UNIVERSITY of MARYLAND
GRADUATE SCHOOL

by Danté Johnson, Luis Schachner, & Raquel Shortt

43rd Annual

Graduate Research Conference

Hosted by The Graduate Student Association
March 26, 2021

GSA Graduate Student Association

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Graduate Research Conference

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In Memory of
Alex Rittle

UMBC Graduate Student Association President
Leader, Friend, & Champion for Fellow Grad Students

UMBC

Cover Art

Doodling with GC-MS Traces of Melanin Molecules

Inspiration: The basic principle of mass spectrometry (MS) is to generate ions from either inorganic or organic compounds by any suitable method, to separate these ions by their mass-to-charge ratio (m/z) and to detect them qualitatively and quantitatively by their respective m/z and abundance in high powered analytical instruments contained electric and magnetic fields. This technique is the basis of our research, and we wanted to share our passion for our science by turning it into art so others can see what we see every day, but in a new and fun way. This piece was created during Black History Month. A mass spectra of the melanin peptide takes the form of curly hair, the crown of a beautiful black woman.

Collaboration of Creators

Danté Johnson and Raquel Shortt
University of Maryland Baltimore, School of Pharmacy, Dept of Pharmaceutical Sciences
Danté and Raquel specialize in novel in cell and in vivo protein footprinting methods coupled with mass spectrometry for the characterization of protein-protein and protein-ligand interaction sites. We use oxidative labeling for the structural characterization of proteins in their native cellular environment.

Luis Schachner
Northwestern
Luis specializes in applying "native" mass spectrometry and other proteomics techniques to the investigation of large biomolecular machines, their metal binding and modifications.
Please check out more art spectra at luisschachner.com as well as Instagram @luis.schachner
Collaborations welcome!

Table of Contents

Bruce E. Jarrell, MD
President
University of Maryland, Baltimore
220 Arch Street
Baltimore, MD 21201
410 706 7002

umaryland.edu

March 16, 2021

Congratulations on your 2021 Graduate Research Conference. If this year has taught us anything it's the importance of understanding that we are interconnected. The instinct to share with one another is so important. The biggest breakthroughs in human health and well-being often happen at the intersection of scholars, schools and disciplines.

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

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

Stay healthy and safe.

Sincerely,

Bruce E Jarrell

Bruce Jarrell, MD, FACS
President

Foreword

Welcome to the 43rd 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 representative of a broad range of UMB graduate research programs, 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) at the University of Maryland, Baltimore will be sponsoring a special award in aging research. University of Maryland Ventures (UM Ventures) will also present their 13th annual Graduate Translational Research Award to recognize important translational research being performed by a UMB graduate student or postdoctoral fellow. We thank the GGEAR and UM Ventures for their continued support of GRC and the outstanding research being conducted by students and postdoctoral 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. We thank alumna, Alyssa Grogan, for joining us during this ceremony that she has also planned in the past!

The GSA gratefully acknowledges those who helped make the GRC possible and successful. We would like to thank 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. A huge thanks to Celeste Gerhart for helping coordinate our lunch option for participants and The Nook Cafe in BioPark for accommodating our needs while we cannot be in person this year. We are grateful for our amazing sponsors, alumni donors, and supporting organizations that drive the success of our event! Another thank you to the UM Foundation for coordinating additional fundraising efforts for this year's virtual GRC. 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 43rd annual Graduate Research Conference, and we hope you enjoy today's program and events!

GSA Executive Board

Emily Smith – President
Lauren McCarthy – Vice President
Gillian Mbambo – Treasurer
Hadley Bryan – Secretary
Sydney Ashton – Public Relations Officer
Katie Gwilliam – Graduate Council Representative

Student Award Winners

The Graduate Student Association would like to congratulate the students who have won our awards during the 2020-2021 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- virtually this year. New this year, the COVID-19 Work from Home Support Award allowed students to access equipment, software, or other items necessary for completing their research from home.

Professional Development Award

Sol Baik
Qingzhao Zhang
Jacquie Cohen Roth

Research Award

Dongyue Yu
Hanover Matz
Katherine Endy

Travel Award

Maria Traficante
Jennifer Kirk

COVID-19 Work from Home Support Award

Benjamin Grosso
Caroline Harmon-Darrow
Chintal Shah
Christine Carney
Haeyoung Lee
Jennifer French
Karehsma Mohanty
Kayleigh Majercak
Lujie Peng
Michael Sikorski
Qingzhao Zhang
Shisi He
Sol Baik
Timileyin Adediran

Abstract Book Images

Danté Johnson and Raquel Shortt in collaboration with Luis Schachner (Front)
Nicole Gould (Back)

43rd Annual Graduate Research Conference

Schedule of Events

Virtual via GatherTown
Friday, March 26th, 2021

8:00 - 9:00 AM	**Check-in & Troubleshoot**	Main Hall
9:00 - 10:30 AM	**Oral Presentations** ***Sessions A & B***	Presentation Rooms 1 & 2
10:30 - 11:30 AM	**Poster Presentations** ***Sessions C & D***	Morning Poster Room
11:30 AM - 1:00 PM	**Lunch Break**	Lounge or take a screen break!
1:00 - 2:00 PM	**Poster Presentations** ***Sessions E & F***	Afternoon Poster Room
2:00 - 2:15 PM	**Break** ***Judges Finalize Scores***	
2:15 - 3:45 PM	**Oral Presentations** ***Sessions G & H***	Presentation Rooms 1 & 2
3:45 - 4:00 PM	**Break** ***Judges Finalize Scores***	
4:00 - 5:00 PM	**GRC Awards & Advancement to Candidacy Ceremony**	Ballroom

GRC Awards & Advancement to Candidacy Ceremony Speaker

Dr. Alyssa Grogan

Alyssa Grogan is a recent graduate from the Program in Molecular Medicine at UMB. Her thesis research, conducted in the lab of Dr. Katia Kontrogianni-Konstantopoulos, focused on understanding the pathophysiology of the giant cytoskeletal protein obscurin in the heart. After defending her Ph.D. in October 2020, she has continued her studies on obscurin as a Post-Doctoral Fellow in the lab. During her time as a graduate student, Alyssa was actively involved with the Graduate Student Association and served as Molecular Medicine representative, Public Relations Chair, Secretary, and a member of the GRC organizing committee.

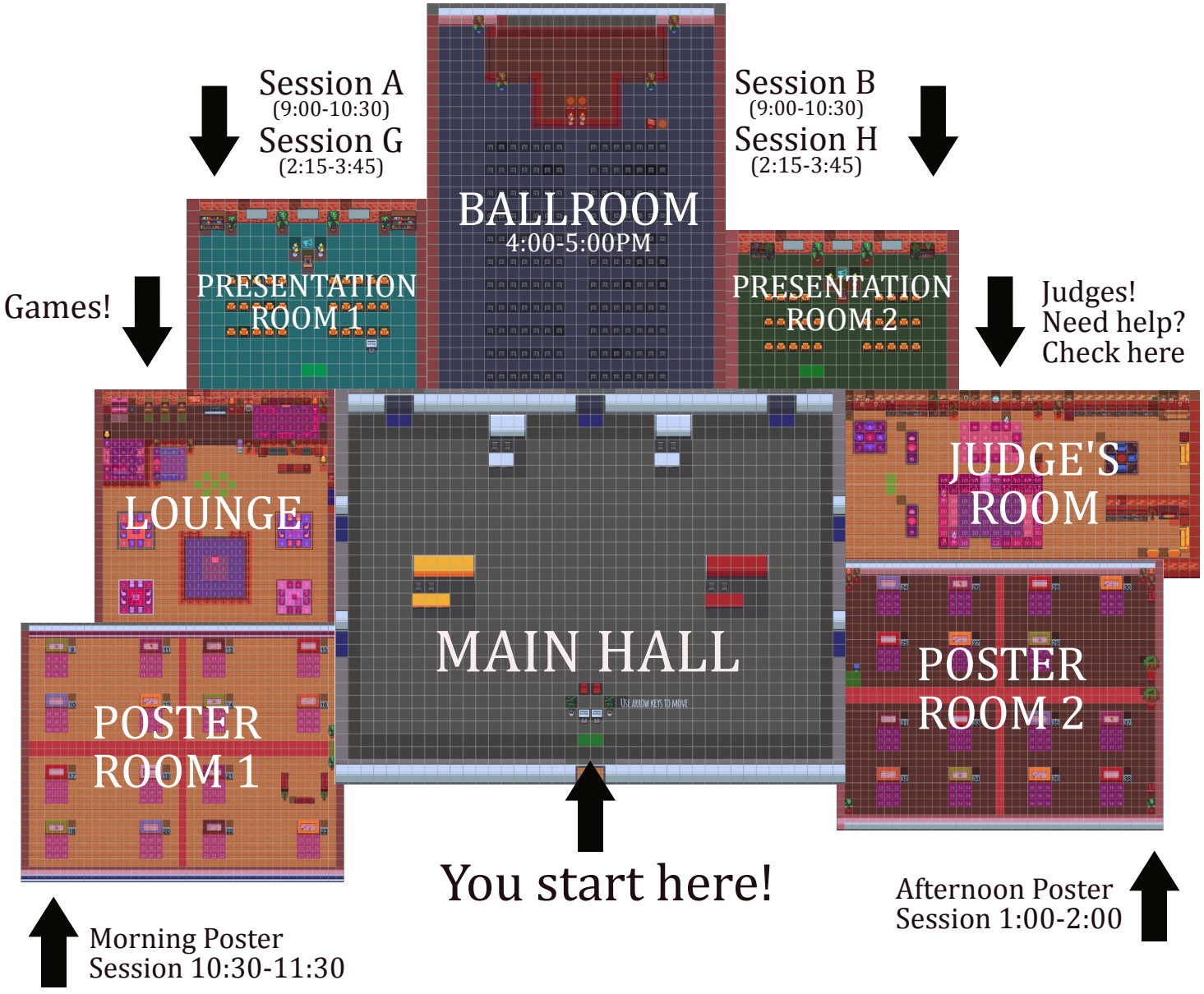
PhD Candidates Recognized

Hadley Bryan
Rainer Butler
Alexandria Chan
Benjamin Diethelm-Varela
Jennifer French-Kwawu
Ioana Ghita
Corbin Goerlich
Kyle Kihn
Jennifer Kirk
Liron Marnin
Franklin Ning
Zahra Rahmaty
Julia Rutherford
Raquell Shortt
Alexandra Soare

43rd Annual Graduate Research Conference

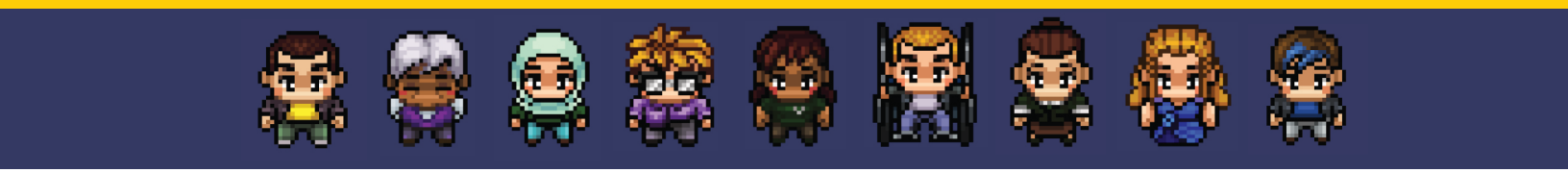
GatherTown Instructions

GatherTown Map

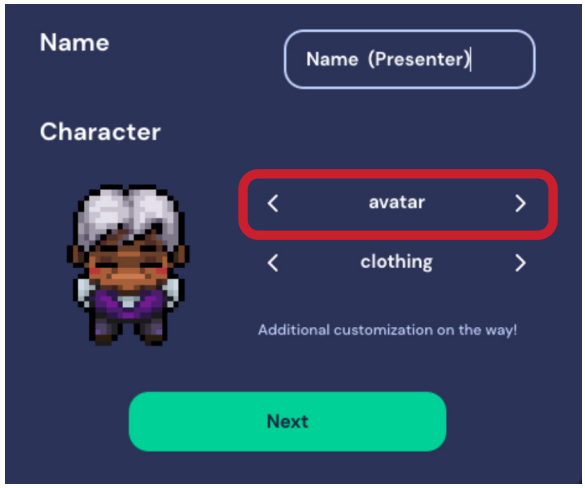


Joining GatherTown for the first time:

Avatar Creation



When you click the GatherTown link- This is what you'll see!

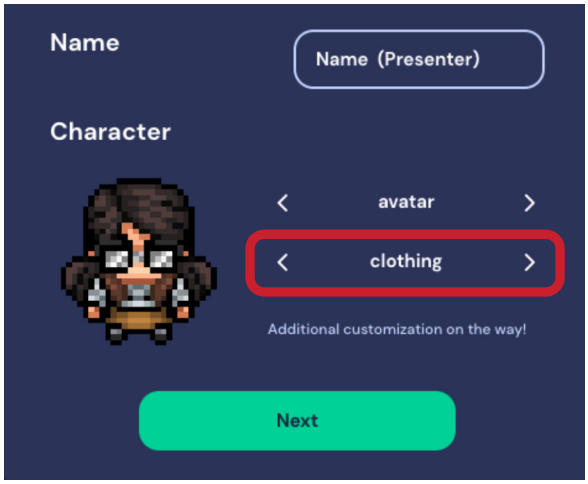


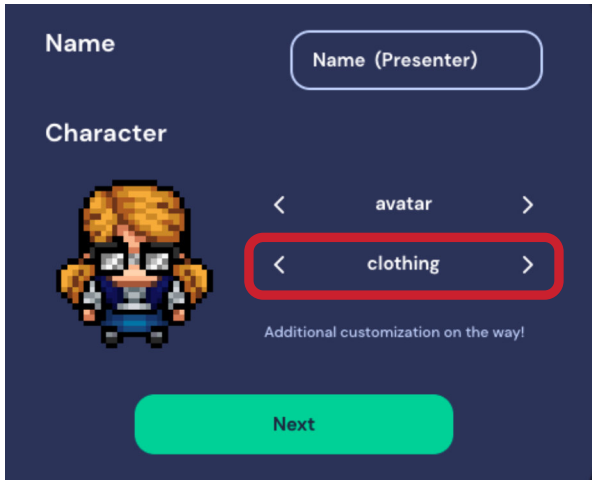
1. Please name your avatar in this format:

   Name (Registration Type)

2. Pick an avatar that you like by clicking these arrows

3. Change hair color and outfit by clicking the these arrows

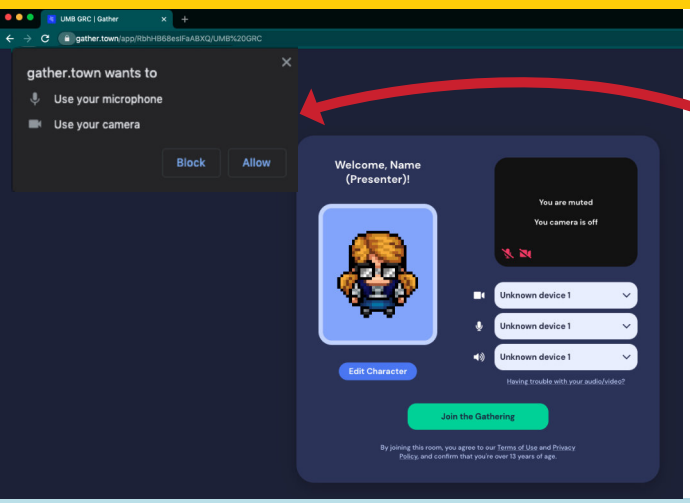




Then click Next!

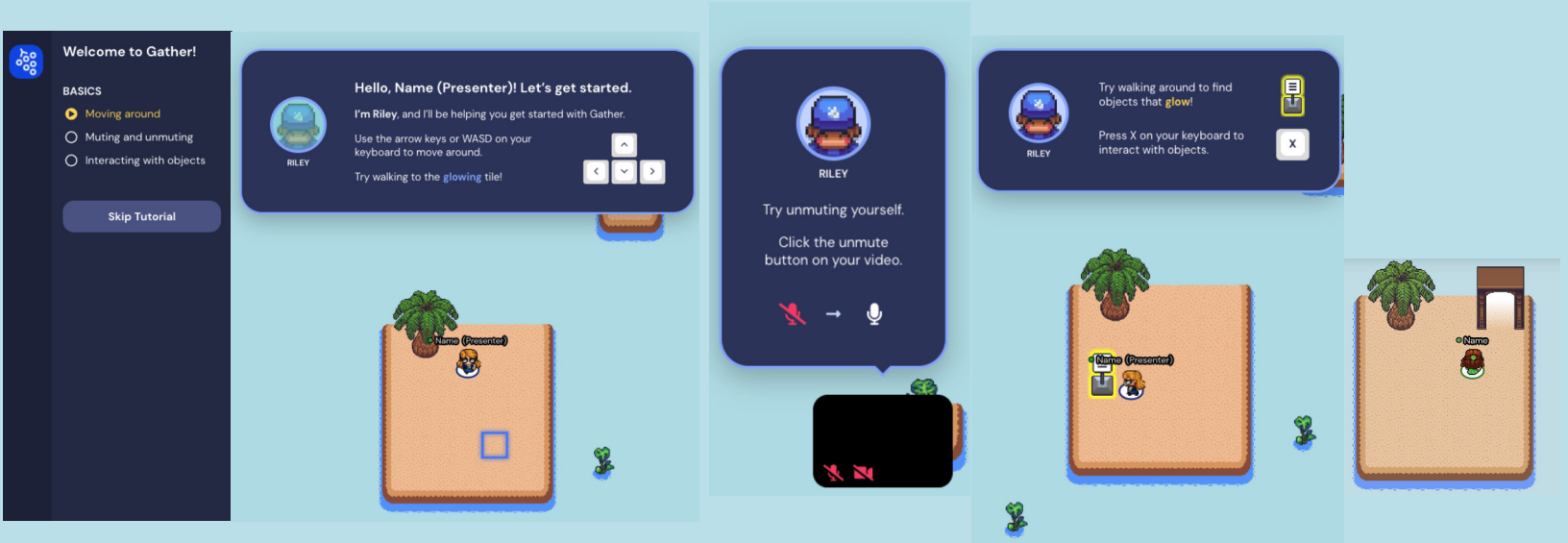
Joining GatherTown for the first time:

Settings & Tutorial



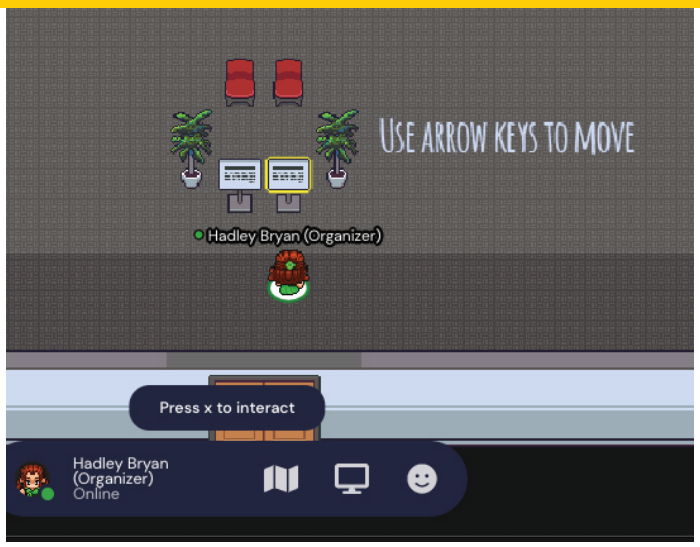
Before you join the gathering, you'll be asked to allow GatherTown to access your camera & microphone. Please click "allow"

If it's your first time in GatherTown you'll see this tutorial next!
You can either "skip tutorial" or continue and "walk through the door" to enter the GRC Map.



Interacting with other people in GatherTown

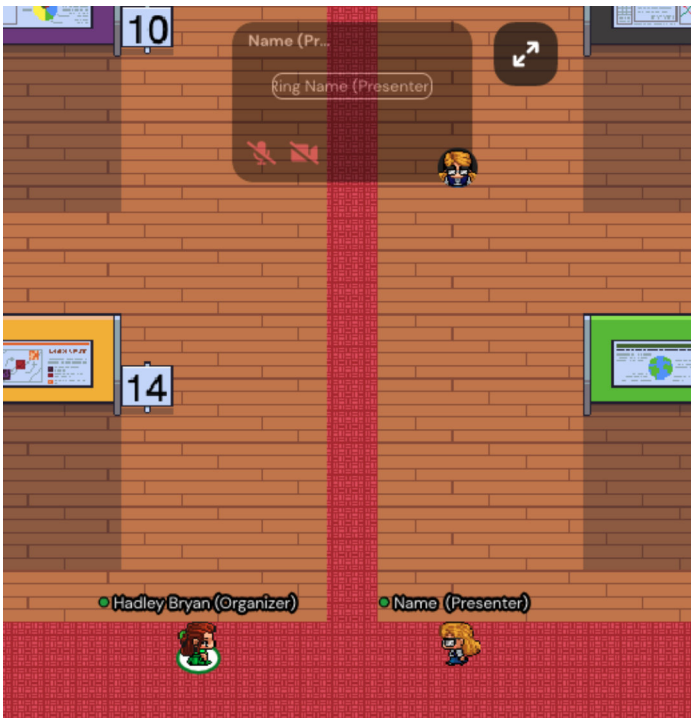
Welcome to UMB GRC!

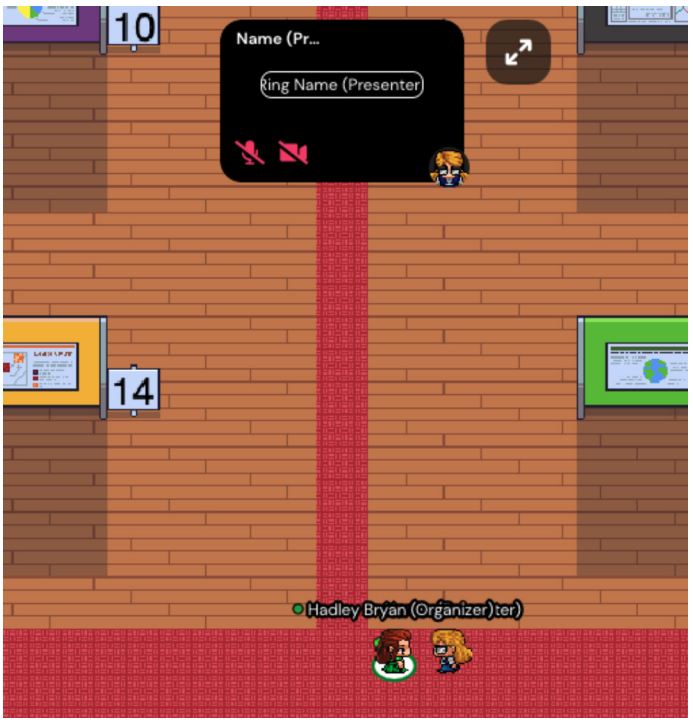


The first thing you'll encounter in our GRC map is a podium: Please press "x" to interact. This will take you to a Google Spreadsheet where you will check in.

Interaction in GatherTown is based on proximity to avatars & objects on the virtual map.

You'll see below, as I move my avatar toward another, a video call starts to appear at the top of my screen. As I get closer, I can turn on my mic & camera to start talking to someone!





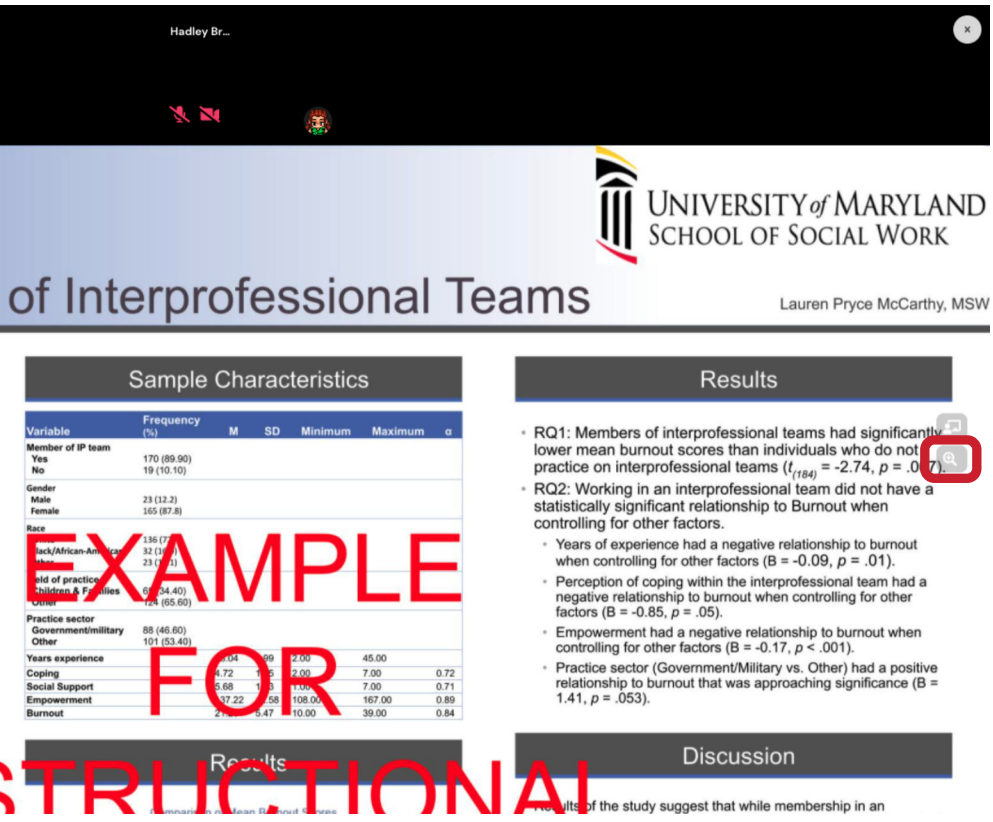
Poster Sessions

10:30-11:30AM & 1:00-2:00PM

For poster sessions:
Posters are numbered by signs to the right of each board.

During your poster session, to interact with presenters/ judges/etc. you should enter the space in front of the poster, indicated by a darker rectangle. This will allow you to discuss the presenter's poster with them.

Just like other objects, press "x" to view each poster.



The presenter's video & anyone else in the space in front of the poster will appear at the top

To zoom in:
press the small magnifying glass on the right, then **click & drag** to view the poster

To exit the poster view:
hit "x" or
click the x in the upper right

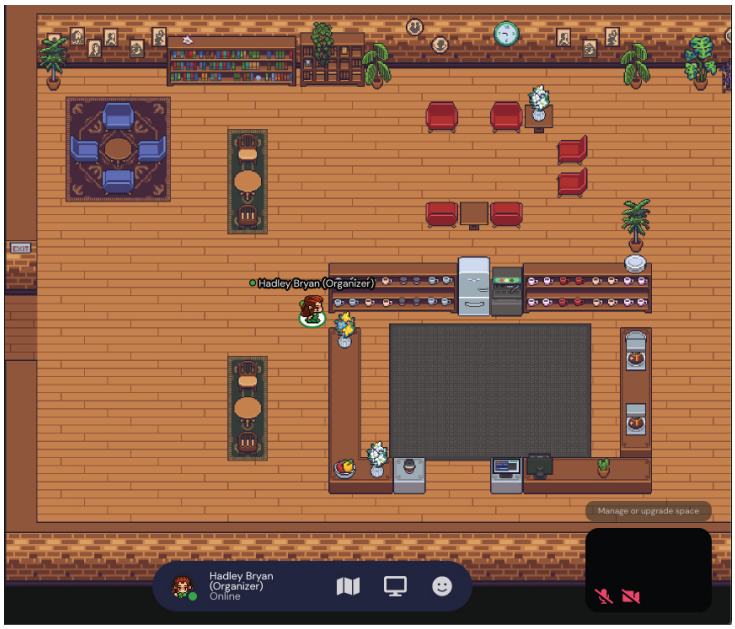
Oral Presentation Sessions

9:00-10:30AM & 2:15-3:45PM

Presenters will move to the megaphone tile when it is their turn to present.
This will allow the presenter to share their screen with all people in the room.

Each presenter will have ~12 minutes to present & ~3 minutes for judges to ask questions.
A volunteer will be in each session to keep time for the presentation and questions.

Judge's Room



Judges will be provided a Google Spreadsheet for their specific session and presenters. These will be shared with volunteers so they can tally scores for each session before the awards ceremony at the end of the day.

You're not required to use the judge's room, but if you need to meet with another judge this is the place! Volunteers will also be here most of the day if you have questions.

THANK YOU!

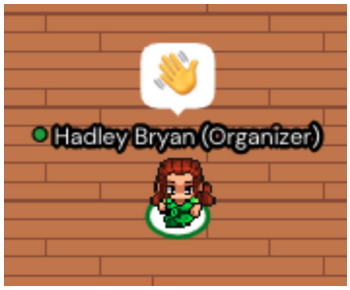
Thank you for taking part in this year's Graduate Research Conference!

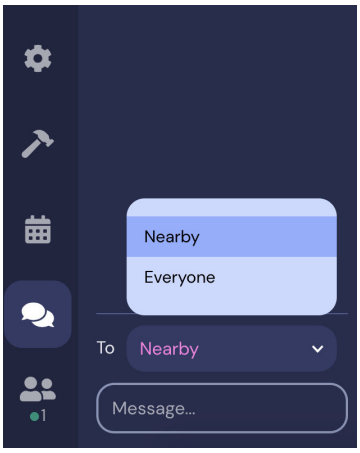
Have questions?

Email Hadley at

umb.gsa.sec@gmail.com

In GatherTown?
Look for my avatar ->





or send me a chat!
<- you will be able to send chats to participants similar to the chat feature in Zoom

Session Assignments

Session A- Oral Presentation Session, 9:00-10:30AM, Presentation Room 1

(*1*) Eman Hefni, (*2*) Sonia Garcia, (*3*) Ioana Ghita, (*4*) Maria Traficante

Session B- Oral Presentation Session, 9:00-10:30AM, Presentation Room 2

(*5*) Stephanie Zalesak-Kravec, (*6*) Douglas Loesch, (*7*) Cooper Roache, (*8*) Chintal Shah

Session C- Poster Session, 10:30-11:30AM, Morning Poster Room

(*9*) Nesreen Alissa, (*10*) Ruth Akinlosotu, (*11*) Alexis Cirko, Kaitlyn Gencarelli, Fahren Nipple, & Jasmine Solano, (*12*) Ahmed Salem, (*13*) Simon Ho, (*14*) Katie Dondero, (*15*) Gretchen Tucker, (*16*) Anju Paudel

Session D- Poster Session, 10:30-11:30AM, Morning Poster Room

(*17*) Raziyeh Baghi, (*18*) Kyle Kihn, (*19*) Shanaliz Natta,
(20) Zachary Fasana, (21) Nicole Gould, (22) Julia Rutherford

Session E- Poster Session, 1:00-2:00PM, Afternoon Poster Room

(*23*) Jennifer Kirk, (*24*) Ebtehal Albeshir, (*25*) Sanjana Rao, (*26*) Rashmita Bajracharya, (*27*) Lori Anderson, (*28*) Kelly Rock, (*29*) Van Anh Nguyen, Paige Cephas, Sarah Pribil, & Flora De Mari Quiroz Moreyra

Session F- Poster Session, 1:00-2:00PM, Afternoon Poster Room

(*30*) Sophie Bruckmeier, (*31*) Juliet Obi, (*32*) Emily Smith, (*33*) Jovanni Ahmad,
(*34*) Ashley Marquardt, (*35*) Christine Carney, (*36*) Abdulrahman Balhaddad

Session G- Oral Presentation Session, 2:15-3:45PM, Presentation Room 1

(*37*) Jamila Asgar, (*38*) Eseosa Fernandes, (*39*) Heather Mutchie, (*40*) Eunsong Park, (*41*) Alexandra Soare

Session H- Oral Presentation Session, 2:15-3:45PM, Presentation Room 2

(*42*) Sydney Ashton, (*43*) Olutomiwa Fadiran, (*44*) Anya O'Neal, (*45*) Mashhood Wani

Abstracts

1. **ANGIOPOIETIN-LIKE 4 IS A CRITICAL FACTOR IN HEAD AND NECK SQUAMOUS CELL CARCINOMA METASTASIS**

Eman Hefni

Hefni E., Menon, D., Armstrong, C., & Montaner, S.

Session A, Oral Presentation

Head and neck cancer represent the 6th most common cancer worldwide and one of the most aggressive malignancies. More than 90% of head and neck cancers are squamous cell carcinomas (HNSCC) that arise in the oral cavity, the oropharynx and the larynx. In the US, this neoplasia accounts for 3% of all cancers, with around 51,000 people diagnosed and 10,000 fatalities every year. HNSCC spreads primarily to the lymph nodes of the neck first before it metastasizes to other areas. The presence of lymph node metastasis has a great impact on the prognosis and survival of affected individuals. Unfortunately, lymph node metastatic tumors occur in about 40% of patients with oral cancer, underscoring the urgency to identify effective targets for the early prognosis and management of HNSCC. Recent data supports a role of Angiopoietin-like 4 (ANGPTL4) as a molecular marker in HNSCC. Compelling evidence suggests a role of ANGPTL4 in cancer dissemination. Indeed, overexpression of ANGPTL4 by cancer cells has been associated with poor prognosis and poor disease-free survival rates. Our research goal is to elucidate the role of ANGPTL4 in HNSCC metastasis, with the ultimate purpose of identifying alternative therapeutic options for this neoplasia. Results: We found that ANGPTL4 expression is elevated in premalignant and malignant oral squamous cell carcinoma cell lines. We found that ANGPTL4 binds to Neuropilins 1 and 2 receptors and induces sprouting of vascular and lymphatic endothelial cells. Inhibition of ANGPTL4 expression in oral malignant cell lines blocked cancer cell proliferation and migration.

2. **RARγ AGONIST EXERTS ANTI-TUMOR FUNCTION ON HUMAN OSTEOCHONDROMAS BY INHIBITING MATRIX SYNTHESIS AND PROMOTING CARTILAGE MATRIX DEGRADATION AND CELL DEATH**

Sonia Garcia

Garcia, S.A., Tian, H., Imamura-Kawasawa, Y., Fisher, A., Cellini, A., Codd, C., Herzenberg, J.E., Abzug, J.M., Ng, V., Iwamoto, M., & Enomoto-Iwamoto, M.

Session A, Oral Presentation

Osteochondromas (OC) are cartilage-capped tumors that arise near growing physis and are considered the most common benign bone tumor in children. Treatment is limited to surgical resection since there are no FDA-approved therapies. Previous translational studies suggested that RARγ agonist suppresses ectopic cartilage formation, including OC in rodent models. Together, this led to a clinical trial to study the efficacy and safety of Palovarotene, a RARγ agonist, for the systemic treatment of multiple OC. The clinical trial was terminated due to concern of the chronic use in children. However, mechanistic studies underlying inhibition of OC formation by RARγ agonist should be useful to develop alternative drug therapies for OC. The purpose of this study was to examine the action of RARγ agonist on human OC. Human OC specimens were obtained at surgery, cultured and treated with RARγ agonist or vehicle. Histological examination demonstrated reduction in cartilage matrix and an increase in production of the NITEGE neoepitope of aggrecan, produced by ADAMTS proteases. Live/dead assay and TUNEL staining demonstrated that RARγ agonist treatment induced

cell death. Strong inhibition of cartilage matrix gene expression and increased expression of extracellular matrix proteases, such as MMP13 in RARγ agonist-treated explants was observed. Ingenuity Canonical Pathway Analysis of differentially expressed genes by RARγ agonists revealed that Interferon Signaling and Retinoic Acid Mediated Apoptosis Signaling pathways were up-regulated. Together, these findings indicate that RARγ agonists may exert anti-tumor function on OC via at least two actions: stimulation of cell death and destruction of cartilage matrix.

3. SOLUBLE IMMUNE BIOMARKERS AS A DIAGNOSTIC TOOL FOR HEAD AND NECK SQUAMOUS CELL CARCINOMA IMMUNE PROFILE

Ioana Ghita

Ghita, I., Theofilou, V. I., Elnaggar, M., Chaisuparat, R., Dyalram, D., Ord, R. A., Webb, T. J., Bentzen, S. M., Lubek, J. E., & Younis, R. H.

Session A, Oral Presentation

Head and neck squamous cell carcinoma (HNSCC) is an immune suppressive tumor with only ~15% response rate to immunotherapy. Here we hypothesize that soluble immune biomarkers in peripheral blood can read the underlying histological tumor inflammation of HNSCC.
Paired tumor tissue and peripheral blood samples were collected from 95 HNSCC patients at the same time point. IHC scoring using PD-L1 and Sema4D immune biomarkers and direct ELISA for plasma were used. IFN-γ signature was analyzed in 10 samples using nanoString. Luminex™ Multianalyte was used to analyze soluble cytokines in plasma.
Our results: 52% of tumors were inflamed (HIS-INF); 40% immune excluded (HIS-IE) and 8% deserted. There was statistically significant correlation between high Sema4D (HsS4D) (67%) in plasma and HIS-IE and between low Sema4D (LsS4D) and HIS-INF (60%) ($p = 0.007$). 75% of the HNSCC patients showed sSema4D in plasma higher than the median in healthy donors (HD). The nanoString gene expression analysis showed HsS4D in plasma to cluster with low IFN-γ signature, HIS-IE subtype. There were statistically significant differences in the levels of IL10, IL17A, IL-1RA and IP10 between HD and HNSCC. Fratalkine, FGF-2, GRO, CD40L were higher in HNSCC HsS4D compared with LsS4D group, but IL10 higher in LsS4D. Comparing with HD, IL10 and IL6 were higher in LsS4D, while IP10 was higher in HsS4D group.
In conclusion, the current work presents a novel technology by which the underlying immune suppressive tumor profile can be diagnosed from a convenient peripheral blood test independent of the morbidity of surgical biopsy.

4. SLC34A2 AS A POTENTIAL BIOMARKER FOR FACIOSCAPULOHUMERAL MUSCULAR DYSTROPHY (FSHD)

Maria Traficante

Traficante, M. K., O'Neill, A., Mueller, A. L., & Bloch, R. J.

Session A, Oral Presentation

Facioscapulohumeral Muscular Dystrophy (FSHD) is the third most common dystrophy, affecting about one in 8500 people. The disease presents as progressive wasting of the face, shoulder girdle, and arm muscles. The cause of FSHD is aberrant expression of the transcription factor DUX4 in skeletal muscle, however the pathophysiology and the mechanism(s) that cause muscle wasting are still unknown. This lack of understanding impedes treatment development, and patients are left with symptom mitigation measures that are less than effective. Recent work from our lab has identified a protein biomarker, the pH-sensitive

Na+-dependent PO42--cotransporter SLC34A2, which is a DUX4 target found both in human biopsies and in our model of human muscle xenografts (Mueller et al., Exp. Neurol. 320: 113011, 2019). In healthy individuals, the cotransporter is expressed in lung, kidney, and gut epithelia, but not in mature muscles. Our previous work has found that SLC34A2 is present in about 1%-2% of FSHD-affected fibers, which correlates with the relatively low prevalence of DUX4 expression we observe in the xenografts. Therefore we hypothesize that SLC34A2 is a surrogate marker for DUX4 expression. We quantified levels of SLC34A2 protein in xenografts as well as patient sera, and we show an increase in SLC34A2 protein levels in FSHD patients compared to healthy controls. With these and future experiments, we aim to investigate the relationship between SLC34A2 protein levels and patient disease progression/severity, and question whether SLC34A2 levels decrease with therapies that suppress DUX4 expression.

5. REGULATION OF RETINOID HOMEOSTASIS BY CELLULAR RETINOL-BINDING PROTEIN, TYPE 1

Stephanie Zalesak-Kravec

Zalesak-Kravec, S. M., Li, W., Yu, J., & Kane, M. A.

Session A, Oral Presentation

Retinoic acid (RA) is the main active metabolite of Vitamin A, an essential diet-derived nutrient. Proper RA signaling is critical for the immune response and gastrointestinal homeostasis, including lineage commitment and maintaining the intestinal epithelial barrier function. Vitamin A deficiency leads to a decrease in RA and can alter the immune response and gut homeostasis. There are many mechanisms in place to maintain RA metabolism, including the expression of cellular retinol binding protein, type 1 (CRBP1). CRBP1 binds to retinol and retinal, protecting them from non-specific oxidation, and facilitating their delivery to the appropriate enzymes for RA biosynthesis. CRBP1 has been shown to be decreased in disease states that display dysfunctional proliferation and differentiation, including cancers and inflammatory disorders. Reduction of CRBP1 levels directly correlates with reduction in RA and restoration of CRBP1 expression has been shown to increase RA levels and positively impact RA-dependent outcomes. Research on the role of CRBP1 in disease has been limited because this protein has proven difficult to quantify. CRBP1 is endogenously lowly abundant and a poor immunogen, making traditional antibody-based detection schemes useless. To solve this problem, we developed a targeted proteomics approach for CRBP1 quantitation. We will utilize this approach to determine the impact of cellular stress on CRBP1 and retinoid signaling using in vitro models of small intestine epithelial cells and an in vivo model of small intestine inflammation. Taken together, these studies will help further our understanding of the mechanisms and impact of CRBP1 loss in disease.

6. CHARACTERIZING THE GENETIC ARCHITECTURE OF PARKINSON DISEASE IN LATINOS: A GENOME-WIDE ASSOCIATION STUDY

Douglas Loesch

Loesch, D. P., Horimoto, A. R. V. R., Sarihan, E. I., Inca-Martinez, M., Mason, E., Cornejo-Olivas, M., Torres, L., Mazzetti, P., Cosentino, C., Sarapura-Castro, E., Rivera-Valdivia, A., Medina, A. C., Dieguez, E., Raggio, V., Lescano, A., Tumas, V., Borges, V., Ferraz, H. B., Rieder, C. R., Schumacher-Schuh, A., Santos-Lobato, B. L., Velez-Pardo, C., Jimenez-Del-Rio, M., Lopera, F., Moreno, S., Chana-Cuevas, P., Fernandez, W., Arboleda, G., Arboleda, H., Arboleda-Bustos, C. E., Yearout, D., Zabetian, C. P., Thornton, T.A., O'Connor, T. D., & Mata, I. F.

Session B, Oral Presentation

Parkinson disease (PD) is the fastest-growing neurodegenerative disease, and as such places ever-increasing worldwide burden on healthcare systems. Despite its global impact, genome-wide association studies (GWAS) and meta-analyses have primarily been limited to individuals of European descent. On behalf of the Latin American Research Consortium on the Genetics of PD (LARGE-PD), we performed the first GWAS of Latin American PD subjects to date. We genotyped 1497 subjects (807 cases) from five South American countries with the MEGA chip from Illumina, followed by imputation using the TOPMed imputation server. We tested variants for association with PD using a generalized linear mixed model, adjusting for age, sex, the first 5 PCs, and relatedness. The SNCA locus achieved GWAS significance (p-value < 5x10-8) and a second locus near NRROS approached GWAS significance (p-value < 1x10-7). Out of 76 known PD risk variants, 83% had a consistent direction of effect and a correlation of 0.82 (p < 2x10-16) between estimated effect sizes. A polygenic risk score (PRS) constructed using the known PD risk variants had an area under the receiver-operator curve of 0.668, a balanced accuracy of 61.7%, a sensitivity of 52.1%, and a specificity of 71.3%. We observed remarkable heterogeneity of the PRS predictive performance by LARGE-PD recruitment site, highlighting the challenges of applying European-ascertained data on a non-European cohort. Overall, we found evidence for a significant, though far from complete, overlap in PD genetic architecture between European-ancestry and South American cohorts.

7. ASSESSMENT OF BEHAVIORAL PHENOTYPES IN D434G AND N999S MOUSE MODELS OF Kcnma1-LINKED CHANNELOPATHY

Cooper Roache

Roache, C.E., Park, S.M., & Meredith, A.L.

Session B, Oral Presentation

Kcnma1-linked Channelopathy is a disorder that is associated with the dysfunction of BK channels – a large-conductance voltage- and calcium-activated K+ channel. Kcnma1 encodes the pore-forming α-subunit of BK channels and are widely expressed across the body, including in the nervous and muscular systems. Within these systems, BK channels affect neuronal excitability and muscle contraction by mediating repolarization and afterhyperpolarization phases of action potential waveforms. In patients, Kcnma1 mutations are mainly associated with epilepsy and movement disorders. Kcnma1 knockout mice display tremors and ataxic movement, indicating an influence of BK channels on movement regulation. In addition, deletion of Kcnma1 in cerebellar Purkinje neurons show reduced basal firing activity, indicating changes in neuronal excitability within the brain area associated with movement regulation. This has been shown to be associated with the behavioral phenotypes of Kcnma1 knockout mice. Thus, CRISPR-generated mice with D434G and N999S Kcnma1 patient mutations were predicted to show altered performance in grip strength and locomotor assays. Locomotor function was assessed by a rotarod assay and grip strength by a hanging wire assay in which mice fall latency times were recorded. D434G mice showed no significant change in rotarod or hanging wire fall latency times compared to wild-type mice. However, N999S mice showed lower fall latency times during both assays compared to wild-type mice, indicating impaired grip strength and locomotor function. These data provide a baseline for characterizing and assessing behavioral phenotypes of patient mutations in mouse models for future investigations into treatment of Kcnma1-linked Channelopathy.

8. DIRECT MEDICAL AND MORTALITY RELATED COSTS AMONG COPD PATIENTS IN THE UNITED STATES

Chintal Shah

Shah, C. H., & Zafari, Z.

Session B, Oral Presentation

AIMS:This study aims to provide a nationally representative estimate of the economic burden of chronic obstructive pulmonary disease (COPD) by examining direct medical costs and mortality costs among individuals aged >=45 years in the United States (US).

METHODS:Data from the Medical Expenditure Panel Survey (2017-2018) and WONDER online tool were used to estimate the direct medical costs and mortality costs associated with COPD. COPD-related costs were determined by: 1) using the sum of disease-specific medical expenditures (attribution approach); and 2) calculating the incremental expenditures using a two-part regression (regression-based approach). For the attribution approach, we directly consolidated data from COPD-specific expenditures reported in MEPS. For the regression approach, we developed a two-part model with a logistic regression to estimate non-zero utilization and a generalized linear model with gamma distribution to estimate costs given a non-zero utilization. Mortality costs were determined using the value of statistical life approach.

RESULTS:The number of patient-years with COPD over two years in a total sample of 23,590 patient-years was 1,073. Among COPD patients, using the attributable approach, the mean annual COPD-related costs per patient were 2018 US $3,386 (Standard Error (SE): $276). Using the regression approach, the mean annual COPD-related costs per patient were $3954 (SE: $578). The mean out-of-pocket costs for COPD-related expenses was $255 (SE: 26) per patient-year. Mortality related costs associated with a COPD patient were estimated at $1,543.86 billion.

CONCLUSION:This study provides updated estimates of the economic burden of COPD among a nationally representative sample of individuals in the US.

9. CURRENT INTERVENTIONS FOR DIABETIC PERIPHERAL NEUROPATHY: DO THEY REDUCE FALL RISK? A SYSTEMATIC REVIEW

Nesreen Alissa

Alissa, N., Westlake, K. P., & Zilliox, L.

Session C, Poster Presentation

Background: Diabetic peripheral neuropathy (DPN) is the most common complication of diabetes, occurring in 50% of diabetics. People with DPN are 15 times more likely to report injury following a fall and feel significantly less safe during standing and walking. Balance training and fall prevention are essential elements of any rehabilitation program for people with DPN.
Objective: To identify rehabilitation interventions with the highest impact on fall-risk outcomes.
Methods: We conducted a systematic review of studies investigating the effects of active rehabilitation interventions on fall-related outcomes in people with DPN. Our search revealed eleven studies fitting the inclusion criteria. Fall risk was identified using fall risk cut-off scores validated in healthy older adults.
Results: Only one active rehabilitation intervention study assessed falls throughout the intervention and prospectively over 6 months. Eleven studies assessed changes in fall risk outcomes from pre- to post-intervention. Fall risk outcome scores fell below their respective fall risk cut offs in the majority of studies. According to established cut-off scores, only two studies resulted in reduced fall risk.
Conclusions: Active rehabilitation interventions improve walking speed, strength, and other static balance tests, however, their effect on fall risk and prospective fall rates remain unclear. Most participants included in these studies were not at risk of falls prior to the intervention, therefore, it is difficult to truly determine

whether these interventions are capable of reducing fall risk. In addition, few studies have prospectively examined the long-term effects of these interventions on balance control and fall rates.

10. INFLUENCE OF ANXIETY-PROVOKING MENTAL STRESS TASK ON REACH TO GRASP BALANCE RESPONSE IN OLDER ADULTS

Ruth Akinlosotu

Akinlosotu, R., Alissa, N., & Westlake, K.

Session C, Poster Presentation

Background: Reach to grasp responses following balance perturbations are important to fall prevention but are often ineffective in older adults. This study aimed to investigate the effect of varied emotional-cognitive stress states on reach to grasp balance responses in older adults.
Methods: 23 healthy older adults (70.5±5.38 years) stood between 2 handrails. A safety harness with integrated loadcell was worn to prevent falls and measure the amount of harness assistance (expressed as percent body weight). With instructions to grasp one rail to restore balance, participants' balance was laterally perturbed using surface translations under three randomly tested conditions: no cognitive task, neutral (verb generation) task, and mental stress task with negative prompts (paced auditory serial addition). Subjective Units of Distress Scores were collected during each condition. The primary outcome was percent stabilizing grasps. Secondary outcomes included percent harness assistance during trials with grasp errors as well as wrist movement time, trajectory distance, and peak velocity.
Results: Perceived level of stress was highest for the mental stress task compared to no task ($p=0.0002$) and neutral task conditions ($p=0.008$). The mental stress condition resulted in the lowest percent of stabilizing grasps ($p = <0.0001$). During trials resulting in grasp errors (i.e., collisions or overshoots), participants required the greatest amount of harness assistance and demonstrated reduced peak velocity of wrist movement ($p=0.0001$) under the mental stress condition.
Discussion and Conclusion: Anxiety provoking cognitive tasks lead to reduced effectiveness of reach to grasp balance responses and should be considered during balance assessment and rehabilitation approaches.

11. THE IMPACT OF COVID-19 ON THE ILLICIT DRUG RELATED DEATHS IN THE STATE OF MARYLAND

Alexis Cirko, Kaitlyn Gencarelli, Fahren Nipple, & Jasmine Solano

Cirko, A., Gencarelli, K., Nipple, F., Solano, J., & Ling, L.

Session C, Poster Presentation

As of March 5, 2021, the 2019 novel coronavirus disease (COVID-19) has caused 2,560,995 deaths worldwide including 533,641 deaths in the United States. While the rising number of COVID-19 deaths have been the news headlines since last year, illicit drug overdose deaths have become another national crisis during the pandemic. The study was to compare the trend and pattern of illicit drug deaths between 2019 and 2020 in Maryland and to evaluate the impact of COVID-19 on the illicit drug related deaths. The Office of the Chief Medical Examiner (OCME) is responsible for medicolegal death investigation of all the non-natural deaths including drug overdose deaths. A retrospective review of all deaths investigated by OCME revealed that there was a 13% increase in illicit drug deaths in Maryland from 2019 to 2020 (N=2268 vs N=2608). More males than females and more African Americans than the other racial groups died of illicit drug overdose based the death rate per 100,000 population. The average number of illicit drug deaths was 189 cases/month in 2019, 206 cases/month prior to pandemic (Jan-March, 2020), a slight drop in April 189 cases during the stay-at-home period, and significant increase 225 cases/month from May to December, 2020.

Fentanyl/fentanyl mixed with other drugs (N=1905 in 2019; N=2298 in 2020, a 17% increase) were the leading cause of illicit drug death, followed by cocaine and heroin/morphine. There was 32% increase in methadone related deaths in Maryland in 2020. Our study showed that COVID-19 pandemic has accelerated overdose deaths in Maryland.

12. POPULATION PHARMACOKINETIC AND PHARMACODYNAMIC MODELING OF HEPARIN IN PEDIATRIC PATIENTS

Ahmed Salem

Salem, A., Moffett, B., Ivaturi, V., & Gopalakrishnan, M.

Session C, Poster Presentation

Unfractionated heparin (UFH) is commonly used anticoagulant in pediatrics due to its short half-life and ease reversibility by protamine sulphate. Current UFH pediatric dosing is challenging and lead to suboptimal outcomes due to lack of pharmacokinetic/pharmacodynamic (PK/PD) pediatric studies and extrapolation of dosage recommendations from adults. The aim of this analysis is to develop a PKPD model of UFH PK, quantified by anti-factor Xa activity, and UFH effect measured as activated partial thromboplastin time (aPTT). Retrospective data including UFH PK, PD and demographics were collected from 633 patients < 19 years old who were admitted to Texas Children's Hospital. Model building was done using 70% of the data while 30% were reserved for model evaluation. Modeling was performed using population approach. A one-compartment model with linear elimination with allometric scaling of weight on Clearance (CL) and volume of distribution (Vd) adequately described UFH PK. An age-dependant maturation function was added to Vd. The typical values of CL and Vd for patient weighing 50 kg is 3.28 L/hr and 8.89 L, respectively. a linear model adequately described UFH-aPTT relationship with estimated intercept of 26.8 seconds and slope of 0.15. The mean absolute percentage error for the PK and PK/PD validation dataset were 28.17% and 18.82%, respectively indicating adequate model predictive performance. A comprehensive population PKPD model of UFH was developed including the whole pediatric age range. The developed model will be used to assess the current pediatric dosage recommendations as well as alternative regimens that could lead to higher therapeutic success.

13. EXPLORING RELATIONSHIPS BETWEEN INSPIRATORY MUSCLE STRENGTH AND FUNCTIONAL CAPACITY IN CHILDHOOD CANCER SURVIVORS: A PILOT STUDY

Simon Ho

Ho, S., York, T., & Marchese, V.

Session C, Poster Presentation

Childhood cancer survivors (CCS) often experience side effects from cancer treatment that impair functional capacity. Inspiratory muscle weakness has been suggested as a potential mechanism for reduced functional capacity in adult survivors of cancer. However, this mechanism has not been well-studied in CCS. The objective of this pilot study was to explore the relationship between inspiratory muscle strength and functional capacity in 10 CCS. Inspiratory muscle strength was measured by maximal inspiratory pressure (MIP) while functional capacity was measured by the two-minute walk test (2MWT), the physiological cost index (PCI) and hemodynamic response to exercise according to changes in heart rate, pulse pressure and rate-pressure product (RPP). Overall, participants' performance in MIP ($p < 0.001$) and 2MWT ($p = 0.005$) was significantly poorer compared to published normative reference values according to age and sex. MIP had a significant

positive relationship with post-activity pulse pressure (Spearman's rank correlation coefficient [rs] = 0.63; p = 0.026). Time since completion of cancer treatment had a significant positive relationship with PCI (rs = 0.59; p = 0.036), heart rate response (rs = 0.59; p = 0.036) and RPP reserve (rs = 0.66; p = 0.018). Our results demonstrate that Inspiratory muscle strength and functional capacity are both impaired in CCS and that a clear relationship exists between these two measures. Inspiratory muscle weakness in childhood cancer should be considered when symptoms of poor functional capacity such as dyspnea arise. Future studies should investigate the effects of inspiratory muscle training in CCS.

14. THE EFFECTS OF 50K ULTRAMARATHON RUNNING ON QUADRICEPS TORQUE AND CIRCULATING INFLAMMATORY CALPROTECTIN

Katie Dondero

Dondero, K.R., Hankerson, I., Nelson, C.M., Prior, S.J., Addison, O., & Landers-Ramos, R.Q.

Session C, Poster Presentation

Purpose: Determine the effects of prolonged running on quadriceps strength and plasma calprotectin levels and examine the relationship between these two factors. Methods: Trained men and women (n=11) age 39 +-7 years participated in a 50k trail run consisting of five 10k laps. Seated knee extensor force was measured before the race, after each lap, immediately post-race and 24h post-race using a hand-held dynamometer. Quadriceps torque (N.m.) was calculated by multiplying tibial length by force. Blood was drawn 30 minutes after participants finished eating their pre-race meal, after the first lap (10k), within 60 minutes of finishing the race and 24h post-race. Plasma calprotectin was measured using an enzyme-linked immunosorbent assay (ELISA). Results: Quadriceps torque did not significantly change from pre-race to lap 1 (P=0.64), but significantly declined post-race (-10%; P=0.047) and returned to pre-race values by 24h post-race (P=0.1). Compared with lap 1, quadriceps torque declined significantly by lap 2 (-9%; P=0.024) but remained unchanged from lap 2 through post-race (P>0.05 for each timepoint). Plasma calprotectin increased 63% at lap 1 (P=0.003), 83% post-race (P=0.001), and returned to pre-race values 24h post-race (P=0.66). Conclusion: The ultrarunners experienced an acute decline in quadriceps torque that coincided with an acute increase in plasma calprotectin concentrations. Both torque and plasma calprotectin returned to pre-race values after 24h. The relationships between calprotectin levels and muscle torque suggest a potential novel role for calprotectin in muscle recovery from an ultramarathon.

15. THE OTHER CAREGIVERS: NON-SPOUSAL MALE INFORMAL CARE PARTNERS FOR PERSONS WITH ALZHEIMER'S DISEASE AND RELATED DEMENTIAS

Gretchen Tucker

Tucker, G. G.

Session C, Poster Presentation

Informal care partners (ICPs) have become an integral part of the long-term care system. ICPs are relied on to provide day-to-day care that is challenging, complex, and often expands several years. The majority of research on informal care partners of persons with Alzheimer's disease and related dementias (ADRD) have focused on spousal caregiving, mother-daughter dyads, and daughters. There is sparse research on non-spousal male ICPs for persons with ADRD. This descriptive qualitative pilot study consisted of in-depth one-on-one interviews with three non-spousal ICPs. Participants consisted of a grandson, son, and former son-in-law. Based on data analysis, there were four primary themes: 1) the male perspective and experience

of caregiving, 2) relationship dynamics, 3) caregiving challenges, and 4) finding meaning within caregiving. Findings suggest that male non-spousal ICPs provide similar assistance as female non-spousal ICPs such as transportation, management medical appointments, and intimate care such as bathing. Beyond the type of care provided, participants discussed gender roles as it related to the types of care they were or were not willing to provide. Implications from the findings are to inform public policies, support services, and medical professionals about the different needs of male non-spousal ICPs and to consider how they may include the ICPs as part of the care recipient's team of care.

16. A DESCRIPTION OF STAFF-RESIDENT INTERACTIONS IN ASSISTED LIVING

Anju Paudel

Paudel, A., Galik, E., Resnick, B., Doran, K., Boltz, M., & Zhu, S.

Session C, Poster Presentation

Background: Positive social and care interactions are vital to understand and successfully accomplish the daily care needs of the residents in assisted living (AL) and optimize their quality of life. Aim: The purpose of this study was to explore and describe the staff-resident interactions in AL. Method: This descriptive analysis utilized baseline data in a randomized trial that included 379 residents from 59 AL facilities. Results: The majority of the interactions observed were positive; almost 25% were neutral or negative. Most interactions were care-related (31.9%) or one-on-one (27.4%), occurred with nursing (40.2%) or support staff (e.g. dining aide; 24.6%), and involved close interpersonal distance (64.6%). Conclusion: Future research should focus on the transition of neutral or negative interactions to positive and explore the factors that might influence neutral and negative interactions. Additionally, innovative approaches are needed to optimize interactions amid physical distancing in the context of the COVID-19 pandemic.

17. IN VIVO EVALUATION OF KNEE MENISCI STIFFNESS DURING DIFFERENT LOADING CONDITIONS USING SHEAR WAVE ELASTOGRAPHY: PILOT STUDY

Raziyeh Baghi

Baghi, R., Huang, M., & Zhang, L.

Session D, Poster Presentation

Background: Meniscal extrusion, the extension of the meniscus beyond the edge of the tibiofemoral joint line, is an independent predictor of osteoarthritis (OA) progression. However, the change from supine to standing, described as dynamic extrusion, is secondary to the changes of elastic properties of the meniscus. Therefore, evaluation of elastic properties of meniscus helps with the earlier detection of knee OA. There is no in vivo study evaluating normal response of the knee components to different loading conditions during daily activities. This study was performed to assess the feasibility of shear wave elastography (SWE) in the evaluation of knee menisci stiffness during rest versus weight bearing.
Method: Six healthy subjects (4 female; 18-35 years old) without history of lower limb injury participated in this study. Knee alignment was measured using a manual goniometer in supine (rest) and standing (weight bearing) positions. Medial longitudinal arch was measured in standing position. SWE measurements of medial and lateral menisci were conducted at supine and standing (double-leg (DS) and single-leg (SS)) positions. Three-way Friedman test was used to compare stiffness quantity between different positions.
Results: All subjects had normal knee alignment. Due to small sample size, no correlation between menisci stiffness and knee alignment could be found. Both medial and lateral menisci showed higher stiffness in DS versus rest position.

Conclusion: Menisci stiffness increases from supine, double-legs standing to single-leg standing

18. HDX-MS GUIDED MODELING AND ENSEMBLE REWEIGHTING APPROACH TO CHARACTERIZE THE STRUCTURE AND DYNAMICS OF CYTOPLASMIC HEME BINDING PROTEIN PhuS

Kyle Kihn

Kihn, K., Wintrode, P., & Deredge, D.

Session D, Poster Presentation

Hydrogen-deuterium exchange coupled with mass spectrometry (HDX-MS) has established itself as a valuable biophysical approach offering meaningful insights into protein structure and dynamics. Recent efforts have aimed to integrate HDX-MS with computational approaches to provide atomistic interpretation of the structural dynamics information garnered. Recently, an HDX-MS based maximum entropy reweighting approach (HDXer) was developed to reweight computationally generated ensembles using HDX-MS data towards high resolution ensemble description of proteins. Here, HDX-MS is used together with enhanced molecular dynamics simulations and HDXer to characterize the structural dynamics of PhuS, a cytoplasmic heme binding protein from P.aeruginosa. Functionally, PhuS shuttles exogenous heme to Heme Oxygenase (HemO) for degradation. Although the crystal structures of unliganded (apo) and heme bound (holo) PhuS are nearly identical, HDX-MS of apo vs holo PhuS revealed large differences in deuterium uptake, notably in C-terminal proximal alpha helices 6, 7 and 8 (a6/7/8). These helices form part of the heme binding pocket and were observed to be mostly labile in apo-PhuS but were largely protected in holo-PhuS. In contrast, the predicted deuterium uptake of a6/7/8 in apo- and holo-PhuS obtained from MD simulations are highly similar to one another and in agreement with the HDX-MS data obtained for holo-PhuS, suggesting that the solution structure of apo-PhuS locally deviates from its crystal structure conformation. The combined use of enhanced sampling MD, HDXer and dimensional reduction reveals an apo-PhuS ensemble in which there is a loss of secondary structure in a6 and the rotation of a7 towards the HemO binding interface.

19. PATHOGENESIS OF SALMONELLA SEROGROUP C1 SEROVARS

Shanaliz Natta

Natta, S. S., Nasrin, S., Sears, K. T., & Tennant, S. M.

Session D, Poster Presentation

Non-typhoidal Salmonella (NTS) are facultative, Gram-negative pathogens that are the leading cause of foodborne infections globally. NTS is responsible for causing gastroenteritis in healthy individuals and invasive disease in infants, the elderly, and HIV-infected patients. Salmonella serogroups B (e.g., serovar Typhimurium) and D (e.g., serovar Enteritidis) are recognized as the most common causes of NTS infections (make up ~60% of NTS infections). However, serogroup C (C1 and C2-C3) are also responsible for a large burden of disease (make up ~30% of NTS infections). In particular, S. Choleraesuis (serogroup C1) has a high predilection for causing invasive disease in humans. We hypothesize that Salmonella serogroup C1 strains possess different pathogenic characteristics than strains of other serogroups. In particular, we hypothesize that they are taken up by macrophages more efficiently and replicate within macrophages more effectively than strains from other serogroups; thereby evading the immune system. A gentamicin killing assay was performed to measure bacterial uptake and intracellular replication using J774 and RAW 264.7 murine macrophage cells. We observed that strains of serogroup C1 were taken up at higher levels by J774 murine macrophage cells than strains of other serogroups, however, there was no difference in intracellular survival

over 20 hours between the serogroups in RAW 264.7 cells. We then evaluated the growth kinetics of S. Typhimurium and S. Choleraesuis in bacteriological media. We performed viable counts and found that S. Typhimurium grew similarly to S. Choleraesuis. In conclusion, my data shows evidence that Salmonella serogroup C1 serovars are more readily phagocytosed than serovars of other serogroups suggesting that these bacteria do indeed possess unique pathogenic mechanisms.

20. DECIPHERING THE LOGIC OF T CELL ACTIVATION BY CONTROLLED PERTURBATION OF SIGNALING FLUX

Zachary Fasana

Fasana, Z., & Singh, N.

Session D, Poster Presentation

To initiate a response, a naïve T cell's receptor engages with antigen presented on major histocompatibility complex and initiates intracellular signals leading to cytokine secretion and cell division. The initial signaling involving a SRC kinase (LCK) soon branches into multiple sub-cascades including PI3K/AKT/mTOR, Calcium-NFAT, PKC-NFKB, and RAS-MAPK. The downstream signal transducer of the RAS-MAPK pathway extracellular-signal-regulated kinase (ERK) is of particular interest to because of its central role in multiple cellular processes. For instance, ERK inhibitors influence the differentiation and expression of IL-4 and IFNgamma by T cells, as well as the induction of master transcription factors for T cell differentiation (GATA3, Tbet, and Foxp3). In model systems, the precise timing, duration and intensity of ERK signals all have differential influences on cell fate. We therefore hypothesized that multiple cell fate decisions in T cell differentiation are also controlled similarly by the dynamics of ERK signals. To evaluate this hypothesis, we need to dissect how RAS-MAPK contributes to each of the precisely orchestrated processes in T cell activation. We therefore designed an approach which utilizes a doxycycline-inducible system to precisely drive the expression of constitutively active and dominant negative mutants of RAS in T cells. This would allow us to finely regulate the strength of flux through RAS-MAPK with temporal precision by administering doxycycline at varying doses and timepoints. To validate this approach, we employ this system in an in vitro model of T cell activation to assess the biochemical and cellular phenotypes influenced by RAS-MAPK during T cell activation.

21. NADPH OXIDASE 2-MEDIATED REACTIVE OXYGEN SPECIES ARE REQUIRED FOR OSTEOCYTE MECHANO-TRANSDUCTION, SCLEROSTIN REGULATION, AND MECHANICALLY-INDUCED BONE FORMATION

Nicole Gould

Gould, N.R, Joca, H.C., Williams, K.M., Lyons, J.S., Hughes, M., Khairallah, R.J., Ward, C.W., & Stains, J.P.

Session D, Poster Presentation

The Wnt/b-catenin antagonist, sclerostin, is critical to controlling load-induced bone formation. Bone-embedded osteocytes reduce sclerostin abundance following mechanical stress, lifting the inhibition of osteoblasts, allowing them to form new bone. Despite the physiological importance, little is known about how sclerostin abundance is controlled in response to mechanical load. We have described a novel osteocyte mechano-transduction pathway in vitro that controls sclerostin abundance through production of reactive oxygen species (ROS) by NADPH Oxidase 2 (NOX2), which triggers calcium influx and the subsequent activation of calcium/calmodulin kinase II (CaMKII), ultimately leading to sclerostin degradation. Here, we

show that inhibition of NOX2-dependent ROS production with gp91-dsTAT prevented mechanical stress-induced calcium influx, CaMKII activation, and sclerostin degradation in cultured osteocytes. Conversely, controlled production of ROS using a photoactivated reagent, KillerRed, in vitro was sufficient to drive CaMKII activation and sclerostin degradation. To model this ex vivo, hydrogen peroxide treatment of intact bones mimicked mechanical stress, resulting in sclerostin degradation. To examine the relevance of NOX2-dependent ROS to load-induced bone formation in vivo, we used a mouse ulnar loading model to stimulate mechano-activated bone formation. We show treatment with apocynin, a NOX2 inhibitor, significantly decreased new bone formation following ulnar loading and blunted the load-induced degradation of sclerostin. Together, these data validate the fidelity of the novel osteocyte mechano-sensing pathway in vivo, provide key insights into osteocyte mechano-transduction and the control of sclerostin, and reveal new therapeutic targets to improve bone mass.

22. PHARMACOLOGIC INDUCTION OF INNATE IMMUNE SIGNALING SUPPRESSES METASTASIS IN TRIPLE-NEGATIVE BREAST CANCER

Julia Rutherford

Rutherford, J. L., McLaughlin, L. J., Topper, M. J., Baylin, S. B., & Rassool, F. V.

Session D, Poster Presentation

Poly (ADP ribose) polymerase inhibitors (PARPi) are FDA-approved for BRCA1/2-mutant triple negative breast cancer (TNBC) and target homologous recombination deficiencies (HRD). DNA methyltransferase inhibitors (DNMTi) increase innate immune signaling in tumors, and when combined with PARPi, cause a broad innate immune response that generates HRD, sensitizing BRCA-proficient cancers to PARPi. We now define the role of treatment-induced innate immune signaling in the tumor on mechanisms of metastasis suppression. This treatment causes decreases in WNT pathway gene expression, as well as protein level decreases in the key WNT effector, β-catenin. Though the WNT pathway is known for its role in cell proliferation, recent studies show that reduction in WNT signaling suppresses invasion. WNT activation was reported to be involved in immunosuppression and immune cell exclusion in the primary tumor microenvironment and was also involved in the programming of immune cells that contribute to premetastatic niche formation, a tumor-favorable environment in a secondary organ. This formation is supplemented by immunosuppressive cells, such as myeloid-derived suppressor cells (MDSCs).

23. BONE-ACTIVE MEDICATION UTILIZATION FROM 2013 TO 2017 AMONG BENEFICIARIES AGED 65+ WITH MEDICARE PART D BY PROVIDER TYPE

Jennifer Kirk

Kirk, J.M., Fleming, S., & Orwig, D.

Session E, Poster Presentation

As the United States' population increasingly consists of older adults aged 65+, an increase is expected in the prevalence of osteoporosis and the number of osteoporotic fractures. Bone-active medications (BAM) delay osteoporosis progression and prevent fragility fractures, but historically low BAM treatment persistence and drug utilization rates exist among at-risk older adults. This research assessed for differences in the BAM utilization rates over five-years in Medicare Part D by provider type: geriatric specialists (GERO), generalists, specialists, nurse practitioners (NP), and physicians' assistants (PA). This longitudinal retrospective analysis included providers with at least one BAM prescription among beneficiaries aged 65+. An analysis of response

profiles was used to model the mean BAM utilization rates overall and by provider group. Of the 50,249 providers included in this analysis, 88.15% were generalists, 5.76% specialists, 1.48% GERO, 2.73% NP, and 1.87% PA. From 2013-2017, the prevalence of BAM utilization was 6%. Over the five years, BAM utilization rates did not change significantly, but provider-specific rates were significantly different ($F=12.53$, $p<.001$). Provider-specific utilization rates were inconsistent with the highest utilization rates and most considerable variation observed among specialists (14.95%). PAs and NPs' BAM utilization rates were stable at around 9.02% and 9.20%, but GERO and generalists exhibited the lowest utilization rates, 4.86% and 5.79%, respectively. While specialists had the higher-than-expected utilization rates, the overall and provider-specific BAM utilization rates were low and did not increase over time. Further research is needed to identify how provider-related factors, like geographic region and clinical training, influence underutilization.

24. MINIMALLY-INVASIVE DENTISTRY VIA DUAL-FUNCTION NOVEL BIOACTIVE LOW-SHRINKAGE-STRESS FLOWABLE NANOCOMPOSITE

Ebtehal Albeshir

Albeshir, E. G., Balhaddad, A. A., Mitwalli, M., Melo, M. A. S., Wang, X., Sun, J., Weir, M. D., & Xu, H. K.

Session E, Poster Presentation

Minimally-invasive treatment is trending to handling caries lesions with a conservative approach to preserve maximum tooth structures. The objectives of this study were to develop a novel low-shrinkage-stress flowable nanocomposite with antibacterial and remineralization properties through the incorporation of dimethylaminohexadecyl methacrylate (DMAHDM) and nanoparticles of amorphous calcium phosphate (NACP), and investigate the mechanical and oral biofilm properties.

Methods:

The light-cured resin was formulated by mixing urethane dimethacrylate (UDMA) and triethylene glycol divinylbenzyl ether (TEG-DVBE).DMAHDM, NACP and glass were incorporated. Flowability test, microtensile strength and surface roughness were evaluated. The antibacterial response of DMAHDM was assessed by using biofilms of human saliva-derived microcosm model. (Virtuoso) was used as a commercial control composite.

Results:

The formula with 45% resin + 5% DMAHDM + 20% NACP + 30% glass had flow rate of (25.0 ± 0.7) mm within the range of ISO requirement. The microtensile was (39.1 ± 4.3) MPa, and the surface roughness was (0.09 ± 0.01) μm, no statistical difference with the commercial control ($p > 0.05$). Human saliva microcosm biofilm colony forming units (CFU) value was reduced by 5-6 logs ($p < 0.05$). Biofilm metabolic activity was also substantially reduced by using NACP and DMAHDM, compared to control composite ($p < 0.05$).

Conclusions: The novel bioactive low-shrinkage-stress flowable nanocomposite achieved strong antibacterial activity without compromising the mechanical properties. This nanocomposite is promising to be used in preventable measures as a pit and fissure sealant, and as a composite in conservative cavities to inhibit recurrent caries and increase restoration longevity.

25. EFFECT OF INTELLIGENT STRETCHING OF SPASTIC ELBOW IN STROKE SURVIVORS

Sanjana Rao

Rao, S., Huang, M., & Zhang ,L.Q.

Session E, Poster Presentation

Upper limb problems, including muscle spasticity, contracture, and weakness, are common after stroke. Elbow joint is one of the frequently and chronically affected structures with a manifestation of reduced range of motion (ROM) and weakness, which significantly impacts activities of daily living. Therefore, management of upper limb motor impairment has been identified as a top priority by stroke survivors, caregivers, and clinicians. The purpose of this study was to assess the immediate effects of strenuous dynamic stretching of elbow joint performed with help of an intelligent stretching device in chronic spastic stroke survivors. The intelligent stretching device could provide intensive and repetitive stretching to the spastic elbow joint in sagittal plane (i.e., flexion and extension) to its extreme positions safely, with control of the stretching velocity and resistance torque to increase ROM, reduce spasticity and joint stiffness. Eight chronic stroke survivors (52.6±8.2 years old, 5 males/3 females) completed a single hourly intervention session. Elbow active and passive ROM, strength and instrumented biceps and triceps tendon tapping test (quantifying the reflex component of the spasticity) were measured before- and after-stretching. Post stretching, there was a significant increase in active ROM of elbow flexion($p=0.026$) and extension ROM($p=0.021$). Also, the spastic elbow flexors showed a trend of an increase in their strength. Since the intelligent stretching had a positive influence on the ROM and strength, it may potentially be used to stretch spastic elbow joints repeatedly and regularly and thereby reduce impairments of stroke survivors and burden on clinicians or therapists.

26. SEX DIFFERENCE IN ALL-CAUSE AND INFECTION-SPECIFIC MORTALITY OVER 10 YEARS POST HIP FRACTURE

Rashmita Bajracharya

Bajracharya, R., Magaziner, J.S., Guralnik, J.M., Shardell, M.M., Rathbun, A.M., Yamashita, T., & Orwig, D.L.

Session E, Poster Presentation

Men die at a twice higher rate than women in the first two years after hip fracture and also experience higher infection-related mortality. Most research has only looked at differences in short-term mortality after hip fracture. The objective was to determine if cumulative incidence of all-cause and infection-specific mortality is higher in men compared to women over ten years. Data came from Baltimore Hip Studies7th cohort. Women were frequency-matched (1:1) to men on timing of fracture to ensure equal numbers of men and women. The association of sex and all-cause mortality was analyzed using Cox proportional hazard model and a cause-specific hazard model for infection-specific mortality. Both models controlled for age, cognition, comorbidity, depressive symptoms, BMI, and pre-fracture ADL limitations. Complete-case sample size was 300 (men=145, women=155). By the end of ten years from the date of hip fracture admission, there were 237 (men=132, women=105) all-cause deaths and 38 (men=25, women=13) infection-specific deaths. Men had significantly higher all-cause mortality risk [73.7% vs 59.3%; HR=2.31(2.02-2.59)] and infection-specific mortality [17.2% vs 8.3%; HR=4.43(2.07-9.51)] compared to women. In addition to sex, older age, cognition, and comorbidities were associated with all-cause mortality whereas only BMI was associated with infection-specific mortality in adjusted models. Men had a significantly higher risk of mortality over 10 years compared to women, specifically two-fold higher risk of infection-specific mortality compared to all-cause mortality. Further research is needed to explain the sex differences in order to implement targeted interventions to reduce long-term mortality rates in men.

27. FALL-RELATED WORRY AND INSOMNIA SYMPTOMS IN OLDER ADULTS

Lori Anderson

Anderson, L. A., Parisi, J. M., & Spira, A. P.

Session E, Poster Presentation

Introduction: Falls are common among older adults and put them at significant risk for poor health outcomes, including mortality, but little is known about the association between fall-related worry and insomnia symptoms in this population. We investigated this association in a large sample of community dwelling older adults.
Methods: We studied 8,245 participants from the 2011 wave of the National Health and Aging Trends Study (NHATS), a nationally representative cohort study of Medicare beneficiaries. Our primary predictor was fall-related worry. Our outcome was insomnia severity, measured as significant insomnia or no significant insomnia..
Results: Participants were grouped into three age categories (65-74, 75-84, 85+) (modal age category = 65-74; 55%); 57% were women and 82% were non-Hispanic White. Overall, 2,251 participants (27%) reported worrying about falling down. Overall, 21% had significant insomnia. In unadjusted analyses, fall-related worry was associated with greater odds of significant insomnia (OR = 2.20, 95% CI: 1.88, 2.59, $p<0.001$). After adjustment for age, race, gender, education, number of health conditions, and depressive and anxiety symptoms, fall-related worry was associated with greater odds of insomnia (OR = 1.42, 95% CI: 1.20, 1.70, $p<0.001$).
Conclusion: After adjusting for potential confounders, fall-related worry is associated with greater odds of insomnia. Greater attention to fall-related worry may help address insomnia in older adults.

28. RECTUS FEMORIS MUSCLE ACTIVATION AND THE RELATIONSHIPS WITH GROSS MOTOR PERFORMANCE IN CHILDREN AND YOUNG ADULTS

Kelly Rock

Rock, K., Gray, V., Lanza, M.B., & Marchese, V.

Session E, Poster Presentation

Gross motor performance in children requires strength and quick, coordinated movements. However, the relationship between neuromuscular activation and gross motor performance in children is not well defined. This study examined maximum quadriceps torque measured by handheld dynamometry and rectus femoris neuromuscular activation measured through rate of activation (RoA) and mean frequency (MNF) measured by electromyography (EMG) during knee extension contractions in healthy school-aged children compared to adults. Additionally, we explored the relationships between maximum torque, RoA, and MNF with gross motor performance as measured by a 15-second two-legged side hop task. Participants were grouped by age, younger children (YC; aged 6 to 8 years; n=6), older children (OC; aged 9 to 11 years; n=10), and adults (aged 19 to 26 years; n=6). The participants performed isometric knee extension contraction to measure maximal torque, early RoA across 50-ms epochs (RoA50-RoA200), and MNF. Maximal torque, normalized to muscle thickness, was lower in YC compared to OC and adults ($p<0.05$). RoA, normalized to the maximal EMG amplitude, was lower among YC and OC compared to adults (RoA150 and RoA200; $p<0.05$). YC performed fewer two-legged hops compared to adults ($p<0.05$). There were significant positive correlations between RoA150 and RoA200 and gross motor performance ($p<0.05$). There were no significant relationships between normalized maximal torque or MNF. Therefore, early and rapid quadriceps muscle activation may be important for gross motor proficiency. Exercise testing and prescription should consider the neuromuscular challenges of tasks that require rapid muscle activation such as agility training.

29. THE IMPACT OF COVID-19 PANDEMIC ON DEATHS DUE TO MOTOR VEHICLE ACCIDENT IN THE STATE OF MARYLAND

Van Anh Nguyen, Paige Cephas, Sarah Pribil, & Flora De Mari Quiroz Moreyra

Nguyen, V. T., Quiroz Moreyra, F. M., Pribil, S. L., Cephas, P. Q., & Ling, L.

Session E, Poster Presentation

This study was to analyze the effects of the COVID-19 pandemic in Maryland on fatal motor vehicle accidents (MVA). This is a retrospective study of MVA related deaths investigated by the Office of the Chief Medical Examiner (OCME) in Maryland from January 2019 to December 2020. Our study yielded a total of 952 fatal MVA cases, 440 cases in 2019 and 512 cases in 2020. Of the 440 cases in 2019, 250 (57%) were drivers (including 13% motorcyclists); 9 (2%) bicyclists; 75 (17%) passengers and 106 (24%) pedestrians. Of 512 cases in 2020, 310 (60) were drivers (including 14%) motorcyclists); 10 (2%) bicyclists; 55 (13%) passengers, and 137 (27%) pedestrians. Of the 560 driver fatalities, there were more whites than African Americans and more males than females. In 2019, more fatal MVA driver deaths occurred in August, September and October (40-49 deaths per month) and less driver deaths in January and December (25-28 deaths per month). While in 2020, more fatal MVA driver deaths occurred in July, August and October (57-68 deaths per month) and less driver deaths in January (N=17) and December (N=20). There was a 20% decrease in the number of fatal MVA driver deaths when comparing April 2019 (N=35) and April 2020 during the state-at-home period (N=28). Of the 243 pedestrian fatalities, in 2019, September had the most deaths (N=14) and March had the least deaths (N=3). In 2020, October had the most deaths (N=17) and April had the least deaths (N=6) during the state-at-home period.

30. AGING INDUCES ASYMMETRIC TRAFFICKING OF PDE11A4 IN THE VENTRAL HIPPOCAMPUS

Sophie Bruckmeier

Bruckmeier, S. R., Pilarzyk, K. N., & Kelly, M. P.

Session F, Poster Presentation

The brain, especially the hippocampus (HIPP), exhibits molecular and morphological hemispheric asymmetries both in the context of regular function and disease. Our lab studies the function of an enzyme that is almost exclusively expressed in the HIPP, phosphodiesterase 11A (PDE11A). PDE11A degrades cyclic nucleotides (cAMP and cGMP), but it is not yet known if it may contribute to hippocampal asymmetries. We have found that PDE11A mRNA expression increases with age in the human HIPP. In mice, we see PDE11A protein expression also increases with age and increasingly accumulates in filamentous “structures” resembling axons. Here, we aim to determine if these age-related increases in PDE11A accumulation occur asymmetrically. Aged C57BL/6J mice not only show more PDE11A-filled structures in the HIPP than do young mice, they also exhibit a greater number of PDE11A-filled structures in the right vs left HIPP. Such an asymmetry was not found in the young C57BL/6J mice. To determine if high PDE11A expression levels are sufficient to drive asymmetries in PDE11A accumulation, we quantified PDE11A-filled structures in young BALB/cJ mice that express as many PDE11A-filled structures as do old C57BL/6J mice. Despite showing a high number of PDE11A4-filled structures in the HIPP, young BALB/cJ mice showed an equal number of PDE11A-filled structures in the right vs. left HIPP. Together, these data suggest that the PDE11A asymmetries observed in aged C57BL/6J mice are not simply driven by higher levels of expression and/or accumulation, but rather by some other age-related mechanism as yet to be determined.

31. A SOLUTION HDX-MS APPROACH IN PROBING THE STRUCTURE AND DYNAMICS OF THE DENGUE NONSTRUCTURAL PROTEIN 5

Juliet Obi

Obi, J.O., Kihn, K.C., & Deredge, D.J.

Session F, Poster Presentation

The number of people infected with dengue virus has increased steadily in recent decades due to a geographical expansion of mosquito vectors, including those that cause dengue fever (DF), making DF a major global health concern. There is no specific treatment for dengue fever currently available, therefore research efforts need to be intensified in the development of antiviral drugs and design of vaccines against the dengue virus. The nonstructural protein 5 (NS5) is highly conserved among flaviviruses. The dengue virus serotype 2 (DENV2) NS5 is a multifunctional protein with an N-terminal methyltransferase, and a C-terminal RNA-dependent-RNA-polymerase (RdRp). The dual enzyme activity of this NS5 protein, and its essential role in dengue viral RNA replication, makes it an attractive antiviral target for the treatment of dengue infection. Hydrogen deuterium exchange coupled to mass spectrometry (HDX-MS) has proven to be a powerful biophysical approach, used to study protein structure and dynamics. We employed solution HDX-MS analysis to probe solvent accessibility and assess the conformational landscape of the DENV2 NS5 protein. We characterized regions with high deuterium uptake in the DENV2 NS5 apo structure and identified regions with EX1 kinetics suggestive of significant conformational changes. We aim to probe these regions further by corroborating our findings with molecular dynamics (MD) simulations. The results obtained from this combined biophysical approach will enable us to identify solvent accessible regions in the DENV2 NS5 protein, which will be further explored with the aim of identifying novel binding site(s) for small molecule inhibitors against the dengue virus.

32. THE ROLE OF COLONIZATION FACTORS IN ETEC PATHOGENESIS IN THE HUMAN ENTEROID MODEL

Emily Smith

Smith, E. M., & Barry, E. M.

Session F, Poster Presentation

Enterotoxigenic Escherichia coli (ETEC) is a primary causative agent of diarrhea in young children in developing countries and of traveler's diarrhea. Following ingestion of contaminated food or water, ETEC adhere to intestinal epithelia and secrete heat-stable toxin (ST) and/or heat-labile toxin (LT), causing dysregulated cellular ion transport and water secretion. Colonization factors (CFs) mediate adhesion and ETEC isolates often harbor genes encoding more than one CF. We hypothesize that expression of multiple CFs by ETEC confers increased adherence and toxin delivery. Clinical strains harboring genes encoding CFA/I and CS21 were studied. Strains deficient in the expression of one or both CFs were engineered and characterized. Adherence assays using intestinal cell lines and the human enteroid model demonstrated that both CFA/I and CS21 are important for ETEC adherence as CF-deficient strains adhered significantly less than the wildtype strain. Antibodies targeting CFA/I on ETEC resulted in a significant decrease in adherence as well. These data provide evidence for the role of both CFs in ETEC adherence. Toxin delivery was measured as a downstream endpoint of adherence. In intestinal cell lines and the human enteroid model, ETEC strains delivered ST to cells over time and resulted in the polarized production of cGMP. CFA/I-CS21 containing strains delivered significantly more ST to cells than CFA/I-only strains, supporting the role of multiple CFs in pathogenesis.

These data suggest that ETEC can express multiple CFs that facilitate increased adherence and toxin delivery, thus supporting the role of multiple CFs in pathogenesis and as new targets for vaccines.

33. INHIBITION OF GPR68 SENSITIZES GLIOBLASTOMA MULTIFORME TO TEMOZOLOMIDE TREATMENT VIA THE Gq/NFK-B PATHWAY

Jovanni Ahmad

Ahmad, J. D., Keyser, B. D., & Williams, C. H.

Session F, Poster Presentation

Glioblastoma Mutliforme (GBM) remains as one of the most aggressive and types cancer. The frontline therapeutic Temozolomide (TMZ), is only effective in 30% of cases and often resistance emerges with recurrence. Therefore, therapies or adjuvants that sensitize GBM to TMZ are of great interest. Here we investigate the role of a proneurogenic GPCR, GPR68, which senses extracellular acidification, in both TMZ sensitive (U87) and resistant (U138) GBM cell lines. Using the GPR68 inhibitor Ogremorphen we show that both lines are sensitive to GPR68, further we show that both lines reduce proliferation and increase cell death. And finally using genetic, protein, and cell-based assays we show that GPR68 inhibition sensitizes U138 to TMZ, and that this is done through down regulation of MGMT, through the Gq/NFk-B pathway.

34. SEX DIFFERENCES IN THE TRANSCRIPTIONAL NETWORKS UNDERLYING PLAYFULNESS SUGGEST A DISTINCT FUNCTION FOR PLAY IN MALES COMPARED TO FEMALES

Ashley Marquardt

Marquardt, A.E., VanRyzin, J.W., Ament, S.A., & McCarthy, M.M.

Session F, Poster Presentation

Social play is a dynamic behavior expressed by most juvenile mammals. While its function is debated, a prevailing hypothesis suggests play serves to sculpt and refine neural circuitry enabling expression of appropriate adult behavior. Importantly, in most species, males play more than females, a sex difference driven by the medial amygdala (MeA). To investigate whether transcriptional signatures underlying play also differ by sex, we performed RNA-sequencing of MeA samples from high- and low-playing juvenile rats of both sexes. Using Weighted Gene Co-expression Network Analysis (WGCNA), we identified 22 co-expression modules, or networks of genes highly correlated in expression across samples. Of the 12 modules (for $p<0.05$) associated with play, almost all (11/12; ~92%) are sex-specific in expression, correlating with expression of play in one sex only. These data suggest there is a distinct transcriptomic profile associated with playfulness in the MeA of males compared to females, a noteworthy finding given the MeA regulates many sex-typical adult social behaviors. We propose that this is no coincidence: play-associated gene networks in the MeA are sex-specific because play modulates circuitry driving different adult behaviors depending on sex. To investigate this, we are currently exploring whether preventing play has distinct functional consequences on various adult behaviors in males and females. Future experiments will also examine the effects of modulating expression of our identified sex-specific gene modules on juvenile playfulness and later-life behavior. Together, these analyses will provide novel insight into the ultimate function of play and how and why this may differ by sex.

35. IMPACT OF PROTEIN CORONAS ON THE SELECTIVITY AND MECHANISMS OF UPTAKE OF Fn14-TARGETED NANOTHERAPEUTICS IN TNBC

Christine Carney

Carney, C.P., Kapur, A., Pandey, N., Dancy, J. G., Wadajkar, A.S., Woodworth, G.F., Winkles, J. A., & Kim, A. K.

Session F, Poster Presentation

There currently are no effective targeted therapeutics for women diagnosed with metastatic triple negative breast cancer (mTNBC), resulting in an overall survival of just ~13 months in these patients. Nanoparticles (NPs) offer the potential to improve the therapeutic efficacy and pharmacokinetic profile of encapsulated drugs through use of passive and active targeting to metastatic tumors. However, effective and active targeting of NPs to tumor cells is complicated by the adsorption of proteins to NP surfaces upon exposure to the systemic circulation. These 'protein coronas' can drastically reduce the blood circulation time and targeting capability of NPs in vivo. We have developed paclitaxel (PTX)-loaded NPs that are engineered for decreased non-specific adhesivity and receptor-targeting ('DART') characteristics. These DARTs selectively bind the Fn14 cell surface receptor, which is overexpressed in numerous solid cancers and their metastases, including mTNBC tumors. We recently demonstrated the enhanced therapeutic efficacy of Fn14-targeted DARTs in comparison to non-targeted NPs and Abraxane, an FDA-approved nanoformulation for mTNBC, in xenograft models of primary and intracranial TNBC. We found that these DARTs retain targeting capability and traffic to Fn14+ tumors in the presence of an endogenous protein corona in vitro and in vivo. Here, we furthered our investigation into the specific mechanisms of DART NP uptake in tumor cells in both the presence and absence of protein coronas using surface plasmon resonance, flow cytometry, total internal reflection fluorescence and confocal microscopy.

36. MAGNETIC-RESPONSIVE PHOTOSENSITIZER NANOPLATFORM VIA Fe_2O_3-TBO IMPROVES PHOTODYNAMIC-INACTIVATION AGAINST CARIOGENIC BIOFILMS

Abdulrahman Balhaddad

Balhaddad, A.A., Xia, Y., Ibrahim, M.S., Weir, M.D., Xu, H.H., & Melo, M.A.S.

Session F, Poster Presentation

Objectives: To develop novel hybrid microemulsions containing toluidine-blue ortho (TBO) and iron oxide (Fe2O3) nanoparticles, guided by magnetic field motion to enhance photosensitizer penetrability into biofilms. Methods: The most effective and biocompatible TBO parameters were investigated using Streptococcus mutans biofilm. Microemulsions were synthesized using TBO as a photosensitizer, essential oil, surfactants, and Fe2O3 nanoparticles at different mass fractions (1, 2.5, and 5 wt.%). The microemulsions were characterized via TEM and thermodynamic stability tests. The antibacterial effect of the Fe2O3-TBO microemulsions was investigated, with and without magnetic field, using 48-h S. mutans biofilms via CFUs and live/dead assays. A preliminary investigation on the antibacterial performance of the Fe2O3-TBO microemulsions was also performed using a saliva-microcosm biofilm model. Results: The TBO concentration of 100 μg/mL demonstrated acceptable biocompatibility. Increasing the energy density dose was associated with significant inhibition ($p<0.05$). The microemulsions were homogenous following the stress tests and stable for six months. The mean size of the magnetic particles ranged between 7 and 11 nm. Increasing the Fe2O3 concentration and using the magnetic field significantly ($p<0.05$) enhanced the biofilm inhibition.

Under the magnetic field with 2.5 and 5 wt.% of the Fe2O3-TBO microemulsion, aPDT reduced the biofilm viability by 100% compared to the control. The aPDT using Fe2O3-TBO microemulsions has shown promising bacterial reductions against total microorganisms' growth, total streptococci, Mutans streptococci, and total lactobacilli. Conclusion: The research results demonstrate a method to improve the current aPDT treatment by applying magnetic forces to effectively direct the TBO into the biofilm.

37. GUT MECHANISMS OF STRESS-INDUCED COMORBID VISCERAL PAIN

Jamila Asgar

Asgar, J., Yang, J., Traub, R., Ravel, J., & Wei, F.

Session G, Oral Presentation

Sufferers of chronic overlapping pain conditions (COPCs) – predominantly women – present with two or more chronic pain disorders. Etiology of COPCs is poorly understood although emotional stress is a well-known contributor and a risk factor. We showed that in female rats with existing neuropathic trigeminal pain (CCI), 3-day forced swimming (FS) stress induced lasting visceral pain hypersensitivity referred to the lower back area (referred hyperalgesia). Individually, neither CCI nor FS produced this comorbid pain phenotype. Accumulating recent evidence supports the importance of gut microbial dysbiosis in the pathogenesis of stress-induced visceral pain. But it is unclear how existing neuropathic pain, stress and gut dysbiosis interact to produce and maintain comorbid visceral pain. We examined fecal microbiota composition of rats with neuropathic trigeminal pain before and after FS stress. Our preliminary data showed extensive compositional changes in the gut microbiome of female rats with referred hyperalgesia. Furthermore, fecal microbiota transfer (FMT) from CCI donors induced referred hyperalgesia in recipients subjected to FS stress. Conversely, FMT from naïve donors attenuated referred hyperalgesia in CCI+FS recipients. These data suggest that CCI-induced gut dysbiosis contributes to comorbid visceral pain in stressed female rats. Understanding complex gut mechanisms of overlapping pain conditions will allow us to develop optimized therapeutic interventions involving targeted modulation of gut microbiota without harmful side effects.

38. INEQUITIES IN FRACTURE CARE-FROM A FOCAL LENS OF RACE AND ETHNICITY

Eseosa Fernandes

Fernandes, E., Slobogean, G., & O'Hara, N.

Session G, Oral Presentation

In the United States, approximately 5.6 million fractures occur each year, corresponding to a 2% incidence. It is projected that in the United States, age-related fractures will increase from 2.1 million yearly in 2005 to over 3 million fractures in 2025, as a result of the growth in the elderly population. This high burden of fractures is particularly concerning, as Improper initial management of fractures can lead to significant long-term morbidity and mortality, especially in the elderly. Racial and ethnic health-care disparities in the U.S. health-care system have been reported in orthopedic surgery specifically. However, there is no consensus on the nature, prevalence or magnitude of healthcare disparities. A clear understanding of the extent and nature of possible disparities within orthopedics is essential for appropriate intervention and advocacy. This study of disparities in fracture care, is particularly important, as the U.S. population ≥50 years of age, who are more prone to fracture, is predicted to increase, eventually reaching 121.3 million people in 2025, with the largest increases expected to occur in nonwhite populations. Our team proposes to conduct a retrospective

cohort study to study this topic, utilizing data from an ongoing multi-center cluster randomized crossover trial on open and closed fractures

39. JOINT COGNITIVE AND PHYSICAL FUNCTION RECOVERY TRAJECTORIES AFTER HIP FRACTURE

Heather Mutchie

Mutchie, H.L., Orwig, D.L., & Gruber-Baldini, A.L.

Session G, Oral Presentation

Introduction: There is a high prevalence of cognitive impairment after hip fracture that impacts physical recovery and mortality. However, research has not extensively studied the co-occurring trajectories of physical recovery with patterns of cognitive recovery over time. This work examines predictive probabilities of functional recovery using cognitive trajectories.
Methods: Hip fracture patients (age ≥65) were recruited from 2006-2011 in the Baltimore area(N=339) within 15 days of admission. Participants were assessed for cognition [Modified Mini Mental State Examination (3MS)] at baseline, 2, 6, and 12 months and tested for physical function [Short Physical Performance Battery (SPPB)] at each follow-up. A joint group-based trajectory model was assessed for the conditional probability of functional trajectory group membership given cognitive trajectory membership.
Results: In the 3MS Impaired Cognition trajectory (3MS ≤78:Group 1), 76% had Severe Functional Limitations(SPPB<3:Group 1), 24% in Very Limited (SPPB3-5:Group 2), none were in Mild Limitation (SPPB 6-10:Group 3). Among the Cognitively Intact (3MS >78:Group 3), 55% were Very Limited (SPPB 3-5:Group 2), and 33% had Mild Limitation (SPPB6-10:Group 3). Those who were cognitively impaired in any 3MS group (3MS <95:Group 1 or 2) were less likely to have Mild Limitations (SPPB 6-10:Group 3).
Conclusions: Cognitive function trajectories had predictive value for physical function recovery. Any level of cognitive impairment predicted functional limitations. Those who were cognitively intact experienced fewer functional limitations.

40. EFFECTS OF MEDICATION-ASSISTED TREATMENT ON TREATMENT RETENTION AND THE ROLE OF PAYMENT SOURCE

Eusong Park

Park, E.

Session G, Oral Presentation

Purpose: Public concerns regarding individuals with opioid use disorder (OUD) in the U.S. have increased due to the alarming death rates each year caused by OUD. Medication-assisted treatment is a proven effective treatment for OUD. This study explores the link between MAT and treatment retention first and then examines the role of payment sources on the link between MAT and treatment retention after allowing for clustering of discharge episodes within states.
Data and Methods: The 2018 TEDS-D (Treatment Episode Dataset-Discharge) for adults with OUD in outpatient service settings (n = 304,979) in 47 states was analyzed using multiple regression.
Results: Male, race other than White and Black, married, receiving MAT, less opioid use, co-occurring mental disorder, residents in Medicaid expanded states, and treatment completion were positively associated with treatment retention. MAT was positively associated with treatment retention, controlling for all covariates. This study also found that different payment sources while receiving MAT had different effects on treatment retention (e.g., Self-pay has longer retention when receiving MAT), compared to Medicaid or private

insurance). Findings also included that substantial variation between states on treatment retention existed when individuals with OUD receive MAT.
Conclusion: Findings underscores the importance of utilizing MAT in the outpatient treatment of OUD. Increasing access to MAT and stabilizing access for individuals with OUD should receive more attention, acknowledging differences in state-to-state substance use treatment infrastructure and policies. In addition, obstructive regulations of each payment source for patients and providers should be identified and modified.

41. IMMUNE EVASION MECHANISMS BY MUCORMYCOSIS CAUSING FUNGI

Alexandra Soare

Soare, A.Y., & Bruno, V.M.

Session G, Oral Presentation

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. Coupled with the unacceptably high mortality rate (70-100% depending on dissemination), there is a clear urgency to understand the host-pathogen interactions in the context of mucormycosis. Mucorales spores can resist killing by macrophages, immune cells that play a crucial role in host defense against microbes. Due to the paucity of knowledge on interactions between macrophages and Mucorales, we sought to characterize the macrophage response to Mucorales. Inducible nitric oxide synthase (iNos) is an enzyme expressed by macrophages in response to pathogens. Activation of iNos leads to the production of nitric oxide (NO), a free radical molecule which is toxic to many pathogens. Transcriptomic data from Mucorales-infected alveolar macrophages showed increased expression of iNos mRNA compared to uninfected macrophages. However, despite the increased expression of iNos mRNA, these macrophages were unable to produce NO, even when co-incubated with NO-producing stimuli. Our experiments demonstrate that this complete reduction of NO is not due to a lack of iNos protein accumulation or detoxification of NO by the fungi. Ongoing experiments are directed towards understanding the mechanism by which Mucorales mold inhibit NO production and how this immunosuppressive activity contributes to disease progression.

42. WORKING FOR PLAY: USING A NEW BEHAVIORAL TASK TO INTERROGATE THE ROLE OF THE BRAIN'S REWARD CIRCUITRY IN DRIVING THE MOTIVATION TO PLAY IN JUVENILE RATS

Sydney Ashton

Ashton, S.E., & McCarthy, M.M.

Session H, Oral Presentation

Rough-and-tumble play is a highly rewarding juvenile social behavior conserved across mammalian species, including humans, and is thought to allow for the development and refinement of a rich repertoire of social skills a mammal will need throughout life. Juvenile males engage in more frequent and intense play than females, but surprisingly we have found that play resulted in greater neuronal activation of brain reward circuitry in females compared to males. Specifically, both the proportion of play-active cells in the ventral tegmental area (VTA) that express] a marker of dopamine (DA) cells as well as the number of play-active DA receptor-expressing cells in the nucleus accumbens (NAc) were greater in females. We hypothesized that

greater activation of the VTA-NAc DA pathway in females leads to increased motivation to engage in playful behavior, without affecting the expression of play itself. To test this, we adapted to juvenile rats an operant social preference task in which the animal must push through a one-way swinging door to physically interact with a playmate. Overall, we found that juvenile rats were willing to push through up to ~200% of their body weight to reach their playmate, demonstrating that early-life social interaction is highly motivating. We found no sex differences in any measure of this task, suggesting that the motivation to play is controlled by a different mechanism than the expression of play. Future experiments will determine a causal role of the VTA-NAc DA pathway by chemogenetically modulating its activity during the social motivation task.

43. GENERATING AN IMPROVED iPSC-CM MODEL SYSTEM FOR STUDYING THE EFFECTS OF Cav1.2 MUTATIONS

Olutomiwa Fadiran

Fadiran, O.O., Vieira, D.C.O., DiSilvestre, D., & Dick, I.E.

Session H, Oral Presentation

Induced pluripotent stem cells (iPSC) are cells taken from patients that have been reprogrammed back into a pluripotent state. These cells can then be differentiated into any type of cell, including cardiomyocytes (CMs). This makes them a useful model system for studying cardiac diseases such as long QT syndrome (LQTS), a condition in which repolarization of the heart is stalled resulting in life-threatening arrhythmias. In particular, mutations within the calcium channel CaV1.2 are known to be causative of LQTS, making iPSC-CMs a useful model system for studying the mechanism of this form of LQTS. However, iPSC-CMs are often immature and don't mimic adult heart cells in several ways. Although iPSC-CMs can produce action potentials (APs) that look similar to mature human CMs, the compliment of channels in these cells seems to differ from typical adult ventricular cells. As a result, we have found that iPSC-CMs do not display the same response to calcium channel blockers such as verapamil as compared to an adult human ventricular CM, demonstrating a need for improvement of the model system. There are two prominent methods known for maturing iPSC-CMs, electrical stimulation and hormone treatment. Here, we treat iPSC-CMs with both methods in an attempt to normalize the response to verapamil, a key readout of normal CaV1.2 contribution to the AP. Optical mapping of wild-type and LQTS iPSC-CMs will be used to measure the AP duration in response to verapamil, thus identifying a method for improving the usefulness of iPSC-CMs in studying LQTS.

44. CD36 ORTHOLOGS EXHIBIT DISTINCT ROLES IN IMMUNITY TO THE LYME DISEASE SPIROCHETE

Anya O'Neal

O'Neal, A. J., Singh, N., Rolandelli, A., Forrest, I. S., Wang, X., Marnin, L., Shaw, D. K., Butler, L. R., Samaddar, S., Snyder, G. A., Do, R., & Pedra, J. H. F.

Session H, Oral Presentation

Ixodes ticks transmit several pathogens of public health importance, including the causative agent of Lyme disease Borrelia burgdorferi. During a blood meal, Ixodes scapularis ticks may acquire bacteria and mount an immune response that limits colonization. Recent studies in these evolutionarily ancient arthropods revealed previously unknown mechanisms of immune recognition, which may have broader implications for the evolution of innate immunity. Our group previously discovered that lipids derived from bacterial infection stimulate tick immune pathways against B. burgdorferi. However, receptors for microbial lipids in I. scapularis remain elusive. Here, we report the tick ortholog of Croquemort, a CD36-like protein originally discovered in

Drosophila, as a plasma membrane receptor for microbial lipids. We determined ligand-protein interactions between the ectodomain of Croquemort and the infection-derived lipid 1-palmitoyl-2-oleoyl-sn-glycero-3-phosphoglycerol (POPG) by pull-down assay and biophysical techniques. Importantly, transcriptional silencing of Croquemort increased B. burgdorferi burden and impaired activation of the immune deficiency (IMD) and Jun N-terminal kinase (JNK) pathways, indicating its direct role in antibacterial immunity. Although CD36 functions are proposed to be conserved from Drosophila to mammals, our findings in ticks reveal distinct functions across evolutionarily distant organisms. We discovered a novel role for mammalian CD36 in Lyme disease pathology. Using murine models and human exome/medical data, we determined that mutations in CD36 cause increased incidence and severity of Lyme disease without affecting bacterial burden. Furthermore, CD36 mutations promote immune dysfunction in affected individuals. Collectively, our findings shed light on the evolution of immunity and contribute to new scientific paradigms in vector-borne diseases.

45. THE ROLE OF RARE HUMAN GENETIC VARIANTS IN LRP1 ON AORTIC ANEURYSM FORMATION

Mashhood Wani

Wani, M.M., Arai, A.L., Migliorini, M., Muratoglu, S.C., & Strickland, D.K.

Session H, Oral Presentation

LRP1 (low density lipoprotein receptor-related protein 1) is a large endocytic receptor that binds over 100 structurally unrelated ligands. Our lab has demonstrated that a sm22 promoter-driven knock-out of LRP1 (smLRP1-/-) results in aortic aneurysms in mice due to fragmentation and degradation of the elastic fibers, further implicating LRP1 in vascular development. The identification of patients with aneurysmal disease harboring missense mutations in LRP1 has allowed for investigations into the role of LRP1 in aneurysm formation. Utilizing both full-length LRP1 (FL-LRP1) as well as a truncated LRP1 that recapitulates ligand binding and endocytic functions of endogenous LRP1, we introduced mutations that correspond to LRP1 variants that segregate in family members afflicted with aortic aneurysms. By means of a receptor-ligand binding assay, we quantified the internalization and degradation of 125I-activated alpha-2-macroglobulin (a2M*). We used two different cell systems for this assay: i) LRP1-deficient Chinese Hamster Ovary (CHO 13-5-1) cells transiently transfected with truncated LRP1 variants or FL-LRP1 constructs and ii) aortic smooth muscle cells isolated from a patient with an abdominal aortic aneurysm and LRP1 missense mutations. The results showed defects in LRP1-mediated internalization of a2M* in LRP1 variants when compared to wild type LRP1. Furthermore, a cycloheximide chase assay has shown significant changes in LRP1 turnover in two different LRP1 variants. Our data highlights the biochemical deficits in different variants of LRP1 that may contribute to the pathogenesis of aortic disease. Pinpointing the role of LRP1 in aneurysm mechanisms will allow for non-invasive interventions to be employed before aortic rupture.

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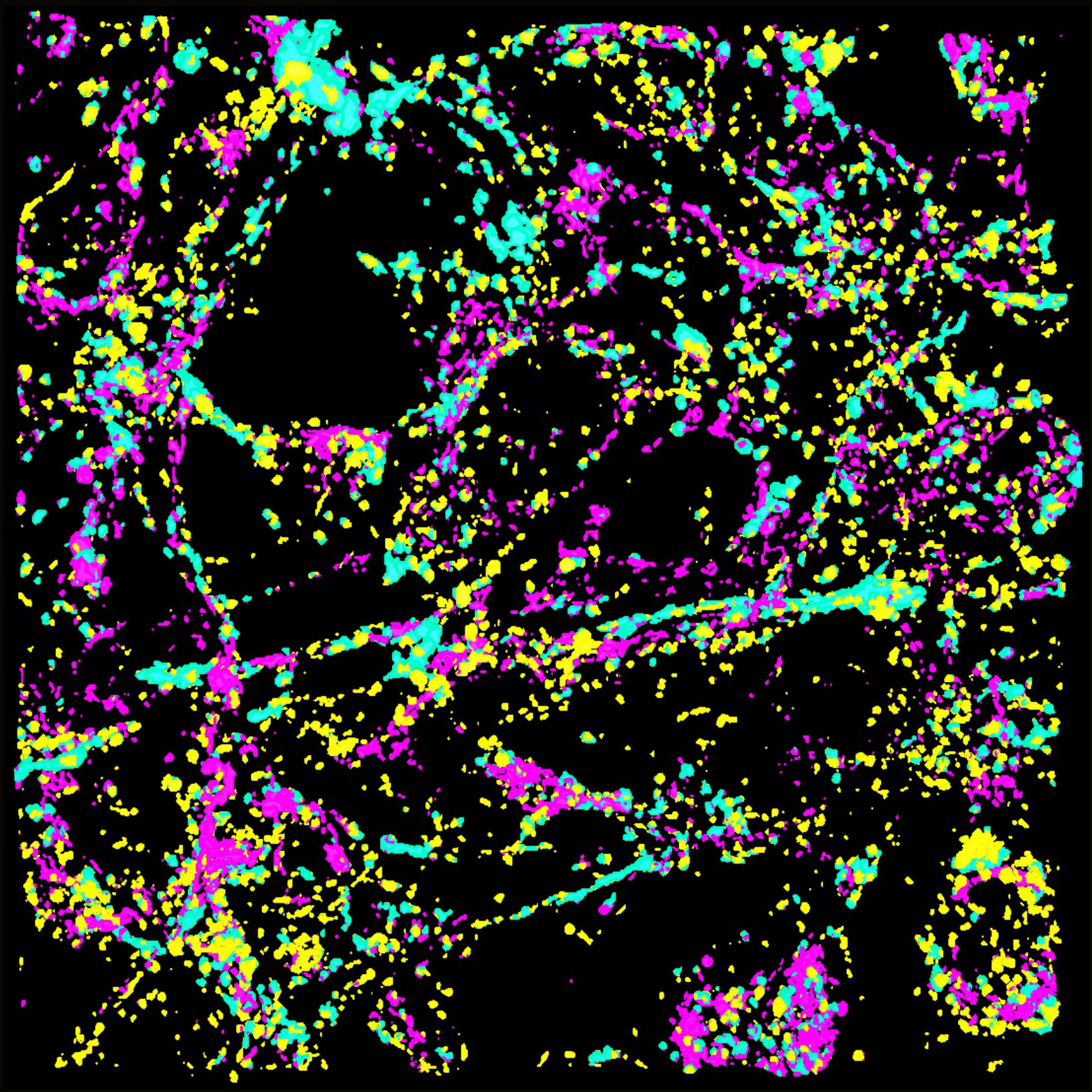

"Fruity Pebbles"

3D reconstruction of GFP-sclerostin,
labeled lysosomes & their co-localization

image by: Nicole Gould