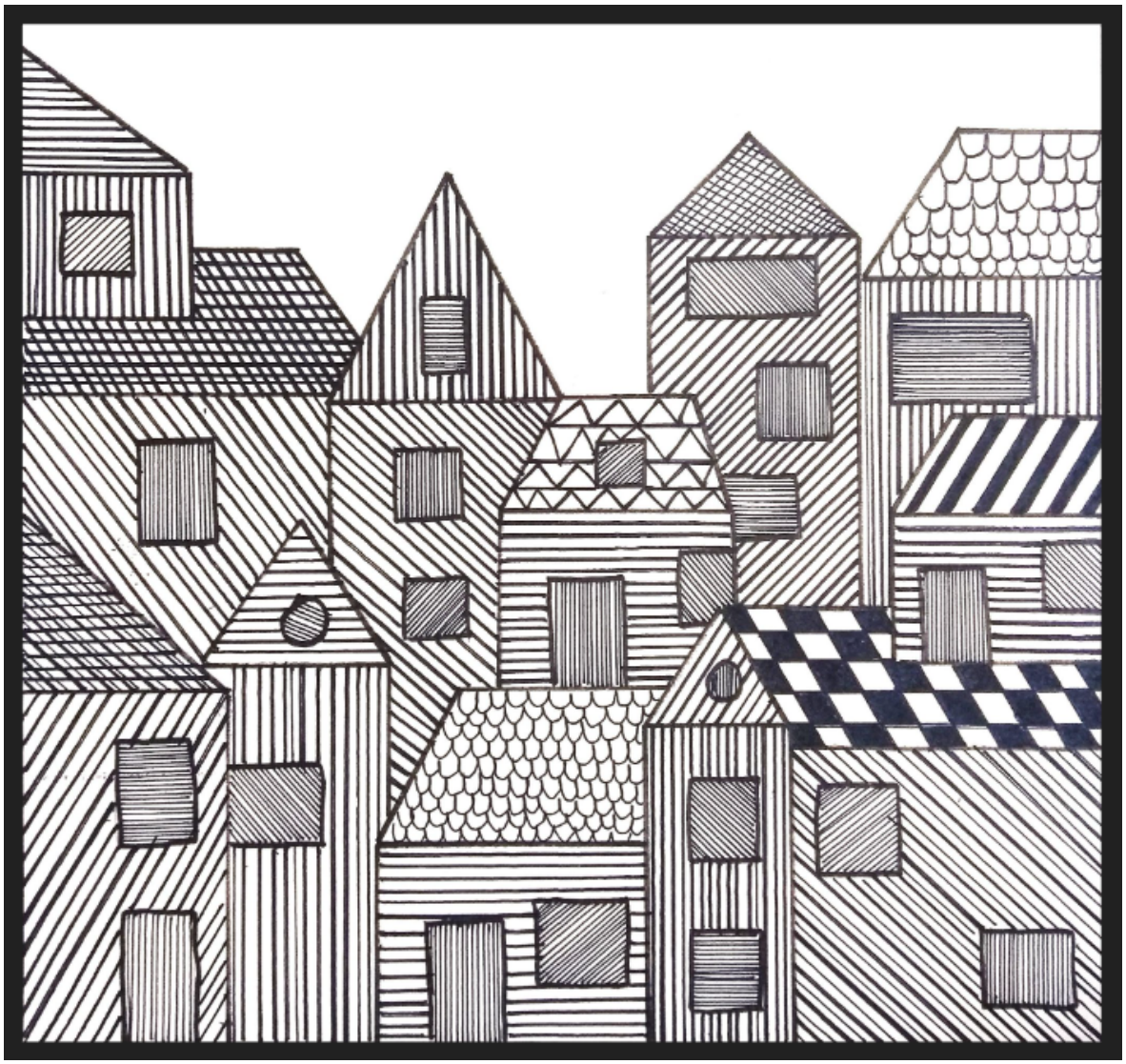
UNIVERSITY of MARYLAND BALTIMORE

# 45th Annual

# Graduate Research Conference



Art by: Margi Parikh

**Friday, March 31, 2023**

# 45th Annual Graduate
# **Research Conference**

Hosted by the Graduate Student Association
Friday, March 31, 2023
SMC Campus Center, Baltimore, MD

Organized by:

**Graduate Research Conference Subcommittee**

Sarah Clem - Chair
Hadley Bryan
Nikita Aggarwal
Makenzy Mull
Tural Mammadli

GRADUATE STUDENT ASSOCIATION

UNIVERSITY of MARYLAND
GRADUATE SCHOOL

Cover Art:

***It's Baltimore Downtown, Baby!***
pen and marker

By: Margi Parikh

Masters in Pharmaceutical Sciences Program

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UNIVERSITY of MARYLAND BALTIMORE

**BRUCE E. JARRELL, MD, FACS**
President

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March 31, 2023

Congratulations on the 2023 Graduate Research Conference. This year marks the 45th year that the University of Maryland, Baltimore (UMB) has hosted this conference for scholars to exchange ideas and information. It serves as a testament that we are interconnected and that the biggest breakthroughs in human health and well-being often happen at the intersection of scholars, schools, and disciplines.

When we see each other as sources of good ideas and work with one another intentionally, we are able to redesign the way we think about problems and come up with creative and innovative solutions. By collaborating and sharing, we can find possibilities where we thought there were none. Working together we can envision new applications for our work, ways to broaden its reach or amplify its impact. Innovation and discovery are two of UMB's core values, and this conference is an example of them at work.

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 E. Jarrell, MD, FACS
President

# Forward

Welcome to the 45th annual Graduate Research Conference (GRC) at the University of Maryland, Baltimore (UMB)! The Graduate Student Association (GSA) is proud to host this conference to allow our researchers, graduate students, professional students, and postdoctoral fellows the opportunity to present their work and discoveries. The interdisciplinary nature of our campus allows us to showcase a variety of research within one conference, including basic, nursing, social, and applied sciences.

This year, we have abstracts from students and postdoctoral fellows representative of every UMB graduate research program, which will be featured in both oral and poster presentations. As in previous years, all students presenting abstracts are eligible to win an award for outstanding presentations in their sessions. Additionally, the Geriatrics and Gerontology Education and Research Program (GGEAR) and the Center for Research on Aging (ORC) at the University of Maryland, Baltimore will be sponsoring special awards in aging research. The Office of Technology Transfer (OTT) will also present the Graduate Translational Research Awards to recognize important translational research being performed by UMB graduate students. We thank the GGEAR and OTT for their continued support of GRC and the outstanding research being conducted by students and fellows on campus. We are also happy to honor the graduate students who have passed their qualifying exam during the last year with the Candidacy Ceremony following the completion of the scientific program and awards of the GRC.

The GSA gratefully acknowledges those who helped make the GRC possible and successful. We would like to thank Interim President Jarrell for his continued support of the students on our campus and their research. Special recognition is deservedly given to Dr. Erin Golembewski, Senior Associate Dean of the Graduate School, for her continued guidance and support, as well as all of the staff of the Graduate School Office. Many thanks are owed to the HS/HSL for all their help with presentation preparations and providing us with the resources necessary to perform informed research. We greatly appreciate the faculty members acting as judges for donating their time, expertise, and critiques. We are grateful for our amazing sponsors and supporting organizations that drive the success of our event! We thank the GSA program representatives and members for their work throughout the year, and especially for their commitment to making the GRC successful. Finally, we would like to recognize the GRC Organizing Committee for their hard work to make the GRC possible and bring together the researchers in our campus community. It is our pleasure to host you at the 45th annual Graduate Research Conference, and we hope you enjoy today's program and events!

**GSA Executive Board**

Rainer Butler - President
Soad Elziny - Vice President
Jernelle Miller - Treasurer
Sarah Clem - Secretary
Jennifer Kirk - Public Relations Officer
Nikita Aggarwal - Graduate Council Representative

# Student Award Winners

The Graduate Student Association would like to congratulate the students who have won our awards during the 2022-2023 academic year. The Professional Development Award allows students to participate in enrichment opportunities like workshops or certificate programs. The Graduate Student Research Award provides funding to those students who need extra resources to complete their studies. The Travel Award supports students so they may attend seminars and conferences in their fields.

**Professional Development Award**

Hadley Bryan

**Research Award**

Jennifer Kirk (Haddock)

**Travel Award**

Jennifer Mariano
Jessica Pottenburgh
Catherine Ladipo
Erika Hermanson
Rex Gonzales
Colin Robertson
Kanwal Mahmood
Jesse Smith
Lujie Peng
Sophie Bruckmeier
Maura Tennor
Nikita Aggarwal
Sanjana Rao
Raziyeh Baghi
Nancy Franke

**Global Travel Award**

Ashley Marquardt
Alexa Ciesinski
Miriam Menken
Morgan Pardue-Kim
Cody Allen-Lis
Kayleigh Majercak
Bernard Davie-Teye

# Schedule of Events

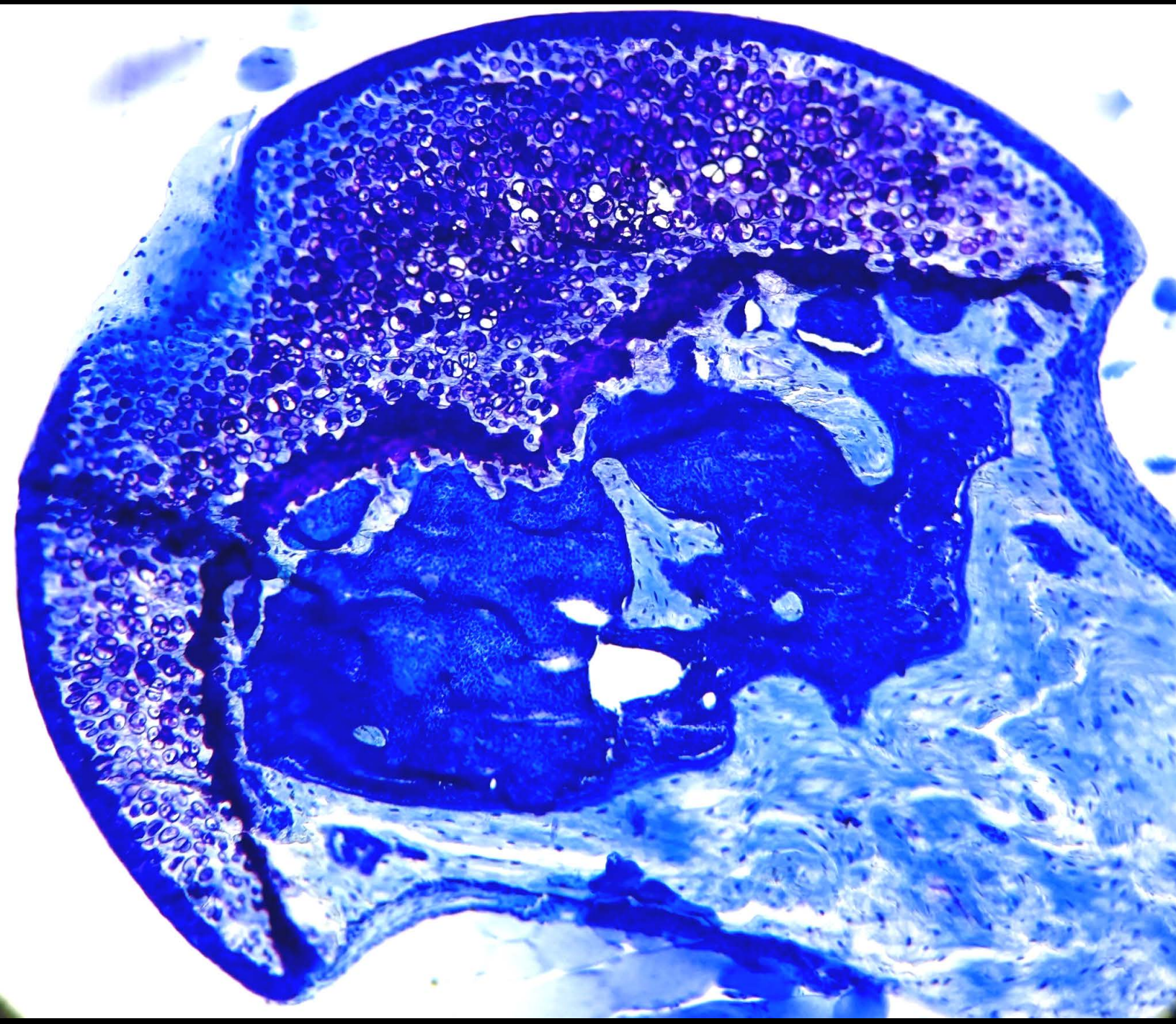

Image by: Jenna Leser, Molecular Medicine

# 45th Annual Graduate Research Conference

## Schedule of Events

SMC Campus Center
March 31st, 2023

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| | | |
|---|---|---|
| **8:00-9:00 am** | **Registration** | **First Floor** |
| **9:00-10:30 am** | **Oral Presentations** | |
| | **Session A** | **Elm Ballroom A** |
| | **Session B** | **Elm Ballroom B** |
| | **Session C** | **Room 351** |
| | **Session D** | **Room 353** |
| **10:30-10:45 am** | **Break** | |
| **10:45 am-11:45 am** | **Poster Presentations Session E & F & G** | **Room 349** |
| **11:45 am-1:00 pm** | **Lunch Break** | **Elm Ballroom** |
| **1:00-2:00 pm** | **Poster Presentations Session H & I & J** | **Room 349** |
| **2:00-3:30 pm** | **Oral Presentations** | |
| | **Session K** | **Elm Ballroom A** |
| | **Session L** | **Elm Ballroom B** |
| | **Session M** | **Room 351** |
| **3:30-4:00 pm** | **Break** *Finalize Scores* | |
| **4:00-5:00 pm** | **GRC Awards & Advance to Candidacy Ceremony** | **Elm Ballroom A** |

# Session Assignments

**Session A – Oral Session, 9:00-10:30 am, Elm Ballroom A**

(#1 Raziyeh Baghi) (#2 Nesreen Alissa) (#3 Christopher Goodis) (#4 Shabnam Lateef) (#5 Ruth Akinlosotu) (# 6 Jennifer Kirk)

**Session B – Oral Session, 9:00-10:30 am, Elm Ballroom B**

(#7 Rex Gonzales) (#8 Amylee Anyoha) (#9 Kuei-Ling Hsu) (#10 Jillian Baker) (#11 Marilyn Bekima)

**Session C – Oral Session, 9:00-10:30 am, Room 351**

(#12 Liron Marnin) (#13 Hephzibah Edwin) (#14 Jenna Leser) (#15 Nidhi Satishkumar) (#16 Aishwarya Iyer) (#17 Jennifer French-Kwawu)

**Session D – Oral Session, 9:00-10:30 am, Room 353**

(#18 Rebecca Lorsung) (#19 Alexandra Soare) (#20 Kaylee Watson) (#21 Julia Rutherford) (#22 Asha Storm) (#23 Vasileios Ionas Theofilou)

**Session E – Poster Session, 10:45-11:45 am, Room 349**

(#24 Nayeon Kim) (#25 Jennifer Mariano) (#26 Katherine Bowers) (#27 Kylie Tomlin) (#28 Ranyah Almardawi) (#29 Shruti Dharmaraj) (#30 Ishraq Alshanqiti) (#31 Ryan Mayers) (#32 Emily McCarthy) (#33 Brandon Lowe) (#34 Parham Habibzadeh)

**Session F – Poster Session, 10:45-11:45 am, Room 349**

(#35 Fayga Smith) (#36 Muhammed Mirza) (#37 Allison Deitz) (#38 Aakash Gnanavel) (#39 G. Mona Saeed) (#40 Miriam Weiss) (#41 Sanjana Rao) (#42 Rosita Asawa) (#43 Maura Tennor) (#44 Patricia Dunlap) (#45 Areej Alfaifi)

**Session G – Poster Session, 10:45-11:45 am, Room 349**

(#46 Yoonzie Chung) (#47 Simon Ho) (#48 Abaneh Ebangwese) (#49 Geralin Love Virata) (#50 Benjamin Grissom) (#51 Francisco Canales) (#52 Gretchen Tucker) (#53 Jon Christofersen) (#54 Aditya Kavuturu) (#55 Emily Smith) (#56 Emmanuel Asiedu)

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

(#57 Andrew Stoltzfus) (#58 Shahd Alajaji) (#59 Rhea Mehta) (#60 Peiyuan Zhang) (#61 Sayan Das) (#62 Jocelyn Brown) (#63 Sorah Levy) (#64 Daniela Fuller) (#65 Susanna Witmer) (#66 Amy Jackson) (#67 Haelim Lee)

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

(#68 Erin Wildermuth) (#69 David Rickert) (#70 Jewel White) (#71 Kanwal Mahmood Hameed) (#72 Anna Maximova) (#73 Sarah Pettit) (#74 Noha Ghonim) (#75 Matthew Eason) (#76 Casey Hofstaedter) (#77 Alli Siclair)

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

(#78 Aarion Romany) (#79 Jacob Shaw) (#80 Abagail Postle) (#81 Nathaniel McClean) (#82 Maxwell Madden) (#83 Heather Buck) (#84 Brent Stewart) (#85 Lamia Mokeem) (#86 Allison Bew) (#87 Abdullah Alhussein) (#88 Isaiah Williamson)

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

(#89 Loretta Anderson) (#90 Kevin Nguyen) (#91 Brianna Scotland) (#92 Linda-Jeanne Mack) (#93 Min Kyoung Park)

**Session L – Oral Session, 2:00-3:30 pm, Elm Ballroom B**

(#94 Kenneth Dietze) (#95 April Cavaletto) (#96 Adarsha Malla) (#97 Aziza Frank) (#98 Melissa Culligan) (#99 Roxy Cundiff-O'Sullivan)

**Session M – Oral Session, 2:00-3:30 pm, Room 351**

(#100 Zachary Noel) (#101 Noah Pollack) (#102 Rebecca Collins) (#103 Alexandria Chan) (#104 Nikita Aggarwal) (#105 Mashhood Wani)

# Abstracts

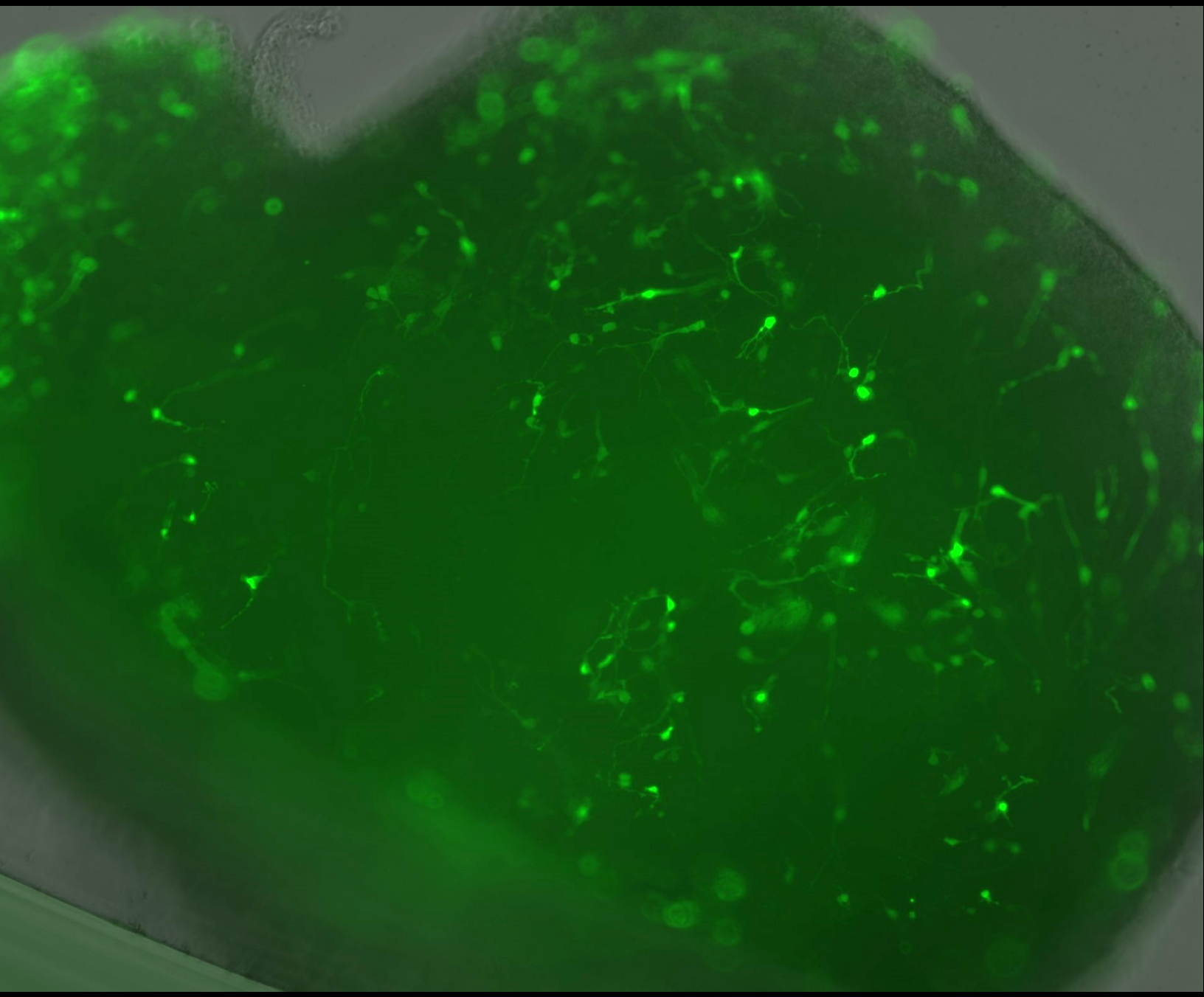

Image by: Shriya Madan, Molecular Medicine

**1. Exploring Strategies for Reducing Knee Medial Compartment Loading: Toward Subject-Specific Training of Medial Knee Osteoarthritis**

**Raziyeh Baghi**

Baghi, R., Ramadan, A., Badhyal, S., Henn, F., Packer, J., Bowman, P., Hochberg, M., Zhang, L.

Session A; Oral Presentation; Ballroom A

INTRODUCTION: Currently most rehabilitation protocols for knee osteoarthritis (KOA) treatment have focused on strengthening the muscles around the knee to potentially reduce the peak knee adduction moment (KAM). However, the evidence to support the efficacy of this approach is limited. In this pilot study, we applied various controlled slow perturbations to the knee using a custom robotic elliptical trainer with the subject making steps without noticing the perturbations. The resulting knee joint loading under the perturbations was investigated to explore potential rehabilitation strategies for reducing the peak KAM and KAM impulse.
METHODS: A customized elliptical trainer with a six degree of freedom goniometer, a 6-axis force/torque sensor, and multi-DOF controlled stepping was used to determine knee moments during stepping. A total of 12 healthy subjects participated in this pilot study. They were asked to perform stepping on the elliptical trainer. During stepping, the footplates were perturbed/moved slowly between the neutral position, toe-in, and toe-out positions; and between the slide-in, neutral, and slide-out positions. Measurements of the knee moment were done in real-time.
RESULTS: Friedman test showed a significant difference between stepping conditions ($P<0.05$). The lowest values of the peak KAM and KAM impulse were observed for the slide out and toe-in foot positioning ($P<0.05$).
CONCLUSION: Considering the efficacy of training on an elliptical trainer with controlled footplate positions for peak KAM and KAM impulse reduction, optimal strategies can potentially be identified for individual subjects with the aim of impairment-specific reduction of the damaging knee joint loading.

**2. Can we objectively measure fear of falling in older adults?**

**Nesreen Alissa**

Alissa, N., Jeon, W., Westalke, K.P.

Session A; Oral Presentation; Ballroom A

Background: Fear of falling (FOF) is highly prevalent in older adults (OA) and is known to negatively influence balance control. Common tools for measuring FOF are subjective, introducing a high level of variability in individuals' perceptions of and thresholds for fear.
Objective: to investigate whether kinematic and psychophysiological measures can objectively measure FOF in OA.
Methods: Sixteen OA were exposed to three random walking trip perturbations. During the 3rd trip trial, participants were engaged in a secondary cognitive task. Kinematic and psychophysiological outcomes as well as subjective measures of anxiety were measured. Relationships between kinematic and psychophysiological measures with subjective FoF and anxiety measures were investigated.
Results: Maximum arm elevation prior to first protective step significantly correlated with SUDS, FES-I, and normalized EDA and HRV. There was no change in arm elevation over the 3 trip trials.
Conclusions: These findings suggest that arm elevation, EDA, and HRV resulting from an unpredictable walking trip perturbation may be used as objective laboratory and clinical indicators of distress, balance confidence, and falls efficacy in OA.
Clinical relevance: Objective measures of FOF could help identify and address the presence of conscious and subconscious FOF in OA and identify changes in balance responses that may be caused by FOF. This research will also help researchers and clinicians avoid the systemic

bias in self-reported scales, and to assess FOF during various task-specific activities rather than being limited to the tasks included in subjective scales.

**3. Discovery of novel BFL-1 inhibitors by computer-aided drug design and screening an in-house library of synthetic BH3 α-helix mimetics**

**Christopher Goodis**

Goodis, C.C., Yu, W., Lowe, B.D., MacKerell, A.D., Fletcher S.

Session A; Oral Presentation;  Ballroom A

Manipulation of cell homeostatic mechanisms is a crucial hallmark of cancer. A key example of this is the B-cell lymphoma 2 (BCL-2) protein-mediated intrinsic apoptotic pathway which is comprised of two sub-families: anti-apoptotic proteins (e.g. BCL-2 and BFL-1) that prevent cell death, and pro-apoptotic proteins (e.g. BAX and BAK) that initiate cell death. These proteins neutralize each other's function through a conserved binding groove on the surface of the anti-apoptotic proteins that recognizes the -helical BH3 domain of the pro-apoptotic counterparts. Once pro-apoptotic proteins are fully sequestered, apoptosis is prevented. However, when a cell undergoes stress, pro-apoptotic proteins are upregulated, dislodging them from their anti-apoptotic counterparts and ultimately causing apoptosis. Cancer cells manipulate this system by overexpressing anti-apoptotic proteins such that all pro-apoptotic proteins are sequestered. Therapeutics dubbed "BH3 mimetics" hoodwink anti-apoptotic proteins into releasing bound pro-apoptotic proteins by themselves binding to the recognition groove. Currently, venetoclax, a BCL-2 selective inhibitor, is the only FDA-approved BH3 mimetic, while multiple clinical trials are on-going for inhibitors that target MCL-1 and BCL-xL anti-apoptotic proteins. BFL-1, in comparison, is far-less studied and remains the underdog of the family, yet BFL-1 overexpression has been implicated in venetoclax resistance. Further, several cancer are dependent on BFL-1, such as melanomas, leukemias and lymphomas. BFL-1 contains a unique solvent-exposed cysteine (Cys55) along with an aspartate (Asp78) within its BH3 binding groove. Towards the development of BFL-1 inhibitors, we present our findings from computer-aided drug design as well as screening an in-house library of synthetic BH3 α-helix mimetics.

**4. Effect of Stroke on Hip Muscle Activity during Voluntary Lateral Steps**

**Shabnam Lateef**

Lateef, S., Lanza, M.B., Gray, V.L.

Session A; Oral Presentation;  Ballroom A

Purpose/Hypothesis: Hip abductor-adductor muscles are important for weight transfer control before taking a voluntary lateral step. Chronic stroke, characterized by residual sensorimotor impairments, may alter the performance of these muscles, which may precipitate a fall. The primary purpose of this study was to examine the role of hip abductor-adductor muscle activation during the weight transfer phase of voluntary lateral steps, and the influence it has on step characteristics in community ambulatory adults with chronic stroke as compared to healthy controls.
Materials/Methods: 20 people with chronic stroke (≥ 50 years) and 10 age-matched healthy controls, were instructed to take a lateral step as quickly as possible in response to a light cue placed six feet in front of them. Rate of muscle activation [RoA] during the weight transfer phase of a voluntary lateral step was measured bilaterally from the Adductor Longus [ADD] and Gluteus Medius [GM] muscles using Electromyography [EMG]. Weight transfer time and step onset time were measured.
Results: People with chronic stroke had reduced paretic ADD and GM activation ($p < 0.03$) during the weight transfer phase compared to healthy controls. The slower the rate of ADD and GM muscle activation of the stance leg during weight transfer, the longer participants, especially people with chronic stroke, took to transfer weight between legs and initiate a lateral step.
Conclusion: People with chronic stroke have an impaired ability to accept weight onto the paretic stance leg. Stroke rehabilitation for fall prevention should emphasize rapid activation of stance leg hip muscles.

**5. Effect of Practice Schedule on Motor Learning of Reactive Balance Responses in Persons with Parkinson's Disease**

**Ruth Akinlosotu**

Akinlosotu R.Y., Alissa N., Westlake K.P.

Session A; Oral Presentation; Ballroom A

Objective: Persons with Parkinson's disease (PwPD) have set-shifting impairments that may limit motor learning of protective responses to prevent falls. This study compares the acquisition and retention of protective stepping stability via blocked versus random practice schedules in PwPD & age-matched controls.
Methods: Twenty PwPD & 20 age-matched controls will experience a slip and trip-like perturbations to induce stepping responses via random and blocked practice schedules. Blocked practice is repeating a task (e.g., slip) severally before the next, while random practice is practicing two tasks (slip & trips) randomly. Each subject will wear a safety harness with an integrated load cell to prevent a fall. Our primary outcome, the margin of stability (MoS) at 1st protective step before, 10 minutes, & 2 days after practice will be analyzed using two ANOVA (Group vs. Trial).
Results: To date, we have assessed four control participants (Ages 50,75, 60 & 80 years) in the blocked group. During the acquisition phase, all four participants improved their MoS from pretest to posttest with a mean MoS change score of 103mm (pretest range: -35mm, to 110mm, posttest range: 57mm to 190 mm). During the retention test, all participants retained/ improved MoS scores. However, the mean MoS change score (77mm) of all participants from the pretest to the retention test was less than from pretest to posttest.
Clinical Relevance: The findings will provide knowledge that may foster the development of robust balance rehabilitation protocols to improve postural responses and reduce falls in PD.

**6. Differences in Self-Reported and Objective Osteoporosis Knowledge: Preliminary Results from a Cross-Sectional Survey Among US Healthcare Providers**

**Jennifer Kirk**

Kirk, J.M., and Albrecht, J.S.

Session A; Oral Presentation; Ballroom A

Background: Disparities in osteoporosis management increase fracture risk and worsen health outcomes among racial and ethnic minorities. Little is known about whether providers' osteoporosis knowledge plays a role in these disparities.
Objective: To evaluate differences between self-rated and objective knowledge of osteoporosis management among geriatricians, general/family practice, specialists [e.g., endocrinologists, rheumatologists, and orthopedic surgeons], and advanced care practitioners in the United States.
Methods: I developed a novel survey to assess self-rated and objective knowledge of osteoporosis management. Self-rated osteoporosis knowledge was calculated as the composite average of the Likert scale responses (Very Poor-Excellent) to two questions (i.e., How would you rate your knowledge of osteoporosis 1. screening and 2. treatment compared to other medical professionals?), with a range of 1-5. Objective knowledge was measured with nine yes/no general knowledge questions (e.g., Increased intake of calcium and vitamin D dietary supplements can promote bone health) and then scored as a percentage (i.e., # of correct responses divided by 9 possible correct responses).
Results: Over the first four months of recruitment, 85 (1.7%) of 5,000 contacted providers responded, with 52 (61.2%) completing the entire survey. While 75% of providers self-rated their knowledge of osteoporosis as above-average to excellent, the median score on the objective assessment was only 55.6%, with the highest score being 77.8% for a single provider.
Conclusions: Preliminary results suggest discordance exists between self-rated and objectively measured osteoporosis knowledge, which may influence disparities in osteoporosis management.

**7. Essential role of obscurin kinase-1 in cardiomyocyte coupling via N-cadherin phosphorylation**

**Rex Gonzales**

Wang, L., Tsakiroglou, P., Gonzales R., Li A., Remedios, C., Wright, N., Kontrogianni-Konstantopoulos, A.

Session B; Oral Presentation; Ballroom B

Obscurins are giant cytoskeletal proteins with structural and regulatory roles. Obscurin-B (~870 kDa), the largest known isoform, contains two enzymatically active Ser/Thr kinase domains, kin1 and kin2, which belong to the myosin light chain kinase (MLCK) family. Kin1 binds to and phosphorylates N-cadherin, a major component of the intercalated disc (ICD), the unique sarcolemmal microdomain that mediates the mechanochemical coupling of adjacent cardiomyocytes. Obscurin-B containing kin1 and N-cadherin co-localize at cell junctions in embryonic rat ventricular myocytes (ERVM), and their co-distribution is regulated by Ca2+. Phosphoproteomics analysis revealed that obscurin-kin1 phosphorylates N-cadherin at Ser-788 located within the juxtamembrane region of its cytoplasmic domain with an apparent Kcat of ~0.29 sec-1. Overexpression of obscurin-kin1 or phosphomimic-Ser-788-Glu N-cadherin in ERVM markedly increases cell adhesion and chemical coupling. Importantly, phosphomimic-Ser-788-Glu N-cadherin exhibits significantly reduced binding to p120-catenin, while overexpression of phosphoablated-Ser-788-Ala N-cadherin increases RhoA activity. Consistent with an essential role of the obscurin-kin1/N-cadherin axis in cardiomyocyte coupling, it is deregulated in end-stage human heart failure. Given the nearly ubiquitous expression of obscurin and N-cadherin, our findings may have broad applicability in deciphering the obscurin-kin1/N-cadherin axis that likely mediates cell coupling in diverse tissues and organs.

**8. Cost-effectiveness Analysis of a Worksite Wellness Program for Reducing Cardiovascular Disease Risk Among Long Term Care Workers**

**Amylee Anyoha**

Anyoha, A., Anderson, L., White-Dumpson, D., Doran, K., Resnick, B., Zhu, S.

Session B; Oral Presentation; Ballroom B

The Worksite Heart Health Improvement Project (WHHIP) was developed to reduce Cardiovascular Disease (CVD) risk among Long Term Care Workers (LTCW). Our prior work has demonstrated the feasibility and efficacy of the program in reducing blood pressure and cholesterol while increasing worker productivity and improving dietary, fitness, and sleep habits.
We propose a cost-effectiveness analysis based on data collected from the WHHIP pilot study. Ninety-eight long-term care staff from four long-term care facilities will be included in the analysis. The facilities will be categorized by intervention or control group. We will focus on hypertension, hypercholesterolemia, and tobacco exposure as risk factors for CVD. The prevalence of these modifiable risk factors in our sample was at least 13.8%, 18.8% and 37% respectively. This oral presentation will discuss methods of an ongoing project. Using a reference case analysis, we will test our hypothesis that the WHHIP is a cost-effective solution to reducing CVD risk among LTCW in comparison to the current standard of no intervention. We will calculate the probabilities of decreasing each risk factor during the study and compare the one-year LTCW cardiovascular disease-related disability costs for hypertension, hypercholesterolemia and tobacco exposure to the cost of the WHHIP. Health costs of CVD at the individual and health care sector levels from the literature will be included. Applying the Markov model will allow us to simulate changes in quality of life and the associated costs. Sensitivity analyses will be performed to measure the accuracy of the model.

**9. Differences in Functional Characteristics of Oral Biofilm in Minority Children with Early Childhood Caries (ECC)**

**Kuei-Ling Hsu**

Hsu, K.L.C, Shaffer, I.N., Fofanov, V. Y., Harro, J.M., Ernst, R.K.

Session B; Oral Presentation;  Ballroom B

ECC often progress at a faster pace, are challenging to treat, and affect minority children disproportionally. Although bacterial biofilms in the dental plaque have been thought to be one of the key factors contributing to the disease process, the functional characteristics and global gene expression patterns remained unclear. This study was to identify the functional transcriptomes of bacteria biofilm from caries active lesions to these in non-caries sites in this population. Paired dental plaque samples were collected from caries active lesions and non-caries sites in the same oral cavity of 19 African American (AA) and Hispanic children with ECC. Total RNA was extracted and RNASeq sequencing was performed using Illumina platform. Altered genes and associated bacterial species were identified using MTSv pipeline, DESeq2 and apeglm. Significant KOs and bacterial species were further mapped using KEGG database to determine the global metabolic pathways. Similar number of significant altered genes were found to be in caries biofilm unique to AA children, whereas extremely high number of genes were found to be significantly upregulated compared to those downregulated unique to Hispanic children. The top bacterial species contributed to the upregulated genes in AA children were quite different from those in Hispanic children. The metabolic pathways of the upregulated genes in AA children were also different from those in Hispanic children. This analysis identified significant differences in the transcriptome profiles in caries biofilm between AA and Hispanic children. Further research using a larger sample size will be needed to confirm these findings.

**10. Development of a sweeping antibody against IL-16 for the  treatment of multiple myeloma**

**Jillian Baker**

Baker, J.M., Atanackovic, D., and Luetkens, T.

Session B; Oral Presentation;  Ballroom B

Multiple myeloma (MM) is an incurable blood cancer resulting from the uncontrolled proliferation of plasma cells. Recently, it has been shown that a unique cytokine, interleukin 16 (IL-16), plays a key role in MM progression. MM cells aberrantly secrete high levels of IL-16 resulting in the increased proliferation of MM cells. Previous cell culture experiments have shown that high levels of IL-16 correlate with disease burden and that blocking IL-16 inhibits MM cell proliferation. The goal of this project is to develop a therapeutic antibody targeting IL-16 for the treatment of MM. Specifically, we have developed sweeping antibodies containing specific modifications that allow for the antibody to clear IL-16. This contrasts with a conventional antibody that only blocks IL-16 from interacting with MM cells but fails to clear it from the bone marrow. We hypothesize that the ability of the sweeping antibody to actively clear IL-16 from the bone marrow will reduce MM cell proliferation and tumor burden. For this purpose, we have developed two high-affinity antibodies targeting IL-16. For the first antibody candidate, we performed an extensive amino acid-substitution screen of an existing humanized anti-IL-16 antibody to introduce the sweeping functionality. The second antibody candidate is a novel fully human sweeping antibody developed in our lab. We are in the process of conducting efficacy analyses in both cell culture and mouse model settings. If successful, these sweeping anti-IL-16 antibodies targeting a cancer-derived growth factor will be the first therapeutics of their kind for the treatment of cancer.

**11. Compliance Considerations in Laboratory Renovations**

**Marilyn Bekima**

Bekima, M. N. and Vucenik, I

Session B; Oral Presentation;  Ballroom B

Many laboratories in the United States were built decades ago. The trend lately has been to update these labs to reflect the latest building and technological safety as well as install the latest state-of-the-art laboratory equipment. Laboratory management constantly seeks to modernize and upgrade laboratories, especially after the COVID

Pandemic where many laboratories unexpectedly acquired new instruments and other supplies to accommodate COVID testing. In addition, the Center for Medicare and Medicaid Services (CMS) regulation in recent years which considers patient experience and satisfaction when making reimbursement payments, has provided additional incentive for hospitals and their laboratories to get a makeover. Renovations and acquisition of new lab equipment is also important because buildings, furniture and equipment age and need to be upgraded.
This article looks at the regulatory considerations and available standards for moving lab equipment to ensure instrument function and patient results are not impacted by move.

**12. Tick regulation of epidermal skin immunity facilitates an advantageous arthropod feeding environment**

**Liron Marnin**

Marnin, L., Bogale, H.N., Laukaitis, H., Rolandelli, A., Valencia, L.M., Park, S., Bencosme Cuevas, E., Galvan, B., O'Neal A.J., Bruno, V.M., Samaddar, S., Butler, L.R., Ferraz, C., Mendes M.T., Singh, N., Cabrera Paz, F.E., Oliva Chavez A.S., Mulenga, A., Serre. D., Pedra, J.H.F.

Session C; Oral Presentation;  Room 351

Hard ticks are hematophagous arthropods of public health importance. Following a tick bite, these arthropods take prolonged, continuous bloodmeals that facilitate pathogen transmission. Successful bloodmeals are attributed to components of the tick saliva that alter inflammation, inhibit hemostasis, and block pain and itch responses in the mammalian skin. Recent studies have reported that extracellular vesicles (EVs) in the saliva enable tick feeding and redirect skin immunity. Here, we provide causality to these findings by showing that tick EVs regulate resident epidermal γδ T cells. Epidermal γδ T cells interact with keratinocytes, which comprise about 95% of the skin epidermal layer, to ensure optimal maintenance of tissue homeostasis and epithelial repair. We demonstrate that Ixodes scapularis ticks significantly reduce epidermal γδ T cells at the bite site for an optimal feeding environment. Using flow cytometry, we profiled the epidermal γδ T cell activation status in the presence or absence of EVs. Furthermore, we employed single cell RNA sequencing coupled with animal models devoid of epidermal γδ T cells to evaluate the directionality of the skin immune response during a tick bite. Collectively, this work broadens our knowledge of immunological mechanisms that occur at the vector-host interface.

**13. Psychological distress symptoms in nurses and their intention to leave:  A Cross-sectional Secondary Data Analysis**

**Hephzibah Edwin**

Edwin, H.S.

Session C; Oral Presentation;  Room 351

Background: A critical nursing shortage exists, and organizations are struggling to retain their nursing workforce. Nurses encounter psychological symptoms, such as feeling anxious, depressed, and worried, which have not been well explored in regards to retention.
Purpose: To examine psychological symptoms of distress among nurses in relation to their intention to leave.
Methods: A secondary analysis of the Nurse Worklife and Wellness Study (Trinkoff et al., 2022) data was done. The psychological distress based on work settings, nurse position (staff, charge, administrators, educators/researchers and APRNs) and years of experience (0-2,3-5, 6-25, >25years) were explored. Multiple linear regression analyses were performed to examine if work setting, position or experience  predicted psychological distress and intention to leave. A mediation analysis was done to examine if psychological distress mediated the association between years of experience and intention to leave.
Results: As years of experience increased, psychological distress and intention to leave decreased. Nurses with less than 2 years' experience had increased psychological distress and higher intentions to leave.  Psychological distress significantly increased intention to leave (B=0.02, 95% CI: 0.005, 0.04). The direct effect of years of experience was negatively associated to the intention to

leave. With psychological distress as a mediator, the association between years of experience and intention to leave was suppressed, resulting in an increase in the intention to leave despite years of experience. Implications: The findings suggest that psychological distress may be contributing to increased intention to leave, so that retention efforts could focus on addressing nursing distress.

**14. Severe Osteopenia and Skeletal Fragility Induced by Conditional Co-Deletion of Camk2d and Camk2g**

**Jenna Leser**

Leser, J.M., Torre, O.M., Gould, N.R., Guo, Q., Buck, H.V., Kodama, J., Otsuru, S., Stains, J.P.

Session C; Oral Presentation;  Room 351

Osteocytes participate in the integration of mechanical, hormonal, and local signals, coordinating an appropriate anabolic or catabolic response from osteoblasts and osteoclasts. Our group previously established in osteocytes, calcium/calmodulin-dependent kinase 2 (CaMKII) is a required signaling effector in response to some bone anabolic cues. Presently, little is known about the role of CaMKII in bone in vivo. Therefore, we conditionally co-deleted the most abundant isoforms of CaMKII in osteocytes (delta and gamma) using osteocalcin-cre, which is expressed in mature osteoblasts and osteocytes, generating Ocn-cre:Camk2d/Camk2g double-knockout (dCKO) mice. Using micro-computed tomography to quantify changes in skeletal microarchitecture, at least 66% of the trabecular bone volume was lost in the femur and vertebra, while 24% of cortical thickness was lost in the femur by 8 weeks old. Four-point bending, a test of bone mechanical properties, showed that in addition to having less bone mass than control mice, dCKO bones are of worse quality. This skeletal phenotype is multifactorial, but appears to be mainly by an unexpected decrease in circulating phosphate, which may be accounted for by both an increase in osteocytic fibroblast growth factor 23 (FGF23), a phosphate-regulating hormone, and a decrease in tissue non-specific alkaline phosphatase (TNAP), a phosphate-hydrolyzing protein, in the bones of dCKO mice. Consistent with this, we observed that dCKO bones were hypo-mineralized with more prominent osteoid seams. Altogether these data confirm an unexpected and yet essential role for osteocyte CaMKIIδ and CaMKIIγ in the maintenance of bone mass and bone quality in mice.

**15. Role of Penicillin Binding Protein-4 (PBP4) in antibiotic resistance and virulence in Staphylococcus aureus**

**Nidhi Satishkumar**

Satishkumar N, Chatterjee S.

Session C; Oral Presentation;  Room 351

Staphylococcus aureus is a Gram-positive pathogen that can cause a wide range of infections in humans. S. aureus is also resistant to antibiotics, notably a class of antibiotics called β-lactams, making it difficult to treat infections and leading to increased illnesses and death. Classical mechanisms of antibiotic resistance in S. aureus have been well described; however, recent years have seen an increase in the prevalence of non-classical β-lactam resistance in S. aureus. Our previous work has identified Penicillin Binding Protein-4 (PBP4) as a novel, non-classical mediator of β-lactam resistance in S. aureus. Mutations associated with the regulatory region of pbp4 result in increased expression of the protein, subsequently leading to enhanced cell wall cross-linking and increased β-lactam resistance. Here, we demonstrate that PBP4-mediated resistance is a phenomenon that is clinically relevant, and can occur independent of classical mechanisms of resistance, thus supplementing them. Along with it role in β-lactam resistance, our studies indicate that PBP4 could potentially mediate resistance to other classes of antibiotics. Finally, using a C. elegans model system, we demonstrate that strains with increased PBP4 expression have decreased virulence, suggesting that increased cross-linking likely came at the cost of virulence.

**16. Investigating the Molecular Pathogenesis of a Novel MYBPC1 Duplication Mutation Linked to Myopathy with Tremor**

**Aishwarya Iyer**

Iyer A., Takagi Y., Wright N., Varney K., Cook M.E., Biancalana V., Spodenkiewicz M., Sellers J., Weber D., Kontrogianni-Konstantopoulos A.

Session C; Oral Presentation; Room 351

Our group identified a novel Leu266Lys267Arg268 (LKR) duplication in the MYBPC1 gene encoding the slow skeletal myosin binding protein-C (sMyBP-C), a critical sarcomeric protein that plays key structural and regulatory roles in striated muscle contraction and relaxation. The resulting clinical phenotype is associated with progressive generalized muscle weakness, skeletal deformities, and a unique myogenic tremor. The molecular mechanism underlying these pathological manifestations is elusive, and currently no therapeutics exist for this emerging sarcomeric myopathy. My work aims to characterize the LKR duplication on a molecular level and delineate the structural and functional alterations that it elicits. This mutation localizes to the M-motif, a sMyBP-C N-terminal region responsible for dynamic interactions with myosin S2Δ and actin to regulate crossbridge cycling. I therefore hypothesize that the duplicated LKR residues alter the biochemical properties of the M-motif, disrupting the sMyBP-C N-terminus structure and function. In vitro motility assays reveal the mutant M-motif to uniquely modulate crossbridge formation and actin movement by dampening actin velocity and increasing actin shearing, compared to the wild-type. Nuclear magnetic resonance experiments suggest that the duplicated residues cause M-motif structural changes on an atomic level and increase binding to S2Δ, evidenced by amide proton chemical shift perturbations. Collectively, through in-silico and in-vitro assays, we have shown, for the first time, that this mutation alters the skeletal M-motif domain structure and augments myosin binding. Ongoing studies will illuminate the molecular and functional basis of this novel myopathy, ultimately aiding in improved understanding of the disease pathogenesis and therapeutic development.

**17. Indigenous American Ancestry Proportions in Reference Panel Causes Different Imputation Performance in Two Distinct Latin American Cohorts**

**Jennifer French-Kwawu**

French-Kwawu, J.N., Borda, V., Leal, T.P., Mata, I., and O'Connor, T.D.

Session C; Oral Presentation; Room 351

Many existing imputation reference panels are based on individuals of European ancestry, making it difficult to reach the same imputation quality in non-European populations as in European populations. Here we aim to analyze how the Indigenous American (IA) ancestry proportions of self-described Latin American (LatAm) individuals included on panels can influence imputation quality in two LatAm populations: a Caribbean Alzheimer's disease (AD) cohort, and the South American populations in the Latin American Research Consortium on the Genetics of Parkinson's Disease (LARGE-PD). We tested three imputation panels with 5,000 individuals from each of three main groups: European American, African American, and LatAm. We modified the composition of LatAm individuals based on IA ancestry, selecting those with the lowest (LP: < 4.8% IA), middle (MP: 13.2% < IA < 23.8%), or highest (HP: > 45.9% IA) proportion. We imputed genotypes on chr 7 and X in both test cohorts, comparing the panels within each population. The proportion of SNPs imputed with $R2 \geq 0.8$ on chr 7 (49.3% LP, 49.9% MP, & 43.6% HP) and chr X (38.0%, 38.5% & 32.8%) in the AD cohort decreased with highest IA ancestry. However, the LP and HP were similar on chr 7 (29.6%, 30.7%, & 29.2%) and chr X (18.3%, 19.5%, & 18.4%) for LARGE-PD. We observed the highest imputation quality overall and for rare SNPs ($0.0001 < MAF < 0.5$) in the MP. These findings highlight how increasing the IA of LatAm individuals in panels may not be beneficial in all LatAm populations.

**18. CGRP Release from Parabrachial Neurons Potentiates Post-synaptic Response in Central Amygdala and Bed Nucleus of the Stria Terminalis, and Activates Oligodendrocytes in Insula**

**Rebecca Lorsung**

Lorsung, R.M, Ji, Y., Alipio, J., Koenig, J., Laub, H., Cramer, N., Masri, R., Keller, A.

Session D; Oral Presentation; Ballroom 353

Despite its prevalence, chronic pain remains largely resistant to therapy. Treatments targeting aversive-affective processing of pain, centered around the parabrachial nucleus (PB), may prove promising. Calcitonin gene-related peptide (CGRP)-expressing PB neurons densely project to several brain structures implicated in aversive-affective pain processing, including the insula, central amygdala (CeA), and the bed nucleus of the stria terminalis (BNST). We are testing the overarching hypothesis that CGRP-expressing PB projections to these brain structures is causally involved in driving the affective component of chronic pain. The first aim of this project is to test whether CGRP release from PB potentiates post-synaptic responses. To test this, we performed whole-cell, voltage-clamp recordings in insula, CeA, and BNST slices from CGRPCre mice. Endogenous, optogenetically-evoked CGRP release from PB terminals in CeA and BNST potentiated evoked excitatory post synaptic currents in a subpopulation of neurons. This potentiation lasted approximately one minute after brief stimulation and was blocked by a CGRP-antagonist. However, in the insula, neither endogenous nor bath applied CGRP potentiated evoked EPSCs. Additionally, neither manipulation affected the amplitude or frequency of spontaneous synaptic inputs to insula neurons, suggesting CGRP does not have a direct effect on insula neurons. RNAscope established that CGRP receptor expression in the insula is restricted to oligodendrocytes and vascular endothelium. These data suggest that PB CGRP release can either alter downstream affective signaling directly through activation of neuronal CGRP receptors on neurons as seen in the CeA or BNST, or cause more subtle shifts in activity via glial activation.

**19. Antifungal effects of nitric oxide against Mucormycosis-causing fungi**

**Alexandra Soare**

Soare, A.Y., Guo, Y., Shetty, A.C., McCracken, C., Ibrahim, A.S., and Bruno, V.M.

Session D; Oral Presentation; Room 353

Mucormycosis is a NIAID-classified emerging infectious disease caused by fungi in the Order Mucorales. Hallmarks of disease progression include angioinvasion and tissue necrosis that often results in significant, irreversible tissue damage or death. While most cases are found in immunosuppressed individuals, mucormycosis is an increasingly common invasive fungal infection. Limited antifungal medications often leave surgical debridement as the only treatment option. The surge of mucormycosis cases among COVID-19 patients has thrust the disease and lack of available treatments into the spotlight. We sought to characterize immune evasion mechanisms by Mucorales fungi. Mice infected with invasion-defective strains demonstrate a global repression of well-known immune pathways compared to mice infected with wild-type strains. One such pathway is the Nos2 pathway, which produces nitric oxide (NO), a signaling molecule and free radical which is toxic to many pathogens, including Mucorales. Follow up studies demonstrate that despite the increased expression of iNos in Mucorales-infected macrophages, these macrophages are unable to produce NO, even when co-incubated with NO-producing stimuli. Our experiments suggest that Mucorales depletes NO through multiple mechanisms including alteration of surrounding metabolic environment to deplete macrophages of nutrients required to mount antimicrobial defenses. This suppressive activity presents NO as a potential novel therapeutic in treating mucormycosis.

**20. The Role of Epitranscriptomics in Wolbachia-mediated Pathogen Blocking Through the Lens of Direct RNA Sequencing**

**Kaylee Watson**

Watson, K., Lindsey, A., Bhattacharya, T., Gasser, M., Hardy, R., Newton, I., Dunning Hotopp, J. C.

Session D; Oral Presentation;  Room 353

Pathogen blocking occurs when the presence of a bacterial Wolbachia endosymbiont reduces viral replication and transmission in its insect host by altering insect virus interactions. This phenomenon is currently being used in many parts of the world as biocontrol for mosquito-transmitted RNA viruses like Dengue, Zika, and Chikungunya. Messenger RNA modifications are proposed as a mechanism of Wolbachia-mediated changes in the insect host Drosophila melanogaster, resulting in reduced transmission of Sindbis virus. In Drosophila melanogaster, Wolbachia modulates the transcription of Dnmt2, which methylates cytosine in RNA. Here we use Oxford Nanopore Technologies (ONT) direct RNA sequencing to detect RNA modifications in both viral and insect host RNA in the Drosophila melanogaster pathogen blocking system. We validated this method with published yeast direct RNA sequencing data supplemented with our own data from a 5-methylcytosine methyltransferase knockout. Relying on both basecalling data and statistical differences in signal, this combining strategy provides us with candidates to further characterize the effects Wolbachia endosymbionts exert on their host in a pathogen blocking system and furthers our understanding of the role of epitranscriptomics in host-microbe interactions.

**21. Tristetraprolin induces an antiproliferative phenotype in TNBC via a novel non-canonical mechanism**

**Julia Rutherford**

Rutherford J.L., Stemberger, M.B., Mahmud, R., and Wilson G.M.

Session D; Oral Presentation;  Room 353

Triple negative breast cancer (TNBC) has a 5-year survival rate of 77%. Recent reports show that 2/3 of TNBC patients develop metastatic disease, the leading cause of death, which lowers the 5-year survival rate to 12%. TNBC's heterogeneous molecular signature has prevented development of successful targeted treatment options. Consequently, further research is needed to identify novel targets. Tristetraprolin (TTP), an RNA-binding protein that destabilizes a variety of mRNAs that encode pro-inflammatory and oncogenic proteins, is potently suppressed in TNBC. TTP repression in tumors correlates with increased disease severity and decreased survival, suggesting a tumor suppressor role in TNBC. To test whether TTP can attenuate the cancer phenotype in TNBC cells, we stably expressed FLAG-tagged TTP in multiple independent TNBC cell lines, then assessed its effects on TNBC proliferation. Using these models, we discovered that TTP drastically reduces the rate of TNBC cell proliferation and stem cell frequency. However, TTP re-expression did not restore rapid decay of known oncogenic mRNA targets, suggesting that its anti-oncogenic functions are independent of its RNA-binding and RNA-destabilizing activities. To discover candidate cellular factors that mediate TTP's anti-proliferative functions, we utilized RNA sequencing to identify genes potently up- or down-regulated in TTP-expressing cells. In addition, pathway analysis revealed that TTP is influential in altering cell growth and metabolic pathways. Collectively, these principal findings establish the non-canonical mechanism of TTP's anti-proliferative function and will identify factors that mediate the anti-oncogenic functions of TTP.

**22. "Precariously Balanced on a Wave of Sick People": a Descriptive Phenomenology Qualitative Study of Nurses' Lived Experiences Three Years into COVID-19.**

**Asha Storm**

Storm, A., Friedmann, E., Scrandis, D., Mooney-Doyle, K., Day, J., & Nelson Goff, B.

Session D; Oral Presentation;  Room 353

Research on the initial impact of the pandemic on registered nurses (RNs) showed high levels of RN traumatic distress. This qualitative study focused on RNs three years after the start of the pandemic to examine the lived experiences of the RNs since the beginning of the pandemic, focusing on distress (peritraumatic distress,

posttraumatic stress disorder, moral distress), personal and professional well-being, and resilience. Participants (n=25) were chosen to maximize the variability of experiences during the pandemic and responded to semi-structured interviews which follow a guide but allow for diversion from the pre-written questions to allow RNs to freely discuss their experiences. Transcripts were analyzed using Giorgi's descriptive phenomenology methodology. RNs described their experiences which fit into three "worlds", the Inner World, the Hospital World, and the Outside World. The Inner World consisted of nurses' personal physical and mental well-being. The Hospital World consisted of nurses' professional well-being, relationships to coworkers and leadership, and moral distress. The Outside World consisted of their feelings toward the future, "dealing with" the outside world's impact, and new experiences of difficulty with patients and families. Nurses expressed a mixture of positive and negative experiences during the pandemic that moved through these three worlds. These results can inform phased pandemic plans and trauma-informed hospital administration and nursing education, and suggest potential areas for change in future pandemics.

**23. Spatial Atlas of Human Gingival Tissues in Health and Disease**

**Vasileios Ionas Theofilou**

Theofilou, V.I, Williams, D.W., Tran, D., Moutsopoulos, N.

Session M; Oral Presentation;  Room 351

The gingival barrier is a unique anatomic location with constant exposure to the exterior environment and a complex immune landscape. Recent single cell RNA sequencing of gingival tissues in health and periodontitis has highlighted diverse cellular populations with distinct transcriptional signatures and inferred functions at the gingival barrier. However, previous work did not provide information related to the spatial distribution of cell subsets in health and disease. We hypothesize that location-specific functions of distinct cell subsets may be important both in tissue homeostasis and in the pathogenesis of periodontitis. The aim of our current project is to generate a spatial atlas of human gingival cell populations in oral health and disease using recently developed spatial transcriptomics (10x Visium Spatial Transcriptomics) and spatial proteomics platforms (iterative bleaching extends multiplexity, IBEX) which we have optimized for oral tissues. Visium 10x Genomics technology allowed for sequencing of tissue area spots (typically 3-30 cells), while computational integration of the Visium-derived dataset with prior single cell RNA sequencing has allowed for visualization of cellular information in discrete capture spots. Furthermore, IBEX has enabled multiplexed imaging of multiple antibodies to provide protein level information at single cell resolution to our datasets. Our preliminary data spatially resolve at an mRNA and protein level immune-functional cellular subsets and their respective microenvironments. They particularly highlight the crevicular epithelium - the barrier site that is directly exposed to the tooth surface and dental microbiome- as an epithelial subpopulation generating antimicrobial defenses, neutrophil chemoattraction and participating in IL17 responses.

**24. The Association Between Psychotropic Drugs and Physical Function in Hospitalized Older Adults with Dementia**

**Nayeon Kim**

Kim, N., Resnick, B.

Session E; Poster Presentation;  Room 349

The aim of this study was to test if the use of psychotropic medications (antipsychotics, sedatives, antiseizure, antidepressants, and anxiolytics) was associated with physical function in hospitalized older adults living with dementia. This study was a secondary data analysis using baseline data from the Function Focused Care for Acute Care Using the Evidence Integration Triangle (FFC-AC-EIT) study. FFC-AC-EIT is an ongoing randomized controlled trial and this study included the first 290 participants. A path analysis was conducted to test the relationship between psychotropic drugs and physical function while controlling for age, gender, race, comorbidities, cognitive function, neuropsychiatric symptoms of dementia, and pain. Overall, 63.4% of

participants took one or more psychotropic drugs, with the most used psychotropic drugs being antidepressants (39%), followed by antiseizure drugs (23.4%), antipsychotics (16.6%), anxiolytics (13.8%), and sedatives (4.1%). No significant association was found between the use of psychotropic medications and physical function. Cognitive function (β=1.489, SE 0.265, p<0.001), comorbidities (β=-2.680, SE 1.093, p=0.014), and pain (β=-2.837, SE 0.865, p=0.001) were directly associated with physical function. Cognitive function was also indirectly associated with function through pain. The findings support prior research showing a lack of association between the use of psychotropic medications and physical function. Additional research may be necessary to investigate the mediating effects of pain between cognition and physical function in older adults with dementia may be needed.

**25. Sex-dependent Progression of the MYBPC1 E248K Myopathy with Tremor in Response to Aging**

**Jennifer Mariano**

Mariano, J.M., Kallenbach, J., Renu, N., Ward, C. W., and Kontrogianni-Konstantopoulos, A.

Session E; Poster Presentation;  Room 349

Myosin-binding protein C (MyBP-C) comprises a family of accessory proteins expressed in striated muscle that function in sarcomeric structure maintenance and actomyosin cross-bridge regulation. Our group has linked mutations in MYBPC1, the gene encoding the slow skeletal isoform (sMyBP-C), to a novel myopathy characterized by muscle weakness, hypotonia, dysmorphia, skeletal rigidity, and most distinctly, a high-frequency low-amplitude tremor. The absence of neuropathy in these patients as well as the restricted expression of sMyBP-C to skeletal muscle suggest that the tremor represents a new entity originating at the level of the sarcomere. Patients harboring the MYBPC1 E248K mutation display generalized myopathy and tremor at birth which stabilizes in adolescence. However, clinical progression of this disease into late adulthood remains unknown.

To study this myopathy, our lab generated a knock-in (KI) murine model expressing the E248K mutation that recapitulates the clinical pathology and disease progression seen in humans.  Using this mouse model, we characterized muscle function of mid- (i.e., 12-month-old) and late- (i.e., 24-month-old) adulthood. We show that in mid-adulthood, the myopathy stabilizes as KI muscles generate comparable specific force to WT. However, in late adulthood, there is a sharp decline in muscle function and specific force production that is sex-specific, with male animals being more severely affected. Further studies are underway to investigate the molecular and structural alterations underlying the manifestation of the disease in response to aging.

**26. Loneliness in LGBTQIA+ Older Adults: A Scoping Review**

**Katherine Bowers**

Bowers, K. MSN, RN, Carpenter, J. PhD, Thornton, M. PhD, Fetting,H. MSN, CRNP, AGNP-C, Johnson,E. MSN, RN

Session E; Poster Presentation;  Room 349

Loneliness in older adulthood is responsible for poor mental and physical health, cognitive decline, and early mortality. Older adults in the LGBTQIA+ community experience additional layers of vulnerability, such as discrimination, higher rates of childlessness, health inequity, and economic disparity that place them at high risk for loneliness. The purpose of this scoping review is to explore the existing literature on loneliness in LGBTQIA+ older adults and identify knowledge gaps to inform future research recommendations. Using the Arskey & O'Malley methodological framework, our team searched PubMed, Embase, CINAHL, PsychINFO, Scopus, and Google Scholar using keywords related to older adults, sexual and gender minorities, and loneliness. We identified 61 articles from 1980 to 2022. Most of the research in this literature reflected studies using descriptive and qualitative approaches. Intervention studies were the least reported. One opinion piece is included. Initial findings highlight associations between discrimination and loneliness, poor

mental health and loneliness, the challenges of HIV in older adulthood and loneliness, and loneliness experienced in caregiving and end of life in LGBTQIA+ older adults. Importantly, many studies emphasized the protective nature of strong social support and community ties against loneliness. Equally, the literature suggests that limited social support is a significant risk factor for loneliness in this population. Older gender non-binary and LGBTQIA+ people of color were underrepresented in many studies. Future research should include intervention research that targets loneliness in this population as well as studies focused on understanding loneliness more comprehensively in underrepresented LGBTQIA+ older adults.

**27. Age-Related Differences in Reactivation-Based Motor Learning**

**Kylie Tomlin**

Tomlin, K., Johnson, B., and Westlake, K.

Session E; Poster Presentation; Room 349

During physical rehabilitation, there is often insufficient time to practice each variation of a motor skill needed in daily life; therefore, the ability to transfer a learned motor skill to a related, untrained task may support functional outcomes. Motor practice can strengthen a motor trace through memory reactivation. We previously demonstrated that fewer, rather than more, practice repetitions of a complex motor task can enhance contralateral skill transfer in healthy, young adults. However, age-related differences in reactivation-based motor learning are unexplored. Here, retention and intermanual transfer of a complex motor task are compared between brief and long reactivation schedules in healthy older adults. Forty healthy, older adults 65-84 years old participated. Participants were randomly assigned to trace an online image of star using an inverted computer mouse in their non-dominant hand either three or ten times per Session Gor seven sessions. Outcomes included speed, accuracy, and skill as defined by a speed-accuracy tradeoff function. Retention skill and intermanual transfer were tested at two-week follow-up. Regardless of group, older adults performed similarly on the task at baseline, retention, and transfer. Compared to younger adults, older adults demonstrated overall lower skill, and brief task reactivation did not significantly benefit intermanual transfer. Results suggest that normal cognitive aging may limit motor trace consolidation and transfer of complex motor tasks. Findings may inform physical rehabilitative approaches for motor learning in older adult patient populations. Future research should investigate conditions of motor practice to optimize functional skill retention and transfer in older adults.

**28. Does Hand Grip Strength Correlate with Shoulder Dysfunction Among Older Women?**

**Ranyah Almardawi**

Almardawi, R.H., Davis, D.L., and Orwig, D.L.

Session E; Poster Presentation; Room 349

Background: Shoulder dysfunction and pain are common problems among older adults. Nearly 20% of those aged 65 and older reported shoulder pain in the 2011 National Health and Aging Trends Study. Shoulder pain and dysfunction may lead to the inability to carry out essential household and daily activities, burdening both patients and society. HGS is commonly tested and considered a reliable measure to assess overall muscle strength and function.
Objective: The aim of this cross-sectional study is to determine the association between hand grip strength (HGS) and shoulder dysfunction. We hypothesize that HGS is correlated with shoulder dysfunction among older women.
Methods: A total of 36 older women volunteers with an age range of 62 to 84 years were included. We assessed the HGS for dominant hands using Jamar Plus Digital Hand Dynamometer. We measured both hands twice and used the strongest measure for the dominant hand.
Degree of shoulder dysfunction was self-reported using the American Shoulder and Elbow Surgeon survey (ASES) [0, worst; 100, best].
Results: Participants had a mean age of 70.9 years (SD:5.7), mean grip strength of 18.2 kg (SD:5.9), and mean ASES score of 86.8(SD: 17.2). A significant and positive

correlation was found between HGS and ASES score (r=0.612, P=0.001).
Conclusion: The moderate correlation of HSG with ASES score supports the hypothesis. The results suggest that future research is warranted to test the feasibility of HSG as a clinical screening tooling for shoulder dysfunction in larger diverse samples of older adults, including men and women.

**29. Excipient-Free Ionizable Polyester Nanoparticles for Lung-Selective and Innate Immune Cell mRNA Transfection**

**Shruti Dharmaraj**

Dharmaraj,S. Chakraborty A, Truong N., Pearson R. M.

Session I; Poster Presentation;  Room 349

Nucleic acid delivery to immune cells has the potential to revolutionize therapeutic outcomes for various diseases. Several viral and non-viral platforms of nucleic acid delivery have been investigated including lipid nanoparticles (LNPs) and polymeric based systems. While LNPs have received significant interest due to the COVID-19 mRNA vaccine, the need for multiple components makes them harder to purify and less stable limiting their cost effectiveness. Similarly, polymeric based platforms generally require functional modifications to the polymer backbone and addition of excipients like lipids or other polymers to effectively deliver nucleic acids to immune cells. Thus, there is need for a nonviral platform with reduced complexity with the adaptability for high-throughput synthesis. Herein, we report the development of a single-component and excipient-free, polyester-based nucleic acid delivery nanoparticle platform comprising ionizable N-methyldiethanolamine (MDET) and various hydrophobic alkyl diols (Cp) that achieves lung-selective nucleic acid transfection in vivo. The polyMDET and polyMDET-Cp polyplexes delivering mRNA to “hard-to-transfect” innate immune cells showed 3-4-fold higher transfection compared to commercially available platforms. After intravenous administration of polyplexes, polyMDET-C4/mRNA and polyMDET-C6/mRNA polyplexes demonstrated a 23- and 12-fold higher lung transfection compared to the spleen respectively. Further characterization revealed transfection in lung macrophages and dendritic cells with low lymphocyte transfection in the spleen. Histology further revealed no detectable levels of organ toxicity or immune cell infiltration. Together the non-inflammatory and lung immune cell tropism provides significant potential of the polyMDET-Cp platform to develop a tolerogenic mRNA vaccine to treat autoimmunity and allergic diseases.

**30. Silencing of nociceptive afferents attenuate hyperalgesia but not condylar degeneration of TMJ after injury.**

**Ishraq Alshanqiti**

Alshanqiti, I., Kumari, S., Hu, J., Chung, M.

Session E; Poster Presentation;  Room 349

A common cause of non-dental pain in the orofacial region is temporomandibular disorder (TMD). One of the painful conditions of TMD is temporomandibular joint osteoarthritis (TMJOA). It causes slow degeneration of subchondral bone and deteriorating of its cartilage, which often is accompanied by pain. However, the mechanistic association of nociceptive afferents and TMJ degeneration is not clearly established. Sixty-five percent of trigeminal ganglia afferents projected to TMJ contain calcitonin gene-related peptides. Approximately half of this co-expresses transient receptor potential vanilloid 1 (TRPV1), which likely mediates pain from TMJ. To determine the contribution of nociceptors to TMJ degeneration and hyperalgesia, we functionally manipulated the TRPV1-lineage afferents in a non-invasive way. We used an inhibitory designer receptor exclusively activated by designer drugs (DREADD), an engineered receptor coupled with inhibitory G protein which can silence targeted neurons upon binding to clozapine-N-oxide (CNO), a specific activator. For targeting the expression of hM4Di, we used TRPV1Cre mice. We used forced mouth opening (FMO) as a model for TMJ injury, leading to TMJ degeneration and hyperalgesia. To activate hM4Di, a CNO-loaded Alzet osmotic pump was implanted in the back of the animal before starting the FMO procedure, which

allows for chronic release for 7 days. We performed micro-computed tomography (μCT) to assess subchondral bone phenotypes in mandibular condyles. Silencing of TRPV1-lineage afferents attenuated spontaneous pain assessed by mouse grimace scale, whereas TMJ degeneration was only modestly affected. Our results suggest that TRPV1 afferent fibers may not be a primary contributor to the degeneration of the TMJ.

**31. Human Induced Microglia Show Impaired Mitochondrial Respiration in Response to High Mobility Group Box 1, a Pro-inflammatory Stimulus Relevant to Neurodegeneration**

**Ryan Mayers**

Mayers, R.P., Zhang, N., Yadava, N., and Polster, B.M.

Session E; Poster Presentation;  Room 349

Nitric oxide (NO)-mediated suppression of mitochondrial oxygen consumption is thought to promote pro-inflammatory, neurotoxic microglia disease phenotypes seen in many neurodegenerative conditions. However, human microglia are reported to show impaired NO production in response to pro-inflammatory stimuli relative to their rodent cell counterparts. We predict that human microglia will lack pro-inflammatory activation-associated mitochondrial respiratory suppression owing to the deficient NO response. Recently, induced microglia-like cells (iMGs) have been derived from peripheral blood mononuclear cells of patients to model human neurodegenerative diseases, enabling efficient study of microglial mitochondrial bioenergetics in response to immune stimulation. Using an established protocol, we derived iMGs from male human PBMCs and validated our differentiation by staining for the microglial markers P2RY12 and CX3CR1. We then treated cells with the endogenous, disease-associated pro-inflammatory stimulus High Mobility Group Box 1 (HMGB1), believed to contribute to cognitive defects in Alzheimer's Disease and traumatic and ischemic brain injury. HMGB1 contributes to neuroinflammation by triggering release of interleukin-1β (IL-1β) mediated by NRLP3 inflammasome activation, so we separately treated iMGs with IL-1β directly. Using a Seahorse XF24 microplate-based respirometer to measure respiration, we found that treatment of iMGs with either stimulus for 18 hours decreased both basal and maximal mitochondrial oxygen consumption rate. Contrary to our expectations, these preliminary data support the conclusion that human male microglia-like cells, like rodent microglia, suppress mitochondrial oxygen consumption in response to disease-relevant pro-inflammatory stimuli. Future experiments will investigate the mechanisms of action and test whether the responses are sex-specific.

**32. Balance Impairments in Pediatric Cancer**

**Emily McCarthy**

McCarthy E, Marchese VG, Rock K, Felter, C

Session E; Poster Presentation;  Room 349

Balance impairments are commonly reported in pediatric cancer, as a direct result of cancer pathology and/or a side-effect of medical treatment. The purpose of this scoping review is to determine causes of balance impairment in children undergoing treatment for cancer/childhood cancer survivors.  A systematic literature search was performed according to PRISMA guidelines. Studies were included if participants were 0-19 years of age with a current or past diagnosis of cancer, an objective outcome measure of balance was reported, and a cause of balance dysfunction was implied. A total of 6639 abstracts and 787 full-text articles were screened for inclusion. A total of 59 full text articles were included in the review. Balance dysfunction was determined to be an impairment caused by cancer pathology or the result of medical treatment.  A total of 23 different outcome measures were used to assess balance function. Chemotherapeutic agents can disrupt sensory integration necessary for balance as a result of peripheral neuropathy, ototoxicity, and central processing impairments. Chemotherapy-induced peripheral neuropathy was commonly associated with balance impairments. Surgical procedures such as solid tumor removal, enucleation or procedures which resulted in limb loss were reported as causes of balance impairment. Multiple studies reported cumulative effects of medical treatments on balance impairments. Causes of balance dysfunction are variable and can be a result of the cancer

itself or the medical treatment to treat cancer. Physical therapists play an important role in assessing balance dysfunction. Further research is needed to identify interventions specific to varying causes of balance impairment.

**33. Design, Synthesis, and Biological Evaluation of Novel Histone Deacetylase 8 (HDAC8) Inhibitors**

**Brandon Lowe**

Lowe, B. D., and Fletcher, S.

Session E; Poster Presentation;  Room 349

Histone deacetylases (HDAC) are enzymes that catalyze the cleavage of acetyl groups from lysine residues of many proteins including histone proteins. Histones bind to DNA and provide structure for chromosomes. With acetyl groups present, the chromosomes are expanded, and the DNA is readily available for transcription. Due to electrostatic interactions, chromosomes condense tightly when histones are deacetylated, blocking the transcription of DNA. Overexpression of HDAC proteins can prevent the transcription of proteins necessary for disease prevention, including cancer, autoimmune disorders, and inflammatory responses. Previous research revealed that HDAC8 expression is linked with lung, colon, and cervical cancer. Subsequent RNA interference knockdown of HDAC8 can slow growth of these cancer cells. HDAC8 expression is also associated with promoting viral entry of Influenza A and other viruses that use endocytosis as a late cell penetration method, although the mechanism is unknown. The FDA has approved four HDAC inhibitors for various cancers, but they exhibit many side effects, which is believed to be due to their pan-HDAC activities. Recently, it was reported that a strategy to acquire HDAC8 selectivity is to construct HDAC inhibitors with an L-shaped configuration. Accordingly, we have designed and synthesized a variety of novel inhibitors spanning several chemotypes, all of which exhibit “L-shapes” and carry the crucial hydroxamic acid functional group to target the active site zinc ion. Additionally, we have recognized and targeted Asp100 and Lys20 residues on the protein surface located near active site entrance. We will present our current status in the discovery of HDAC8-selective inhibitors.

**34. Long-lived Plasma Cells and Beyond: Vaccine Discovery Platforms and Diagnostic Markers for a Durable Antibody Response**

**Parham Habibzadeh**

Habibzadeh, P., Tehrani, Z. R., Flinko, R., Chen, H., Abbasi, A., Yared, J. A., Ciupe, S. M., Lewis, G. K., Sajadi, M. M.

Session E; Poster Presentation;  Room 349

Antibodies are crucial components of protection against various infectious diseases, including Coronavirus Disease 2019 (COVID-19). Generation of a stable long-lived plasma cell (LLPC) population is the sine qua non of a durable humoral immune response after vaccination or natural infection.
In this project, using both classic immunologic assays (e.g., ELISA, ELISPOT) and more recently developed techniques (e.g., single cell sequencing), we study the bone marrow samples of HIV elite neutralizers and patients following COVID-19 vaccination or infection. We have been able to show a significantly decreased LLPC population against SARS-CoV-2 spike protein compared to those against tetanus antigen which is known to elicit long-lived antibody response. We were also able to identify a significant difference in subgroup analysis based on disease severity in those who have had natural SARS-CoV-2 infection highlighting different mechanisms in the generation of LLPCs following infection (i.e., extrafollicular response vs. follicular response). In addition, we have developed statistical models in order to characterize the durable vs. non-durable antibody responses. Through our single cell transcriptomics studies, we were also able to characterize transcriptomics signature associated with long-term survival of plasma cells.
The two major outcomes of this project, developing a vaccine discovery platform for eliciting a durable antibody response and also a blood test for assessing humoral immune response durability within a short period following

vaccination, have the potential to be used for public use and benefit.

**35. Joshi & Merchant, M.D., P.A.: A Retrospective Case Study of New Patients in December 2022**

**Fayga Smith**

Smith, F., Sultani, Z.

Session F; Poster Presentation;  Room 349

This retrospective case study analyzes new patients treated by Joshi & Merchant M.D., P.A. in December 2022. This is a psychiatric office located in Columbia, MD and is owned by Dr. Milan Joshi. The practice includes four physician assistants and three nurse practitioners, all working in a collaborative patient-centered team that specializes in treating adults over age 18. Howard county is racially diverse and one of the wealthiest counties in the United States. There were a total of 88 new patients, with 69% female and 31% male patients. The analysis shows that new patient age percentages reflect the county demographics, excluding young adults ages 18-25 which is disproportionately higher. Although Howard County is a racially diverse community, 78% of new patients seen in this practice reported a white race. The majority of new patients were from Howard County, reflecting the location of the practice. The variety of neighboring counties patients traveled from may be attributed to the wide range of referrers. A majority of patients presented with a complaint of anxiety, followed by depression. This is further reflected in the number of patients diagnosed with generalized anxiety disorder and major depressive disorder. GAF, a scale utilized by clinicians to document global functioning, was on average 70 at the initial encounter, indicating new patients were moderately functioning adults. Of note, there was no significant difference in the number of patients who had previously been treated by a psychiatrist.

**36. Characterization of androgen receptor (AR), endocannabinoid (EDC) receptors, and complement proteins in the developing amygdala**

**Muhammed Mirza**

Muhammed Z. Mirza, Miguel Perez-Pouchoulen, Jonathan W. VanRyzin, and Margaret M. McCarthy

Session F; Poster Presentation;  Room 349

The medial amygdala (MeA) is a sexually dimorphic brain region important for determining sex differences in play behavior. The MeA is differentiated by hyperactive microglial phagocytosis of Astrocyte Progenitors (APs) in males during neonatal development (VanRyzin, 2019). Masculine levels of testosterone correlate with an increase in EDCs, particularly 2-AG, and increased microglia phagocytosis. This process can be mimicked in female rats by increasing testosterone or activating the cannabinoid receptors with agonists. The astrocytes targeted for phagocytosis were also enriched with complement proteins. We examined ARs, EDC receptors, and complement proteins, to better characterize the players involved in this event.
We arrived at two hypotheses. The hunting hypothesis states that APs produce EDCs which microglia detect in a chemotaxis fashion and follow down a gradient to then consume the astrocytes. The farming hypothesis states that EDCs are produced by other cells in the area activating a complement protocol in the microglia which then tag the APs for phagocytosis.
Confocal images following RNA Scope were acquired to determine the expression of AR, CB1 and CB2 receptor across varying cell types allowing precision co-localization of multiple cellular markers. There was little colocalization observed between AR and microglia (Iba1); however, the AR and CB2 receptor colocalized with the astrocyte marker (GFAP). A microglia deficient environment was induced from PN0-2 which significantly decreased Iba1 ($p=0.003$) by PN4 compared to the control. We will use this approach to further investigate complement protein C3 and C1qa in the microglia deficient environment to test the “farming hypothesis”.

**37. Self-Compassion, Childhood Emotional Neglect, and  Posttraumatic Growth: Parental Well-Being During COVID-19**

**Allison Deitz, LCSW-C**

Deitz, A. H. H.

Session F; Poster Presentation;  Room 349

Background: The CoronaVirus Disease 2019 (COVID-19) pandemic forced parents to contend with balancing remote learning for school-aged children and remote work for themselves, or finding safe childcare if they were essential workers. Self-compassion is key in promoting posttraumatic growth (PTG), a component of well-being; however, parents with histories of childhood emotional neglect may struggle to practice self-compassion when their own affectional needs were chronically unmet earlier in life, carrying implications for both parental and child well-being in recovering from the pandemic.
Objective: To examine the relationship between childhood emotional neglect and pandemic-related PTG, and the moderating role of self-compassion.
Participants and Setting: The sample consisted of 436 parents (ages 19-66; M = 37.62 years, SD = 9.31) from across the U.S.
Methods: An online cross-sectional survey collected information on pandemic- and parenting-related stresses, childhood emotional neglect, self-compassion, psychological distress, and pandemic-related PTG. Multivariate regression analyses were conducted to analyze relationships amongst childhood emotional neglect, self-compassion, and pandemic-related PTG.
Results: Higher self-compassion significantly predicted higher pandemic-related PTG. The interaction between childhood emotional neglect and self-compassion was significant; specifically, when self-compassion was lower, greater childhood emotional neglect predicted lower pandemic-related PTG.
Conclusions: Findings emphasize the utility of self-compassion in promoting pandemic-related PTG, especially for adults who may not have had compassion shown to or self-compassion modeled for them in childhood. Self-compassion is a freely accessible, portable practice that individuals can implement successfully with minimal instruction. Mental health clinicians may be able to identify points of intervention wherein self-compassion may stimulate pandemic-related PTG.

**38. Medicolegal Investigation of Sudden Unexpected Infant Deaths in Maryland: a retrospective forensic autopsy study 2016-2021G**

**Aakash Gnanavel**

Gnanavel, A., Landry, A., Lozano, E.R.

Session F; Poster Presentation;  Room 349

According to the CDC, there are about 3,400 sudden unexpected infant deaths (SUID) in the United States each year. These deaths occur among infants less than one-year-old and have no immediately apparent cause. The three commonly reported types of SUID to include sudden infant death syndrome (SIDS), unknown cause, and accidental suffocation and strangulation in bed.
The office of the Chief Medical Examiner (OCME) is responsible for the medicolegal investigation of all the sudden unexpected deaths in the State of Maryland. This study aims to identify the trend and pattern of sudden unexpected infant death and its risk factors.
During the six years, 465 infants died suddenly and unexpectedly in Maryland. The yearly SUID ranged from 64 to 88 cases, averaging 77.5 cases. More male infants (N= 259, 55.7%) died suddenly and unexpectedly than female infants (N= 206, 44.3%). Most of the SUID cases were African American infants (N= 265, 57%), 149 (32%) were white infants, and 51 (11%) were other-race infants.
The OCME has witnessed a sharp decline in SUID in Maryland, and the number dropped from more than 100 cases annually before 2000 to 75 cases in 2021. There has been a significant diagnostic shift from SIDS (more than 90% of cases in 2019) to Sudden Unexplained Death in Infancy (unknown cause) (86%) and accidental asphyxia (17%) during 2016 and 2021. During 2016-2021, 21 infants died of accidental asphyxia, and 27 died from homicide, which was preventable deaths.

**39. Exploring Barriers and Strategies to Improve Physical Impairments and Functional Disability in Patients Post Hand, or Wrist Surgery.**

**G. Mona Saeed**

Saeed, GM, Marchese, VG

Session F; Poster Presentation;  Room 349

Purpose: In patients with musculoskeletal conditions, the primary focus of rehabilitation has been evaluating physical impairments (pain and muscle force production) and functional disability, however, more attention is being brought to the role of psychosocial factors (self-efficacy and kinesiophobia). In patients post hand or wrist surgery, this pilot study aimed to 1. Explore relationships between psychosocial barriers, physical impairments and functional disability; and 2. Identify if focus of attention strategies can create a distraction to decrease pain, improve muscle force production and functional disability.
Methods: Ten participants underwent a single-session crossover design while playing a video game. Outcome measures, Numeric Pain Rating Scale (NPRS), General Self Efficacy Scale (GSES), Tampa Scale of Kinesiophobia-11 (TSK-11), muscle force production, and Quick Disabilities of Arm, Shoulder & Hand (QDASH), were completed at three time points (baseline, after each external/internal focus of attention training).
Results: Spearman's correlations tests identified a strong positive correlation between the TSK-11 and the QDASH (r =0.71, p =0.02). No other outcome measures were identified to have a significant correlation. Friedman's tests determined that there were significant differences at the three time points, NPRS scores worsened from baseline to after external focus training while muscle force production and QDASH scores improved from baseline to after internal focus training.
Conclusion: Hand therapists need to consider the role of not only physical impairments and functional disability, but psychosocial factors, to provide comprehensive care to the post-surgical patient.

**40. Nociceptive and Transcriptomic Responses in a Swine Diabetic Wound Model Treated with a Topical AT1R Antagonist**

**Miriam Weiss**

Weiss, M.N., Mocci, E., Zhu, S., Renn, C.L., and Dorsey, S.G.

Session F; Poster Presentation;  Room 349

Painful ulcers are prevalent among diabetic patients. Proinflammatory angiotensin 1 receptors (AT1R) are upregulated in diabetic skin and thus have been suggested as targets for wound healing. Here, we investigated the effects of topical valsartan, an AT1R antagonist, on pain and gene expression changes in swine diabetic wounds. Swine were selected because their skin structure and diabetes pathologies resemble those of humans.
Eight wounds were surgically induced in diabetic, hyperglycemic Yucatan miniature swine. AT1R antagonist was applied to four wounds and vehicle to the other four. Nocifensive testing was conducted at baseline, then weekly beginning seven days after wound induction. Mechanical and thermal stimuli were applied to the wound margins until a nocifensive reaction was elicited. Tissue from the dorsal horn, dorsal root ganglion, and wounds were sequenced and analyzed with DESeq2. Unbiased pathway analysis using Metascape was conducted on differentially expressed genes.
There was no significant difference in mechanical tolerance between valsartan- and vehicle-treated wounds (p=0.106). Thermal tolerance was significantly higher in valsartan-treated wounds (p=0.015). Analysis of differentially expressed genes revealed two enriched pathways of interest: interleukin-18 signaling in dorsal horn laminae IV-V and sensory perception of mechanical stimulus in wound tissue.
Topical AT1R antagonist was associated with a decrease in diabetic wound-related thermal hyperalgesia, but not mechanical allodynia. RNA-seq analysis of differentially expressed genes revealed several pathways of interest for future pain research. The model created in this study may be valuable for future diabetic ulcer research and after further, larger studies, could improve diabetic wound care.

**41. Effect of robot-aided hand rehabilitation on motor recovery post stroke**

**Sanjana Rao**

Rao,S., Koh,K., Baghi,R., Zhang,C., Xu,D., Oppizzi,G., Kamper,D., Kehs,G., Zhang,L.Q.

Session F; Poster Presentation; Room 349

Robot-aided UE training has been established as a safe and feasible treatment to complement rehabilitation post stroke. There have been several rehabilitation robots developed to train the proximal UE, achieving outcomes comparable to dose-matched conventional therapy. However, distal UE function is essential for the execution of activities of daily living and is often severely impaired post stroke, with low probability of regaining its full functional use. A robotic hand training helps in delivering intensive, high-dosage training and also provides direct quantitative feedback to patients about their performance, which can enhance motivation and potentially help in restoration of their hand function. The purpose of this study was to determine the efficacy of robotic hand rehabilitation device in improving the UE motor function in stroke survivors.The study was conducted with 18 sub-acute stroke survivors.The subjects underwent a robotic hand training for 3 sessions/week over 6 weeks. The hand training was provided using Hand of Hope exoskeleton.The outcomes were evaluated using the following: UE-Fugl-Meyer Assessment (FMA), Action Research Arm Test (ARAT), Grip and Pinch Strength measurement, Wolf Motor Function Test (WMFT) and robotic measures- X-tau matrix depicting the wrist-finger coupling.We found significant improvements in the hand function measures post 6 weeks of training. Improvements were noted in FMA(p=0.04), WMFT(p=0.016), Grip Strength and Pinch Strength (p=0.013), Key Pinch Strength (p=0.018), and ARAT(p=0.008) measures.This study shows that a myoelectric hand robotic training via biofeedback system can potentially promote recovery of UE function.

**42. Serological Responses to Malaria Variant Surface Antigens in Malawian Infants**

**Rosita Asawa**

R. R. Asawa, B. Hritzo, Aa Ouattara, A. A. Berry, L. R. Andronescu, B. Shrestha, A. Sharma, R. Nakajima, A. Jain, O. Taghavian, A. Jasinskas, P. L. Felgner, J. Chinkhumba, D. Mathanga, M. A. Travassos, M. K. Laufer

Session F; Poster Presentation; Room 349

The Plasmodium falciparum parasite is the deadliest and most prevalent malarial species in Africa, disproportionately affecting young children aged 1-5 years old. Maternal antibodies present at birth are thought to protect infants from severe manifestations of malaria for the first 6 months of life. Identifying specific protective maternal antibodies could inform vaccine development for young children in malaria-endemic areas. During the blood phase of the malaria life cycle, the parasite expresses variant surface antigens, the most studied of which is the highly diverse P. falciparum erythrocyte membrane protein 1 (PfEMP1) found on the surface of infected red blood cells that allow it to bind to host endothelium and evade host immunity. We hypothesized that serological responses to PfEMP1, both the intensity of the responses and the number of variants recognized, in cord blood at birth would correlate with subsequent risk of malaria. We collected serum from cord blood at delivery in Liwonde, Malawi, and instances of malaria infection were tracked quarterly for 2 years. Serum samples were then probed for serological responses using a protein microarray containing 259 fragments of PfEMP1. Analyses of infants experiencing infection within the first 6 months of life showed few differences from infants who remained healthy in early life. Preliminary results suggest that maternal antibodies to a wide range of PfEMP1 antigens did not predict susceptibility to clinical malaria for infants in the first 6 months of life. These results have the potential to inform vaccine development methods against P. falciparum malaria.

**43. Parental Self-Compassion and Psychological Distress During the COVID-19 Pandemic**

**Maura Tennor**

Tennor, M. K.

Session F; Poster Presentation; Room 349

The COVID-19 pandemic has been detrimental to mental health, particularly for parents. Interventions are desperately needed to ameliorate parental difficulties (and by extension, those of their children), as there is currently no end in sight for the pandemic. Given the frequent need for social distancing and isolation as well as the fact that therapists are in short supply, remedies that can be applied on one's own are needed. Self-care, particularly the self-compassion component of self-care, has significant potential as a reliable and valid intervention for parental well-being. The study objective was to examine the association between parental self-compassion and distress. This study found higher parental self-compassion was associated with lower distress, greater parental age to be associated with lower distress, and high levels of parental education to be associated with higher distress. Promotion of better self-care, and self-compassion in particular, will help to stop the spread of mental health issues during this difficult time.

**44. Development of a Conceptual Framework for Data-Centric Machine Learning in Nursing**

**Patricia Dunlap**

Ball Dunlap, P. A.

Session F; Poster Presentation;  Room 349

Background: There is inadequate nursing literature mentioning the data-centric perspective, including its application to AI and machine learning in nursing. This distinction lives in the realms of Data and Computer Sciences disciplines. Further concept clarification is warranted to ensure cogent usage of the data-centric concept in nursing practice and its alignment with other fields.
Objective: To elucidate the nursing body of knowledge about the data-centric artificial intelligence phenomenon via a nursing-specific conceptual analysis methodology.
Method: The concept of interest was analyzed using Norris' Concept Clarification methodology to clarify, define, and advance nursing knowledge. This method was employed because it refines concepts that may be used in nursing without an explicit, shared, and conscious agreement about their properties or meanings attributed to them.
Result: A nursing-specific operational definition was derived from the conceptual analysis, including an exemplar.
Conclusion: Having a data-centric machine learning operational definition and exemplar, further exploration of exploiting this approach as an intervention for pressing nursing EHR technology problems (i.e., documentation burden) can commence. Data-centric machine learning allows nurses to sit at the conversation table and drive their data's effective use and representation for improved experiences with digital health tools, especially custom AI-enabled solutions.

**45. COVID-19 Disease Associated Oral Microbiome Dysbiosis and Risk of Oral Opportunistic Infections**

**Areej Alfaifi**

Alfaifi, A. A ,Sultan, A. S , Jabra-Rizk, M.

Session F; Poster Presentation;  Room 349

Despite the myriad oral manifestations during COVID-19 and presence of SARS-CoV-2 in saliva, the oral cavity remains an underappreciated site. However recently, SARS-CoV-2 was shown to replicate in salivary gland cells resulting in inflammation and tissue destruction. Saliva contains antimicrobial peptides considered integral components of innate immunity crucial for oral health. Most notable is histatin-5 exclusively produced in salivary glands with unique potent antifungal activity against Candida albicans. In this project, we hypothesize that SARS-CoV-2 mediated salivary gland destruction compromises histatin-5 production, predisposing patients to oral candidiasis. To that end, we are using our customized immunoassay to measure salivary histatin-5 levels in a prospective study using stratified COVID-19 cohorts. Additionally, to identify potential COVID-19 associated pathologic dysbiotic shifts in the oral microbiome, we are performing comprehensive metagenomic analysis on clinical oral samples. Thus far, preliminary data indicate a trend with decrease in salivary histatin-5 and increase in Candida during COVID-19,

continuing post COVID-19 recovery, potentially part of long COVID-19 syndrome. To provide lacking mechanistic insights into the pathophysiology of salivary gland dysfunction during COVID-19, we are performing in situ hybridization coupled with immunofluorescence for co-localization of SARS-C0V-2 and histatin-5, respectively, in salivary gland tissue from deceased COVID-19 patients. Preliminary findings indicate diminished or absent histatin presence in salivary gland acini with proliferating SARS-CoV-2 providing first direct evidence associating SARS-CoV-2 with histatin-5 production. Based on these novel findings, our immunoassay for salivary histatin-5 evaluation may be a valuable tool for identifying predisposition to candidiasis in acutely ill and recovered COVID-19 subjects.

**46. Understanding the Association between Economic Hardship and Parental Psychological Distress during the COVID-19 Pandemic**

**Yoonzie Chung**

Chung, Y.

Session G; Poster Presentation;  Room 349

Since March 2020, the COVID-19 pandemic has sparked concerns and fear throughout the world as well as in the United States. Economic recession spurred by COVID-19 put a myriad of families at risk of financial insecurity. The Family Stress Model (FSM) posits that economic burden positively affects parents' psychological distress, leading to adverse child outcomes. Applying FSM to the association between economic hardship and parental psychological distress, the current study sought to identify whether economic hardship is associated with parents' psychological distress during the COVID-19 pandemic. These research questions guide the current study: 1) Is economic hardship associated with parents' psychological distress during the COVID-19 pandemic? 2) Which economic hardship item is more strongly associated with parental psychological distress during the COVID-19 pandemic? Data regarding parents residing in the United States was collected via Qualtrics (n= 436) from June through August 2022. The independent variable, economic hardship, was measured with the income subscale of the Covid Family Stressor Scale (CoFaSS), and the dependent variable, parental psychological distress, was measured with Kessler 6-item scale. Using multiple regression analysis, the current study found that total economic hardship is positively associated with parental psychological distress ($B = 1.025$, $p < .001$). Among economic hardship items, going into financial debt is strongly associated with parental psychological distress ($B = 1.951$, $p < .001$). It suggests that economic support for families experiencing economic hardship during the pandemic is urgently needed.

**47. Diaphragm Function and Breathing Performance on the Six-Minute Walk Test in Children with Sickle Cell Disease**

**Simon Ho**

Ho, S., Rock, K., Marchese, V.

Session G; Poster Presentation;  Room 349

Background: Skeletal muscle dysfunction has been implicated in the development of exercise intolerance in sickle cell disease (SCD). The objective of this study was to explore differences in the diaphragm, which is a skeletal muscle, and breathing performance during the six-minute walk test (6MWT) in children with SCD.
Methods: Diaphragm function was measured by maximal inspiratory pressure and diaphragm ultrasonography (thickness and excursion). Breathing performance during the 6MWT (respiratory frequency [fR], tidal volume [VT], minute ventilation [VE], and oxygen consumption [VO2]) was measured via breath-by-breath expired gas analysis. Rate of perceived exertion (RPE) was measured by the Borg 0–10 category ratio (CR-10) scale.
Results: Diaphragm thickness at total lung capacity, thickening fraction, and excursion time during quiet breaths and deep breaths (DB) were greater in children with SCD versus controls ($p < 0.05$ for all). Yet, 6MWT distance was shorter in children with SCD ($p = 0.01$). VT, VE, and VO2 were also lower ($p < 0.05$ for all). DB excursion correlated positively with 6MWT distance ($r = 0.648$, $p = 0.023$) and negatively with RPE ($r = -0.759$, $p = 0.003$). RPE correlated

negatively with distance (r = -0.680, p = 0.015). DB excursion time correlated positively with distance (r = 0.611, p = 0.035), VT (r = 0.770, p = 0.009), VE (r = 0.736, p = 0.015), and VO2 (r = 0.751, p = 0.012).
Conclusions: Children with SCD likely have respiratory system inefficiencies that lead to different breathing patterns and strategies, ultimately contributing to exercise intolerance.

**48. Factors Associated with a Reduction in Modifiable Risk Factors, with a Focus on Physical Activity (PA), Healthy Diet, and Sleep Among Long Term Care (LTC) Workers Diagnosed with Diabetes (DM)**

**Abaneh Ebangwese**

Ebangwese, A., Doran, K., Resnick, B., and Zhu, S.

Session G; Poster Presentation;  Room 349

LTC workers provide most of the care for older and disabled adults, however, since the pandemic, LTC facilities have been struggling with staff turnover rates which have been reported to be as high at 75% and mostly due to chronic health issues. According to the CDC, DM, along with heart disease and cancer are the most prevalent chronic diseases and the leading causes of death and disability in the United States. But all Americans do not share this burden equally. The prevalence is higher in low-income minority groups which LTC staff are predominantly a part of. Prior studies have shown that certain wellness behaviors such as increased physical activity, a healthy diet, and enough quality sleep decreases risk for DM. However, LTC workers exhibit poor adherence to healthy behaviors compounding the prevalence of experiencing health disparities. One study even showed that those diagnosed with DM were 1.50 times more likely to fail to maintain the recommended PA minutes per week. This presentation will discuss the secondary data analysis methods I will conduct for my dissertation as well as for the parent project (a worksite wellness intervention within LTC). My dissertation aims to identify health-promoting factors associated with increased engagement in PA, healthy diet, and quality sleep in LTC workers diagnosed with DM. These wellness behaviors have been shown to reduce DM risk. Ultimately, improving LTC workers' health by reducing modifiable DM risk factors through identifying ealth-promoting will be an important step towards reducing turnover and health disparities in this population.

**49. Examining the Effects of Chronic Stress on BLA-VP Circuit Activity During Social Interaction in Mice**

**Geralin Love Virata**

Virata, G.L.V., Campbell, R.R., Martinez, D., and Lobo, M.K.

Session G; Poster Presentation;  Room 349

Chronic stress causes disruptions to the brain's reward circuitry that are theorized to promote depressive symptoms, such as anhedonia and social avoidance. Human studies suggest hypofunction of the ventral pallidum (VP), a major region within the reward circuit, is linked to motivational deficits and depressive symptoms. However, how stress changes VP activity, resulting in these disruptions is still unknown. The VP receives input from the basolateral amygdala (BLA), a region involved in emotional processing and learning that undergoes stress-induced changes in neural activity. Therefore, we focused on examining BLA inputs to the VP (BLA → VP) and how stress-induced alterations to this circuit promote social avoidance in mice. We hypothesized that chronically stressed, socially avoidant mice will have decreased BLA → VP circuit activity. To test this, we used retroAAV-GFP to label BLA → VP cells and subjected mice to physical stress using a chronic social defeat paradigm with male mice. We assessed whether chronic stress alters Fos protein expression, a neural activity marker, in BLA → VP cells, following a social interaction test, and have observed decreased expression in BLA → VP cells in stressed mice compared to unstressed controls. On-going experiments include examining Fos BLA → VP activity analysis in female stressed mice using a witness defeat paradigm. Overall, understanding how chronic stress disturbs neural circuitry to promote depression-like behaviors will provide useful insight for future therapeutic development.

**50. Heroin-induced Genomic Regulation of Ventral Pallidum and Nucleus Accumbens Neuron Subtypes.**

**Benjamin Grissom**

Grissom, B.H., Campbell, R., Cortes-Gutierrez, M., Qamar, B., Mitra S., Ament S.A.*, Dietz, D.M.*, and Lobo, M.K.*

Session G; Poster Presentation; Room 349

Opioid dependence is associated with long-lasting changes in the mesolimbic dopamine system, but the cell type-specific gene regulatory networks mediating these effects are poorly understood. To address this, we sequenced the nuclear transcriptomes (snRNA-seq) and chromatin accessibility states (snATAC-seq) of 279,219 single cells in the nucleus accumbens (NAc) and ventral pallidum (VP) from rats in the context of heroin self-administration. We produced detailed atlases for the cell type diversity in each brain region, characterizing ten transcriptionally distinct subtypes of spiny projection neurons in the NAc and >20 transcriptionally distinct neuronal subtypes in VP, representing the first detailed single-cell genomic atlas for this brain region. We characterized cell type-specific changes in gene expression and chromatin accessibility in rats that self-administered heroin vs. controls, at 1 or 14 days of abstinence, to gain insight into both acute and persistent effects on gene regulation. We integrated these data to model the gene regulatory networks mediating the effects of heroin. Our results provide insight into the gene regulatory mechanisms mediating the persistent effects of opioids in the brain.

**51. The Regulation of Peripheral T Cell Function by Neurotransmitters**

**Francisco Canales**

Canales, F.J., Singh, N.J.

Session G; Poster Presentation; Room 349

The nervous and immune systems are known to regulate each other's functions to maintain host health. T cells are central players in cellular immunity. Previous work from our lab suggested that neurons may specifically modify T cell responses by using certain neurotransmitters and neurotransmitter receptors (NRs). The pattern of NR expression in T cells indicates that distinct subsets of T cells engage different NRs; but their specific roles and mechanisms of action are not known. In order to investigate two of these molecules (SigmaR1 and VIPR1 NRs) I am using parallel strategies to generate T cell-specific NR knockouts. The SigmaR1 receptor is known to be a non-opioid intracellular receptor that interacts with a variety of psychotomimetic drugs. There is also some evidence of T cell specific function for SigmaR1. I am using a retroviral CRISPR construct that will conditionally knockout the SigmaR1 gene in mature T cells, allowing us to characterize the alterations in T cell function that may result from this change. The VIPR1 receptor senses Vasoactive Intestinal peptide (VIP) which stimulates vasodilation, myocardial contractility, and decreases arterial blood pressure. Previous work in the lab showed that pretreatment of T cells with VIP affects T cell differentiation. We are generating a T cell-specific knockout animal model by using VIPR1-floxed mice crossing to CD4-Cre. These studies will identify how different NRs induce T cell specific changes and help modulate immunity.

**52. Multi-Method Study to Assess Gender and Racial Disparities in Unmet Dementia-Related Care Needs among Non-Spousal Informal Care Partners of Community-Dwelling Persons with Alzheimer's Disease and Related Dementias**

**Gretchen Tucker**

Tucker, G.G., Gruber-Baldini, A., Samus, Q., Girling, L., Eckert, J.K., Wallace, B., Orwig, D.

Session G; Poster Presentation; Room 349

Research related to informal care partners (CPs) of persons with dementia has focused on spousal and female non-spousal CPs; little is known about male non-spousal CPs. To address this gap, a secondary data analysis of two cohort studies that enrolled dyads of persons with dementia and their CPs was employed to improve the understanding of CP dementia-related care needs by spousal status and gender. The unmet dementia-related care needs were

measured using the Johns Hopkins Care Needs Assessment. The assessment consists of six domains and 18 binary items of CP unmet needs (e.g., memory disorder education, general health care, daily living, and informal support) yielding a summary score range 0-100. Of the 595 CPs, 69% (413) were non-spousal, 24% (140) were male and a greater percentage were African American (320 (55%)). CPs' average age was 63±11.85 years and 80±9.81 for care recipients and the average years of education for CPs was 15±3.11. There were differences in specific unmet needs by spousal status in which non-spousal CPs (vs spousal) had higher unmet needs regarding decision-making (80% vs. 58%; p<.0001); spousal CPs had higher unmet needs related to informal support (50% vs. 40%; p=0.03) and meaningful activities (23% vs. 15%; p=0.02). However, the mean percentage of unmet needs was not different for spousal status and gender. In conclusion, overall unmet needs of CPs were not different by spousal status or gender, but there were differences in some of the specific types of unmet needs by spousal status.

**53. Induction of Ferroptosis in Diverse Cancer Types Using Small Molecules**

**Jon Christofersen**

Christofersen, J. R., Neitzel, L.R., Cornell, J. L., Kocinsky, S., Rea, S. L., Williams, C. H., Hong, C. C.

Session G; Poster Presentation; Room 349

Highly acidic tumor microenvironments have been linked in proliferation and survival in diverse cancer types. Aerobic glycosylation results in an acidic milieu in a process called the Warburg effect (thought to be a driver of cancer). We previously identified a class of small molecules, Ogremorphins (OGM), which have been seen to selectively inhibit GPR68, a pH sensing receptor. Our lab has evaluated the role of GPR68 in multiple cancers and found that it is protective against ferroptosis. Previously, we validated this in glioblastomas prompting us to further comprehend the role of this in cancer types originating from other organs.

The cell lines evaluated here were treated with low and high dose OGM as well as erastin as a positive control. During ferroptosis, lipids in mitochondrial membranes become free radicals. We used the compound, Liperfluo, to measure lipid peroxisome levels intracellularly. Cell Titer Glo was used to detect ATP for measuring cell survival. cDNA was generated from these cell lines to measure the expression of GPR68 and additional components of the ferroptosis pathway. This was necessary to assess if levels of GPR68 correlate to lipid peroxides levels during knockdown.

We found that a broad range of cancer cells originating from various organs are sensitive to OGM and erastin. Additionally, we tested primary cells and found they were sensitive to OGM and erastin. However, we found there was not a strong association between GPR68 and sensitivity to OGM suggesting that levels of expression do not control the ferroptotic response in these cells.

**54. Targeting EGFR to Enhance Natural Killer T Cell- Mediated Killing of Lung Cancer Cells**

**Aditya Kavuturu**

Kavuturu A., Webb T.J.

Session G; Poster Presentation; Room 349

Lung cancer is the most lethal and second most diagnosed type of cancer in American men and women in 2022, and non-small cell lung cancer (NSCLC) accounts for 85% of lung cancer cases. Epidermal growth factor receptor (EGFR) mutation is the second most common mutation, after KRAS, in NSCLC, and patients with EGFR mutant lung cancers eventually develop acquired resistance to EGFR tyrosine kinase inhibitors (TKIs), such as gefitinib and erlotinib. Novel therapeutic strategies, such as targeted therapy in combination with immunotherapy, are being developed to overcome resistance in NSCLC patients. For example, Natural Killer T (NKT) cells are being combined with EGFR TKIs in ongoing clinical trials, but it is unclear whether there are synergistic effects. We tested the hypothesis that treatment with EGFR TKIs blocks the production of immunosuppressive factors by lung cancers and sensitizes the cancer cells to NKT cell-mediated killing.

A549 lung cancer cells were treated with increasing concentrations of cisplatin, gefitinib, and erlotinib, and we measured levels of vascular endothelial growth factor (VEGF), a potent immunosuppressant, and killing of 2D monolayer and 3D spheroid cultures. We also assessed NKT cell-mediated cytotoxicity in the presence and absence of immune checkpoint blockade. We found that treatment with EGFR TKIs reduces production of VEGF. In addition, we found that combining EGFR TKIs with chemotherapy induces cytolysis, and the addition of NKT cells further enhances tumor cell death. These studies suggest that the combination of EGFR TKIs with immune modulation has therapeutic potential in lung cancer.

**55. The role of the minor CF CS14 in ETEC adherence to HT29 intestinal cells and the human enteroid model**

**Emily Smith**

Smith, E.M., Papadimas, A., Gabor, C., Wu, T., and Barry, E.M.

Session G; Poster Presentation; Room 349

Enterotoxigenic Escherichia coli (ETEC) is a primary causative agent of diarrhea in travelers and young children in low-to-middle-income countries. ETEC adhere to intestinal epithelia via colonization factors (CFs) and secrete heat-stable toxin (ST) and/or heat-labile toxin (LT), causing dysregulated ion transport and water secretion. There are over 30 CFs identified, including major CFs prevalently associated with moderate-to-severe diarrhea (MSD) and minor CFs in which their role in pathogenesis is less understood. The Global Enteric Multicenter Study (GEMS) identified CS14, a class 5a fimbriae, as the only minor CF associated with MSD and was recommended for inclusion in ETEC vaccines. Despite detection of CS14 in ETEC isolates, its role in adherence and functional cross reactivity to other 5a fimbriae are not understood. We hypothesize that CS14 expression increases adherence and that adherence is CS14-specific with minimal cross reactivity with other class 5a fimbriae, using HT29 intestinal cells and human enteroid monolayers. ETEC isolates expressing CS14 from the GEMS were evaluated. Western blots and electron microscopy demonstrated CS14 expression in isolates grown on CFA agar and the iron chelator deferoxamine mesylate. Expression of CS14 resulted in significantly increased adherence to intestinal cells. Anti-CS14 antibodies and anti-CS4 antibodies, but not anti-CFA/I antibodies, inhibited adherence by ETEC isolates, suggesting specific inhibition with some class 5a cross reactivity. Altogether, these data demonstrate that targeting CS14 in ETEC isolates is sufficient for adherence inhibition with cross reactive inhibition by antibodies to CS4. These data provide support for CS14 as a vaccine antigen in current vaccine strategies.

**56. Angiopoietin-like 4 increases cancer cell resistance to chemotherapy through enhanced HR-mediated DNA damage repair**

**Emmanuel Asiedu**

Asiedu, E.B., Kumar, A., and Montaner, S. M

Session G; Poster Presentation; Room 349

DNA-damaging drugs such as platinum-based chemotherapies and topoisomerase inhibitors represent a major paradigm for cancer treatment. In many patients, however, resistance to these drugs develop over time, through various mechanisms. One prominent mechanism of resistance in cancer cells is enhanced DNA repair. Angiopoietin-like 4 (ANGPTL4) has been associated with increased cell survival, proliferation, migration, invasion, anoikis resistance, metabolism, angiogenesis, and drug resistance in cancers. Very little is known about how ANGPTL4 impacts DNA repair and how this affects drug sensitivity and resistance in cancer cells. Using a CRISPR/Cas9 generated ANGPTL4 KO HNSCC cell line, we have shown that the loss of ANGPTL4 sensitizes cells to killing by cisplatin and camptothecin. Further, ANGPTL4 loss increased γH2AX foci, decreased RAD51 foci, and decreased homologous recombination repair efficiency. These results so far suggest that ANGPTL4 might allow cancer cells to resist therapy by elevating DNA damage repair and can be a useful drug target considering its pleiotropic functions in cancer progression.

**57. Zinc Fingers are a General Target for Persulfidation by Hydrogen Sulfide (H2S)**

**Andrew Stoltzfus**

Stoltzfus, A. T., Vignane, T., Li, H., Worth, M. M., Filipovic, M. R., Michel, S. L. J.

Session H; Poster Presentation;  Room 349

Persulfidation (or "sulfhydration") of protein thiols by the gasotransmitter hydrogen sulfide (H2S) has been recently established as an important signaling event associated with oxidative stress and cellular aging. While H2S, mostly bisulfide (HS-) anion at physiological pH, likely does not persulfidate protein thiols directly due to incompatible electric potential, it may act through small-molecule thiols (ex: glutathione) to add a sulfur to cysteine thiols (CysSH CysSSH). This highly reactive persulfide species can alter protein function and/or scavenge intracellular radical species during oxidative stress by direct reaction with radicals. Zinc finger proteins (ZFs) are potential targets for this PTM as they contain Cys-rich zinc-binding domains and our laboratory has previously reported the direct reaction of the ZF protein TTP with H2S. This reaction requires O2 and involves in-situ persulfidation. To understand how general ZF persulfidation is, we applied a persulfide-specific proteomics approach and observed a trend between Cys content of ZF domains and frequency of persulfidation. A series of TTP variants were prepared and analyzed for H2S reactivity via cryo-electrospray ionization mass spectrometry, as well as UV-visible, circular dichroism, and fluorescence spectroscopies. We found that all peptide variants bound Zn(II) and were persulfidated by H2S to some extent, with higher Cys content contributing to greater persulfide labeling and ROS in the -CCCH and -CCCC peptides. Current work is focused on proteomic classification of persulfidated ZFs and elucidating the radical mechanism of this PTM using chemical tags, fluorescence, and spin-traps.

**58. Detection of Intracranial and Extracranial Carotid Calcifications in Cone Beam Computed Tomography Utilizing a Deep Learning Convolutional Neural Network Image Segmentation Approach**

**Shahd Alajaji**

Alajaji, S. A., Amarin, R., Masri, R., Tavares, T., Kumar, V., Price, J. B., Sultan, A. S.

Session H; Poster Presentation;  Room 349

Background and Aims: Atherosclerosis is a major risk factor for myocardial infarction and stroke. Carotid calcifications (CC), a reliable indicator of future myocardial infarction and stroke, can incidentally be detected on routine head and neck cone beam computed tomography (CBCT) during routine dental visits. CBCT can identify and quantify calcifications as small as 1mm3 and even mild calcifications are proven to be associated with significant coronary artery disease. This study aimed to leverage a deep learning convolutional neural network image segmentation approach to accurately detect and segment incidental CCs on CBCT images.
Methods: Transfer learning via a U-Net based neural network architecture was utilized. A total of 138 axial CBCT images were included and distributed as 60% training, 10% validation, and 30% testing.
Results: Mean training and validation accuracy for extracranial image segmentation was 92% and 82%, respectively. Pixel testing accuracy for extracranial CC was 92%, with an area under the curve (AUC) of 1.0, a sensitivity of 100%, and a specificity of 69%. Intracranial CC detection had a pixel testing accuracy of 38%, AUC of 0.5, a sensitivity of 93%, and a specificity of 8%.
Conclusion: The deep learning model showed excellent sensitivity for the detection of extracranial and intracranial CC. The findings of this study highlight the potential to utilize AI methods for medical image analysis. The findings also demonstrate how AI can alert the clinician to discovery of serious incidental pathology and the potential to enhance early detection of future cardiovascular complications.

**59. The Mediating Role of Pain Severity in the Association Between Depressive Symptoms and Gait Speed**

**Rhea Mehta**

Mehta, R., Shardell, M., Ryan, A., Dong, Y., Beamer, B., Hochberg, M., Rathbun, A.

Session H; Poster Presentation; Room 349

Knee osteoarthritis (OA) and comorbid depression adversely impact gait speed over time. Depression can alter pain tolerance and perception; therefore, self-reported knee pain severity may mediate the relationship between depressive symptoms and gait speed, but this has not been evaluated longitudinally using repeated measures data. Thus, we assessed whether knee pain severity mediates the association between depressive symptoms and gait speed over time. Participants (n=2,222) from the Osteoarthritis Initiative with radiographic knee OA (Kellgren-Lawrence grade ≥ 2) in at least one knee were included. Depressive symptoms were assessed using the Center for Epidemiologic Studies Depression Scale (CES-D; range 0-60) at baseline and first two annual follow-up visits. The twenty-meter gait speed (meters per second) outcome was assessed at the second through fourth annual follow-up visits. Knee pain severity was assessed as a mediator and measured using the Western Ontario and McMaster Universities Osteoarthritis (WOMAC) pain subscale at the first through third annual follow-up visits. Linear regression mediation using a version of the Sobel-Goodman approach was the primary method of analysis. Indirect and direct effects of depressive symptoms on gait speed for each one-unit CES-D score were -0.001 ($p < 0.001$) and -0.003 ($p = 0.020$) standard deviations, respectively. Thus, approximately 24% of the association between depressive symptoms and gait speed was mediated by knee pain severity across time. The current results support the need for simultaneous, multidisciplinary interventions for both depressive symptoms and knee OA pain to prevent future decline in physical performance.

**60. Parents' Problem-Solving and Psychological Distress During Covid-19: Mediating Effect of Preparedness for Caregiving**

**Peiyuan Zhang**

Zhang, P.

Session H; Poster Presentation; Room 349

Background: Covid-19 has severely impacted every aspect of human life, especially parents' well-being. Parents psychological distress substantially increased. Problem-solving, as one of the most effective coping strategies, has been found to decrease psychological distress among parents. However, the specific mechanism between the coping strategy of problem solving and psychological distress remains under-investigated.
Aims: This study examined whether (1) problem-solving is associated with psychological distress among parents during Covid-19 and (2) preparedness for caregiving mediates the association between problem-solving and psychological distress.
Methods: A national cross-sectional study was conducted in June 2022. The study sample included 436 participants with at least one child under 18 years old during Covid-19. A mediation analysis was conducted.
Results: Problem-solving confidence was statistically associated with decreased psychological distress among parents during Covid-19 in the total effect model ($b = -.14$, $p <. 01$). When preparedness for caregiving, the mediator, was included, the direct effect of problem-solving confidence was no longer significant, but the indirect effect via preparedness for caregiving was statistically significant ($b = -. 06$, $p <$ .01). It explained the 43% effect of the association between problem-solving and psychological distress.
Conclusions: Future practice efforts may focus on enhancing parents' problem-solving and their preparedness for caregiving to address the negative influence of the

**61. BECC470, a Synthetic TLR4 Ligand Augments Immunogenicity and Protective Efficacy of Influenza Vaccine**

**Sayan Das**

Das, S., Baracco, L., Varisco, D.J., Frieman, M.B. and Ernst, R.K.

Session H; Poster Presentation; Room 349

Viral infections continue to be a leading cause of morbidity and mortality worldwide. To combat this, effective vaccines can be generated by combining antigenic targets with vaccine adjuvants to increase immunogenicity, cross-protection, antigen sparing and effectiveness in immunocompromised individuals. In this study, rHA was adjuvanted with BECC470, a rationally designed synthetic TLR4-based ligand to generate an efficacious candidate vaccine.

Mice immunized with 40 ng of rHA(H1) adjuvanted with BECC470 showed ~1.5–2 log increase in anti-HA IgG1 and IgG2a titers, compared to groups adjuvanted with PHAD or MPL. In agreement with the antibody titers, groups of mice immunized with rHA adjuvanted with BECC470 lost less weight upon intranasal influenza virus challenge, when compared to control or unadjuvanted groups. Lung viral titers, evaluated day 7 post-infection, showed that all BECC470 immunized mice had cleared the virus with minimal airway bronchiolar and periarterial inflammation. To evaluate cellular responses, cytokine response was evaluated from cells isolated from lungs and spleen of mice immunized with BECC470 along with PHAD and MPL as controls. Cells isolated from groups immunized with BECC470s secreted higher level of IFN-gamma, IL-12p70 and IL-17a when compared to unadjuvanted/control groups.

Additionally, 1/120th dose of a quadrivalent Flu vaccine (Flucelvax) adjuvanted with BECC was able to generate immunoglobulin response comparable to full dose of the vaccine in immunized mice.

In summary, BECC470s not only enhances immune response but also enables antigen sparing making it an excellent candidate for a turnkey vaccine adjuvant not only for influenza but also potentially for other diseases.

**62. Racial Disparities in Social Activity Participation between Black and White Americans**

**Jocelyn Brown**

Brown, J.L.

Session H; Poster Presentation;  Room 349

Arthritis is a leading cause of disability in the United States with over 54 million Americans suffering from the disease. According to cumulative disadvantage theory, Black Americans face systemic racism that exposes them to disadvantageous health pathways and barriers throughout their lives, leading to a higher risk of developing arthritis and greater disability compared to their white counterparts. While research has shown that Black Americans with arthritis are more physically inactive than white Americans, little is known about the impact of arthritis on their social activities. Activity theorists posit that social activity participation is crucial for physical and mental well-being as people age. To examine this issue, the present study investigated how arthritis affects social activity participation among Black and white Americans. Using data from the Behavioral Risk Surveillance System, the study analyzed responses from 4,111 participants (including 9% Black Americans) and conducted a binary logistic regression controlling for covariates such as education, sex, marital status, and self-rated health. The analysis found that Black Americans with arthritis were 1.65 times the odds than white Americans with arthritis to report that their arthritis impacted their social activity participation (OR = 1.65, SE = 0.23, $p < 0.05$). These findings suggest that arthritis is a significant barrier to social activities, further affecting the quality of life of this population. Further research should identify the mechanisms underlying this relationship and develop interventions to address activity constraints among Black Americans living with arthritis.

**63. Examining Relationships Between Nursing Home Facility Factors, Pain, and Race**

**Sorah Levy**

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

Session E; Poster Presentation;  Room 349

Pain is pervasive among nursing home (NH) residents with dementia and racial disparities exist in pain management approaches and outcomes across facilities. The purpose of this study was to examine the interaction between nursing home facility factors (NHFF) and race in relation to pain among NH residents with dementia.

This secondary analysis used baseline data from the EIT-4-BPSD study. Measures included demographic and health information collected from medical charts, NHFF (e.g., size, staffing levels, star rating, profit status), and pain scores based on the Pain Assessment in Advanced Dementia (PAINAD) Scale. Linear mixed models analyzed the association between NHFF, residents' pain, and interactions by race, controlling for age, gender, function, and comorbidities.
The sample included 553 residents from 55 NH. The majority of NHs were for-profit (n=34, 60.7%). The mean age of residents was 83 (SD=10.4), the majority were female (n = 398, 72%), White (n = 419, 76%), and had minimal pain (M = .7, SD = 1.5). After adjusting for residents' demographic and health characteristics, there were no significant associations between NHFF and pain and no significant interactions by race ($p > 0.05$).
Findings suggest NHFF were not associated with pain and no racial differences in these associations emerged. This study was limited in that the sample was relatively homogenous, from a single region of the country, and participants had minimal pain. Further research in more diverse samples across geographic regions may augment identification of racial differences in the associations between NHFF and pain among NH residents with dementia.

**64. Small Molecules to Enhance iPSC-derived Cardiomyocyte Proliferation for Heart Repair**

**Daniela Fuller**

Fuller, D.T., Ali, S., Abedin, T.T., Neitzel, L.R., Hudson, J., Williams, C.H., Hong, C.C.

Session H; Poster Presentation;  Room 349

Heart failure, which is one of the leading causes of death worldwide, is characterized by the irreversible loss of cardiomyocytes. Over the past few decades, there has been significant interest in exploring strategies to revive the inherent regenerative potential of the heart for repairing the damaged heart tissue. Alternatively, others have been developing engineered heart tissue constructs using patient-derived induced pluripotent stem cells (iPSCs) to be transplanted into failing hearts as autologous cardiac patches to augment cardiac function. However, iPSC derived cardiomyocytes proliferate slowly and their low proliferation rate represents an important bottle neck for generating these tissue constructs. Moreover, while various approaches to promote cardiac regeneration in vivo involving direct reprogramming to induced cardiomyocytes (iCMs) or induction of cardiomyocyte proliferation have been proposed, they are limited by strikingly low efficiency or pro-tumorigenic potential. The Hong lab has conducted an unbiased phenotypic screening and identified a group of structurally related small molecules that enhance proliferation in human induced pluripotent stem cell-derived cardiomyocytes (iPSC-CMs). These small molecules, which are not toxic, are unique among pro-proliferative compounds in that they do not disrupt cardiac function in engineered heart tissue constructs and do not induce unwanted proliferation in non-cardiomyocyte cells. Mechanistically, they potentiate Wnt signaling, a pathway known to be involved in regeneration. This study identifies novel therapeutic targets for heart failure as well as potential lead compounds for future regenerative therapies.

**65. Stressors of Long-Term Care Facility Nursing Assistants During the COVID-19 Pandemic Utilizing Ecological Momentary Assessment, Wearable Sensors, and End-of-Day Reconstruction**

**Susanna Witmer**

Witmer, S., Doran, K., Chen, K., Yoon, L., Ebangwese, A., Shifali, S., Fischer, E.R., and Charan, D.

Session H; Poster Presentation;  Room 349

Stress within LTC facilities results in high staff turnover, staffing crisis, and adverse events among the residents. Identifying and understanding stress among LTC workers and finding solutions is imperative to reduce the consequences of stress. A single LTC facility quantitative/qualitative mixed pilot study was conducted to identify stressors among LTC workers. Eight nursing assistants with smart phone accessibility were included. Those with acute heart disease or taking heart rhythm medications at the time of study were excluded to minimize

interference with the wearable sensor/watch data. Participants wore a sensor watch for two 8-hour working shifts, which collected biophysical changes related to stress responses. Participants completed two Ecological Momentary Assessment (EMA) surveys on each shift and rated the intensity of stressor(s) they experienced. After shifts were completed, participants met with a research team member to reconstruct their workday to contextualize the EMA and wearable sensor/watch data. In total, 83 stressful events (average 5.19 events per shift) were identified. Wearable sensor/watch data identified 53 events in total; of those, 26 events (49%) were substantiated by EMA and then verified by the end-of-day interviews. Nursing assistants reported mild to low moderate stress levels, which stemmed from sources from work demands and pressure, heavy workloads and staffing, safety issues or COVID-19 concerns, disrespect from residents and families. As one of the first studies utilizing EMA and objective measures of stress while on-the-job in LTC workers, these findings provide insights to develop on-the-job stress reduction and wellness programs for LTC workers.

**66. A Scoping Review of Telehealth Palliative Care in Nursing Homes: Characteristics and Outcomes**

**Amy Jackson**

Walton, L., Courtright, K., Demiris, G., Gorman, E., Jackson, A., Carpenter, J.

Session H; Poster Presentation; Room 349

Background: A significant portion of seriously ill older adults spend their last days in nursing homes (NHs) but may not have access to palliative care. However, telehealth palliative care may improve specialist access and end-of-life experiences among older adults in NHs.
Objective: To synthesize telehealth palliative care evidence in NHs, service characteristics, and outcomes to provide recommendations for practice, research, and policy.
Design: We searched Medline (Ovid), Embase (Elsevier), Cochrane Library (WileyOnline), Scopus (Elsevier), CINHAL (EBSCOhost), Trip PRO, and Dissertations & Theses Global (ProQuest) on 10 June 2021, with an update on 06 January 2022. We included observational and qualitative studies, clinical trials, quality improvement projects, and case and clinical reports that self-identified as telehealth palliative care for NH residents.
Results: The review yielded eleven eligible reports in the United States and internationally from 2008 to 2020. Reports described live video as the preferred telehealth delivery modality with goals of care and physical aspects of care being most addressed. Findings in the reports focused on five patient/family-centered outcomes: symptom management, quality of life, advance care planning, healthcare use, and evaluation of care. Advantages to telehealth palliative care include increased completion of goals of care and decrease in healthcare use. Disadvantages included technological difficulties and increased NH financial burden.
Conclusions: Future studies should focus on inclusive telehealth palliative care access, feasibility, cost, care experience, and outcomes relevant to underrepresented and diverse populations and settings. More research may support policy changes to bolster payment models and practice recommendations supporting telehealth palliative care.

**67. COVID-19 Family Stress and Positive Psychological Change: Moderating Effect of Sense of Community**

**Haelim Lee**

Lee, H.

Session H; Poster Presentation; Room 349

Background: COVID-19 pandemic posed unprecedented stress in every aspect of parents' lives. Still, the relationship between COVID-19 family stress and parents' positive psychological change as a form of personal growth has not been fully explored. Understanding the community context to which the family belongs is essential as it helps explain how families respond to this shared trauma.
Methods: Data was collected from 436 adult parents in the U.S. who have at least one child under 18 via Qualtrics online survey panels in 2022. Multivariate regression

analyses were conducted to examine the moderating effect of a sense of community on the relationship between COVID-19 family stress and positive psychological change. Relevant covariates included race, ethnicity, gender, employment, age, and income.
Results: Results showed that COVID-19 family stress was not significantly associated with positive psychological change among parents (b=-.10, p= .079). A brief sense of community did not moderate the association between COVID-19 family stress and positive psychological change (b=.07, p= .139). On the other hand, a brief sense of community was positively associated with positive psychological change (b=.17, p= .000). Compared to White parents, Black/African American (b=.16, p= .017) and Asian, American Indian, or Alaskan Native parents had significantly higher levels of positive psychological change (b=.22, p= .034).
Implications: Social work practitioners and policymakers could employ these results in offering community resources that can strengthen community connectedness. Implementation of long-term community-level initiatives promoting mental health and positive personal growth of parents in the COVID-19 context is needed.

**68. Identifying cell-type-specific transcriptomic effects of anti-sense oligonucleotide gene therapy treatment in Huntington Disease**

**Erin Wildermuth**

Wildermuth, E, Cortés-Gutiérrez. M, Bragg, R, Cantle, J, Malaiya, S, Carroll, JB, Ament, SA

Session I; Poster Presentation;  Room 349

As a monogenic disorder, Huntington's disease (HD) is at the forefront for gene-therapy innovation in neurodegeneration. In particular, several approaches are being evaluated to reduce the levels of toxic huntingtin (HTT) protein in the brain. One challenge to clinical innovation is our ability to discern detailed information about how HD and its potential therapeutics impact the brain. Single-nucleus RNA sequencing is a cutting-edge technology capable of providing this level of detail. Here, we studied cell type-specific transcriptomic effects of HD mutations in the striatum of a knock-in mouse model, HttQ111/+. Further, we examined the cellular impacts of a non-allele specific Htt-lowering antisense oligonucleotide (ASO). We characterized substantial transcriptional effects of the HD mutation in spiny projection neurons, the cell type most vulnerable to HD neurodegeneration. Surprisingly, Htt-lowering ASO treatment exacerbated many of these transcriptional changes. Understanding these cell type-specific effects of ASO treatment could aid in the interpretation of Htt-lowering toxicity that has recently been observed in human patients.

**69. Host peptidoglycan recognition proteins and NOD receptors modulate the immune response to Bordetella pertussis**

**David Rickert**

Rickert, D. M., Himmelberger, R. E., Carbonetti N. H., Skerry, C. M.

Session I; Poster Presentation;  Room 349

Pertussis disease is associated with severe pulmonary inflammation and there is an urgent need to understand the mechanisms of pathogenesis to aid development of host-directed therapeutics. Bordetella pertussis produces a myriad of toxins to facilitate its pathogenesis, including tracheal cytotoxin (TCT), a monomeric fragment of peptidoglycan (PGN). We have identified the PGN recognition proteins (PGLYRP) and the host immune receptors, NOD1/2 as key players in the host response to infection. We hypothesized that TCT mediates pulmonary inflammatory pathology in mice and that therapeutic targeting of TCT may prevent this. To determine the contribution of TCT to host inflammatory responses, we infected mice with a mutant strain of B. pertussis which secretes excess TCT (TCT+). Mice challenged with TCT+ strain had increased pulmonary pathology supporting the idea that TCT drives pertussis pathogenesis. Further, we theorized TCT could be modulating inflammation via intracellular PGN sensors, NOD1 and NOD2, so we used cell reporter systems to determine if TCT stimulates responses via the NOD receptors. We characterized the interaction of TCT with human and mouse NOD1 and

NOD2 and found TCT to be a potent stimulus mNOD1, implicating the receptor TCT-mediated pathogenesis. Previous work demonstrated PGLYRPs mediate host inflammatory responses to B. pertussis. To determine if PGLYRPs can modulate TCT-sensing by NOD receptors we used a HEK293-NOD reporter assay. PGLYRP1 and PGLYRP4 were found to increase NOD1 responses to TCT and decrease responses to NOD2. Together, these data reveal a novel mechanism through which inflammatory responses to B. pertussis TCT are determined.

**70. Brain-Power & Placebo: Structural Brain Differences among High and Low Placebo Responders with Temporomandibular Disorders**

**Jewel White**

White, J.N., Wang, Y., Massalee, R., Colloca, L.

Session I; Poster Presentation;  Room 349

Background: Placebo effects, as a form of top-down descending pain modulation, have a definitive neurobiological basis involving distinct cortex activations. The fMRI blood-oxygenation-level-dependent (BOLD) signal changes related to placebo effects have been widely examined. However, neurobiological predictors of placebo responses among individuals with chronic pain, such as differences in brain structure, remain largely unknown. To address the gap, we assessed the placebo responses of participants diagnosed with Temporomandibular Disorders (TMD) and identified each participant as a placebo responder or non-responder. We then performed voxel-based morphometry (VBM) analysis of fMRI T1-weighted images to determine between and single-group correlations between local grey matter volume (GMV) and placebo responses in this cohort.
Methods: The classical conditioning with verbal suggestions paradigm was used to study placebo phenotypes. fMRI Software Library (FSL) VBM-analysis was used to detect GMV changes in TMD patients.
Results: Data on 72 TMD participants in Phase 2 of our study identified 32 TMDs as responders, and 40 as non-responders. Behaviorally, responders exhibited significantly greater differences in visual analogue scale (VAS) pain ratings than non-responders ($F_{1,69}=60.41$, $p<0.001$) controlling for age, sex and race. Between-group correlation analysis did not reveal a correlation between GMV and HPR/LPR status. Rather, single-group correlation analysis revealed a significantly positive correlation between placebo responses and GMV in all TMD patients ($p<0.05$, FWE-corrected) in the lingual gyrus, parahippocampal gyrus, temporal occipital fusiform cortex, supramarginal gyrus, and superior parietal lobule. The results from this study suggest a role for changes in brain structure in the placebo responses of TMD patients.

**71. Targeting Amino Acid Metabolism in Acute Myeloid Leukemia**

**Kanwal Mahmood Hameed**

Mahmood Hameed, K., Bollino, D. R. and Emadi, A.

Session I; Poster Presentation;  Room 349

Acute Myeloid Leukemia (AML) is a highly aggressive form of blood cancer characterized by the disruption of normal blood cell production/function. Due to the dependence of glutamine observed in AML, glutamine metabolism has been explored as a potential target for treatment. Our group has previously confirmed the sensitivity of AML to glutamine depletion using Rylaze, an FDA-approved Erwinia asparaginase (also called crisantaspase), to deplete exogenous glutamine. However, following crisantaspase-induced glutamine depletion we identified an increase in plasma levels of serine in vivo and upregulation of the serine biosynthesis enzyme, phosphoglycerate dehydrogenase (PHGDH), in vitro. We hypothesized that the increase in serine could be a resistance mechanism and that targeting both glutamine and serine would lead to an increased anti-AML effect.  Indeed, CRISPR-cas9 knockout of PHGDH in AML cell lines resulted in a ~250-fold decrease in the IC50 value of Rylaze compared to parental AML cell lines.
Moreover, we found synergistic anti-proliferative effects when BI-4916, a PHGDH-inhibitor, was used in combination with Rylaze in AML cell lines and primary AML cells. This combinatory treatment also led to increased cell death, decreased production of glutathione, a major

antioxidant in the cell, and inhibition of protein synthesis as determined by the eIF4E/4E-BP1 mRNA translation-initiation factor proteins. Ongoing work is focused on the transcriptomic analysis of this combinatory treatment in AML cell lines. A better understanding of the relationship between serine and glutamine metabolism may guide future therapeutics aiming to identify and target resistance mechanisms in AML.

**72. Altering stem cell factor and c-kit signaling impacts the proliferation of hippocampal mast cells in early postnatal development**

**Anna Maximova**

Maximova, A. A., Blanchard, A. C., McCarthy M. M.

Session I; Poster Presentation; Room 349

While inflammation in the neonatal brain has been linked to the progression of neuropsychiatric diseases, less well understood is the role immune cells normally play in neurodevelopment. Mast cells (MCs) are an innate immune cell that can release substances such as histamine, cytokines, and growth factors during host defense, allergy, or inflammation. Our lab established that MC activation in the preoptic area (POA) during a critical period can alter synaptic patterning and adult behavior in a rat model. A robust MC population lines the ventricles next to the developing hippocampus, which peaks in cell number at postnatal day 7, declines during week 2, and is absent into adulthood. This population is also highly proliferative, a key difference from POA MCs. This project investigates this difference in proliferative capacity by studying c-kit, a receptor tyrosine kinase, and its ligand, stem cell factor (SCF), both of which regulate peripheral MC proliferation. We characterized the expression of both SCF and c-kit across the first few weeks of life via RT-qPCR, showing a peak in SCF expression in the hippocampus at PN4 before the MC peak at PN7. Inhibiting SCF or c-kit interactions via blocking antibodies both in vitro and in vivo caused a significant reduction in hippocampal MC proliferation but not in total MC numbers. Addition of exogenous SCF results in increased hippocampal MC proliferation, but not total MC numbers as well. Further studies will use SCF/c-kit signaling as a tool to manipulate hippocampal MCs and study their impact on early neurodevelopment.

**73. Epidemiological Characteristics of Firearm Homicide Fatalities in Maryland: A retrospective forensic autopsy study 2016-2021**

**Sarah Pettit**

Pettit S.M., Bass B., Eiker G., Sloulin L., Pauli E., Li L.

Session I; Poster Presentation; Room 349

According to the American Medical Association and the American Public Health Association, firearm violence in the United States is classified as a significant public health threat. This study aims to assess firearm homicide fatalities in Maryland from 2016 through 2021. The Office of the Chief Medical Examiner (OCME) is responsible for medicolegal investigation of all the violent deaths in the State of Maryland. This study was conducted by reviewing homicide records at the OCME. The goal of this study is to describe epidemiological characteristics of firearm homicide fatalities in Maryland.
During the six-year period, there were 3605 homicides in Maryland with an average of 586 homicide deaths per year. The yearly homicide cases increased 15.4% in Maryland from 2016 to 2021. Of the 3605 homicides, 2905 (80.6%) were due to firearms. Firearm-related homicides disproportionately affect people of color, especially African Americans. More than 86% of homicide victims were African Americans when compared with Whites (8.5%) and other races (4.8%). The male-to-female ratio was 8:1 among firearm homicides. Most homicide victims were 20-29 years of age (41.9%). More than 58% of fatal homicides occurred in Baltimore City. Postmortem toxicology analysis indicated that 44.1% of firearm homicide victims tested positive for non-controlled substances (e.g., diphenhydramine and lidocaine) and alcohol, followed by 34.4% who tested positive for schedule II controlled substances (e.g., cocaine and fentanyl). Firearm homicide is a serious public safety and public health issue. More research is needed to address the risks of firearm injuries and firearm injury prevention programs.

**74. Biodegradable Nanogels for Controlled Release of Artemisinin-derived Drug to Treat Leukemia**

**Noha Ghonim**

Ghonim, N.A., Tabassum, S., Mott, B.T., Lapidus, R.G., Rudek, M.A., Civin, C.I., and Lowe, T.L.

Session I; Poster Presentation; Room 349

Leukemias are devastating blood cancers that affect all ages, with 470,000 newly diagnosed cases and about 300,000 deaths annually in the world. A two-carbon linked dimeric artemisinin analog (herein called ART631) is a potent anti-leukemic drug at nanomolar concentrations, but it has limiting water-solubility. Additionally, clinical artemisinin analogs characteristically have short in vivo half-lives that require frequent dosing to maintain pharmacologically active plasma concentrations. The purpose of this project is to develop an ART631 loaded biodegradable nanogel system (NanoART631) (US Provisional No. 63/334,896) that can enhance the water solubility and sustain the release of ART631, as a potential antileukemic. NanoART631 increased ART631's water solubility > 400-folds. The z-average diameter NanoART631 was 100-200 nm in PBS at 37°C, with a polydispersity index < 0.3 and a -11 - -15 mV zeta potential. In MTT assays, NanoART631 formulation had IC50 ~50 nM after one day incubation with MOLM 14 cells and killed 88% and 98% of the AML cells at 4 nM after 2 and 3 days of incubation, respectively. In contrast, NanoART631 was not toxic to ARPE-19 cells or DPSCs at a nanoparticle concentration of 1 mg/mL, which contained ~79 µM ART631. The single-dose IV maximal tolerated dose (MTD) of NanoART631 in NRG mice (n=3) was 500 mg/kg (containing ~25 mg/kg ART631). Empty nanoparticles had no clinical toxicity to mice at the same and higher IV doses. In conclusion, the innovative NanoART631 has potential as an effective antileukemic therapy that addresses the limited solubility and in vivo half-life of artemisinin analogs.

**75. Overexpression of the Obscurin Pleckstrin Homology Domain in Triple Negative and HER2 Positive Breast Cancer Cells Reduces Invasion and Chemoresistance to Doxorubicin**

**Matthew Eason**

Matthew Eason, Se Jong Lee, Poornima Dubey, PhD, Anthony Kim, PhD, Konstantinos Konstantopoulos, PhD, and Aikaterini Kontrogianni-Konstantopoulos, PhD

Session I; Poster Presentation; Room 349

New therapies targeting metastatic spread and treatment resistance are greatly needed to improve breast cancer patient survival. Recently, obscurin, an ~800kDa scaffolding protein localized to the cell membrane, has risen to the spotlight as an overlooked metastasis suppressor commonly lost in breast cancer. Specifically, breath epithelial cells lacking obscurins undergo epithelial-mesenchymal transition (EMT), and demonstrate increased migration, invasion, and chemoresistance. Biochemical studies in our lab have linked breast epithelial obscurin loss to an increased activation of the pro-metastatic PI3K/Akt2 signaling pathway. Mechanistically, the obscurin pleckstrin homology (PH)-domain binds the SH3-domain of the p85 regulatory subunit of PI3K. Thus far, due to obscurin's massive size, gain of function/rescue experiments of obscurin have not been feasible. To combat this challenge, we have generated a mini-obscurin peptide construct composed of an obscurin core functional unit: a myristilated obscurin PH-domain fused to a Myc-Tag. We hypothesized that restoration of the obscurin PH-domain in obscurin-low breast cancer cells will reduce PI3K/Ak2 pathway activity to block metastasis and reduce chemoresistance. We report that overexpression of a myristilated obscurin PH-domain in MDA-MB-231 (triple negative breast cancer) and SKBr3 (HER2 positive breast cancer) cells reduces PI3K/Akt2 pathway activity. Furthermore, the mini-obscurin-PH peptide reduces cellular filopodia formation, 3D collagen-1 matrix spheroid invasion, and synergistically increases cancer cell apoptosis in response to the anthracycline chemotherapy doxorubicin, at non-cardiotoxic doses. Together, these data support the marked clinical impact that exogenous delivery of the obscurin PH-domain in patient breast cancer cells may have on disease progression and chemotherapy response.

**76. Pseudomonas aeruginosa Lipid A 2-hydroxylation Impacts Host Recognition and Response in CF Macrophages**

**Casey Hofstaedter**

Hofstaedter, C.E., Met, C.M., Chandler, C.E., Gillespie, J.J., Rasko, D.A., Harro, J.M., Kopp, B.T., Ernst, R.K.

Session I; Poster Presentation; Room 349

Pseudomonas aeruginosa (Pa) is a Gram-negative bacterium capable of causing chronic, severe lung infections in cystic fibrosis (CF) patients. Pa undergoes functional and structural alterations while adapting to the CF airway. One change involves structural modification of lipid A, the membrane-bound component of LPS and TLR4/MD-2 complex ligand. These modifications influence signaling through TLR4, impacting the host immune response, and ultimately treatment and clinical outcomes. Our group has recently identified two dioxygenases, LpxO1 and LpxO2, that perform site-specific 2-hydroxylation of Pa lipid A secondary acyl chains. To investigate the relevance of these enzymes in CF clinical isolates, we performed whole-genome sequencing on longitudinal isolates from 15 patients. We identified 3 strains with independent lpxO2 mutations and 2 strains with lpxO1 mutations resulting in premature stop codons and non-functional proteins. MALDI-TOF mass spectrometry revealed loss of 2-hydroxylation on lipid A, further confirming loss-of-function mutations. Next, LPS stimulation assays were performed using NF-kB reporter cell lines. We found decreased TLR4 recognition when lpxO2-dependent hydroxylation was absent from lipid A. Further, we performed LPS stimulations on primary monocyte-derived macrophages (MDMs) from healthy and CF subjects. Following LPS stimulation, CF MDMs demonstrate decreased absolute cytokine production compared to healthy MDMs. Interestingly, in healthy MDMs, both lpxO1 and lpxO2 mutants showed decreased cytokine production compared to wild-type; however, CF MDMs revealed decreased cytokine production for only lpxO2-deficient LPS. This suggests CF macrophages recognize lipid A structural variation differently and may help us understand why lipid A structure is altered during chronic lung infection in CF.

**77. Chronic Ethanol Exposure Degrades Perineuronal Nets and Induces GABA Synapse Elimination in the Dorsal Striatum**

**Alli Siclair**

Patton, M.S., McKeon, P.N., VanRyzin, J.W., Patton, M.H., Heckman, M., Mathur, B.N.

Session I; Poster Presentation; Room 349

Persistent drinking in the face of a negative consequence, or compulsive drinking, is a prominent feature of alcohol use disorder. Parvalbumin-expressing striatal fast-spiking interneurons, comprising ~1% of the total striatal neuronal population, are necessary for the expression of compulsive-like drinking in mice. However, how chronic ethanol exposure modulates the physiology of dorsal striatum fast-spiking interneurons is unknown. Here, we found that chronic ethanol exposure reduces GABAergic, but not glutamatergic, transmission onto dorsolateral striatum fast-spiking interneurons. These results correspond with a significant loss of GABAergic synapses predominantly on the soma and proximal processes of fast-spiking interneurons where extracellular matrix perineuronal nets are enriched. We found that chronic ethanol exposure degrades perineuronal nets in the dorsal striatum, and that enzymatically degrading perineuronal nets similarly reduces GABAergic transmission onto dorsolateral striatum fast-spiking interneurons. Collectively these data suggest that chronic ethanol exposure degrades perineuronal nets to downregulate GABAergic synaptic transmission onto fast-spiking interneurons. This study provides new insight into the pathophysiology of chronic ethanol exposure on a habit center in the brain.

**78. Mechanism of the Heat-Induced Polymorphic Self-Assembly of Chitin**

**Aarion Romany**

Romany A., Payne G. F., Shen J.

Session J; Poster Presentation;  Room 349

Chitin is the second most abundant polysaccharide on earth. Owing to Its high tensile strength and biodegradability, its derivatives have been found in diverse application such as tissue engineering, drug carriers and wound dressing. However, to make functional material from chitin a primary challenge is to find effective and environmentally friendly ways to dissolve it in solution. Hence, a detailed understanding of chitin's crystalline structure and mechanism of sol-gel transition is important. Over the years, chitin's crystalline structure has been elucidated via X-ray diffraction and electron microscopy, but its self-assembly remains elusive. Additionally, chitin's gelation behavior was shown to exhibit temperature dependence. Suggesting self-assembly is accelerated at high temperatures. Contradicting the common belief that hydrogen bonding, which is thought to be the driving force for chitin chain association, weakens with increasing temperature. Intrigued by this contradiction, we perform microsecond timescale all-atom molecular dynamics simulations to elucidate the heat-induced self-assembly of chitin. In agreement with experiment, we find that high temperatures enhances self-assembly.  Additionally chitin self-assembly proceeds through two distinct mechanisms.

**79. Nanoparticle Biomolecular Corona as a Platform to Predict Endotoxemia Disease Severity**

**Jacob Shaw**

Shaw J.R., Caprio N., Weldemariam M., Tran A., Jones J., Kane M., Pearson R.M.

Session J; Poster Presentation;  Room 349

Despite significant advancements in mass spectrometry techniques, the discovery of disease-specific biomarkers in blood remains extremely difficult, often due to their low plasma abundance. Intravenously administered nanoparticles (NPs) rapidly adsorb and concentrate blood components to form a biomolecule coating termed the nanoparticle "biomolecular corona" (NP-BC). Researchers have demonstrated NP-BCs' ability to concentrate low abundance plasma proteins through electrostatic interactions. Additionally, the NP-BC fingerprint has been discovered to be unique based on the individuals' disease state and blood protein composition. Given this, the NP-BC is a promising platform that allows for the concentration and analysis of low abundant biomarkers for disease diagnostics.
Herein, we describe the use of poly(lactic-co-glycolic acid) (PLGA) NPs as a platform to concentrate and identify disease-specific plasma biomolecules with low plasma abundance. We evaluate this phenomenon in an endotoxemia mouse model of sepsis due to its highly dynamic plasma composition. Our results revealed the existence of disease severity-specific NP-BC signatures. Comprehensive lipidomics and proteomics analysis of these biomolecules resulted in the discovery of over 300 biomolecules that were specifically enriched in the NP-BC but were undetectable in whole plasma variants. Of these concentrated biomolecules, we used multi-omics integration to identified a panel of pro-inflammatory mediators that were used to predict host disease severity. Our data identifies multiple biomolecular signals associated with disease progression and highlights the robust ability of NPs to concentrate low abundance biomolecules, circumventing the common issue of low abundance impeding diagnostic workflows.

**80. Chronic administration of aromatase inhibitor, letrozole, reduced fear acquisition in male mice**

**Abagail Postle**

Postle, A. F., Gould, T. D.

Session J; Poster Presentation;  Room 349

Introduction: Post-traumatic stress disorder (PSTD) is a debilitating disease with a lifetime prevalence of 6.8% and available treatments are not sufficient for most individuals. Fear acquisition (FA) and extinction (FE) are pre-clinical models of fear learning and exposure therapy, respectively. Exposure to stress increases fear acquisition and time to extinction, which implicates stress-dependent mechanisms in these behaviors.  In females, the gonadal hormone,

estradiol (E2), mediates stress-induced delays in FE in both humans and rodents. However, while testosterone is aromatized to E2 in the male brain the role of E2 on FA and FE in males is less well understood.
Methods: C57B/6J male mice underwent either orchiectomy or chronic letrozole treatment to study the role of E2 on acquisition and extinction of fear memories. Half of the animals underwent subthreshold social defeat stress (SSDS) prior to fear acquisition to determine if E2 modulates stress-induced dysregulation of FA and FE. Using E2 receptor-beta (ERB) KO animals we determined if lack of ERB throughout life changes FA or FE.
Results: We found no effect of orchiectomy on fear acquisition or extinction. Letrozole treatment decreased fear acquisition but had no effect on FE. Male ERB KO animals showed no differences from WT controls in FA or FE. There was no effect of SSDS.
Conclusion: Chronic aromatase inhibition in the male mouse decreases fear acquisition in a stress and ERB independent manner. Overall, these studies suggest a novel pathway for decreasing fear acquisition in males: aromatase inhibition.

**81. Investigating the Requirement of ERK2 Cysteine 252 in Mediating the Effects of a Function-Selective ERK1/2 Inhibitor in A375 Melanoma Cells**

**Nathaniel McClean**

McClean, N. J., Grogan, L.

Session J; Poster Presentation;  Room 349

Many proliferative diseases—including cancers—result from a dysregulation in the extracellular signal-regulated kinase 1/2 (ERK1/2) pathway. The ERK1/2 pathway regulates both the normal and disease states of cells and is a major player in disease when constitutively active. Most inhibitors of ERK1/2 target the ATP-binding site which shuts off all downstream signaling events, often leading to off-target toxicity and eventual drug resistance. Our lab is developing function-selective kinase inhibitors which target substrate binding regions distinct from the ATP-binding site. We identified a novel function-selective inhibitor, SF-3-030, that binds cysteine residue 252 (C252) of ERK1/2, distinct to the ATP-binding site, near a region (F-site recruitment site) that mediates interactions with oncogenic immediate early gene transcription factors, such as c-Fos. SF-3-030 inhibits proliferation and expression of c-Fos and c-Myc—potential targets for melanoma treatment—in PDGF stimulated cells containing constitutively active ERK1/2. My study aims to understand the importance of C252 for the biological effects observed via SF-3-030 treatment of melanoma cells. Preliminary studies involving immunoassay and cell viability assays using A375 with ERK2 deletion of C252 suggest differential viability and protein expression with SF-3-030 treatment compared to wild-type. In addition, preliminary studies on ERK2 protein containing mutations at C252 suggest changes in protein secondary structure. Elucidating the importance of C252 may contribute to the development of SF-3-030 as a function-selective ERK1/2 inhibitor as a novel cancer therapeutic.

**82. Serotonin Control of the Claustrum**

**Maxwell Madden**

Madden, M. B., Mathur, B. N.

Session J; Poster Presentation;  Room 349

Cognitive flexibility deficits are a major contributor to diminished life and therapeutic outcomes across myriad neuropsychiatric disorders including Alzheimer's, depression, and schizophrenia. The classical psychedelic, psilocybin, induces long-lasting improvement of cognitive flexibility, but the mechanism of this action is unknown. The claustrum, a subcortical nucleus, connects frontal cortical and parietal cortical network nodes and is required for optimal task performance in tasks requiring cognitive flexibility. Both the claustrum and cortical networks are disrupted by acute psilocybin; psilocybin challenge both depresses claustrum activity and disrupts functional connectivity between the claustrum and cortical networks. Thus, we hypothesize that acute psilocybin and serotonin suppresses frontally directed control of cortical networks through claustrum. To test this, we employ whole-patch clamp electrophysiology and pharmacology in mouse claustrum slices to assess the serotonin receptors

subtypes involved in psilocybin action on claustrum function. These data provide avenues toward understanding the subjective and therapeutic effects of psychedelic drug treatment.

**83. Nitric Oxide's Role in Mechanically-Stimulated Sclerostin Degradation**

**Heather Buck**

Buck, H.V., Torre, O.M., Gould, N.R., Ward, C.W., Stains, J.P.

Session J; Poster Presentation; Room 349

A threshold of fluid-shear stress (FSS) to osteocytes elicits NOX2-derived reactive oxygen species that induce TRPV4 to initiate calcium influx, which activates calmodulin-dependent kinase II (CaMKII) to regulate the lysosomal degradation of sclerostin. Here, we extend our discoveries identifying nitric oxide (NO) as a regulator of lysosome activity and sclerostin degradation downstream of mechano-activated Ca2+ influx.
Pharmacological inhibition of nitric oxide synthase (NOS) activity in Ocy454 osteocyte-like cells prevents FSS-induced sclerostin degradation. Conversely, a 5-minute treatment of Ocy454 cells with a NO donor is sufficient to induce the rapid lysosomal degradation of sclerostin, independent of CaMKII phosphorylation. Together these data show that NO is necessary and sufficient for sclerostin protein control. To interrogate the hierarchy of NO production within the mechano-transduction cascade that controls sclerostin protein abundance, we subjected Ocy454 cells to FSS in the presence of NOX2 or TRPV4 antagonists. Blocking NOX2 and TRPV4 prevents FSS-induced NO production, supporting that NO production is downstream of these signal transducers. Consistent with this hierarchy, NO was insufficient to induce Ca2+ influx in Ocy454s.
To understand the source of NO, qPCR revealed that NOS3 is the predominant NOS gene expressed in Ocy454s. Preliminary data shows that siRNA knockdown of NOS2 and NOS3 abrogates FSS-induced sclerostin degradation and that NOS2/3 knockdown may play a role in CaMKII regulation. In conclusion, it seems that NOS3- and NOS2-dependent NO plays an important role in the post-translational degradation of sclerostin protein, suggesting a link between mechano-activated NO production and physiological responses initiating de novo bone formation.

**84. Differential Claustrum Responses to Experimental Pain in Chronic Pain Patients and Healthy Controls**

**Brent Stewart**

Stewart, B. W., Han S. W., Keaser M., Lee H., Chen S., Mathur B., Seminowicz D.

Session J; Poster Presentation; Room 349

The claustrum is hypothesized to support initiation of cortical networks for cognitive control. Claustrum activity increases at the onset of a difficult cognitive task known to induce activity within Fronto-Parietal Network (FPN) regions. Experimental pain similarly increases activity within FPN regions, and chronic pain patients exhibit altered cognitive control network dynamics compared to healthy controls. Predicting that claustrum activity increases at the onset of a painful stimulus, and that claustrum activity differs between chronic pain patients and healthy controls, claustrum activity was recorded via Blood Oxygenation Level Dependent (BOLD) fMRI during blocks of painful thermal stimulation and non-noxious warmth in samples of healthy controls (n = 34) and migraine patients (n = 105). Claustrum activation was detected at the onset of noxious thermal stimulation but not non-noxious warmth. Migraine patients exhibited significantly greater right claustrum activation at the onset of pain than controls. Altered claustrum function may underlie altered cognitive control network recruitment in chronic pain patients.

**85. Formulation and Characterization of Bioactive Nano-core-shell System for Improving Dental Resins**

**Lamia Mokeem**

Lamia S. Mokeem, Abdulrahman A. Balhaddad, Isadora Garcia, Yucheng Lan, Michael D. Weir, Mary Anne S. Melo

Session J; Poster Presentation; Room 349

Aim: Here, we synthesized and characterized a superparamagnetic, chlorhexidine releasing, silanized with antibacterial quaternary ammonium (SiQuac), iron oxide -silica mesoporous framework core-shell system, Fe3O4@m-SiO2@CHX_SiQuac, for novel bioactive framework for smart dental adhesives.
Methods:
Core-mesoporous shells were synthesized by dissociating TEOS hydrolysis and condensation reaction. The synthesized nanoparticles' structure and composition were characterized by TEM, XRD, N2 adsorption-desorption by BET, EDX, and TGA analysis. Next, CHX loading and release profiles of the Fe3O4@m-SiO2@CHX were measured using UV-Vis and HPLC in pH 5.5 and 7.4. In addition, the influence of the silane-coupling agent on the preparation and CHX releasing profile was investigated.

Results: The framework Fe3O4@m-SiO2@CHX_SiQuac was successfully synthesized for the first time. TEM showed a high mesoporous shell, mean size core of 173 ± 34 nm, and shell thickness of 15.4± 5 nm. XRD showed that the structures have a high degree of crystalline, TGA showed that the structure is approximately stable up to 186 °C, N2 Adsorption and Desorption showed porous size 16 and 13.2 nm respectively. Encapsulation efficiency measurement indicated that about 7.4 mg/mL of
Conclusion: This study introduced the significance of a multifunctional framework based on a core-shell system as a potential modifier of resin-based dentin adhesives. This system, Fe3O4@m-SiO2@CHX_SiQuac, could be potentially used in adhesive and restorative dentistry.

**86. Epidemiological Profiles of Firearm Suicide Deaths in the State of Maryland: A Retrospective Forensic Autopsy Study 2016-2021**

**Allison Bew**

Bew, A., McConnell, C., Flannery, G., Tibbs, M., Watson, J. K., Ling, L. M.D.

Session J; Poster Presentation; Room 349

The objective of our study was to document the epidemiologic characteristics of victims of suicide due to firearm injuries in the state of Maryland from 2016 to 2021 in our forensic autopsy population. This study was a retrospective review of autopsy cases of all suicide deaths caused by firearms investigated by the Office of the Chief Medical Examiner (OCME) in Maryland over a 6-year period from January 2016 to December 2021.
From 2016 to 2021, 1556 deaths were certified as firearm suicide. Firearm injury was the leading cause of suicide in Maryland, followed by hanging and drug overdose. Of the 1556 suicidal firearm caused deaths, 1398 (89.8%) were males and 155 (10.0%) were females with male/female ratio of 10 to 1. The majority of firearm suicide victims were white (N=1236, 79.4%) with African American (N=253, 16.3%), and Hispanic (1.8%) or others (2.4%). Their age ranged from 11 to 101 years with a mean age of 51 years. Our study revealed that more than 90% suicide victims resided in suburban and rural areas. Postmortem toxicology analyses showed that 486 of the 1556 suicides cases (32%) were tested positive for alcohol and 853 of the 1556 suicide cases (55%) had tested positive for varying illicit and prescription drug(s).
In the United States, firearm injury was the leading method of suicide. Addressing the problems of intentional firearm injuries in our society is worthy of public attention. Further study will be done on the risks of suicide in the State of Maryland.

**87. Incorporation of Calcium Phosphate and Calcium Fluoride Nanoparticles with Antibacterial Monomer in Novel Low-Shrinkage-Stress Composite**

**Abdullah Alhussein**

Alhussein, A.H., Alsahafi, R., Balhaddad, A.A., Hack, G.D., Oates, T.W., Sun, J., Weir, M.D., and Xu, H.K.

Session J; Poster Presentation; Room 349

Objectives: Dental composites are one of the most used dental materials for tooth cavity restorations. However,

recurrent caries is among the most common causes of dental restoration failure due to the lack of bioactivity and marginal leakage resulting from polymerization shrinkage. Our objective was to develop a novel low-shrinkage-stress resin composite with antibacterial and remineralizing properties.
Methods: The low-shrinkage-stress resin composite was formulated by mixing urethane dimethacrylate (UDMA) with triethylene glycol divinylbenzyl ether (TEG-DVBE), and then incorporating 3% dimethylaminododecyl methacrylate (DMADDM), and 20% nanoparticles of amorphous calcium phosphate (NACP), or 20% nanoparticles of calcium fluoride (nCaF2). The flexural strength and elastic modulus of the resin composite were tested, as well as its antibacterial effect against Streptococcus mutans biofilms and cytotoxicity against human gingival fibroblasts and dental pulp stem cells.
Results: The incorporation of 3%DMADDM with 20%NACP or 20%nCaF2 into a low-shrinkage-stress composite demonstrated a comparable flexural strength to the commercial control ($p>0.05$). However, the novel composite demonstrated a lower elastic modulus than the commercial control ($p<0.05$). The novel composite showed the lowest biofilm CFU, lactic acid, and biofilm biomass, compared to controls ($p<0.05$). The low-shrinkage-stress resin composite with the incorporation of DMADDM and NACP or nCaF2 exhibited comparable cell viability to the commercial group ($p>0.05$).
Conclusion: The novel dental composite with antibacterial and remineralization properties demonstrated a potent antibacterial action against Streptococcus mutans with good mechanical properties and excellent cytocompatibility. The designed formulations could be used as a strategy to prevent secondary caries around dental restorations.

**88. Effects of Cocaine on Mitochondria in Brain Reward Regions**

**Isaiah Williamson**

Williamson, I., Calarco, C., Barrett, C., Lobo, MK.

Session J; Poster Presentation;  Room 349

Stimulant drugs, such as cocaine, have been shown to alter gene expression throughout the brain, leading to changes in neuron morphology and function and, ultimately, to changes in behavior. In addition to this, the function of energy homeostasis in the brain has become an area of investigation for its role in reward and motivation, specifically following the use of drugs. Previous work shows that mitochondrial function in the nucleus accumbens (NAc) is critical for expression of cocaine-seeking behavior after IV self-administration (IVSA) in mice. NAc is a central hub for integrating reward-related behavior, and cocaine IVSA causes many transcriptional expression changes in genes related to mitochondrial function in multiple brain reward-related brain regions connected to NAc. To understand transcriptional and mitochondrial changes in input regions to NAc, we are examining gene expression changes and mitochondrial morphological changes in medial prefrontal cortex, basolateral amygdala, and ventral hippocampus in a circuit specific manner, focusing on cells in these regions that project to NAc. Preliminary data show the success of two different methods of circuit labeling – labeling both ribosomes and mitochondria. These results give insights into which mitochondrial-related genes are most changed following IVSA, thus providing the genes to focus on in future steps, aiding in understanding the pertinent molecular mediators and transcriptional regulators involved in mitochondrial morphology and, ultimately, cocaine-seeking behavior.

**89. Falls Risk Among High- and Low-Frequency Sleep Medication Users With and Without Dementia**

**Loretta Anderson**

Anderson, L.R., Wennberg, A.M.

Session K; Oral Presentation;  Ballroom A

Introduction:  Sleep disturbances and falls are common in older adults, particularly in people living with dementia (PLWD).  Increasing sleep disturbances occur with increasing age, and one third of those 65 and older experience falls at least once per year.  Sleep medication

use is associated with falls in older adults, but little is known about its impact in PLWD. This study seeks to determine if there is a differential association between high- and low- frequency sleep medication use among those with and without dementia.
Methods: Using data from the 2011 National Health and Aging Trends Study (n=8,245), we used logistic regression models to examine the association of high- versus low-frequency sleep medication use with falls in community-dwelling older adults with and without self-reported dementia.
Results: In our fully adjusted model, PLWD (n=176), high-frequency sleep medication users were more likely to fall than low-frequency sleep medication users (OR=3.86, 95% CI: 1.31, 11.37). Among those without self-reported dementia (n=6,658), high-frequency sleep medication users were more likely to fall than low-frequency sleep medication users (OR=1.40, 95% CI: 1.11, 1.77).
Conclusion: After controlling for potential confounders, PLWD who have high - frequency sleep medication use are almost 4 times more likely to experience falls than PLWD who have low-frequency sleep medication use. Reducing sleep medication use in older adults with and without dementia may help reduce the risk of falls and fall-related outcomes in older adults. Future studies to examine sleep medication alternatives may be warranted.

**90. Genetic Risk of BMI, Blood Pressure, and Smoking is More Strongly Associated with Early Than Late Onset Ischemic Stroke**

**Kevin Nguyen**

Nguyen K, Xu H, Gaynor B, Cole J.W., Malik R, Dichgans M, Kittner SJ, and Mitchell BD

Session K; Oral Presentation; Ballroom A

Objective: We employed Polygenic Risk Scores (PRS) and Mendelian Randomization to assess the association and causal effect of conventional stroke risk factors (RFs) with the onset of early onset stroke (EOS) versus late onset stroke (LOS).
Methods: We calculated PRS for risk factors (BMI, hyperlipidemia, type 2 diabetes, blood pressure, and smoking) in EOS cases (n = 6,728) and controls and LOS cases (n = 9,272) and controls followed by a comparison of the odds ratios to determine if the genetic component for RFs differs between EOS and LOS. Mendelian randomization analyses were used to infer causality of strongly correlated RFs SNPs with risk of EOS stroke.
Results: BMI PRS was more strongly associated with EOS (OR = 1.19; p = 1.16E-33) than with LOS (OR = 1.01; p = 0.299). PRS for both DBP and SBP were also more strongly associated with EOS (DBP OR = 1.30 p = 3.28E-66, SBP OR = 1.32 ; p = 2.16E-70) than for LOS (DBP OR = 1.13; p = 3.05E-20, SBP OR = 1.17; p = 1.06E-29). Smoking PRS was also more associated with EOS (OR = 1.16 p = 7.92E-24) than with LOS (OR = 1.04; p = 2.85E-03). There was little difference in the association with lipids and T2D PRS.
Conclusion: The genetic component of BMI, blood pressure, and smoking are more strongly associated in EOS compared to LOS. This suggests that control of these risk factors is particularly important in young adults in the prevention of EOS stroke.

**91. Antigen-Specific Modulation of Immune Responses Using Ovalbumin-poly(lactic-co-glycolic acid) Nanoparticles**

**Brianna Scotland**

Scotland, B. L., Cottingham, A. L., Singh, N. Pearson, R. M.

Session K; Oral Presentation; Ballroom A

Autoimmune and allergy diseases affect millions worldwide and are caused by immune dysregulation and inflammation. Current treatments for these diseases are immunosuppressive and noncurative. Therefore, there is an unmet demand for the development of innovative immunotherapies that can safely address the underlying cause. Nanoparticulate-based immunotherapies, specifically polymeric nanoparticles (NP) comprised of poly (D, L-lactic-co-glycolic acid) (PLGA) and poly(D, L- lactic acid) (PLA), have been shown to have inherent immunomodulatory properties and promising results in modulating antigen (Ag)-specific T cell responses. Current

methods for Ag association with NPs, such as encapsulation and surface conjugation, suffer several limitations, such as significant burst release, uncontrolled Ag loading, and possible immune recognition. Here, we describe the development of ovalbumin (OVA) protein-PLGA bioconjugate NPs (NP-OVA) to overcome these limitations. Through this design, we can elucidate the relationship between NP design parameters on restoring dysregulated immune responses in an Ag-specific manner. We successfully synthesized NP-OVA with three precise Ag loadings of 2, 8, and 25 μg OVA/mg. NP-OVAs displayed minimum surface Ag detection and a reduced burst release. NP-OVAs (8 and 25 μg OVA/mg) upregulated MHC-II presentation and CD80/86 expression on Dendritic cells. Flow cytometry analysis demonstrated induction of OVA-specific CD4+ T cell CD25 expression and proliferation in an Ag loading-dependent manner in response to NP-OVAs. Ag-encapsulated NPs were employed as a control. A similar Ag loading-dependent trend was observed in INFγ and IL-2 cytokine secretion. Overall, precise delivery of Ag using NP-OVA has the potential to aid in designing nanoparticle-based immunotherapies for Ag-specific immunomodulation.

**92. Caregiver distress and access to childcare in the time of COVID-19**

**Linda-Jeanne Mack**

Mack, L.-J. M., Lee, H., Deitz, A. Chung, Y.

Session K; Oral Presentation; Ballroom A

Starting in March of 2020, the COVID-19 pandemic required families to shift their daily routines immediately. Mandated lock downs closed schools and childcare facilities leaving parents to make immediate adjustments to their routines, often times with little access to natural social supports (Chen, et al., 2022; Russell et al., 2020). To meet the new demands, many parents quit their jobs as part of the “great resignation” or as “essential workers” had to make other arrangements for their children. Two years after the initial lockdowns, parents continued to report high level of psychological distress (Bastiaansent, et al., 2021; Chen, et al., 2022; Gawlik & Mazurek Melnyk, 2022; Igielnik, 2022; LePage & Javais, 2022). To capture the experiences of parents later into the COVID-19 pandemic, 440 parents were surveyed by a convenience sample through Qualtrics, resulting in a final sample of 436.
Psychological distress was measured by the Kessler 6 scale (Kessler, et al., 2003). COVID-19 family related stressors were measured by the COVID-19 Family Stressors Scale (Prime et al., 2021). Social supports and access to childcare were measured by the Family Resource Scale’s Social Time Subscale which asked ten items about their access to basic social support needs including access to childcare and babysitting (Brannan, et al. 2006). Access to childcare was associated with psychological stress during the COVID-19 pandemic ($p<.05$). Access to basic social resources ($p<.001$), COVID-19 stressors ($p<.001$), essential work status ($p<.001$), and stay at home parenting ($p<.01$) are associated with parental stress during the COVID-19 pandemic.

**93. Challenges and Opportunities in Enhancing the Elder Care Workforce**

**Min Kyoung Park**

Park, M. K., Taylor, J., Hochman, M., and Martin, D.

Session K; Oral Presentation; Ballroom A

Addressing workforce challenges affecting long-term care and related industries must be informed by a conceptual framework that acknowledges employer needs and the unique circumstances affecting employees. In fall 2022, we hosted a state-wide geriatric workforce summit with a two-fold purpose: (1) identify challenges with recruitment and retention in long term care workforce and (2) formulate opportunities to build a pipeline of talent while being adaptive to a new generation of employees. Frontline staff, licensed professionals, managers, and directors attended the half-day event to share their perspectives on factors influencing recruitment and retention of employees in the senior service and care sector and identify strategies to reverse current trends resulting in the shrinking of the eldercare workforce. In addition to wages and benefits, small group discussions identified barriers permeating from ageism, low employee morale, and a lack of mentorship

and career development opportunities within organizations. Participants shared ideas about the role institutions of higher education and area health education centers can play in overcoming some of the identified challenges. In this session, we will share the findings of our geriatric workforce summit and exchange ideas that can make delivery of long-term care services and supports to older people an attractive career choice.

**94. Determining Kinetics and Key Modulators of CAR T Cell-Mediated Trogocytosis**

**Kenneth Dietze**

Dietze, K. A., Luetkens, T.

Session L; Oral Presentation; Ballroom B

CAR T cells have revolutionized the field of cancer immunotherapy, specifically in the treatment of hematological malignancies. CAR T cell therapy combines elements of B cell antigen recognition with T cell activation, resulting in a transgenic T cell capable of recognizing whole surface antigen with high specificity and affinity. Although CAR T cells have shown remarkable clinical success, the majority of patients receiving CAR T cell therapy relapse within a few years of treatment. Several mechanisms have been implicated in CAR T cell-mediated relapse, including CAR T cell-mediated trogocytosis (CMT). During CMT, targeted tumor-associated antigens are extracted from the tumor cell surface, along with fragments of lipid membrane, and subsequently incorporated into the membrane of the CAR T cell. CMT thereby causes antigen-negative tumor cells that are now invisible to the CAR T cells and antigen-positive CAR T cells that are killed by other CAR T cells. To date, the subcellular and molecular processes causing CMT remain poorly characterized and CMT has not yet been observed in-vivo. We have developed a highly sensitive luciferase complementation assay to uncover the kinetics of CMT. Using this assay, we found that inhibition of the cysteine protease Cathepsin B reduces CMT. By overexpressing the endogenous Cathepsin B inhibitor Cystatin A, we show that we can reduce CMT without compromising antitumor efficacy. We believe our results will aid in the development of improved CAR T cell products which minimize trogocytosis and thereby reduce the number of relapses in patients receiving CAR T cell therapy.

**95. Associations between Romantic Relationship Quality, COVID-19 Stress, and Psychological Distress among Parents of Minors**

**April Cavaletto**

Cavaletto, A., Zhang, P.

Session L; Oral Presentation; Ballroom B

Background: While world disasters can have a negative impact on romantic relationships, high quality relationships are associated with positive individual outcomes and may act as a buffer against negative mental health outcomes during times of hardship. Thus, this study explores the associations between relationship quality, COVID-19 stress, and psychological distress, and the potential moderation effect of relationship quality on the association between COVID-19 stress and psychological distress.
Methods: A national cross-sectional study was conducted in June 2022, in which participants completed an online survey related to experiences during COVID-19. The study sample included 370 adults who had minor children during COVID-19 and were in a relationship of at least 1 month. A linear regression was used to analyze the relationships between psychological distress and the independent variables. An interaction model was conducted to test the moderation of relationship quality. Models controlled for gender, relationship status, income, division of household labor, essential worker status, and household COVID-19 status.
Results: Participants who experienced more stress from changes in their daily routines due to COVID-19 reported more psychological distress ($b = 2.19$, $p < .001$) and participants who reported higher relationship quality reported less psychological distress ($b = -0.20$, $p < .001$). However, relationship quality did not moderate the relationship between COVID-19 stress and psychological distress.
Implications: Implications for practice and policy to address parental mental health during the pandemic will be

discussed, including relationship interventions and policies that directly impact COVID-19 stressors.

**96. Leveraging Surgical Resection to Study Recurrent Growth Patterns of Glioblastoma**

**Adarsha Malla**

Malla A.P., Anastasiadis, P., Alomari, S., Kedda J., Pacis, P., Brem, H., Tyler, B., Woodworth GF.

Session L; Oral Presentation; Ballroom B

Glioblastoma (GBM) is the most common primary intrinsic adult brain cancer and is virtually an incurable disease. While preclinical models have been used to identify promising therapeutic strategies for GBM, these have all shown limited efficacy or failed at the clinical trial stage. These disappointing results highlight a compelling need for the field to advance our preclinical models to better recapitulate key features of GBM pathobiology and treatment. Here, we leverage a clinical neurosurgical resection device adapted for rodents to safely and precisely perform standard-of-care resective brain tumor surgeries. Using this resection platform, we are able to perform biopsies and gross total resections, extend animal survival, collect viable tissue for glioma stem cell culture, and study recurrent tumor growth patterns. This new platform serves as a robust tool to study multiple aspects of GBM pathobiology and brings a number of capabilities from the bedside back to the bench.

**97. Gallium-Salophen Complexes as Dual-Targeting Inhibitors of the Heme Sensing and Utilization Systems of Pseudomonas aeruginosa**

**Aziza Frank**

Frank, A.F., Centola, G., Hom, K., Xue, F., Wilks, A.

Session L; Oral Presentation; Ballroom B

Pseudomonas aeruginosa (Pa) is a gram-negative opportunistic pathogen posing a great danger to immunocompromised patients. With an estimated 32,000 infections and 2,700 deaths reported by the CDC in 2017, new therapeutic strategies are needed to overcome multidrug resistant (MDR) Pa infection. Iron, an essential micronutrient for Pa's virulence and survival, is limited within the host during infection. Pa has adapted to acquire iron in the form of heme via two non-redundant heme uptake systems, Pseudomonas heme uptake (Phu) and heme assimilation (Has) system. The high-capacity Phu system is primarily used to acquire heme during chronic infection. The Has system allows for extracellular heme sensing and signaling in the environment during acute infections. Additionally, the Has system involves a secreted hemophore HasAp which tightly binds heme and releases it to outer-membrane receptor, HasR. Release of heme from HasAp to HasR, triggers extra cytoplasmic function (ECF) sigma factor signaling cascade resulting in the increased production of HasAp. Internalized heme is eventually oxidatively cleaved by heme oxygenase (HemO) to release iron, CO, and biliverdin isomers b and d (BVIXb/d), known to post-transcriptionally upregulate the Has system. Thus, our lab aims to target HasAp and HemO to attenuate Pa infection by utilizing Gallium-Salophen (GaSal) complexes. GaSal targets heme sensing and signaling by binding to HasAp and blocking the ECF sigma factor signaling cascade. Additionally, internalized GaSal binds and inhibits the heme-degrading enzyme HemO. These GaSal analogs will result in iron-dysregulation rather than iron-starvation leading to reduced virulence and antibiotic resistance factors.

**98. Perceptions and measurements of dyspnea and quality of life experienced by malignant pleural mesothelioma patients before and after lung-sparing surgery: A pilot mixed methods study**

**Melissa Culligan**

Culligan, M., Klinedinst, N., Mooney-Doyle, K., Regan, M., Tod, A., Friedberg, JS.

Session L; Oral Presentation; Ballroom B

Objective: Pleural mesothelioma (PM) is a rare, debilitating cancer of the pleural space with a median overall survival of 12-18 months. Key factors contributing to these poor

survival rates include a heavy symptom burden and decreased quality-of-life. Dyspnea is one of the most common, debilitating symptoms experienced by PM patients. Lung-sparing surgery for PM is considered an investigational treatment intended to palliate symptoms, improve breathing function, prolong survival, and maximize quality-of-life. However, not all PM patients experience a comparable level of dyspnea palliation and improvement in quality-of-life following lung-sparing surgery. A clear understanding of who these patients are and what physiological, psychological and situational factors may be contributing to these unfavorable outcomes has not been reported in the literature.
Methods: The overall objective of the study is to gain an enriched understanding of how lung-sparing surgery for PM impacts participants experience of dyspnea and how that experience compares with quality of life. This prospective convergent longitudinal mixed methods study will focus on situational, physiological and psychological factors associated with the experience of dyspnea by comparing dyspnea scores, quality-of-life and the patient's lived experience of dyspnea before and after lung-sparing surgery for PM.
Results: Study is open to enrollment.
Conclusions: This study has potential to inform further research focused on the development of novel and innovative interventions focused on improving quality-of-life and palliation of the physical, psychological and situational factors that contribute to the intensity, timing, distress and quality of PM patients' lived experience of dyspnea, before and after lung-sparing surgery.

**99. Religion/spirituality is related to expectation but not placebo effects**

**Roxy Cundiff-O'Sullivan**

Cundiff-O'Sullivan, R. L., Raghuraman, N., Wang, Y., and Colloca, L.

Session L; Oral Presentation;  Ballroom B

Religious beliefs influence the understanding and interpretation of health and disease, but how religiosity influences placebo effects is unknown. This study examined the association between religiosity and placebo effects in healthy control and temporomandibular disorder (TMD) participants (374 Christian, 140 Non-Christian, 94 Atheist). Heat pain intensity applied to the forearm was assessed using a visual analogue scale (0-100) in a classical conditioning placebo paradigm. Participants were told green screens signaled pain relief via a sham electrode whereas red screens signaled full painful stimulation. Red and green screens were paired with high- and low-pain during conditioning and medium-pain during testing. Participants reported expectation and religion and completed the Chronic Pain Coping Inventory and Pain Catastrophizing Scale. The association between religiosity and TMD pain severity and interference was also examined. There was no effect of group or religion on placebo effects, although Christians reported greater expectation than Non-Christians and Atheists. Christians endorsed the highest use of guarding, resting, seeking help, relaxing, social support, catastrophizing, and soothing self-statements as coping strategies, yet Christians had greater pain severity than Atheists. This study is among the first to find an association between religiosity and expectation but not placebo effects.

**100. The Effects of "Ungrading" Individual Readiness Assurance Tests: A 2x2 Crossover Study Analyzing Assessment Scores**

**Zachary Noel**

Noel, Z.R. Cestone, C., Kulo, V., Gordes, K., Sweet, M.

Session M; Oral Presentation;  Room 351

Objective: Individual readiness assurance tests (iRATs) are frequently graded in team-based learning (TBL) classrooms, with the goal of incentivizing pre-class preparation. The objective of this study is to determine whether shifting to an ungraded iRAT process affects student preparation and learning, as measured using assessment scores.
Methods: Using a 2x2 crossover design in a second-year pharmacotherapy course, students were assigned to one of two iRAT grading sequences: graded/ungraded (G/UG) or ungraded/graded (UG/G). In the G condition iRATs were

graded based on correctness and in the UG condition based on completion. Each period consisted of four iRATs, four team readiness assurance tests (tRATs), and one examination. Repeated measures MANOVA was used to test within-subject differences of mean iRAT, tRAT, and examination scores across grading conditions. Bonferroni correction was used for post-hoc testing.
Results: All 91 students in the course were included in the analysis. There was a statistically significant main effect for iRAT grading condition on assessment scores, $F(2,88) = 3.851$, Wilk's $\Lambda = .992$, $p = .025$. Univariate analysis demonstrated a significant difference only in iRAT scores, with the mean score higher in the G condition (72.51% versus 67.99%; $p = .011$). Examination scores (81.07% versus 80.32%, $p = .397$) and tRAT scores (96.5% versus 96.5%, $p = .867$) were similar in the G and UG conditions.
Conclusions: Students demonstrated a modest reduction in iRAT scores when it was "ungraded"; however, tRAT and examination scores remained markedly similar, suggesting that overall learning was similar irrespective of iRAT grading condition.

**101. Comparative Analysis of Enterovirus-D68 3A Non-Structural Protein, and its Interactions with Host Protein Lis1, in Related Enteroviruses**

**Noah Pollack**

Pollack, N.A., Jassey, A., Jackson W.T.

Session M; Oral Presentation;  Room 351

Enteroviruses, members of the picornavirus family, are small, non-enveloped, positive sense single stranded RNA viruses. Notable members of the family that cause human disease include polio, enterovirus-d68 (EV-D68), coxsackievirus B3, and rhinovirus. Despite their relatedness, there have been multiple unique phenotypes described amongst similar enterovirus non-structural proteins. We seek to compare the functionality of 3A and its interaction with host protein Lis1 between enteroviruses. In multiple enteroviruses, including polio and coxsackievirus, 3A has been implicated in membrane rearrangement and blocking endoplasmic reticulum to Golgi trafficking. However, it is yet to be determined the individual role of EV-D68 3A. Due to significant amino acid differences at key regions of the protein, we propose EV-D68 3A has unique properties during infection when compared to polio 3A. Overexpression of EV-D68 3A colocalized with the endoplasmic reticulum marker calnexin as well as altered calnexins localization. Human Lis1, a member of the dynein motor complex, is most notable for its role during brain development and neuronal migration. However, it has also been implicated in vesicle movement throughout the cell. Lis1 interacts with polio 3A and this interaction hinders its ability to block ER to Golgi trafficking, however, the role of Lis1 during infection by other picornaviruses is unknown. Overexpression of Lis1 caused a decrease in polio and coxsackievirus B3 release from cells, but greatly increased rhinovirus 16 release. These data and future experiments suggest an independent usage or role of Lis1 during enterovirus infection.

**102. Short-term Regulations for Laboratory Developed Tests**

**Rebecca Collins**

Collins, R., Dasi, D., Bekima, M., Liebhardt, P., Vucenik, I.

Session M; Oral Presentation;  Room 351

In recent years, there has been an increase in technology startups opening and operating laboratories. Some of these companies make exaggerated claims of revolutionizing medicine by introducing new technology that is not always based on sound science and uses data that has not been validated by peer review.
These companies have been able to operate with little to no supervision by exploiting the loopholes and lack of regulation for laboratory developed tests (LDTs), the category under which they operate. We propose short-term regulations for LDTs that may be put in place to enhance patient safety while the VALID Act; legislation that will regulate laboratory developed tests long-term, is undergoing review in Congress.

**103. A Polypharmacological BCL-2/HDAC Dual Inhibitor Strategy to Mitigate MCL-1 Upregulation in Venetoclax Resistance**

**Alexandria Chan**

Chan, A. M., Wuytz, Z. N., Eberley, C., Lowe, B. D., Drennen, B. J., Civin, C. I., Fletcher, S.

Session M; Oral Presentation; Room 351

Cancers depend on several pathways for survival, causing resistance to treatment through the upregulation of key proteins. Therefore, multifactorial treatments are required to maintain therapeutic efficacy. Combination treatments are commonly used, however, another method termed "polypharmacology" can be implemented. These compounds contain pharmacophores for two or more proteins, resulting in several advantages including an increased therapeutic effect due to the simultaneous presence of both pharmacophores in tissues.
The B-cell lymphoma-2 (BCL-2) family of proteins are regulators of cell death consisting of pro and anti-apoptotic proteins. In malignant cells, anti-apoptotic proteins, such as BCL-2, are overexpressed allowing the cells to survive. Venetoclax is an FDA-approved BCL-2 inhibitor that is efficacious towards several cancer types. However, resistance commonly occurs due to the upregulation of other proteins including histone deacetylases (HDACs), which play key roles in epigenetic regulation, including the downregulation of pro-apoptotic proteins, directly nullifying the anti-tumor activity of venetoclax. Prior research has shown efficacy in resistant cells using a combination treatment of venetoclax and an HDAC inhibitor. Given the potential benefits of polypharmacology, we have developed novel BCL-2/HDAC dual inhibitors for cancer treatment, including venetoclax-resistant populations. Currently, there are four FDA-approved HDAC inhibitors; however, these show considerable toxic effects as pan-inhibitors. To mitigate these effects, we propose to target only one HDAC isozyme and have designed dual inhibitors of BCL-2/HDAC1 and BCL-2/HDAC6. We hypothesize these inhibitors will be efficacious against venetoclax-resistant populations while also avoiding the undesirable effects of pan-HDAC inhibition.

**104. Forms of Labor Control Utilized on Victims of Labor Trafficking**

**Nikita Aggarwal**

Aggarwal, N. and Finigan-Carr, NM

Session M; Oral Presentation; Room 351

There are likely to be more than 40 million women, men, and children who are being forced to work under threat. While not a recent phenomenon, labor trafficking as a form of modern slavery has engendered intersecting layers of exploitation of immigrants due to the rigorous changes in global labor market trends. It is critical to understand the role institutional actors play in exacerbating the vulnerabilities of migrant workers. The current paper aims to explore control through various forms of restriction faced by those forced into the informal labor market. Using administrative data from a global repository of reports on human trafficking, this cross-sectional study examined whether the type of labor and recruiter relationship predict the experiences of exploitation among the victims of forced labor (N= 734) coerced to work in the sectors of agriculture, construction, and domestic work. The findings from the regression analysis indicated that both adult women and men tend to experience at least one form of restriction in their workplaces. Additionally, the findings suggested that individuals who were forced into labor by brokers, local recruiters, etc. have higher odds of facing at least one form of restriction than those who were forced by family members. The study examines more subtle, invisible, and incessant forms of control that come into existence due to the nature of the informal work sector. Findings emphasize that future research should consider how the role of recruiters influences the association between types of forced labor and other intangible forms of control.

**105. Low Density Lipoprotein Receptor-related Protein 1 (LRP1) Facilitates SARS-CoV-2 Viral Entry**

**Mashhood Wani**

Wani, M.M., Migliorini, M., Strickland, D.K.

Session M; Oral Presentation; Room 351

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the causative agent of COVID-19, uses the viral spike (S) protein for host cell attachment and entry. With SARS-CoV-2, the S protein undergoes cleavage into the S1 and S2 subunits at a furin cleavage site during cellular assembly. Subsequent activation of the spike protein resulting in membrane fusion occurs via proteolytic processing through TMPRSS2 and Cathepsin L. The ability of the viral transmembrane S protein to interact with cellular receptors facilitates cell entry into endosomal compartments and is a critical determinant of viral infectivity. While ACE2 is a known receptor SARS-CoV-2, we interrogated other known endocytic receptors implicated in viral entry. Harnessing biochemical and cellular-based approaches, we have shown that the Spike protein of SARS-CoV-2 binds directly, with high affinity, to low density lipoprotein receptor-related protein 1 (LRP1). Our data further reveals that LRP1- expressing cells internalize $^{(125)}$I-labeled spike protein to a much greater extent than LRP1-deficient cells. To study these observations further, we generated pseudovirions expressing SARS-CoV-2 spike protein on their surface, and investigated their internalization in HEK293T cells stably transfected with ACE2. When HEK293T/ACE2 cells were transfected with LRP1, we noticed a substantial increase in pseudovirion internalization in the presence of LRP1, suggesting that LRP1 cooperates with ACE2 in mediating SARS-CoV-2 internalization into endosomal compartments. We also demonstrated that purified soluble forms of ACE2 can interact with LRP1. Together, these data reveal that LRP1 interacts with the Spike protein and may synergize with ACE2 to promote SARS-CoV-2 internalization.

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