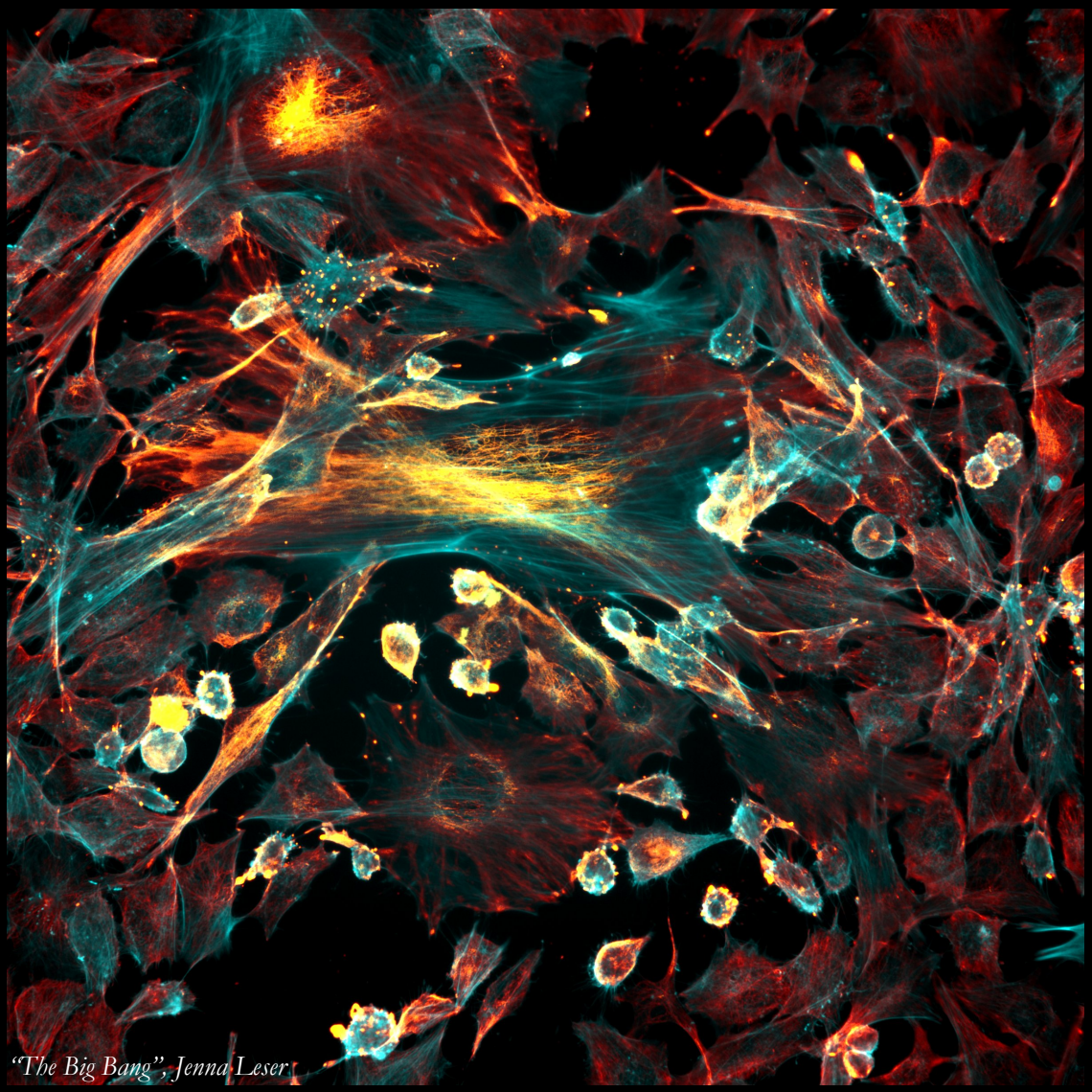
UNIVERSITY of MARYLAND
THE FOUNDING CAMPUS

42nd Annual
Graduate Research Conference



"The Big Bang", Jenna Leser

SMC Campus Center
March 6th, 2020
Baltimore, MD

graduate
student
association

Hosted by the Graduate Student Association

Sponsored by

THE ANNIE E. CASEY FOUNDATION

UNIVERSITY of MARYLAND
THE FOUNDING CAMPUS

42nd Annual Graduate Research Conference

Presented by:

graduate student association
UNIVERSITY of MARYLAND

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THE ANNIE E. CASEY FOUNDATION

41st Annual Graduate Research Conference

presented by the Graduate Student Association

Contents:

UNIVERSITY of MARYLAND
BALTIMORE

BRUCE E. JARRELL, MD, FACS
Interim President

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March 6, 2020

Congratulations on your 2020 Graduate Research Conference. Your instinct to share with one another is so vital to your individual and collective success. Each of us must understand how our colleagues contribute to our joint mission – and it's important that we consider our work in that context rather than in isolation. In fact, one of UMB's Core Values – those principles at the very heart of our mission – is Collaboration.

Why is Collaboration so important? It is because the biggest breakthroughs in human health and well-being often occur at the intersection of scholars and schools and disciplines. Our commitment to talk and work with each another – and to redesign the way we think about the problems that confound us – is when we can unleash the necessary creativity and innovation. That is when we see possibilities open up before us and new avenues emerging from dead ends. That is when we dream up new applications for our work, ways to broaden its reach, or pathways to amplify its impact.

I wish you the best of luck at your Conference – and that you will truly live the core value of Collaboration now and into the future.

Sincerely,

Bruce E. Jarrell

Bruce E. Jarrell, MD, FACS
Interim President

Forward

Welcome to the 42nd annual Graduate Research Conference (GRC) at the University of Maryland, Baltimore (UMB)! The Graduate Student Association (GSA) is proud to host this conference to allow our researchers, graduate students, professional students, and postdoctoral fellows the opportunity to present their work and discoveries. The interdisciplinary nature of our campus allows us to showcase a variety of research within one conference, including basic, nursing, social, and applied sciences.

This year, we have abstracts from students and postdoctoral fellows representative of every UMB graduate research program, which will be featured in both oral and poster presentations. As in previous years, all students presenting abstracts are eligible to win an award for outstanding presentations in their sessions. Additionally, the Geriatrics and Gerontology Education and Research Program (GGEAR) and the Center for Research on Aging (ORC) at the University of Maryland, Baltimore will be sponsoring a special award in aging research. The Office of Technology Transfer (OTT) will also present their 12th 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 OTT for their continued support of GRC and the outstanding research being conducted by students and postdoctoral fellows on campus. We are proud to host our keynote speaker, Dr. Donna Calu, a UMB alumna who is now an Assistant Professor in the Department of Anatomy and Neurobiology. 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. After the Advancement to Candidacy ceremony and GRC awards, there will be a reception and social hour.

The GSA gratefully acknowledges those who helped make the GRC possible and successful. We would like to thank Interim President Jarrell for his continued support of the students on our campus and their research. Special recognition is deservedly given to Dr. Erin Golembewski, Senior Associate Dean of the Graduate School, for her continued guidance and support, as well as all of the staff of the Graduate School Office. Many thanks are owed to the HS/HSL for all their help with presentation preparations and providing us with the resources necessary to perform informed research. We commend our keynote speaker, Dr. Donna Calu, for her contributions to the field of science and sharing her message with our campus. We greatly appreciate the faculty members acting as judges for donating their time, expertise, and critiques. We are grateful for our amazing sponsors and supporting organizations that drive the success of our event! We thank the GSA program representatives and members for their work throughout the year, and especially for their commitment to making the GRC successful. Finally, we would like to recognize the GRC Organizing Committee for their hard work to make the GRC possible and bring together the researchers in our campus community. It is our pleasure to host you at the 42nd annual Graduate Research Conference, and we hope you enjoy today's program and events!

GSA Executive Board

Megan Lynch – President
Emily Smith – Vice President
Heather Mutchie – Treasurer
Lauren McCarthy – Secretary
Tyree Williams – Public Relations Officer
Katie Gwilliam – Graduate Council Representative

2020 GRC Organizing Committee

Liana Andronsecu, Hadley Bryan, Alyssa Grogan, Gillian Mbambo, Tim Mowry, Kelly Rock, and Lauren McCarthy

Student Award Winners

The Graduate Student Association would like to congratulate the students who have won our awards during the 2019-2020 academic year. The Graduate Student Research Award provides funding to those students who need extra resources to complete their studies. The Travel Award supports students so they may attend seminars and conferences in their fields.

Professional Development Award

Eryn Dixon, 2019

Travel Award

Maria Ibrahim, Third Quarter 2019
Brian Johnson, Third Quarter 2019
Ivie Conlon, Third Quarter 2019
Eryn Dixon, Third Quarter 2019

Husam Albarmawi, Fourth Quarter 2019
Basant Motawi, Fourth Quarter 2019
Paige McKeon, Fourth Quarter 2019
Gideon Wolf, Fourth Quarter 2019

Todd Becker, First Quarter 2020
Sara Daniel, First Quarter 2020
Marie Hanscom, First Quarter 2020
AbdulRahman Balhaddad, First Quarter 2020

Sol Baik, Second Quarter 2020
Rachel Margolis, Second Quarter 2020
Shalini Sahoo, Second Quarter 2020

Abstract Booklet Images
Jenna Leser (Front)
Phyo Nay Lin (Back)

Keynote Speaker Biography

Dr. Donna Calu

Assistant Professor of Anatomy and Neurobiology, University of Maryland, Baltimore School of Medicine

I graduated from University of Maryland, College Park with BS in Biology. I completed my PhD at University of Maryland Baltimore (UMB), Program in Neuroscience, working with Geoffrey Schoenbaum to study the role of amygdala neural activity in attention and associative learning. As a postdoc in the laboratory of Yavin Shaham at the National Institute on Drug Abuse (NIDA), I used an optogenetic approach to examine the role of prefrontal cortex in driving palatable food relapse. I started my lab as an Early Independent Scientist at NIDA, building a research program investigating the behavioral and brain basis of addiction vulnerability. I moved back across town to UMB Department of Anatomy and Neurobiology in September of 2015. The Calu lab conducts behavioral and systems neuroscience studies to elucidate the brain systems driving individual differences in reward learning and motivation that predict addiction vulnerability. We probe amygdala, cortical and striatal brain circuitry, prior to drug experience, to determine how engagement of these brain pathways during learning relates to addiction vulnerability phenotypes. We also examine how these brain systems are changed by voluntary drug experience and dependence to drive drug seeking and drug taking. These preclinical studies may yield new biomarkers of addiction vulnerability and identify new prevention and diagnostic strategies for treatment of addiction.

42nd Annual Graduate Research Conference

Schedule of Events

SMC Campus Center
March 6th, 2020

8:00-9:00 am	**Breakfast & Registration**	**Second Floor**
9:00-10:30 am	**Oral Presentations**	
	Session A	**Elm Ballroom A**
	Session B	**Elm Ballroom B**
10:30-10:45 am	**Coffee Break**	
10:45 am-11:45 am	**Poster Presentations**	**Room 349**
	Session C	
	Session D	
	Session E	
11:45 am-1:00 pm	**Lunch**	**Elm Ballroom**
	Dr. Donna Calu	
1:00-2:00 pm	**Poster Presentations**	**Room 349**
	Session F	
	Session G	
	Session H	
2:00-2:15 pm	**Coffee Break**	
2:15-3:45 pm	**Oral Presentations**	
	Session I	**Elm Ballroom A**
	Session J	**Elm Ballroom B**
4:00-5:00 pm	**Candidacy Ceremony and GRC Awards**	**Elm Ballroom A**
5:00-7:00 pm	**Reception & Social Hour**	**Second Floor**

Session Assignments

Session A – Oral Session, 9:00-10:30 am, Elm Ballroom A
(#1 Emily Smith) (#2 Jack Henderson), (#3 Phyo Nay Lin), (#4 Tyree Wilson), (#5 Gideon Wolf) (#6 Jennifer Kirk)

Session B - Oral Session, 9:00-10:30 am, Elm Ballroom B
(#7 Aksinija Kogan), (#8 Rashmita Bajracharya), (#9 Ivana Alexander), (#10 Rachel McPherson), (#11 Paige Zambrana), (#12 Amy Nelson)

Session C – Poster Session, 10:45-11:45 am, Room 349
(#13 Todd Becker), (#14 Danielle Phillips), (#15 Kimberly Leffler), (#16 Nancy Franke), (#17 Jennifer Kirk), (#18 Lindsey Clark, (#19 Franklin Ning), (#20 Jeffrey Inen), (#21 Gillian Mbambo), (#22 Anh Tran)

Session D – Poster Session, 10:45-11:45 am, Room 349
(#23 Sydney Stern), (#24 Adrienne Kambouris), (#25 Mashhood Wani), (#26 M. Doyinsola Ismail), (#27 Ramon Martinez), (#28 Amy Defnet)

Session E – Poster Session, 10:45-11:45 am, Room 349
(#29 Yulemni Morel), (#30 Isadora Garcia), (#31 Ghalia Bhadila), (#32 Darex Vera-Rodriguez, (#33 Kyle Kihn), (#34 Alexandria Chan), (#35 Ellis Tibbs), (#36 Zahra Rahmaty), (#37 Benjamin Diethelm-Varela), (#38 Anya O'Neal)

Session F – Poster Session, 1:00-2:00 pm, Room 349
(#39 Eusong Park), (#40 Ji Hyang Cheon), (#41 Yao Wang), (#42 Shawna Murray-Brown), (#43 Payal Chatterjee), (#44 Ritika Kurian), (#45 Brandi Hobbs), (#46 Courtney Mason), (#47 Dongyue Yu)

Session G – Poster Session, 1:00-2:00 pm, Room 349
(#48 Muddassar Iqbal), (#49 Christina Stennett), (#50 Lora Stojanovic), (#51 Jessica Allen), (#52 David Langan), (#53 Hanover Matz), (#54 Erika Lipford), (#55 Michael Creed), (#56 Anna Dellomo), (#57 Jenna Leser), (#58 Elizabeth Humphries)

Session H – Poster Session, 1:00-2:00 pm, Room 349
(#59 Cassandra Jordan), (#60 Stephanie Zalesak), (#61 Lorreen Agandi), (#62 Rayyan Alfirdous), (#64 Paige Mathena), (#65 Lori Anderson).

Session I – Oral Session, 2:15-3:45 pm, Elm Ballroom A
(#66 Asmita Adhikari), (#67 Alex Casella), (#68 Allison Gerber), (#69 Kelly Rock), (#70 Abdulrah Balhaddad), (#71 Saovleak Khim)

Session J – Oral Session, 2:15-3:45 pm, Elm Ballroom B
(#72 Nicole Gould), (#73 Angela Lee), (#74 Ashley Marquardt), (#75 M. Doyinsola Ismail), (#76 Liana Andronescu), (#77 Alyssa Grogan)

Abstracts

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

Emily Smith

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

Session A; Oral Presentation; Ballroom A

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) expressed on the bacterial surface mediate adhesion. We hypothesize that ETEC that harbor genes encoding more than one CF must efficiently regulate multiple CFs for adherence and toxin delivery. Clinical strains harboring genes encoding CFA/I, CS21, and/or CS14 were studied. After growing strains in different media, we determined that CFA/I expression was restricted to CFA agar whereas CS21 was expressed in all growth conditions. CS14 expression was restricted to CFA agar with an iron chelator. Adherence assays using the ex vivo human enteroid model demonstrated that strains H10407, CVD19, and CVD30 adhere to monolayers in a CFA/I-dependent manner. CVD30 that expresses high levels of CFA/I and CS21 had increased adherence compared to H10407 that only expresses CFA/I, providing evidence for the role of both CFs in adherence. LT intoxication induced a concentration- and time-dependent increase in cAMP in T84 cells and enteroid monolayers, and ST intoxication induced a concentration-dependent increase in cGMP in T84 cells. Infection with H10407 or CVD19 demonstrated that ETEC delivers LT to cells. These data suggest that ETEC can differentially express multiple CFs and allow for increased adherence, thus supporting the role of multiple CFs in pathogenesis and proposing new targets for vaccines.

2. RESOLVING A PROTON-BINDING SITE IN THE SODIUM-PROTON ANTIPORTER NHAA BY CONTINUOUS CONSTANT PH MOLECULAR DYNAMICS

Jack Henderson

Henderson, J.A., Huang, Y., & Shen, J.

Session A; Oral Presentation; Ballroom A

Prokaryotic sodium-proton antiporters, such as NhaA from Escherichia coli, are important model systems for understanding the medically relevant human analogs which are drug targets for the treatment of heart diseases. In NhaA there are two proton binding sites, one being Asp164 which is supported by biochemical and biophysical experiments, but the identity of the second proton binding site is a topic of debate. Recent mutagenesis experiments suggest Lys300 may not be the second proton binding residue, as Lys300 mutants remained electrogenic. Here we used continuous constant pH molecular dynamics to investigate the second proton binding site in NhaA. Calculated pKa values of the wild type and mutants (K300A, K300R, and K300Q D163N) suggest that Asp133, a residue close to

Asp164 and Asp163, can serve as an alternative proton-binding site in place of Lys300. Together with conformational details, our work supports the salt-bridge model in which Lys300 is a second binding site that participates in electrogenic sodium transport by NhaA.

3. THE EFFECT OF ZSCAN4 ON TELOMERE CHROMATIN REMODELING

Phyo Nay Lin

Lin, PN., Gupta, A., Brown, R. A., & Zalzman, M.

Session A; Oral Presentation; Ballroom A

Telomeres are repetitive DNA sequences at the ends of linear chromosomes that protect the coding regions of DNA. Telomeres become shorter with every cell division and hence operate as a biological clock to eventually lead to replicative senescence. Therefore, factors regulating telomeric chromatin impact cell replicative lifespan, tumor formation and growth. We have previously reported that the murine Zinc Finger and SCAN Domain Containing 4 (mZscan4) has a role in telomere homeostasis and genomic stability in mouse embryonic stem (mESCs) cells. It was further shown to promote nuclear reprogramming during the generation of induced pluripotent stem cells and is involved in increasing the developmental potency of mESCs. Additional reports suggest that transient expression of Zscan4 in mESCs correlates with chromatin de-repression. However, to date, the function of human ZSCAN4 in cancer and its contribution to the epigenetic landscape changes at telomeric chromatin remain to be determined. In this study, we define the effect of ZSCAN4 on telomeric chromatin remodeling in human cancer cells. Understanding the mechanism by which ZSCAN4 affects the telomeric chromatin maintenance is important for designing new therapeutic approaches to target cancer cell replicative lifespan.

4. INTEGRATION OF HEME UPTAKE AND UTILIZATION INTO THE SRNA REGULATORY NETWORK OF PSEUDOMONAS AERUGINOSA

Tyree Wilson

Wilson, T., Mourino, S., & Wilks, A.

Session A; Oral Presentation; Ballroom A

Pseudomonas aeruginosa (Pa) is a gram-negative opportunistic pathogen that requires iron for survival and virulence. Pa can acquire iron through several mechanisms including iron siderophores, the ferrous iron uptake system (Feo) or via heme uptake and metabolism. Pa encodes two interdependent heme uptake systems, the heme assimilation system (Has) and the Pseudomonas heme utilization (Phu) that have non-redundant roles in heme sensing and uptake, respectively. Once heme is taken up into the cytoplasm it is bound to PhuS which functions as a specific heme chaperone to the iron regulated HemO releasing iron and biliverdin-gamma/beta. In addition to its role in regulating heme flux through HemO, we have recently uncovered a link between PhuS and the iron-regulated sRNAs, PrrF1 and PrrF2. PrrF1 and PrrF2 expression is negatively regulated by Fur and hence de-repressed under iron-starvation. PrrF sRNAs bind to complementary sequences of their target mRNAs causing the RNAseE and Hfq-dependent degradation of genes encoding iron containing protein as an iron sparing response. Furthermore, the unique tandem arrangement of prrF1 and prrF2 encodes an

overlapping sRNA PrrH, whose expression was reported to be heme dependent. Interestingly, the prrF1/F2 tandem arrangement is found upstream of the phu system and only in pathogenic P. aeruginosa that also encodes PhuS. This led us to hypothesize that there is a functional link between PhuS and the prrF1/F2 (prrH) regulon that is critical for adaptation to heme as an iron source. Studying this functional link will provide potential therapeutic strategies for treating Pseudomonas infection.

5. THERAPEUTIC MANIPULATION OF MEMORY T CELL HOMEOSTASIS IN VIVO.

Gideon Wolf

Wolf, G. & Singh, N.

Session A; Oral Presentation; Ballroom A

The accumulation of a memory T cell repertoire with specificities to multiple pathogens, collectively keeps the host safe against prevalent environmental threats. Other than booster vaccinations which narrowly increase the frequency of a single antigen-specific cohort, there are no viable strategies available to globally alter the total memory T cell population in vivo. Since memory T cells are thought be maintained by trophic signals from cytokines or self-MHC- both of which are available from endogenous antigen-presenting cells (APC)- we hypothesized that enhancing APC numbers in vivo can be a viable strategy to amplify memory T cells. Towards this end we treated mice with FMS-like tyrosine kinase 3 ligand (Flt3l) or specific self-peptides known to increase the peripheral survival of cohorts of CD4 T cells. After an acute expansion of dendritic cells (DCs) following Flt3l treatment, we observed an increase in effector memory CD4s and CD8s, but not in naïve T cells. Over the short term, this increase was independent of alterations in the thymus. On cessation of Flt3l treatment, the increase in DCs was not sustained, and the population of memory T cells also returned to steady state, suggesting restoration of competitive homeostasis. In contrast to this global effect, administering an endogenous self-peptide used by a small subset of peripheral T cells did not significantly alter the overall number or distribution of the memory repertoire. Taken together, these data suggest new options to manipulate memory T cell populations in clinically relevant situations.

6. SEX DIFFERENCES IN BONE-ACTIVE-MEDICATION UTILIZATION BEFORE AND AFTER HIP FRACTURE

Jennifer Kirk

Kirk, J.M., Orwig, D., Gruber-Baldini, A., Hochberg, M.C., Magaziner, J.S., & Rathbun, A.M.
Session A; Oral Presentation; Ballroom A

Bone-active-medications (BAMs), including prescriptions (RxBAMs), calcium and vitamin D, increase bone mineral density and reduce osteoporotic fracture risk, yet utilization rates post-hip fracture are low and it is unclear who is taking these medications before and after hip fracture. This study examined the prevalence of BAM use (reported by self or proxy) by sex at the time of hip fracture and over the year post-fracture. Calcium, vitamin D, and RxBAM utilization was assessed at baseline (within 22-days of admission, 2,6, and 12-months). The sample included 328 older adults 65+ from the Baltimore Hip Studies' seventh cohort. A complete case analysis (n=285) was used with generalized estimating equations (GEE) to assess baseline characteristics that predict the probability of BAM use during follow-up. Prior to the fracture, there were sex differences in

medication use such that fewer men than women took calcium 17% versus 56%, RxBAMs 8% versus 24.8%, either calcium or vitamin D with RxBAM 5% versus 18%, and 42% versus 2.0% took neither. These differences remained over the year post-hip fracture. During follow-up, only 12(3.5%) participants took RxBAM the entire study. Of RxBAM users 90(27.4%), there were few new users (36), and many participants stopped or never started treatment. Unadjusted models showed sex-differences in BAM and RxBAM use. After controlling for baseline use, sex-differences were no longer significant. Adjusted GEEs detected men had OR=0.58, 95%C.I.[.37,1.00], p=.19 of RxBAM use. RxBAM use was low especially in men and may contribute to the high rates of preventable secondary osteoporotic fractures and post-fracture mortality.

7. DNA METHYLTRANSFERASE INHIBITORS PROMOTE HOMOLOGOUS RECOMBINATION DEFICIENCY THROUGH INDUCTION OF IMMUNE SIGNALING, SENSITIZING ACUTE MYELOID LEUKEMIA CELLS TO PARP INHIBITORS

Aksinija Kogan

Kogan A., McLaughlin L., Baer, M.R., Baylin, S.B., Topper, M., & Rassool, F.V.

Session B; Oral Presentation; Ballroom B

Acute myeloid leukemia (AML) patients unfit for intensive chemotherapy are treated with DNA methyltransferase inhibitors (DNMTis). However, while many AML patients respond to DNMTis, responses are not durable. We previously reported a novel treatment strategy for AML that combines DNMTis with poly (ADP-ribose) polymerase inhibitors (PARPis), drugs classically used to treat breast and ovarian cancer patients with BRCA mutations and homologous recombination defects (HRD).
We have now identified a novel mechanism through which DNMTis may sensitize BRCA-proficient AML cells to PARPis. This mechanism is tied to the capacity of these drugs to reprogram cancer signaling networks. We show that treatment with the DNMTi decitabine (DAC) at a low concentration (10nM) can directly induce HRD, by significantly down-regulating key genes central to HR activity, including multiple genes in the Fanconi anemia (FA) pathway, as a mechanism for enhanced PARPi sensitivity. We have previously shown that DNMTis activate innate immune pathways involving interferon (IFN) beta and tumor necrosis factor (TNF) alpha, a phenomenon known as viral mimicry. We now show for the first time that immune signaling is linked to induction of HRD. Importantly, we identified a common immune signaling pathway induced by both DNMTis and PARPis: cytoplasmic double-stranded DNA sensing through signaling of the cyclic GMP-AMP Synthase - Stimulator of Interferon Genes (cGAS-STING) pathway. Our data suggest that STING may be a central signaling hub linked to HRD and also suggest ways in which epigenetic therapy, inhibitors of DNA damage response proteins, and targeted immune therapy can synergize to treat AML.

8. CHANGES IN HEALTH-RELATED QUALITY OF LIFE (HRQOL) IN ADULTS WITH POSITIVE DEPRESSION SCREENING OVER A PERIOD OF A YEAR: ASSESSING DIFFERENCES BY ANTIDEPRESSANT USE AND AGE

Rashmita Bajracharya
Bajracharya, R., Castillo, W.C., Qato, D. & Olives, E.V.

Session B; Oral Presentation; Ballroom B

Background: Little information is available regarding HRQoL outcomes of antidepressant use in oldest-old (≥80 years).
Methods: To obtain adequate sample of oldest-old, we pooled thirteen panels (2004-2017) from Medical Expenditure Panel Survey of community-dwelling individuals with each panel followed for 2 years. Components of Short-form12, Mental Component Score (MCS) and Physical Component Score (PCS), was used to measure HRQoL. We compared longitudinal changes in HRQoL among 10,658 individuals with depressive symptoms by age categories (20-29, 30-39, 40-49, 50-59, 60-69, 70-79, ≥80 years) using Cohen's-d. We also estimated if effect of antidepressant use on HRQoL is different by age categories using generalized estimating equations.
Results: Only younger age categories 20-29 [effect size (ES)=0.64] and 30-39 (ES=0.56) had a statistically meaningful increase in MCS. PCS increased in a positive direction for all age categories, but the increase was not statistically meaningful. Compared to no antidepressant use, those who used antidepressants had a statistically significant increase in MCS of 8.42 only for 20-29. For all other age categories, MCS changed in a negative direction (30-39=-2.93, 40-49=-2.55, 50-59=-2.37, 60-69=-3.34, 70-79=-1.42, ≥80=-3.43). Compared to no antidepressant use, those who used antidepressants had a statistically significant increase in PCS of 22.11 only for 20-29. For other age categories, PCS changed in a negative direction (30-39=-1.13, 40-49=-1.68, 50-59=-0.94, 60-69=-0.60, 70-79=-1.27). For ≥80, increase of 0.89 in PCS was observed for antidepressant users compared to non-users but the association was not significant.
Conclusion: ≥80 benefitted the least from antidepressant use with regards to improvement in MCS.

9. BAND OF BROTHERS: VIETNAM VETERANS' ATTITUDES/BELIEFS ABOUT MILITARY SERVICE AND THEIR IMPACT ON PTSD RECOVERY

Ivana T. Alexander

Alexander, I. T., Peeples, A. D.l & Havrilla, S.

Session B; Oral Presentation; Ballroom B

Vietnam era veterans suffer unique and significant challenges related to their physical and mental health that can be linked to their military service. Veterans Health Administration (VHA) data estimates that 18% of Vietnam era veterans meet the full diagnostic criteria for PTSD. This figure is much larger when considering veterans who exhibit clinically significant PTSD symptoms. Despite efforts to engage this aging cohort of veterans in evidence-based treatment programs for PTSD, little research has focused on the attitudes and perceptions related to patriotism, military service, experiences with Veterans Affairs' services and providers and how these beliefs affect their treatment trajectory, either through the development of protective social factors or barriers that hinder treatment recovery. Successfully engaging this population of veterans in ongoing treatment requires a comprehensive understanding of how their post-war return and subsequent interactions both with social systems and systems of care impact their perceptions of recovery and treatment outcomes. This paper explores the impediments and opportunities for PTSD treatment engagement and recovery embedded in Vietnam era veterans' attitudes and beliefs about their military service and the

systems and institutions at the core of providing care. The findings are drawn from a qualitative pilot study with Vietnam era veterans who have had recent engagement with a trauma-focused treatment program at a VA Medical Center. The veterans (n=12) each participated in a two-interview research protocol that examined narratives related to their thoughts, feelings, and impressions of treatment and recovery in PTSD.

10. GENDER DIFFERENCES IN STAFF-RESIDENT INTERACTIONS IN NURSING HOMES

Rachel McPherson

McPherson, R. E. Resnick, B. M., & Galik, E.

Session B; Oral Presentation; Ballroom B

Communication and interactions are an integral part of care in long-term care settings. The Quality of Interactions Schedule (QuIS) was developed to measure the quality of verbal and nonverbal interactions among nursing staff and older adults initially for those in acute care and later used as well in a variety of long term care settings. Following a brief observation period, interactions between staff and residents are categorized into positive social, positive caring, neutral, negative protective, and negative restrictive. Little research has been done to describe the quality of care interactions between staff and male versus female residents. The purpose of this study was to describe gender differences in the quality of interactions. Data for the present study was based on baseline data from the Evidence Integration Triangle for Behavioral and Psychological Symptoms of Dementia (EIT-4-BPSD) implementation study. A total of 553 residents from 55 settings were included in the analyses. The findings indicate that there were no significant differences in the quality of staff interactions with male or female residents. The majority of the interactions were positive social, positive care, or neutral. There were 31 negative protective and 23 negative restrictive interactions. Future work should focus on eliminating neutral and negative interactions across both genders.

11. ENVIRONMENTAL HARMONIZATION IN MULTI-APPLICATION SUNSCREEN USE: IN VITRO PERMEATION TESTING TO HEALTHY VOLUNTEERS

Paige Zambrana

Zambrana, P. N. Hammell, D., & Stinchcomb, A. L.

Sunscreens are used every day by Americans as a means of reducing the risk of photoaging and skin cancers, such as melanoma and basal cell carcinoma, and are often added to daily-use cosmetic products. The ultraviolet (UV) filters in these products have predetermined maximum percentage levels. Oxybenzone, one of the most common UV filters, has a maximum percentage set at six. Because of the nature of sunscreens applied to large areas of the body multiple times a day during elevated temperatures and humidities, accumulation of UV filters on the skin is significant. This could represent significant systemic exposure, especially to children who have a higher surface area to body weight ratio. Our in vitro studies mimicking multiapplication use with heat resulted in a maximum 2-fold increase in oxybenzone flux and cumulative skin permeation from some sunscreen products tested, and revealed different permeation abilities of each formulation tested. Based on these results, we designed in vivo studies to focus on sunscreen reapplication with different sunscreen formulations in the presence of controlled skin surface temperature and humidity. The

overall goal of this project is to generate a streamlined and validated approach for permeation testing of currently marketed and future sunscreen products. This will generate more accurate information of the potential total permeation of oxybenzone in worst-case scenarios, and show the difference that formulation makes, advocating for final formulation permeation testing. Reliable in vitro-in vivo correlations may enable in vitro testing use for future sunscreen studies, decreasing the need for costly clinical trials.

12. ALTERING MECHANISMS OF FRAILTY IN PERSONS LIVING WITH HIV

Amy Nelson

Nelson, A.K.

Session B; Oral Presentation; Ballroom B

Background: People living with HIV now have nearly equal lifespans to the general population, yet they experience frailty, a vulnerability to stressors caused by lack of physiologic reserves, more often and ten years earlier than those without HIV. In geriatrics, frailty is associated with decreased muscle strength and increased systemic inflammation. Less is known about mechanisms driving early frailty in HIV or effective interventions for this aging population.

Impaired cellular energy metabolism by mitochondria may contribute to the muscular weakness and ongoing inflammation accompanying frailty in HIV and driving early presentation. This study will examine the impact of six weeks of moderate exercise on cellular energy metabolism, inflammatory markers and frailty phenotype in people living with well-controlled HIV.

Research Plan: Fifteen subjects with HIV, aged 50 to 65, will be recruited to complete three study visits over twelve weeks. Each visit will assess frailty score, collect blood samples for cellular oxygen consumption testing, inflammatory markers and complete questionnaires on pain, depression, polypharmacy, comorbidities and duration of infection. After visit two, subjects will complete six weeks of an aerobic exercise intervention, with 30 minutes of escorted walking at 100 steps/minute three times weekly.

Expected Outcome: The addition of moderate aerobic activity is expected to increase cellular oxygen consumption and decrease inflammatory markers in this population. These changes are expected to correlate with frailty phenotype and highlight the ability of the mitochondrial mechanisms of frailty to be altered by simple physical activity.

13. THE IMPACT OF SOCIAL IDENTITY ON PERCEIVED CAREER SELF-EFFICACY IN MASTER OF SOCIAL WORK STUDENTS

Todd Becker

Becker, T.D.

Session C; Poster Presentation; Room 349

Despite the National Association of Social Workers' mission to improve human wellbeing particularly for marginalized communities, social workers often do not reflect the communities they serve. The Council on Social Work Educational Policy and Accreditation Standards has led social work education to emphasize developing dominant social groups' abilities to work with marginalized groups. This orientation how a student's marginalized background could actually contribute to effective practice in the field. This cross-sectional study recruited a

convenience sample of current MSW students (N = 310) from five of the top 20 ranked schools in the U.S. An OLS regression assessed the relationship age, race, Hispanicity, gender, sexual orientation, BSW attainment, and previous work with marginalized communities had on career self-efficacy. The overall model was not statistically significant, suggesting individual-level variables are insufficient in predicting career self-efficacy in a sample of MSW students. Longitudinal designs and a more nuanced measure of self-efficacy for social work students could provide further information.

14. PERCEIVED QUALITY OF EDUCATIONAL EXPERIENCES AND MSW STUDENTS' SELF-AWARENESS OF PRIVILEGE AND OPPRESSION AS IT RELATES TO HETEROSEXISM

Danielle Phillips

Phillips, D.R.

Session C; Poster Presentation; Room 349

Social work education is grounded in values that promote social justice, self-determination, and ethical practices when working the marginalized individuals such as individuals who identify as LGBTQ. It is assumed that students' implicit biases are explored while receiving a Master of Social Work (MSW); however, research indicates that students are often not trained to assess personal biases and beliefs that results in the continued oppression of individuals who identify as LGBTQ. This cross-sectional study explored the associations of age, gender, sexual orientation, and race and MSW students' self-awareness of privilege and oppression as it related to heterosexism using data collected from MSW students at five top 20 MSW programs in the United States. The overall model was statistically significant, $F(10, 300) = 4.159$, $p = .001$, $R2 = .122$, and Adjusted $R2 = .092$. There were positive associations between individuals who identified as gay/lesbian, bisexual, or other identified sexual orientation and MSW students' self-awareness of privilege and oppression as it related to heterosexism. Black or African American race were statistically significant and negatively associated with MSW students' self-awareness of privilege and oppression as it related to heterosexism when compared to White participants. Age was the best predictor of self-awareness of privilege and oppression as it related to heterosexism among MSW students indicating that for every year older a participant was there was a drop in self-awareness. Results indicate that MSW students from diverse backgrounds would benefit from education that promotes cultural competence and self-awareness.

15. INDIVIDUAL CHARACTERISTICS ASSOCIATED WITH COLOR-BLIND RACIAL ATTITUDES IN MSW STUDENTS

Kimberly Leffler

Leffler, K.

Session C; Poster Presentation; Room 349

This research is based on the Critical Race Theory (CRT) perspective as well as aspects of cultural competency in social work practice. A sample of 305 Master of Social Work (MSW) students from five MSW programs across the United States are included in this study's analytic sample. A multiple linear regression was conducted to explore which individual characteristics are associated with MSW student's color-blind racial attitudes using the Color-Blind Racial Attitudes Scale (CoBRAS). Results found

that a student's age, gender, and sexual orientation are all associated with CoBRAS scores. Whether a student had received a BSW degree and their program concentration were also associated with CoBRAS scores. Within this sample Race was not found to be associated with CoBRAS scores.

16. UNDERSTANDING PRIVILEGE AND ENGAGING IN ACTIVISM

Nancy Franke

Franke, N.

Session C; Poster Presentation; Room 349

To best serve clients and be effective "social change agents", social workers must unpack their own privilege and understand and work to dismantle interconnected systems of oppression. One way to do so is through engaging in social activism. This exploratory cross-sectional study considered the relationship between knowledge of racial and heterosexual privilege, intersecting demographic characteristics, and participation in political and social activism among a sample of 310 master of social work students. Knowledge of heterosexual privilege was positively associated with engagement in political and social activism. People who identified as bisexual, gay, lesbian, or queer, as well as macro-focused students had higher rates of activism. There was a significant difference in activism according to an intersectional race and gender variable and a race and sexual orientation variable as well. Limitations and implications are discussed.

17. Differences in One-Year Gait Speed Trajectories between Depression Subtypes in Older Adults After Hip Fracture

Jennifer Kirk

Kirk, J., Magaziner, J., Shardell, M., Orwig, D., Gruber-Baldini, A., Ryan, A., Hochberg, M.C., & Rathbun, A.

Session C; Poster Presentation; Room 349

Fifty-percent of older adults, who fracture a hip, experience depressive symptoms associated with poorer functional recovery. However, depressive symptoms are heterogeneous and non-specific(somatic, emotional, and behavioral). This study assessed differences in gait-speed trajectory by depression subtypes in older adults after hip fracture.

Participants(n=304)were older adults in the Baltimore Hip Studies 7th cohort(N=362) who provided data on baseline depressive symptoms using the 20-Item Center for Epidemiological Studies Depression Scale and three-meter gait-speed(meters-per-second [m/s])assessed at 2,6,or 12-months post-fracture. Posterior probability estimates from a latent class analysis assigned participants to one of four depression subtypes: Asymptomatic, Catatonic, Anhedonic, or Melancholic. Weighted estimating equations evaluated gait-speed trajectories by baseline subtype. Models estimated between-group differences comparing Catatonic, Anhedonic, and Melancholic subtypes to Asymptomatic participants.

Catatonic subtype had slower gait-speed compared to Asymptomatic group during the post-fracture recovery period:β=-0.034(95%CI:-0.129,0.060) at 2-months and β=-0.030(95%CI:-0.124,0.065)12-months. There was gait-speed difference between Melancholic and Asymptomatic subtypes at 2-months(β=0.002;95% CI:-0.105,0.109); however, the direction and magnitude of differences at 6-months(β=-0.054;95%CI:-0.170,0.060) and 12-months(β=-0.030; 95%CI:-0.140,0.081)were similar to

Catatonic participants. No consistent association between Anhedonic depression and post-fracture gait-speed trajectory was observed. Time-specific differences comparing Catatonic, Anhedonic, and Melancholic subtypes to Asymptomatic participants did not reach significance($p>.05$).

While associations between depression subtypes and gait-speed trajectories were not statistically significant, clinically significant differences in gait-speed are 0.03-0.05m/s, Catatonic and Melancholic depression may have an impact on functional recovery. Perhaps, depression subtypes that exhibit psychomotor agitation symptoms(difficulty concentrating, decreased energy and movement), negatively affect older adults' ability to engage in and adhere to rehabilitation during post-fracture recovery.

18. DEVELOPMENT OF A CONCEPTUAL FRAMEWORK FOR FATIGUE IN COPD

Lindsey Clark

Clark, L. A., & Klinedinst, N. J.

Session C; Poster Presentation; Room 349

Over 11 million people have chronic obstructive pulmonary disease (COPD) in the United States, and over 50% suffer from fatigue daily. Fatigue leads to negative outcomes such as limited quality of life and frequent exacerbations. The mechanism of fatigue in COPD is not well understood, thus treatment is limited.

A scoping review was conducted to evaluate potential mechanisms of fatigue in adults with COPD. Given the limited evidence for mechanisms of fatigue in COPD, studies included evaluated the relationship or mechanism of fatigue in adults with COPD and suggested potential biologic mechanisms in other chronic inflammatory diseases.

The most commonly suggested mechanism for fatigue in COPD is lack of oxygenation. However, treatment methods such as aerobic exercise and supplemental oxygen do not resolve fatigue. In other chronic diseases, fatigue is associated with inflammation and reduced energy production at the cellular level. Particularly in lung diseases, there is an increased energy demand due to inflammation in the lungs. Inflammation damages cellular mitochondria, which can affect cellular energy metabolism. Mitochondrial function is reduced in COPD, but the relationship to fatigue is not well established.

A conceptual framework was developed to synthesize a potential mechanistic component of fatigue in COPD. Fatigue is conceptualized as an imbalance in energy supply and demand in adults with COPD compared to healthy individuals. Systemic inflammation from COPD can damage mitochondria, and when combined with lower cellular oxygen supply, reduces cellular energy production. This causes adults with COPD to feel fatigued and react by slowing down or resting.

19. INTERFERONS ALPHA AND GAMMA WITH MONOCYTES AS A THERAPEUTIC STRATEGY FOR OVARIAN CANCER.

Franklin Ning

Ning, F., Duemler, A., Green, D.S.
Zoon, K., & Annunziata, C. M.

Session C; Poster Presentation; Room 349

Background: In the presence of pro-inflammatory cytokines, monocytes are cytotoxic to tumor cells. We previously showed that monocytes stimulated with interferon alpha and gamma result in synergistic killing of ovarian cancer cells in vitro. Here we better characterize monocyte differentiation and their ability to induce cell death through co-culture experiments with spheroids and in vivo mouse experiments.
Methods: OVCAR8 cells were grown in ultra-low attachment conditions for three days before being co-cultured with human monocytes as well as interferon gamma and interferon alpha. Monocytes and OVCAR8s were assayed by flow cytometry for markers of differentiation and viability, respectively. To observe any differences in survival, Foxn1nu athymic mice were injected intraperitoneally with 2*10^6 OVCAR8 cells. Two weeks later, 20*10^6 monocytes and IFN were injected intraperitoneally. Subsequent mouse experiments analyzed monocyte differentiation towards M1 or M2 phenotypes by flow cytometry with or without exposure to tumor cells and/or interferons.
Results: Ovarian cancer cell spheroids showed decreased viability in the presence of monocytes combined with interferon. We show that monocytes also express a spectrum of M1/M2 phenotype when stimulated to IFN or exposed to tumor cells. Mice treated with a combination of interferons and monocytes performed significantly better than either treatment alone or vehicle.
Conclusion: Monocytes combined with interferons alpha and gamma are effective at killing ovarian cancer cells in laboratory models. Phenotypic analyses show a novel pattern of differentiation markers. Future studies will look at modifying the dose schedule to maximize cancer cell death and exploiting interactions with other immune cells.

20. TOWARDS EFFICIENT AND PRECISE IN VIVO GENOME ENGINEERING

Jeffery Inen

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Session C; Poster Presentation; Room 349

Human development is underscored by the complex interactions between multiple cell types over space and time. In order to better translate this understanding for therapeutic success, it is paramount that we develop models that can faithfully recapitulate these intricacies. In contrast to both in vitro and in direct, transplant-based in vivo models, autochthonous, in vivo models preserve the endogenous tissue and its complex microenvironment while leaving the immune system intact. Despite the application of CRISPR/Cas9 mediated genome editing to develop these models faster, cheaper, and with greater throughput, homology directed repair (HDR) remains a notoriously inefficient process in mammalian cells. This inefficiency challenge is particularly salient for direct in vivo applications where enrichment strategies commonly used in vitro cannot be used. While many investigators have previously optimized various aspects of CRISPR/Cas9 mediated HDR, most of these optimizations were performed separately and in a variety of different contexts. In this study, using two independent systems, we examine the combined effect of Cas9 and donor template variants that were all previously

shown to separately improve HDR efficiency. Our findings show that while a high fidelity Cas9 does not improve knock-in (KI) over Wt, the combination of Cas9 (Wt) fused to Ctip, an enzyme critical in the endogenous HDR pathway, and an homology mediated end joining (HMEJ) donor template leads to 20-25 fold increase in total KI efficiency and a 40% increase in biallelic modification. Finally, we explore the use of this technology in neural progenitors directly in the embryonic mouse brain.

21. DIFFERENTIAL CHEMOKINE GENE EXPRESSION PATTERNS IN MALARIA-PROTECTED AND MALARIA-SUSCEPTIBLE INDIVIDUALS

Gillian Mbambo

Mbambo, G., Dwivedi, A., Lyke, F.E., & Silva, J.C.

Session C; Poster Presentation; Room 349

In malaria endemic regions, there are populations of individuals who are either clinically immune or clinically susceptible to Plasmodium falciparum infections regardless of comparable exposure. For our study, individuals with no clinical malaria episodes are classified as malaria-protected individuals due to acquired protective immunity whereas individuals with at least 2 clinical malaria episodes are classified as malaria-susceptible individuals. To identify critical differences in immune responses between malaria-susceptible and malaria-protected children, we use RNAseq to characterize host gene expression profiles. To determine host factors that confer susceptibility to vs protection from P. falciparum infections, we examined the immunological responses from stimulated Peripheral Blood Mononuclear Cells (PBMCs) collected over a transmission season with samples from the beginning of the malaria season (Day 0), peak malaria season (Day 90) and the end of malaria season (Day 150). We hypothesize that children with acquired protective immunity exhibit a higher expression of genes involved in the activation of an immune response or genes that play a role in immune effector function. To address our hypothesis, we used PBMCs collected from children (4-6 years of age) who participated in the FMP2.1/ASO2 adjuvanted AMA-1-based blood-stage vaccine. PBMCs were stimulated with P. falciparum schizonts (Pfsz), Staphylococcus aureus enterotoxin B (SEB) as a positive control, and media as a negative control. We found that there was differential chemokine expression at the beginning of the malaria transmission season (day 0), where PBMCs from malaria-protected individuals express high levels of CXCL10, CXCL11, CXCL9, and CCL8.

22. CERAMIDE ANALYSIS ON A MALDI-TOF PLATFORM: MATRIX, ADDUCT, AND FRAGMENTATION OPTIMIZATION

Anh Tran

Tran, A, Q., & Jones, J, W.

Session C; Poster Presentation; Room 349

Ceramides are pivotal membrane lipids associated with various biological functions, many of which can affect cell signaling and membrane biophysical properties. Due to their low endogenous abundance, ceramide analysis is challenging.

In literature, ceramides are often analyzed using electrospray ionization (ESI) mass spectrometry (MS), while few highlight advantages of analyzing ceramides using Matrix-Assisted Laser Desorption/Ionization

(MALDI) coupled to Time of Flight (TOF) MS. MALDI-TOF analysis offers unique advantages including low sample consumption, high throughput screening, and potential compatibility to mass spectrometry imaging.

In biological derived total lipid extracts, ionization often favors abundant phospholipids. Our data shows that the MALDI matrix THAP (2,Äô,4,Äô,6,Äô-trihydroxyacetophenone) reduces signal intensity of many phospholipids, resulting in observation of ceramide peaks. Furthermore, the addition of lithium into the system reduces spectral complexity and boosts the intensity of ceramides by consolidating ceramide adducts (protonated, sodiated and potassiated) into a single lithiated adduct peak. Therefore, THAP doped with LiCl was our matrix-system of choice for ceramide analysis.

In order to aid analysis and further add lithium into samples, a base hydrolysis method was developed using lithium hydroxide. This procedure selectively hydrolyzed phospholipids with acylglyceride structures, leaving behind the unreactive ceramides, therefore reducing sample complexity during MS analysis. Current data suggests the use of our optimized LiOH hydrolysis along with LiCl-THAP matrix-system yields mass spectra that biases towards ceramide detection in liver samples.

Additionally, we are pursuing the use of tandem mass spectrometry via laser-induced dissociation (LID) on the MALDI-TOF MS platform to obtain information about ceramide,Äôs structural features.

23. DUAL ACTIVATION OF THE CAR AND NRF2 IMPROVES THE EFFICACY:TOXICITY RATIO IN CYCLOPHOSPHAMIDE AND DOXORUBICIN-BASED TREATMENT OF TNBC

Sydney Stern

Stern, S., Liang, D., Li, L., Kareem, A., Hu, T., Kurian, R., Heyward, S., Hong, C., Xue, F., & Wang, H.

Session D; Poster Presentation; Room 349

Triple negative breast cancer (TNBC) accounts for 10-20% of all breast cancer cases and has poor prognosis. The absence of targetable sites leaves cytotoxic chemotherapy to be the standard treatment. Cyclophosphamide (CPA) and doxorubicin (DOX) are among the most commonly used chemotherapeutic agents for TNBC, while often associated with meager outcomes due to drug resistance and intolerable toxicities. As a prodrug, CPA relies on hepatic CYP2B6 for bioactivation to its active metabolite, 4-hydroxycyclophosphamide. The constitutive androstane receptor (CAR) is a master regulator of CYP2B6 expression in that activation of CAR leads to CYP2B6 induction and subsequent CPA bioactivation. DOX, on the other hand, is often associated with a dose-limiting cardiotoxicity. Activation of nuclear factor erythroid 2-related factor (Nrf2) has been implicated in the protection against DOX-induced cardiotoxicity. Here, we identified compound DL7076 as a novel dual-activator of CAR/Nrf2. We showed that DL7076 concentration-dependently induced the expression of CYP2B6 in human primary hepatocytes and HO-1, a Nrf2 target gene, in cardiomyocytes, respectively; while the expression of these genes in TNBC cells was not significantly altered. Functionally, DOX-induced cytotoxicity was efficiently reversed by co-administration of DL7076 in H9c2 cells (a rat cardiomyoblast cell line) but not in TNBC cells. Moreover, using a hepatocyte-H9c2-TNBC coculture model, we showed

that co-administration of DL7076 with CPA/DOX selectively enhanced the cytotoxicity in TNBC cells, while protected H9c2 cells from the chemo-related oxidative stress, apoptosis, and cell death. Collectively, our results establish DL7076 as a novel compound that can improve the efficacy:toxicity ratio of CPA/DOX-based TNBC treatment.

24. THE ROLE OF SINC IN CHLAMYDIAL PATHOGENESIS

Adrienne Kambouris

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Session D; Poster Presentation; Room 349

Chlamydial pathogenesis requires intracellular growth in a vacuolar 'inclusion' where the bacteria replicate and differentiate. We have previously identified SinC, a novel type III secreted effector protein of Chlamydia psittaci. SinC translocates to the nuclear inner membrane of the infected and neighboring, uninfected cells. Using BioID, we observed that translocated SinC is proximal to MAVS as well as LEM domain proteins of the host cell including intrinsically disordered proteins LBR, emerin and MAP-1, that control multiple essential pathways of the host.

The highly conserved SinC ortholog of Chlamydia caviae GPIC, a pathogen of guinea pigs that does not infect humans, also targets the nuclear inner membrane. In order to assess the effect of SinC on gene expression in C. caviae-infected cells, RNA-seq was performed on HeLa cells infected with C. caviae WT and an isogenic sinC mutant at 12 and 36 hours post-infection (hpi). Infection with the mutant revealed a decrease in expression of genes involved in cholesterol biosynthesis and RNA sensing innate immunity at 12 hpi. We hypothesize that this occurs through interactions of SinC with its host targets. Further characterization of SinC may lead to a better understanding of some of the most severe chlamydial infections and in time to novel immunological or therapeutic means of interfering with these infections.

25. RECEPTOR DYSFUNCTION IN MULTIPLE HUMAN LRP1 VARIANTS ASSOCIATED WITH AORTIC ANEURYSMS

Mashhood Wani

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Session D; Poster Presentation; Room 349

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.

26. RISK OF SUBSEQUENT CARDIOVASCULAR EVENTS AMONG MEDICARE BENEFICIARIES DIAGNOSED WITH OBSTRUCTIVE SLEEP APNEA, TREATED WITH CONTINUOUS POSITIVE AIRWAY PRESSURE

M. Doyinsola Ismail

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Session D; Poster Presentation; Room 349

Obstructive sleep apnea (OSA) is associated with an increased risk of cardiovascular disease (CVD). We evaluated the incidence of new CV events among Medicare beneficiaries with and without pre-existing CVD who were newly diagnosed with OSA and subsequently initiated Continuous Positive Airway Pressure (CPAP) therapy.

We conducted a retrospective analysis of a 5% sample of Medicare claims data including adults ≥ 65 years who were newly diagnosed with OSA and initiated CPAP 2009-2013. CVD was operationalized as ischemic heart disease and cardiovascular or peripheral procedures. Person-time at risk was summed from the date of first PAP charge to the earliest of either new CV event date or the end of observation (24 months). Incidence rates were estimated by dividing new CV events by person-months.
4,289 Medicare beneficiaries met study criteria. Mean age was 72±5 years, 90% were white, and 55% were male. 38% had pre-existing CVD and 62% had no prior history of CVD. In the 2-year period following CPAP initiation, beneficiaries without prior CVD had a 10% risk of having a new CV event compared to 74% among those with pre-existing CVD. The incidence rate among those without prior CVD was 5.2 new CV events per 100 person-years (95% CI = 4.6-5.4), compared to 74.5 new CV events per 100 person-years among those with pre-existing CVD (95% CI= 70.4-78.2).
Among beneficiaries newly diagnosed with OSA who initiated CPAP, those with prior CVD history were seven-times more likely to experience subsequent adverse cardiovascular events relative to beneficiaries without pre-existing CVD.

27. MECHANISMS OF A FUNCTION-SELECTIVE ERK INHIBITOR AND INDUCTION OF APOPTOSIS IN MELANOMA CELLS

Ramon Martinez

Martinez, R.

Session D; Poster Presentation; Room 349

Various cancers can contribute their proliferative phenotypes to mutations conferring constitutive activity of the extracellular signal-regulated kinase (ERK1/2) signaling pathway. Recent drug design trends have suggested that shifting the design of inhibitors from targeting the catalytic core of a kinase to allosteric inhibition may prove as a promising alternative to therapeutic development. We previously identified a novel thienyl naphthalene sulfonate compound that shows functionally-selective inhibitory activity against ERK2 by blocking F-site containing substrates, including Fos family proteins. Proteomic analysis of drug-treated melanoma cell lysates suggests treatment with this compound results in defects in mitochondrial function as well as upregulation of markers suggestive of activating an oxidative stress response. Immunoblot analysis demonstrated the upregulation of the nuclear factor erythroid 2-related factor 2 (Nrf2), which is known to play a role in regulating the oxidative stress pathway. While studies with inhibitors reactive oxygen species (ROS) show generation of ROS with compound treatment, cell viability studies have indicated that ROS is only partially responsible for the growth inhibition of melanoma cells. Mass spectrometry suggests that the novel compound may interact with ERK2 via covalent modifications on a unique cysteine residue. However, in vitro experiments with N-acetyl cysteine (NAC) shows that the compound does not form random interactions with cysteines, and suggests protein coordination with the compound is required for adduct formation. In these studies, we provide insight into the interactions this novel compound makes with the ERK2 protein, and the transcriptomic and proteomic responses that result in oxidative stress and melanoma cell death.

28. COMPARISONS OF ATP-COMPETITIVE (TYPE I) VERSUS FUNCTION-SELECTIVE (TYPE IV) ERK INHIBITORS TO PREVENT AIRWAY SMOOTH MUSCLE CELL PROLIFERATION IN ASTHMA

Amy Defnet

Defnet, A.E., Huang, W., Kane, M.A., Deshpande, D.A., & Shapiro, P.

Session D; Poster Presentation; Room 349

Hyperproliferation of airway smooth muscle (ASM) cells is a characteristic of airway remodeling associated with inflammatory diseases, such as asthma. Currently, there are no effective therapies to stop ASM cell proliferation that contributes to debilitating bronchoconstriction. Previous studies have shown that stimuli such as growth factors, cytokines, and cellular stress induce signaling through the extracellular signal-regulated kinases (ERK1/2) in ASM cells making them a potential therapeutic target. Although several Type I selective ATP-competitive inhibitors of ERK1/2 have been developed, these compounds block all enzymatic activity, including ERK1/2 functions in normal cells not associated with disease. To mitigate off-target toxicity, we previously identified a novel function-selective Type IV ERK2 inhibitor, referred to as SF-3-030. In the current studies, SF-3-030 was compared to known Type I inhibitors, ulixertinib and Vx-11e, in regulating platelet-derived growth factor (PDGF) induced ASM cell proliferation. We show that both the type I and IV inhibitors can prevent PDGF-mediated proliferation of human ASM cells through the disruption of activator protein-1 (AP-1) activity along with the inhibition of several key signaling pathways associated with asthma pathogenesis. Proteomic analysis of PDGF-stimulated ASM cells showed that SF-

3-030 regulated a subset of proteins that were affected by ulixertinib. Additionally, functional studies of IL-6 secretion and soluble collagen were performed to further explore proteomic results. These data suggest that Type IV function-selective inhibition of ERK2 is sufficient to mitigate ASM cell proliferation in asthma while reducing possible off-target effects seen with Type I ATP-competitive inhibitors.

29. QUANTITATION OF VINYL ETHER PHOSPHATIDYLETHANOLAMINE: APPLICATION TO TRAUMATIC BRAIN INJURY

Yulemni Morel

Morel, Y., Sarkar, C., Lipinski, M. M., Kane, M. A., & Jones. J. W.

Session E; Poster Presentation; Room 349

Traumatic brain injury (TBI) is a major health concern worldwide resulting in approximately 50,000 deaths annually. TBI can result in a cascade of biological events including autophagy impairment, due to degradation of lysosomal membranes. Previous data has shown vinyl ether phosphatidylethanolamine (PE) were differently expressed in brain lysosomes from mice exposed to TBI compared to sham. Vinyl ether PE are comprised of an ether-linkage at the sn-1 position with an adjacent cis double bond. This unique structural arrangement provides functional implications for membrane dynamics. The sn-2 position of vinyl ether PE are reservoirs of polyunsaturated fatty acids, that when enzymatically cleaved provide an integral pathway for the production of secondary messenger molecules including eicosanoids. These data suggest vinyl ether PE as potential diagnostic biomarkers have the ability to provide unique insight into the pathogenesis of neurodegeneration following TBI.

We have developed a quantitative assay based on liquid chromatography tandem mass spectrometry (LC-MS/MS) that can effectively detect and quantify vinyl ether PE in biological samples. The LC-MS/MS method uses selected reaction monitoring (SRM) to simultaneously monitor precursor-to-product transitions optimized to provide structure specificity at both the sn-1 and sn-2 position. The chromatography involves a HILIC separation to achieve lipid class separation and allow for internal standard co-elution with all monitored transitions. Our quantitative assay was applied to brain lysosomes and tissue from a controlled cortical impact TBI mouse model. We will present our findings on assay validation and the prospect of vinyl ether PE as quantitative diagnostic biomarkers for brain injury.

30. ANTIBACTERIAL RESPONSE OF ORAL MICROCOSM BIOFILM TO NANO-ZINC OXIDE IN DENTAL ADHESIVE

Isadora Garcia

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Session E; Poster Presentation; Room 349

Objectives: Various nanoparticles are currently under investigation to impart biointeractivity for dental materials. This study aimed to: (1) formulate an experimental dental adhesive containing ZnO nanoparticles; (2) evaluate its chemical and

mechanical properties; and (3) assess the antibacterial response against oral microcosm biofilm.
Methods: Nanosized ZnO was chemically and morphologically evaluated. ZnO was incorporated at 0 (GCTRL), 2.5 (G2.5%), 5 (G5%) and 7.5 (G5%) wt.% in an experimental dental adhesive. The adhesives were evaluated for the degree of conversion (DC), flexural strength (FS), and elastic modulus (E). The antibacterial activity was evaluated using a 48 h-microcosm biofilm model after the formation of acquired pellicle on samples' surfaces. Colony-forming units (CFU), metabolic activity, and live/dead staining were assessed.
Results: Nanosized ZnO presented characteristic peaks of Zn-O bonds, and the particles were arranged in agglomerates. The DC ranged from 62.21 (±1.05) % for GCtrl to 46.15 (±1.23) % for G7.5% ($p<0.05$). G7.5% showed lower FS compared to all groups ($p<0.05$). Despite achieving higher E ($p<0.05$), G2.5% did not show differences for GCtrl regarding the FS ($p>0.05$). G7.5% had lower CFU/mL compared to GCtrl for mutans streptococci ($p<0.05$) and total microorganism ($p<0.05$), besides presenting lower metabolic activity ($p<0.05$) and higher dead bacteria via biofilm staining.
Conclusion: The physicochemical properties of the dental adhesives were similar to commercial adhesives and in compliance with ISO recommendation. G7.5% restricted the growth of oral microcosm biofilm without impairing the physicochemical performance.

31. NOVEL NANO-STRUCTURED THERAPEUTIC ANTI-CARIES DENTAL ADHESIVE REDUCES BIOFILM PATHOGENICITY AND PROTECTS TEETH

Bhadila Ghalia

Bhadila, G. Y., Weir, M. D., Melo, M. A. S., & Xu, H. H. K.

Session E; Poster Presentation; Room 349

Replacement of failed dental restorations costs the U.S. billions of dollars annually. This is attributed mainly to secondary caries due to dental biofilm. The objectives of this study were to: (1) develop a novel nano-structured dental adhesive with antibiofilm and remineralization properties using dimethylaminohexadecyl methacrylate (DMAHDM) and nanoparticles of calcium fluoride (nCaF2); (2) evaluate the dentin bond strength, the cariogenic pathogenicity of Streptococcus Mutans (S. mutans) biofilm, and lactic acid production; (3) investigate the effects of DMAHDM on fluoride ion release. Four groups were tested: (1) commercial control adhesive, (2) Experimental control adhesive, (3) Experimental control + 20% nCaF2, and (4) Experimental control + 20% nCaF2 + 5% DMAHDM. The anticariogenic properties were assessed by biofilm colony-forming units counts (CFU), metabolic activities, biofilm biomass, acid neutralizing activities, and lactic acid production of biofilms grown on adhesive resins. Adding nCaF2 and DMAHDM did not compromise the bond strength ($p > 0.1$). The nCaF2-DMAHDM-containing adhesive decreased the S. mutans biofilm CFU by 4 orders of magnitude, showed more than 3-fold decrease in metabolic activity, 10-fold decrease in lactic acid production, and more than 2-fold decrease in biofilm biomass, compared to controls ($p < 0.05$). The nCaF2-DMAHDM-adhesive was able to shift the acidic cariogenic biofilm environment (pH = 4) to a safe pH of 7. The new adhesive had the ability to release high levels of Ca and F ions to remineralize tooth structures. This novel

nano-structured therapeutic adhesive was able to mitigate the cariogenic potential of S. mutans, while providing tooth-strengthening ions.

32. DESIGNING SPECIFIC INHIBITORS TO TARGET S100B IN MELANOMA

Darex Vera-Rodriguez

Vera-Rodríguez, D.J., Young, B., S Spriggs, S., Yu, W., Wilder, P.T., MacKerell, A.D., & Weber, D.J.

Session E; Poster Presentation; Room 349

Malignant melanoma (MM) is statistically defined as the most dangerous form of skin cancer, causing a large majority of skin cancer deaths. Previous studies demonstrate S100B as a tumor marker in MM, a protein that interacts with the tumor suppressor p53, inhibiting p53 function. With the goal of blocking this interaction, three binding sites on S100B for small molecules have been identified. However, developing drugs specific for S100B over other S100-family members still remains a challenge.

This project aims to identify S100B-specific small molecule inhibitors and understand the basis of their specificity over other S100 family members (specifically S100A1). To identify S100B-specific compounds, an NMR fragment-based screening approach was run with S100B and S100A1. A 2D-[1H,15N] HSQC of S100B bound to a non-specific fragment showed multiple chemical shifts perturbations (CSPs) including residues V13, F43, L40, F73, and C84 (Figure 1). Interestingly, fewer and less pronounced CSPs were observed for a S100B-specific fragment. In combination with the fragment-based screening approach, Site-Identified Ligand Competitive Saturation (SILCS) molecular dynamics (MD) simulations were performed to determine potential S100B binding sites that could explain the CSPs. Results show a strong hydrophobic pocket comprised by helices 1, 2, and 4 from Calcium-bound S100B (Figure 2) at low free energy (GFE) levels. Residues residing in this novel binding site are consistent with CSPs for compounds that bind S100B, several which are involved in binding to the S100B-specific fragment. These data provide important information relevant to developing S100B-specific drugs to treat MM.

33. MOLECULAR DYNAMICS, HDX, AND MODELING: A MULTIFACETED APPROACH TO MODEL SOLUTION STRUCTURAL ENSEMBLES

Kyle Kihn

Kihn K. C., Wintrode P.L., & Deredge J.

Session E; Poster Presentation; Room 349

Hydrogen-Deuterium exchange coupled with mass spectrometry (HDX-MS) is a powerful biophysical technique which allows probing of the structure and dynamics of conformational ensembles of proteins in solution. To take further advantage of this experimental technique, computational HDX prediction tools are being developed which estimate protein amide backbone protection factors from molecular dynamics simulations. These calculated protection factors can be further transformed to kinetic deuterium uptake curves and correlated to the experimental uptake data. With these correlations, structures and simulation can be validated and the resolution of HDX-MS data increased. In combination with enhanced sampling molecular dynamics, clustering algorithms, and maximum entropy reweighing, improved ensemble refinement can be achieved, allowing for representative

ensembles to be extracted from simulated data. This clustering and refining of ensembles enable improved computational and biophysical analysis of structurally relevant conformations. We have applied this modeling and reweighing approach to the heme binding protein PhuS from P.aeruginosa. Here, we used HDX-MS together with enhanced molecular dynamics simulations and a maximum entropy ensemble reweighting approach to decipher functionally important structural features of PhuS, a cytoplasmic heme binding protein from P.aeruginosa. Additionally, we uncover large structural difference between the heme bound and apo in solution conformations, which are not apparent in the static crystal structures. The uncovering of these biologically relevant ensembles will potentially allow for the discovery of new druggable sites within the PhuS protein.

34. DUAL INHIBITION OF HDAC6 AND THE PROTEASOME AS A POLYPHARMACOLOGIC METHOD FOR TREATMENT OF HEMATOLOGICAL MALIGNANCIES

Alexandria Chan

Chan, A. M., Mitchell, A., & Fletcher, S.

Session E; Poster Presentation; Room 349

Cancer cells adapt for survival through activation of multiple pathways, leading to resistance often seen in chemotherapies. One method used to combat these multifactorial diseases is polypharmacology, commonly thought of as “one drug multiple targets”. Proteasome inhibitors are known to cause resistance in patients; the proteasome is responsible for the degradation of damaged, misfolded, or unwanted proteins in the cell. Cancer cells often produce an increased amount of ineffective proteins that need to be degraded. Proteasome inhibition causes accumulation of these proteins, resulting in cell death. One method of resistance is the aggresome pathway, mediated by histone deacetylase-6 (HDAC6). This pathway trafficks unwanted proteins into aggresomes where they are stored until degradation by lysosomes. Upregulation of HDAC6 in malignant cells and the lack of adverse effects from knockdown of this protein make it an ideal target for cancer treatment. HDAC inhibitors have three groups: zinc binding, linking, and capping. Selectivity for HDAC6 over other family members can be achieved by the manipulation of this model, specifically increasing linking and/or capping group size. The wider binding pocket of HDAC6, compared to other isoforms, readily accommodates these bulky groups. Increase in selectivity also attenuates the cytotoxic effects of pan-HDAC inhibition. Recent literature shows the dual proteasome/HDAC inhibition has a synergistic effect, leading to increased cell death and decreased cell proliferation. Therefore, we have assembled a library of dual proteasome/HDAC6 inhibitors by enhancing existing proteasome inhibitors through addition of various linkers and zinc binding groups for selective inhibition of HDAC6.

35. FINE-TUNING NOTCH EXPRESSION BY LYMPHOCYTIC GRANZYME B PRODUCTION

Ellis Tibbs

Tibbs, E., & Cao, X.

Session E; Poster Presentation; Room 349

Notch signaling has been studied for many years and has been found to play a role in many aspects of cellular development, tissue homeostasis, and progression of disease. Upon interaction with its ligand, Delta-like-4,

the Notch1 molecule undergoes two proteolytic cleavage events. This eventually leads to the translocation of the intracellular domain (NICD) into the nucleus. Once there, NICD interacts with transcription factors such as CBF1/RBPJ. Recently, Notch has been found to play a role in the Th1/Th2 imbalance found in many diseases. Using a software to determine possible cleavage target sites for Granzyme B (GzmB), two were found following the start site of NICD. Thus, we hypothesize that Granzyme B production plays a functional role in the translocation of intracellular Notch1 in affecting CD4+ and CD8+ T lymphocyte activation.
We test our hypothesis by stimulating T lymphocytes collected from transgenic mice that are deficient in GzmB and measuring intracellular and extracellular Notch1 expression compared to wildtype following in vitro aCD3-CD28 stimulation. Flow Cytometry was used to measure Notch expression. Preliminary results show that 24hrs after stimulation, CD8+ and CD4+ T cells from GzmB-deficient mice show 12% and 6%, more NICD expression than WT counterparts and 19% and 14% more extracellular Notch1 expression, respectively. These results show that the presence of GzmB can cause an alteration in the fine-tuning expression of Notch1. This work helps us understand the role of Granzyme B in Notch activation and differentiation of lymphocytes.

36. OBESITY CORRELATES IN PRESCHOOL AGE CHILDREN

Zahra Rahmaty

Rahmaty, Z.

Session E; Poster Presentation; Room 349

Childhood obesity is a public health issue. Almost 24% of preschoolers had obesity in the 2006 national dataset. Diet quality is one of the critical factors contributing to obesity. Food neophobia is a strong factor in determining children's diet, its effect was not consistent with children's weight status. Also, caregivers' weight status was a predictor of children’s obesity in some studies, but the result was not consistent through literature. This study aims to find correlates of obesity in children, test the effect of caregivers' weight status and children's food neophobia scores on childhood obesity.
Methods: A cross-sectional, secondary data analysis of baseline data of CHAMP study was done. CHAMP is a 3-arm cluster randomized-control trial aiming to increase healthy habits in preschoolers. Child and family-level factors were put in the GLMM to find obesity correlates. Descriptive statistics were used to show participant characteristics. Obese and non-obese children were compared for their characteristics by independent t-test and chi-square test.
From the 816 participated children, 25% were obese. Obese children had higher proportion of obese caregivers and higher proportion of food insecurity at home. Caregivers' BMI and light physical activity were the only significant correlates of obesity while controlling for other factors. This study showed that researchers can expect obesity in children of obese caregivers. Obesity prevention programs should focus on these caregivers even before children reach the cut points of obesity. Although CFNS could not predict children's weight in this study this relationship should be investigated in a longitudinal study

37. A STUDY ON THE STEREOCHEMISTRY OF HCAR ACTIVATOR CITCO

Benjamin Diethelm-Varela

Diethelm-Varela, B., Hom, K., Liang, D., Deschamps, J., Imler, G., & Xue, F.

Session E; Poster Presentation; Room 349

The human constitutive androstane receptor (hCAR) is a xenobiotic receptor which enhances the metabolic activation of the cytotoxic prodrug, cyclophosphamide, thus improving the therapeutic index of the chemotherapeutic regimen CHOP. CITCO (6-(4-chlorophenyl)imidazo[2,1-b][1,3]thiazole-5-carbaldehyde-O-(3,4-dichlorobenzyl)oxime) is the prototypical hCAR activator, serving as a lead compound for novel activator design. This compound has two stereoisomers, and the activity of each is currently unknown. In this work, we aimed to characterize the stereochemistry and behavior in solution of CITCO in order to better understand this pharmacological tool.
Using chemical synthesis and characterization by 1H-NMR, NOESY, X-ray crystallography, and HRMS, we discovered that CITCO is synthesized stereoselectively as the E isomer regardless of the reaction conditions. The Z isomer forms in solution and is isolable. NMR kinetic data shows that CITCO experiences time- and concentration-dependent stereoisomerization in solution, both from E to Z and from Z to E. The equilibrium position is concentration-dependent. When assaying conditions mimicking those used for biological hCAR activation, rapid isomerization ensues, leading to a mixture of isomers within 3 hours.
As hCAR activation reporter assays usually take 24 hours to measure activity, our finding suggests that all CITCO activity reported so far comes from a mixture of isomers regardless of the original composition. Further studies are needed to characterize the isomerization mechanism, and to unambiguously determine the activity of each isomer in order to undertake rational hCAR activator design.

38. TICK CROQUEMORT BINDS TO INFECTION-DERIVED LIPIDS AND ELICITS BORRELIA BURGDORFERI IMMUNITY IN THE VECTOR

Anya O'Neal

O'Neal, A.J.

Session E; Poster Presentation; Room 349

Innate immunity in evolutionarily ancient chelicerates reveals distinct signaling networks when compared to insects. For instance, lipids derived from microbes stimulate humoral immunity, which is protective against infection by the Lyme disease spirochete Borrelia burgdorferi in Ixodes scapularis ticks. Bona fide lipid receptors for microbial immunity in chelicerates remain elusive. Here, we report the I. scapularis protein Croquemort, a CD36-like scavenger receptor for lipids when using a pull-down assay combined with surface plasmon resonance, tryptophan fluorescence quenching and hydrophobic probe assays. Furthermore, we determined ligand-protein interactions between the I. scapularis ectodomain of Croquemort and the 1-palmitoyl-2-oleoyl-sn-glycero-3-phosphoglycerol (POPG) microbial lipid. The tick Croquemort has a canonical scavenger receptor-type fold with a large open cavity or pocket where POPG may be inserted. We found residues likely to affect the structural integrity of I. scapularis Croquemort and uncovered critical POPG molecular interactions at the entrance and inner lining of the ectodomain pocket or cavity. Importantly, metabolomics analysis revealed that B. burgdorferi increases the presence of POPG in tick cells and transcriptional silencing of croquemort increases B. burgdorferi

bacteremia in I. scapularis. Deciphering how Croquemort regulates immune signaling pathways in I. scapularis ticks are currently being done through reductionist approaches, such as ectopic expression and genome editing technologies, and single-cell and bulk RNA sequencing. Collectively, our findings shed light onto tick-Borrelia interactions and contribute to new scientific paradigms in arthropod immunity.

39. EFFECTS OF INDIVIDUAL CHARACTERISTICS AND EXPERIENCES ON MSW STUDENTS' ADVOCACY

Eusong Park

Park, E.

Session F; Poster Presentation; Room 349

Social work education ought to train students to engage in the work of advocacy because the primary goal of a social worker is to support people in need. However, literature is lacking to show the relationship between individual factors and MSW students' advocacy. This study examines individual factors that influence activity in anti-racism advocacy and political-social advocacy among MSW students. The research team sent an online survey link to the current MSW students of five schools in the U.S. Data analyses included hierarchical regression. The results indicate that people who identify as bisexual and queer, studying a macro concentration, having work experience with people who are marginalized had positive associations with having a high anti-racism advocacy score; cisman and having a BSW had negative associations with having a high anti-racism advocacy score. The results also indicate that people who identify as bisexual and queer, studying a macro and a combined concentration, and having work experience with people who are marginalized had positive associations with having a high political social advocacy score. Findings suggest that MSW educators could pay more attention to the populations with certain demographic characteristics that tend to have lower rates of advocacy and encourage them to become actively involved in promoting the wellbeing of those who are marginalized.

40. DOES THE CLASSROOM EXPERIENCE OF SUPPORTING MULTICULTURALISM PREDICT CULTURAL AWARENESS AND CLASSISM AWARENESS OF SOCIAL WORK STUDENTS?

Ji Hyang Cheon

Cheon, J.H.

Session F; Poster Presentation; Room 349

Cultural awareness is a key factor in the process of developing cultural competence that social workers should demonstrate in social work services. Previous research has investigated contributing factors to build cultural awareness including class structure (included curriculum or standalone class), teaching methods (lecture only or other), but the results were not consistent. Only a few studies have examined the role of a culturally competent instructor in improving students' cultural competence. There have been no studies to investigate the relationship between the role of the instructor and classism which is one aspect of cultural diversity.
Three hundred eleven students in five MSW programs were participated the survey.
Only cultural awareness has been positively associated with classism awareness. However, the relationship between classroom experience and cultural awareness strengthened negatively, changing to be statistically significant depending on the

perceived course content coverage of cultural competence of MSW students.
The findings indicate that the increase of exposure to the content of cultural competence may have a positive effect on cultural and classism awareness. However, as cultural and classism awareness increases, students may use stricter criteria to evaluate the instructor's support of multiculturalism. This project concludes with practice and policy implications, including the potential benefits of expanding content coverage of cultural competence in MSW programs, as well as hiring culturally competent instructors. In the future, it is necessary to conduct research on whether the more students are exposed to the contents of cultural diversity, the more rigorously they evaluate the cultural competence of the instructors.

41. GENDER IDENTITIES AND GENDER INEQUALITY: AN EXAMINATION OF AWARENESS OF SEXISM AMONG MSW STUDENTS

Yao Wang

Wang, Y.

Session F; Poster Presentation; Room 349

There have been concerns on gender imbalance and inequality among the field of social work in terms of both clinical practice and academia. One of the goals of social work education is to recognize social injustices in our society and raise the awareness of these systematic privilege and oppression. Previous studies show that there are gender differences in the field of social work, in terms of salary, leadership, status-related positions and workload. Few studies examined how social work courses or trainings address the issues related to sexism. This study is going to fill out the gap in the literature.

42. MSW PROGRAM CULTURAL AWARENESS PREDICTING STUDENT ANTI-RACIST BEHAVIORS

Shawna Murray-Browne

Murray-Browne, S.

Session F; Poster Presentation; Room 349

Masters level students across the country come into the social work profession in an effort to help racial and ethnic minorities who continue to endure racism and oppression. However, while the current racially charged political climate in the United States has led to an overflow of activism and advocacy, the same students are in classrooms in Schools of Social Work, avoiding discussions about these tough topics. This cross sectional study explores whether there is a relationship between MSW program ratings in cultural awareness and MSW student color-blind attitudes and antiracist behaviors. Informed by critical race theory, insight around the current state of social work education and the implications for social justice oriented social work education is explored.

43. POLARIZABLE GENERAL FORCE FIELD FOR DRUG-LIKE MOLECULES: DRUDE GENERAL FORCE FIELD (DGENFF)

Payal Chatterjee

Chatterjee, P.

Session F; Poster Presentation; Room 349

The classical Drude oscillator polarizable force field offers an explicit treatment of induced electronic polarization presently not

addressed in the commonly used additive force fields. Such an empirical approach leads to an improved and more accurate representation of electrostatic interactions in Molecular Mechanics and Molecular Dynamics (MD) simulations. The Drude Polarizable Force Field presently include topologies and parameters for biomolecules such as proteins, lipids, carbohydrates, and nucleic acids along with a limited set of small molecules. To expand the coverage of small molecules to include a wider-range of drug-like molecules, thereby encouraging its' usage in drug design, we hereby aim to extend the Drude Polarizable force field to a wide range of small molecules – Drude General Force Field (DGenFF). This effort will also include an automation of the process of optimization of parameters for small molecules, using both experimental and Quantum Mechanical (QM) data as the target. Such automation will help in expanding the coverage of available parameters to overlap with that of the vast chemical space relevant to drug design.

44. CITCO AS AN ADJUVANT THERAPY ENHANCES EFFICACY OF CHOP IN NON-HODGKIN'S LYMPHOMA.

Ritika Kurian

Kurian, R., Hedrich, W., Mackowiak, B., Li, L., & Wang, H.

Session F; Poster Presentation; Room 349

Non-Hodgkin lymphoma (NHL) is a common form of blood cancer originating in the lymph or lymphatic system. CHOP comprising of cyclophosphamide (CPA), doxorubicin, vincristine, and prednisone is a first-generation chemotherapy regimen widely used for the treatment of NHL, yet poor survival rates have been reported in stage III or IV patients; calling for an improvement of this frontline therapy. Pharmacologically, CPA, a prodrug, needs be bioactivated to its active metabolite 4-hydroxy-CPA. This metabolic activation is primarily mediated by CYP2B6, which is transcriptionally regulated by the constitutive androstane receptor (CAR). We have previously demonstrated that CITCO, a selective CAR activator, can robustly induce hepatic CYP2B6 and enhance antineoplastic effect of CHOP towards lymphoma cells in vitro. Here, we investigate CITCO as an adjuvant drug candidate facilitating CHOP-based treatment of NHL in a human CAR transgenic mouse model. Our results demonstrate that CITCO is well-tolerated via IP, IV, or oral administration in hCAR-TG mice; and CITCO pretreatment followed by CHOP regimen leads to significant suppression of NHL xenograft growth. CITCO treatment markedly induced the expression of Cyp2b10 (murine ortholog of human CYP2B6) and the formation of 4-hydroxy-CPA in vivo. Our data indicate that compared to other administration routes CITCO gavage induces Cyp2b10 expression to a similar or greater extent although with low serum exposures. Collectively, our findings uncover CITCO as an effective facilitator for CHOP-based NHL treatment in vivo; and the unique pharmacokinetic-pharmacodynamic feature of CITCO makes it a promising candidate for potential adjuvant treatment with CHOP regimen in clinic.

45. FRANCISELLA TULARENSIS PHAGOSOMAL TRANSPORTERS FPTA AND FPTF ARE CRITICAL FOR PATHOGENESIS

Brandi Hobbs

Hobbs, B. E., & Barry, E. M.

Session F; Poster Presentation; Room 349

Francisella tularensis (Ft) is a Gram-negative, facultative intracellular bacterium that is a Tier 1 Select Agent of concern for biodefense for which there is no licensed vaccine. A subfamily of 9 Francisella phagosomal transporter (fpt) genes belonging to the Major Facilitator Superfamily of transporters was identified as critical to pathogenesis and potential targets for attenuation and vaccine development. We hypothesize that fptA and fptF gene products contribute to virulence by facilitating the intracellular replication niche. fpt deletion mutants were generated in Ft Live Vaccine Strain (LVS). Mutations in fptA and fptF resulted in reduced intracellular replication at 24-hours post-infection and LVSΔfptF induced reduced cytotoxicity at 48-hours post-infection in murine peritoneal macrophages ($P < 0.05$). Mutants were able to re-infect neighboring cells in no-gentamicin conditions permitting cell-to-cell spread, though this was delayed at 48-hours post-infection vs. LVS ($P < 0.05$). In vivo, an i.n. dose of 1x103 CFU of LVS results in death of 87.5% of mice by day 10 post-infection. Mutant strains LVSΔfptA and LVSΔfptF were attenuated with LD50 values of >2x10^3 and >1x10^4 respectively. The bacterial burdens of LVSΔfptA and LVSΔfptF mutant strains at 6-days post-infection were significantly reduced compared to that of LVS in spleens, lungs and livers ($P < 0.05$), and LVSΔfptA and LVSΔfptF mutant strains were cleared from the host by 21-days post-infection. These results support a fundamental necessity for fptA and fptF gene products in the pathogenesis of Ft and support their further consideration as targets for the development of live attenuated vaccines.

46. CD5 CONTROLS THE CELL-TO-CELL HETEROGENEITY IN SURVIVAL BY MODULATING NFKB CYTOPLASMIC RESERVES IN PERIPHERAL T CELLS

Courtney Matson

Matson, C.A., Choi, S., Zhao, B.
Livak, F., Love, P.E., & Singh, N.J.

Session F; Poster Presentation; Room 349

A critical component of adaptive immunity is the ability of rare antigen-specific T cells to activate and proliferate to combat foreign pathogens. Oftentimes there is heterogeneity among these responses, even between T cells bearing receptors capable of recognizing the same antigen. Although it is known that some of this variation correlates with the amount of the surface receptor CD5 – where CD5-high T cells respond to a higher extent than their CD5-low counterparts – the underlying molecular mechanism is not known. We find that CD5 regulates the intracellular levels of the NFκB inhibitor, IκBα, by post-translational stabilization of the protein. This stabilization is independent of two canonical binding partners of CD5, SHP-1 and casein kinase II. The higher IκBα expression allows T cells to retain a proportionally greater amount of NFκB in a cytoplasmic reservoir without significant nuclear translocation. Upon antigen-driven activation, TCR signals result in phosphorylation and degradation of IκBα, releasing the cytosolic NFκB to enter the nucleus and drive gene expression. Importantly, at this time, CD5-high T cells with a greater NFκB reservoir would allow for a more robust NFκB-dependent gene expression. Consistent with this postulate, we find a higher survival advantage for CD5-high relative to CD5-low thymocytes ex vivo, which was abrogated when NFκB signaling was inhibited. Taken together, our data reveal an intriguing mechanism where disparate cytoplasmic pools of a key signaling molecule held in an inactive state prior to T cell activation regulates peripheral T cell responses.

47. GRISEOFULVIN AND ITRACONAZOLE AS BCS CLASS II DRUG MODELS FOR SOLUBILITY BOOST VIA BETA CYCLODEXTRIN DERIVATIVES COMPLEX FORMATION

Dongyue Yu

Yu, D., Popescu, C., & Hoag, S.W.

Session F; Poster Presentation; Room 349

INTRODUCTION: Itraconazole (ITZ) and griseofulvin (GSF) are both antifungal antibiotics and have low water solubility. The aim of this study is to assess beta cyclodextrins derivatives' ability to enhance ITZ and GSF solubility by complex formation evaluated by phase solubility technique and Differential Scanning Calorimetry (DSC).

METHODS and MATERIALS: Two hydroxypropyl beta-cyclodextrins Kleptose® HPB = HPBCD with MS=0.65; Kleptose® HP =HPCD with MS=0.85, a methylated beta-cyclodextrins Kleptose® Crysmeb and a sulfobutylether beta-cyclodextrin (SBEBCD Captisol®) were evaluated for their solubilization potential of ITZ and GSF.
For the phase solubility study, an excess amount of API was added to 10 mL of aqueous solutions of increasing CDs concentrations (20, 40, 80, 160, 200 mM) in deionized water. The filtered supernatants were analyzed by UPLC and 1ml was placed on the stability chamber for 6 and 12 months. Also, 2 mL of each filtered sample was lyophilized and analyzed using DSC to confirm inclusion complex formation.

RESULTS: The cyclodextrin derivatives solubility time increase X=S/S0 at 100mM concentration ranking for ITZ is as follows : Crysmeb (966X) >HPBCD (452X) > HPBCD (366X) > SBEBCD (31X) while for GSF there are very minor differences :Crysmeb (5.1X) >SBEBCD (5X) > HPBCD (4.8X) > HPCD (4.2X) .DSC analysis is confirming the complex formation for both ITZ and GSF by endothermic peak disappearance in the thermograms display in all freeze-dried sample.

CONCLUSION: The type of cyclodextrin derivative selection is critical for ITZ solubilization (highest efficiency S/S0=966 in presence of methylated beta cyclodextrins Crysmeb) while for GSF is not.

48. ROLE(S) OF THE TANDEM-REPEAT GALECTIN-9 IN ADHESION OF INFLUENZA A VIRUS TO HUMAN AIRWAY EPITHELIAL CELLS

Muddassar Iqbal

Iqbal, M., Feng, C., & Vasta, G.

Session G; Poster Presentation; Room 349

Galectins are a family of galactose-binding lectins with members (galectin-1 to -15) classified as proto-, chimera- and tandem-repeat types based on their domain organization. Galectins have been implicated in diverse processes including embryonic development, immune regulation, and tumor metastasis. Recently, galectins have been identified as pattern recognition receptors (PRRs), being upregulated during certain infections, binding to galactose residues exposed on pathogen surfaces, and acting as defense factors. For some pathogens, however, these protective role(s) have been subverted to facilitate their attachment to and entry into host cells.
The protective role of the proto type galectin-1 (Gal1) against influenza A virus (IAV) infection has been previously reported. Studies in our lab, however, have shown that upon exposure of airway epithelial cells to

IAV, both Gal1 and the chimera type galectin-3 (Gal3) are secreted to the host airway lumen and bind to the cell surface galactosyl moieties that have been exposed by desialylation by the viral neuraminidase. Both galectins can directly cross-link the pneumococci to the epithelial cell surface, potentially promoting a secondary bacterial infection.
The protective role of the tandem-repeat galectin-9 (Gal9) against IAV infections has also been previously reported, but the mechanism(s) involved are not fully understood. We propose that as a multivalent binding protein, Gal9 may be able to cross-link pathogens to the desialylated cell surface, and enhance pathogen adhesion and entry. We are initially testing this hypothesis in an *in vitro* model aimed at assessing the capacity of Gal9 to cross-link IAV (PR8) to untreated and desialylated glycoproteins and A549 airway cells. Experiments to investigate the Gal9-mediated IAV adhesion to the desialylated cell surface will be followed by the assessment of Gal9-mediated viral entry and replication.

49. VAGINAL MICROBIOTA COMPOSITION PRIOR TO AND AFTER LUBRICANT USE

Christina Stennett

Stennett, C., Tuddenham, S., He, X., Robinson, C. K., Ravel, J., Ghanem, K. G., & Brotman, R. M.

Session G; Poster Presentation; Room 349

There is some evidence to suggest that vaginal lubricants disrupt protective lactobacilli in the vaginal microbiota. Lubricants may deplete vaginal lactobacilli and thereby increase susceptibility to sexually infectious disease acquisition.

The Human Microbiome Project (HMP) study involved 125 young women who self-collected vaginal samples daily for 10 weeks and reported lubricant use and sexual activity daily. We selected women who reported vaginal lubricant use with condomless vaginal intercourse and analyzed samples approximately 1 day prior to and 1 day following lubricant use. The race-matched controls also reported condomless vaginal intercourse but did not use vaginal lubricants (also sampling ~1 day pre- and post-intercourse). Vaginal microbiota was characterized on each sample by amplicon sequencing of the V3-V4 hypervariable regions of the 16S rRNA gene, and pre-to-post differences in the most abundant taxa was assessed with generalized linear multilevel models.

The 22 cases and 22 controls were mostly African American and had average age of 30. While the pre-to-post-exposure L. crispatus relative abundances for controls were even, cases had slightly lower L. crispatus abundance in post-exposure samples. Among cases whose “pre” sample was L. iners-dominated but also had a sizeable proportion of L. crispatus present, L. crispatus abundance diminished considerably after lubricant exposure in the “post” sample.

In this small matched secondary analysis of young women, we observed modest differences in the pre-to-post-exposure vaginal community composition between cases and controls. Future research designed for this purpose should be larger and should evaluate the particular lubricant components on the vaginal microbiota.

50. INFLAMMATION SIGNALING IS INVERSELY LINKED TO DNA REPAIR SIGNALING AND CAN ENHANCE PARPI EFFICACY IN BRCA

PROFICIENT OVARIAN AND BREAST CANCERS.

Lora Stojanovic

Stojanovic, L, McLaughlin, L, Kogan, A, Topper, M, Baylin, S., & Rassool, F.V.

Session G; Poster Presentation; Room 349

Poly (ADP-ribose) polymerase inhibitors (PARPi) are small molecule inhibitors of PARP enzymes that are currently approved by the FDA for the treatment of BRCA deficient ovarian cancer (OC) and breast cancer (BC) patients. However, PARPi fail for the majority of sporadic OC and BC with intact BRCA1/2 genes and other BRCA-proficient cancers thus novel approaches must be explored in order to expand the use of PARPi. We show, for the first time, an inverse relationship between Fanconi anemia related genes and type 1 interferon (IFN) pro-inflammatory response, as well as Fanconi anemia related genes and TNFα/ NFkB gene signaling, which was validated in METABRIC triple negative BC (TNBC) and TCGA Serous Ovarian Cystadenocarcinoma datasets. Using this basal inverse correlation between DNA repair and innate immune signaling, treatment of BRCA proficient cells with TNFα or IFNβ results in a transcriptional downregulation of FA and HR gene expression. Furthermore, HR activity was significantly downregulated. Treatment with ruxolitinib to block effects of IFNβ signaling, was able to fully rescue HR activity thus highlighting the link between innate immune signaling and DNA repair. Investigation into the relationship between innate immune signaling and DNA repair is a novel approach in understanding of DNA repair regulation and can additionally expand PARPi efficacy in BRCA proficient OC and BC to exploit the relationship between these pathways.

51. IMMUNOGENICITY OF A LIVE ATTENUATED SALMONELLA TYPHIMURIUM VACCINE IN AGED MICE

Jessica Allen

Allen, J. C., Toapanta, F. R., & Tennant, S. M.

Session G; Poster Presentation; Room 349

Older individuals (≥65 years) are more susceptible to non-typhoidal Salmonella (NTS) infections and experience more severe disease compared to younger adults. NTS account for a high burden of foodborne infections and deaths worldwide, in which younger adults generally develop gastroenteritis that resolves after several days. However, hospitalization and mortality rates of older NTS-infected individuals drastically increase with age. Due to this public health concern, we have developed a live attenuated vaccine, CVD 1926, against a common Salmonella serovar, S. Typhimurium. CVD 1926 is immunogenic and provides protection in adult mice (6-to 8-week old). However, primary vaccine responses in older individuals fail to generate complete protection due to progressive immune senescence. Indeed, we show that vaccinated aged (18-month-old) mice produce reduced humoral and T cell mediated responses compared to adult mice. To evaluate the immunogenicity of CVD 1926, both adult and aged mice received two doses of CVD 1926 perorally and were subsequently assessed for S. Typhimurium-specific IgG and intestinal T cell responses. Of the vaccinated mice, 60% of adult mice demonstrated detectable IFN-γ levels in CD4 central memory and CD8 memory T cells. In contrast, IFN-γ was detected in CD4 central memory in 20% of aged mice and in CD8 memory T cells from 40% of aged mice. Collectively, the reduction in antibody titers and T cell responses

represent decreased immunogenicity in aged mice. In line with other reports of poor vaccine responsiveness among the elderly, there is an age-associated inferior immune response following CVD 1926 vaccination.

52. MODULATION OF PATHOPHYSIOLOGICAL PROCESSES OF AUTOIMMUNE ARTHRITIS BY INDOLE-3-ACETIC ACID AND INDOLE-3-ALDEHYDE

David Langan

Langan, D. P., Meka, R. R., & Moudgil, K. D.

Session G; Poster Presentation; Room 349

Rheumatoid arthritis (RA) afflicts 0.5-1% of US adults, making it one of most common autoimmune diseases. Clinical RA is characterized by swelling of the joints of both extremities. Environmental factors, including diet and microbiome dysbiosis, are disease-modifying factors for RA. Indole-3-acetic acid (I3AA) and indole-3-aldehyde (IAld) are derived from both the diet and gut microbiota. We hypothesized that I3AA and IAld, ligands for the aryl hydrocarbon receptor (AhR), regulate critical AhR-dependent arthritis-related processes, namely production of pro-inflammatory cytokines, angiogenesis (new blood vessel formation), and osteoclastogenesis (bone resorption). We tested this using in vitro models of these 3 processes. Both I3AA and IAld inhibited IL-1β and IL-6 expression (by RT-qPCR), in RAW264.7 (RAW) cells treated with M. tuberculosis H37Ra sonicate (H37Ra) or LPS compared with vehicle control. Additionally, I3AA-treated RAW cells cultured in the presence of receptor activated nuclear-factor kappa beta (RANKL) formed fewer osteoclasts along with reduced expression of tartrate-acid phosphatase (TRAP) and cathepsin-K expression (CatK) (by RT-qPCR), compared to vehicle-treated cells; whereas, IAld-treated cells formed more osteoclast along with more TRAP and CatK expression. Human umbilical vein endothelial cell (HUVEC) tube formation (Matrigel assay), indicative of angiogenesis, was inhibited by I3AA, while IAld had minimal or no effect. These preliminary results suggest that I3AA and IAld are capable of modulating key RA-disease processes . We plan to examine the effect of AhR inhibitors on these processes, and to assess whether I3AA and/or IAld can confer protection against arthritis in a rat model of RA.

53. BASIC AND APPLIED COMPARATIVE IMMUNOLOGY: LESSONS FROM THE NURSE SHARK B CELL RESPONSE

Hanover Matz

Matz, H., & Dooley, H.

Session G; Poster Presentation; Room 349

Comparative model systems outside the conventional research of mouse and man can provide novel insights on the evolution of the immune system and new molecular tools for therapeutics and diagnostics. Cartilaginous fishes are the oldest extant taxonomic group to possess an immunoglobulin-based adaptive immune system. By investigating the evolution of the humoral response in nurse sharks (Ginglymostoma cirratum), we have identified primordial B cell selection structures that we hypothesize preceded mammalian germinal centers. To identify these structures, we immunized animals with the fluorescent antigen phycoerythrin (PE). Through immunofluorescent microscopy and in situ hybridization experiments, we have characterized patterns of antigen presentation, T cell interaction, and AID expression in B cell follicles of the shark spleen. Our results

show distinct sites where PE is presented to B cell clones expressing IgNAR (immunoglobulin new antigen receptor), a heavy-chain only immunoglobulin class in sharks. We hypothesize that these sites underpin the basic principles of B cell selection and can reveal factors that shape the clonal diversity of the immune response. Additionally, we have shown the applied value of studying the nurse sharks by generating single-domain variable regions (VNARs) from an IgNAR phage display library derived from animals immunized with HER1 and HER3, receptors upregulated in breast cancer. These recombinant VNAR domains, potential alternatives to mammalian antibodies, were found to bind their respective target antigens with high specificity via ELISA. At the crossroads of this basic and applied research we hope to use comparative immunology to improve vaccine designs and develop alternative therapeutic strategies.

54. ELUCIDATING THE LOCALIZATION OF ESTROGEN AND ESTROGEN-RELATED RECEPTORS IN THE INNER EAR

Erika Lipford

Lipford, E., Shuster, B., Milon, B., McMurray, M., Olszewski, R., Hoa, M., Mong, J., & Hertzano, R.

Session G; Poster Presentation; Room 349

Hearing loss is the most common sensory impairment, affecting hundreds of millions of people worldwide. Although both men and women are impacted by hearing loss, the incidence rate differs considerably between the two sexes. Cross-sectional studies have reported the prevalence of bilateral high frequency hearing loss to be 2.7 times higher in males compared to females. While sex differences in hearing loss were once attributed to a disparity in occupational noise exposure and anatomical variation between males and females, recent studies have implicated estrogen as having a protective effect against high frequency noise-induced hearing loss in females. Estrogen receptors signal through canonical and non-canonical pathways, impacting the central and peripheral auditory physiology. While the localization of the estrogen receptors (ERs) within the auditory system has been examined, the roles of estrogen-related receptors (ERRs) in auditory function require further investigation. In mouse models, the conditional knockout of estrogen-related receptor β (Esrrβ) or estrogen-related receptor γ (Esrrγ) leads to the development of hearing loss. The aim of this study is to elucidate the localization and expression of estrogen receptors α and β and estrogen-related receptors α, β, and γ within the inner ear of adult B6CBAF1/J mice. Using RNAscope, a method of in situ hybridization, we are able to localize the expression of ER and ERR mRNA in the cochlea. Our results give insight into the molecular mechanism through which both estrogen receptors and estrogen-related receptors grant protection against hearing loss.

55. SIX1 TRANSCRIPTION FACTOR ENHANCES HUMAN ERYTHROPOIESIS VIA GATA1

Michael Creed

Creed, T.M., Eberly, C.L., Kim, M., Cutler, J.A., Civin, C.I., Pandey, A., & Kingsbury, T. J.

Session G; Poster Presentation; Room 349

Erythropoiesis is orchestrated by the coordinated action of multiple transcription factors. The master erythropoietic regulator GATA1 is modulated by multiple co-

regulatory factors, such as FOG1, and cooperates with additional erythroid transcription factors such as KLF1. Though the PAX-SIX-EYA-DACH network (PSEDN) of transcription factors has been well characterized in the formation of several organ systems, a role for PSEDN members in hematopoiesis has only recently been recognized. Here, we studied the PSEDN member SIX1 and discovered its ability to drive erythroid differentiation of human hematopoietic cells. Enforced overexpression (OE) of SIX1 in human TF1 erythroleukemia cells or primary CD34+ hematopoietic stem-progenitor cells (HSPCs) stimulated the generation of erythroid cells, as determined by increased numbers of cells expressing erythroid-selective surface markers (CD235ahiCD71hiCD34-), erythroid gene RNA quantitation and hemoglobin protein levels (HBB). Conversely, SIX1 knockout in TF1 cells or primary HSPCs reduced erythropoiesis. Gene set enrichment analysis (GSEA) of global RNA-seq data conducted in TF1 cells showed that SIX1 OE broadly regulated GATA1 target genes, including those involved in heme metabolism. Additionally, multiple approaches, including proximity ligation assays, demonstrated that SIX1 associates with GATA1 in TF1 cell lines. Functionally, this interaction of SIX1 with GATA1 increased GATA1 transcriptional output as measured by luciferase reporter assays. Taken together our results suggest that SIX1 stimulates erythropoiesis via multiple mechanisms, including increased GATA1 function. Our findings provide the first demonstration of a role for the PSEDN in erythropoiesis and reveal physical and functional interactions between two developmental transcriptional networks.

56. PARP INHIBITOR RESENSITIZES TKI-RESISTANT AML TO TKI

Anna Dellomo

Dellomo, A. J., Lapidus, R. S., Karbowski, M., Baer, M. R., Kingsbury, T. J., & Rassool, F. V.

Session G; Poster Presentation; Room 349

Internal tandem duplications within the juxtamembrane domain of fms-like tyrosine kinase 3 (FLT3-ITD) are present in 20-25% of patients with acute myeloid leukemia (AML) and confer poor prognosis. FLT3-ITD is a constitutively active form of the receptor and aberrantly signals through STAT5 which can feedback to stabilize FLT3 through the downstream effector, Pim-1. Tyrosine kinase inhibitors (TKI) have clinical effects in FLT3-ITD AML but responses are limited due to the development of resistance through various means, including point mutations in the FLT3 tyrosine kinase domain. Novel therapies are therefore required to overcome TKI-resistance.

Poly (ADP-ribose) polymerase (PARP) 1 functions by poly-ADP-ribosylating (PAR) itself and other proteins primarily to catalyze DNA repair but also to regulate activity of proteins involved in other processes. Recent studies show that cotreatment of PARP inhibitor (PARPi) and TKI can effectively induce synthetic lethality in TKI-sensitive FLT3-ITD AML, however, the effects of PARPi in TKI-resistant disease has yet to be explored.

We now show that, compared to TKI-sensitive counterparts, point-mutated TKI-resistant FLT3-ITD AML have significantly increased ROS, PARP1, and phospho-STAT5 (pSTAT5), and loss of PARP1 reduces pSTAT5 and downstream targets. STAT5 was also found to have putative PARylation sites and immunoprecipitates with PAR, suggesting that PARP1 may play a direct role in regulating STAT5. Finally, we found that

PARPi with TKI is synergistically lethal in TKI-resistant cells suggesting a model whereby PARPi resensitizes cells to TKI by decreasing PARP1 effects on STAT5 and its downstream targets. Therefore, this combination has potential for treatment of TKI-resistant AML.

57. COLCHICINE IMPROVES MUSCLE FUNCTION, ENHANCES BONE MASS, AND REDUCES WHITE ADIPOSE TISSUE IN AGED BUT NOT YOUNG MICE

Jenna Leser

Leser, J.L., Gould, N.G., Shi, G., Spita, N., Mull, M.L. , Riddle, R.C., Ward, C.W., & Stains, J.P.

Session G; Poster Presentation; Room 349

We recently described a mechano-transduction pathway in bone where a subset of detyrosinated microtubules regulates a signal cascade that converges on a key mechano-responsive protein, sclerostin. Additionally, bone derived sclerostin increases white adipose tissue (WAT) accumulation. Further, this same subset of detyrosinated microtubules regulates the mechano-responses of skeletal muscle. Here, we show detyrosinated microtubules are increased in the muscle and bone of aged (78-week) compared to young mice (16-week). We hypothesized increased detyrosinated microtubules contributes to age dependent defects in muscle function and bone mechano-responsiveness, leading to sarcopenia and osteopenia, and accumulation of WAT. We treated 16-week and 78-week C57BL/6 mice with colchicine (1mg/L, drinking water, 8 weeks), a microtubule destabilizing drug, anticipating that targeting microtubules might restore mechano-transduction, increasing bone formation, improving muscle function, and reducing white adipose accumulation in aged mice. Consistent with our hypothesis, colchicine treated aged mice showed significantly increased bone formation on the cortical surface (300% increase, $p=0.0496$) and decreased bone derived sclerostin. Additionally, these mice exhbited improved in vivo muscle contraction velocity (40% increase, $p=0.0106$) and power (20% increase, $p=0.0058$). Finally, colchicine treated aged mice showed reduced WAT mass (50% reduction of inguinal fat, $p=0.0199$, 60% reduction of gonadal fat, $p=0.0038$) and adipocyte size (30% reduction, $p<0.0001$). In contrast, young colchicine treated mice, which do not have an over-abundance of detyrosinated microtubules, had no significant effects on bone, muscle or WAT. These data show that targeting the aging microtubule network restores mechano-responsiveness to improve aging dependent sarcopenia and osteopenia, and diminish WAT.

58. GENOME-WIDE ASSOCIATION STUDY IDENTIFIES NOVEL RISK LOCI FOR MOOD DISORDERS IN A FOUNDER POPULATION

Elizabeth Humphries

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Session G; Poster Presentation; Room 349

Despite successes of genome-wide association studies (GWAS) of psychiatric traits in large case-control cohorts, identifying causal variants and interpreting their biological mechanisms has proven difficult.

Two issues inherent to case-control GWAS contributing to these difficulties are the small effect sizes of individual risk variants and genetic heterogeneity across sub-populations. Studying genetic risk for psychiatric disorders in population isolates could overcome these challenges, as certain functional alleles are highly enriched relative to the broader population, and some of these alleles may have substantial effects on disease risk. Anabaptists comprise several related founder populations, such as Old Order Amish (OOA) and various Mennonite groups, who originated from Western Europe in the 17th century, with little or no non-Anabaptist gene flow for the last 300 years. In this study, we combined neuropsychiatric and genetic data from 3 studies of Anabaptist families affected with severe mental illnesses with additional OOA population controls (n=2601). We also obtained quantitative behavioral and neurocognitive phenotypes in 428 of these subjects, recruited as part of the Amish Connectome Project. Here, we performed a genome-wide association study in this population. We identified four genome-wide significant risk loci. The relative risk associated with these risk variants appears larger than previously described risk variants for mood disorders. We also identified one locus contains a deleterious protein-coding variant in CUX1 that is below the adjusted p-value for all Amish-enriched, deleterious protein-coding variants. CUX1 is a novel risk gene for mood disorders that has previously been implicated in autism.

59. NEONATAL DEFICIENCIES IN NK CELL-ACTIVATING CYTOKINES IN THE CONTEXT OF BORDETELLA PERTUSSIS INFECTION

Cassandra Jordan

Jordan, C. M.. Mitchell, A. E., & Carbonetti, N. H.

Session H; Poster Presentation; Room 349

Whooping cough, caused by the bacterium Bordetella pertussis, has seen a resurgence in recent years, in part due to the switch from the whole cell vaccine to acellular vaccine. Although both adults and infants present as a severe paroxysmal cough, infants disproportionally experience a fatal health decline. Our lab aims to develop a better understanding of the biological interactions against B. pertussis and develop therapeutics to potentially limit the number of infant deaths. Disease progression in infant and adult mouse models show some parallels to human disease. Adult mice exhibit severe lung pathology, but overcome infection, while infant mice experience mild lung pathology, develop leukocytosis, bacterial dissemination, and can succumb to infection. We hypothesize that this discrepancy in response to infection is due to a deficiency in neonatal Interferon gamma (IFN-g) production by Natural Killer (NK) cells, which can activate protective T-helper 1 (Th1) cells. We further hypothesize that this deficiency is in part due to the inability of neonatal antigen presenting cells, such as macrophages and dendritic cells, to produce the NK activating cytokines, Interleukin (IL) 12, IL15, and IL18, when exposed to B. pertussis. To test this hypothesis, we will isolate splenic antigen presenting cells from infected and uninfected infant and adult mice, incubate with heat killed B. pertussis, and analyze for the production of IL12, IL15, and IL18. We have examined differences in cytokine expression and will further determine will whether NK cells from infant and adult mice can produce IFN-g when activated by these cytokines.

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

Stephanie Zalesak

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

Session H; Poster Presentation; Room 349

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 propose 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 an in vitro and vivo models of small intestine inflammation. Taken together with the application of targeted CRBP1 quantitation, these studies will help further our understanding of the mechanisms and impact of CRBP1 loss in disease.

61. QUANTITATIVE ANALYSIS OF COMPARTMENTS IN THE LEG TO DETERMINE INCISION PLACEMENT

Loreen Agandi

Agandi, L.

Session H; Poster Presentation; Room 349

Compartment syndrome is characterized as excess swelling within the compartment leading to an increase in pressure in a limited space. The lower leg fasciotomy is a common procedure performed to mitigate the effects of compartment syndrome. To relieve the increased compartment pressures associated with compartment syndrome, a two- incision fasciotomy is commonly performed. On the lateral side of the leg, our study shows that the anterior compartment is commonly missed due to incision placement ending up too posterior relative to the position of the intermuscular septum between the anterior and lateral compartments. This results in the surgeon proceeding posteriorly and identifying the septum between the lateral and superficial posterior compartments, misidentifying it as the septum between anterior and lateral compartments. The lower leg will be divided evenly into fourths, starting at the head of the fibula and ending at the lateral malleolus, circumferentially measured and analyzed via CT and MRI scans. The angle from the center of the fibula to the center of the tibia and out to the septum will be measured to quantify for variability in participant's intermuscular septum relative to the bony landmark architecture. Performing an incorrect fasciotomy can be detrimental to a person's livelihood, resulting in possible death or amputation. By assessing the circumferential distance from the tibial spine

to the fibula we can determine if the recommendation of changing the lateral incision surgical technique to two fingers posterior to the tibia will result in lateral leg decompression performed correctly.

62. DEVELOPING BIOFILM-PENETRATING NANO-BASED PHOTOSENSITIZERS FOR DENTAL TISSUES DISINFECTION

Rayyan Alfirdous

Alfirdous, R., Balhaddad, A., Garcia, I., Ibrahim, M., Rolim, J., Gomes, E., Martinho, F., Collares, F., Xu, H., & Melo, M.A.

Session H; Poster Presentation; Room 349

Objective: This review clusters the growing field of nano-based platforms for antimicrobial photodynamic therapy (aPDT) targeting pathogenic oral biofilms and increase interactions between dental researchers and investigators in many related fields.
Background data:Clinically relevant disinfection of dental tissues is difficult to achieve with aPDT alone. It has been found that limited penetrability into soft and hard dental tissues, diffusion of the photosensitizers, and the small light absorption coefficient are contributing factors. As a result, the effectiveness of aPDT is reduced in vivo applications. To overcome limitations, nanotechnology has been implied to enhance the penetration and delivery of photosensitizers to target microorganisms and increase the bactericidal effect.
Materials and methods:The current literature was screened for the various platforms composed of photosensitizers functionalized with nanoparticles and their enhanced performance against oral pathogenic biofilms.
Results: The evidence-based findings from the up to date literature were promising to control the onset and the progression of dental biofilm-triggered diseases such as dental caries, endodontic infections, and periodontal diseases. The antimicrobial effects of aPDT with nano-based platforms on oral bacterial disinfection will help to advance the design of combination strategies that increase the rate of complete and durable clinical response in oral infections.

63. THE ROLE OF MAST CELLS IN SHAPING NEONATAL BRAIN DEVELOPMENT

Alexa Blanchard

Blanchard, A.C., Pickett, L., Reinl, E., & McCarthy, M.

Session H; Poster Presentation; Room 349

The critical period of sexual differentiation in rats occurs perinatally when the estradiol levels peak in the male CNS around birth, driving different neural growth patterns and microglial phagocytic programs in males and females. The preoptic area (POA) is a hypothalamic region that drives sexual and social behaviors, which is reflected on the cellular level by sex-specific differences in neuron number, spine density, and immune cell activation states. Recently mast cells have been shown to play a crucial role in masculinization of the POA to promote neural dendrite formation crucial for male copulatory behavior in adulthood. Though mast cells are known to respond to the estradiol surge in males and drive sex-specific neural changes, the factors recruiting mast cells to the parenchyma and their brain-specific activities are poorly understood. Here, we sought novel insights into the mechanism by which mast cells gain access to brain tissue and exert their influence on neurodevelopment.
Establishment of a flow cytometric protocol to isolate mast cells from the postnatal rat

brain enabled characterization of their phenotype, intracellular contents, and migration patterns in the postnatal period. Immunohistochemical analysis on a developmental time course of mast cell infiltration revealed brain region specificity and differing replication patterns across developmental timepoints. Utilizing methods including in-vitro assays, depletion studies, in-situ hybridization, and gene expression analysis, continued exploration of mast cell biology in this tissue context will illuminate the role of the innate immune system in shaping sex-specific brain developmental paradigms.

64. PROSTAGLANDIN E2 SIGNALING RESTRICTS ACTIVATION OF THE CGAS-STING PATHWAY

Paige Mathena

Mathena, R.P., Perkins, D.J., & Vogel, S.N.

Session H; Poster Presentation; Room 349

The Cyclic GMP-AMP synthase-Stimulator of Interferon Genes (cGAS-STING) pathway acts as a sensor for cytosolic double stranded DNA (dsDNA) from self or microbial sources. Activation of cGAS/STING drives a potent inflammatory response, including production of the cytokine type I interferon (IFN) through activation of the kinase TBK1 and the transcription factor IRF3. Appropriately controlling cGAS/STING activity is critical to prevent autoimmune damage, but how the immune system accomplishes this is an open question. Production of the small lipid prostaglandin E2 (PGE2) has been shown to limit IFN production in other contexts. The goal of this study was to test the hypothesis that PGE2 feedback could additionally be a mechanism controlling the cGAS-STING pathway, preventing over-activation. We utilized the chemotherapeutic drug 5,6 Dimethylxanthenone-4-acetic acid (DMXAA), which directly activates murine STING independent of cytosolic dsDNA. We found that in murine embryonic fibroblasts (MEFs) and primary murine macrophages, exogenous PGE2 can suppress DMXAA induced STING signaling pathways. MEFs or macrophages initially receiving PGE2, followed by DMXAA, showed decreased activation of both TBK1 and IRF3. Additional data suggests the effect of PGE2 may be mediated at the level of STING activation. This result argues that PGE2 signaling may be a physiologically relevant mechanism to restrict cGAS/STING activation.

65. FALL RELATED WORRIES AND INSOMNIA SYMPTOMS AS MODIFIABLE RISK FACTORS FOR ALZHEIMER'S DISEASE: DATA FROM THE NATIONAL HEALTH AND AGING TRENDS STUDY

Lori Anderson

Anderson, L.R., Parisi, J.M., Munro, C.A., & Spira, A.P.

Session H; Poster Presentation; Room 349

Increased sleep disturbances occur with increasing age, and sleep disturbances are associated with poor cognitive outcomes, including dementia. Women are more likely to have sleep problems with increasing age, and women are twice as likely as men to develop Alzheimer's disease. Finally, older adults are more likely to experience falls with increasing age, and worldwide, a third of those 65 and older experience falls at least once per year.
Methods: Using data from 7,075 survey respondents in 2012 of the National Health and Aging Trends Study, we examined the association between fall-related worry and

insomnia symptoms in adults aged 65 and older. Logistic regression models were developed to examine the relationship between fall-related worry and insomnia symptoms in older adults, controlling for common covariates.
Results: Fall-related worry was associated with a higher odds of insomnia symptoms, after adjusting for race, age, gender, and education (OR= 2.20, 95% CI: 1.88, 2.59), plus number of health conditions (Model 2) (OR= 1.87, 95% CI: 1.58, 2.20), plus anxiety and depression (Model 3) (OR= 1.42, 95% CI: 1.20, 1.70), $p < 0.001$ for all three models.
Conclusions: After accounting for potential confounders, older adults who worry about falling are more likely to experience insomnia symptoms than those who do not worry about falling. Fall-related worry and insomnia symptoms are both modifiable risk factors, and future studies might be well-suited to examine interventions in which to reduce the risk of both, hence possibly reducing the risk of cognitive decline and Alzheimer's disease.

66. INVESTIGATION OF DISSOLUTION PERFORMANCE OF ITRACONAZOLE AMORPHOUS SOLID DISPERSIONS USING HPMCAS -L, -M AND -H GRADES

Asmita Adhikari

Adhikari, A.

Session I; Oral Presentation; Ballroom A

Poor solubility of oral formulations and the formulation challenges associated with it has been a concern in drug development and design. Spray-dried amorphous solid dispersions have become a common approach to enable formulation of poorly soluble drugs. HPMCAS has been observed to inhibit the crystallization tendency of supersaturated solution of itraconazole by enhancing the kinetic solubility and thermodynamics of poorly soluble drugs. However, this supersaturation can be transient resulting in initial surge of dissolution rate followed by decrease in concentration due to nucleation and crystallization. We hypothesize the rate and extent of supersaturation attained by different grades of polymer is different. The aim is to investigate the influence of polymer on supersaturation profile and compare the dissolution performance of amorphous solid dispersions (ASDs) prepared by spray drying technique using -L, -M and -H grades of HPMCAS polymer in Simulated Intestinal fluid w/o enzyme (USP SIF, pH 6.8) media. We also hypothesize that the dissolution performance of spray dried dispersions (SDDs) can be linked to potential changes in solid state due to precipitation over time. Characterization of amorphous solid dispersions is performed by assessing glass transition temperature (Tg) and we aim to characterize the solid-state changes in itraconazole amorphous solid dispersions using various grades of HPMCAS relevant to intestinal transit time of 5 hours.

67. REGULOME-WIDE ASSOCIATION STUDY IDENTIFIES TRANSCRIPTION FACTOR NETWORKS ASSOCIATED WITH RISK FOR SCHIZOPHRENIA

Alex Casella

Casella, A.M.

Session I; Oral Presentation; Ballroom A

More than 90% of genetic risk loci for complex traits are located in non-coding regions, suggesting that regulatory regions may be involved in the development of these traits. It is thought that disruption of transcription factor (TF) binding sites may be a mechanism by which risk variants affect

these phenotypes, but we lack adequate tools to connect these disruptions to genetic risk. Here, we developed a method, the Regulome Wide Association Study (RWAS), to test for associations of binding sites for specific TFs with genetic risk for a trait. Predicted binding sites for 842 TFs were derived from a new database of DNase I footprints, and the density of footprints was calculated within known tissue-specific enhancer regions. Next, we calculated genetic associations within each enhancer using summary statistics from large genome-wide association studies, and then tested for the over-representation of predicted binding sites for each TF in the enhancers associated with a trait of interest. To demonstrate our approach, we applied RWAS to identify TFs whose predicted binding sites in the human brain were overrepresented in enhancers associated with genetic risk for schizophrenia (SCZ). Notably, several of the TFs identified in our model are known to be master regulators of neuronal development and have been linked to SCZ in previous studies, including MEF2C and members of the POU family. Here we have developed a generalizable approach that integrates GWAS summary statistics with footprint-derived regulatory networks in order to identify TF target networks associated with disease risk.

68. EXTRACELLULAR ASSEMBLY OF HETERODIMERIC IL-12 CYTOKINE CONFERS PROTECTION AGAINST SYSTEMIC BUT NOT LOCAL LEISHMANIA MAJOR INFECTION

Allison Gerber

Gerber, A. N., & Singh, N. S.

Session I; Oral Presentation; Ballroom A

Upon infection, naïve T cells differentiate into effector subsets to generate an appropriate response to pathogens. In order to skew T cells towards the proper effector response, dendritic cells (DC) release specific cytokines. IL-12 is a heterodimeric cytokine made up of two subunits – p40 and p35. IL-12 is an important cytokine for the differentiation of IFNγ producing T cells. Assembly of IL-12 is thought to occur only when both relevant subunits are expressed inside a DC, allowing for covalent linkage and secretion. Intriguingly, the p40 subunit is also released from DC as a monomer with unknown function. We previously hypothesized that monomeric p40 can bind p35 released by another cell in the extracellular space. To test this hypothesis in a physiological setting, in vivo bone marrow chimeras were set up using p40-/- and p35-/- cells and infected with Leishmania major, a parasite which requires IL-12 induction of IFNγ for clearance. Chimeric mice were able to induce IFNγ production by T cells, suggesting that functional IL-12 assembly can occur in the extracellular milieu from component peptides. Intriguingly, we find that extracellular IL-12 was sufficient to control the parasite at disseminated infection sites, such as the liver and spleen, but not the primary site of infection. This suggests that not only are dendritic cells capable of skewing T cell differentiation but there is also a tissue specific component that can dictate T cell responses.

69. RELATIONSHIPS BETWEEN QUADRICEPS MUSCLE STRENGTH AND THICKNESS IN HEALTHY CHILDREN: IMPLICATIONS TO MUSCLE PERFORMANCE TESTING

Kelly Rock

Rock, K., Nelson, C., Addison, O., & Marchese, V

Session I; Oral Presentation; Ballroom A

Background: Muscle performance is important for physical function. Muscle thickness (MT) and strength are clinically-relevant correlates of muscle performance. Examination of knee extension strength at multiple testing positions using handheld dynamometry and quadriceps MT using ultrasonography are valid, reliable and practical, but have not been explored together in healthy children.

Methods: In 16 children (6-11 years), knee extension joint torque (KEJT) was measured in seated and supine with 90° and 35° of knee flexion by handheld dynamometry, and rectus femoris (RF) and vastus lateralis (VL) MT were measured by ultrasonography. Relationships between KEJT and MT were assessed using Pearson product-moment coefficients. One-way repeated-measures ANOVA tests were conducted to compare the effect of strength testing positions on KEJT.

Results: Significant positive correlations existed between RF MT with supine KEJT at supine 90° ($r=0.78$, $P<0.001$), supine 35° ($r=0.74$, $P=0.001$), seated 90° ($r=0.67$, $P=0.004$), and seated 35° ($r=0.65$, $P=0.007$), but no significant relationships existed between KEJT and VL MT. There was a significant main effect of strength testing position on KEJT ($P<0.001$). Pairwise comparison identified significant differences in KEJT between knee positions 90° and 35° in sitting and in supine ($P<0.001$), and between seated and supine testing positions when the knee was positioned in 90° of flexion ($P<0.001$), but not when the knee was positioned in 35° of flexion.

Conclusions: The results of this study suggest RF MT may be useful in examination of muscle performance in children, and strength testing positions should be considered during baseline and post-intervention testing.

70. ANTIBACTERIAL DENTAL COMPOSITE INHIBITS THE GROWTH OF BIOFILM DERIVED FROM ROOT CARIES PLAQUE ISOLATED FROM PATIENTS

AbdulRahman Balhaddad

Balhaddad, A.A., Ibrahim, M.S., Garcia, I.I., Collares, F., Weir, M.D., Hockin H. K. X. &, Melo, M.S.

Session I; Oral Presentation; Ballroom A

Aims: Resin composites as chosen material for restorative management of root caries have no antibacterial functionality, and instead, are highly susceptible to accumulate biofilms (dental plaque). This study aims to investigate the effect of dimethylaminohexadecyl methacrylate (DMAHDM) and nano-sized amorphous calcium phosphate (NACP) on the mechanical behavior and the antibacterial response of bioactive composite.
Methods: The effect of 20% NACP on two levels (presence/absence) and DMAHDM concentration (%wt.) in three levels (0, 3, and 5) were evaluated. Plaque samples isolated from patients with root carious lesions were used to initiate a 48h-old plaque-derived biofilm. The antibacterial properties were assessed via surface charge density, metabolic activity (MTT), colony-forming unit counts (CFU), and lactic acid (LA) production. Mechanical properties were measured via flexural strength and elastic modulus. Two-way ANOVA and Tukey's multiple comparison tests were performed to detect the significance of the variables.
Results: DMAHDM-NACP demonstrated excellent mechanical properties compared to commercial controls ($p=>0.05$). The charge density increased by 8-12-fold with increasing the DMAHDM concentration and the addition of NACP ($p=<0.01$). All the investigated

formulation revealed higher antibacterial properties compared to the control. 5%DMAHDM-20%NACP demonstrated the most significant antibacterial action among the experimental groups. 5%DMAHDM-20%NACP reduced the metabolic activities and LA production by around 90% (p=<0.01). 5%DMAHDM-20%NACP also reduced the growth of total microorganisms, total streptococci, Mutans Streptococci, and Lactobacilli by 4-7 log compared to control. Conclusion: DMAHDM-NACP composite showed acceptable mechanical properties and high bacterial reduction. DMAHDM-NACP composites are promising to inhibit the bacterial growth over composite, thereby inhibiting secondary caries.

71. MOLECULAR DYNAMICS, HDX, AND MODELING: A MULTIFACETED APPROACH TO MODEL SOLUTION STRUCTURAL ENSEMBLES

Saovleak Khim

Khim, S., Jean-Baptiste, U., Altas, B., & Poulopoulos, A.

Session I; Oral Presentation; Ballroom A

Brain development relies on temporal and spatial regulations, the synchrony of molecules that act in concert to direct proper wiring. Subsequently, circuit-specific remodeling results in structural and functional consequences. We utilize synthetic biology, in utero electroporation and in vivo genome editing to reveal circuit level and subcellular endophenotypes, an index used to simplify more complex phenotypes seen in neurodevelopmental and psychiatric disorders like ASD, Autism Spectrum Disorder, and Schizophrenia. Here, we have identified a family of proteins called PTPRs, protein tyrosine phosphatase receptors, that are tightly regulated during development. Currently, we are focused on two subfamilies of PTPRs: Type IIa and Type IIb. Each may have a role as an inhibitory or attractive guidance cue for axonal growth in various brain regions. Our study uses CRISPR knockouts (KO) and overexpression (OE) to observe the effects of these PTPRs on circuit formation in the mouse model. PTPRδ KO, a Type IIa PTPR, revealed a loss of cortico-perirhinal and cortico-striatal projections, regions important for visual perception, memory, cognition, and executive functions. PTPRδ OE showed inappropriate outgrowth of axons within the corpus callosum, crucial for the integration of information from the left and right hemispheres. These findings suggest that type IIa PTPRδ may bind with its substrates to act as an “exit” sign that signals axons to innervate its target. Further studies are underway to explore how different subfamilies and variants of PTPRs coordinate to produce proper wiring and function.

72. MECHANO-RESPONSIVE SCLEROSTIN PROTEIN IS RAPIDLY DEGRADED THROUGH THE LYSOSOME IN OSTEOCYTES

Nicole Gould

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

Session J; Oral Presentation; Ballroom B

The skeleton adapts to its mechanical environment by sensing mechanical signals and transducing them into biological signals that direct bone remodeling, the concerted action of bone resorbing osteoclasts and bone forming osteoblasts. Mechano-sensitive osteocytes control bone formation in part through the expression of the Wnt/B-catenin

antagonist, sclerostin. Following mechanical stimulus, sclerostin protein levels are reduced, lifting the inhibition on osteoblasts to allow for bone formation. Despite the physiological importance, little is known about how sclerostin abundance is controlled in response to mechanical load. Here, we show that sclerostin is rapidly degraded after mechanical stimulation in vitro and in vivo. Specifically, within five minutes of the application of mechanical stress, sclerostin protein is degraded. In vitro, we show that blocking lysosomal function, but not proteasomal degradation or secretion, prevents rapid sclerostin degradation. Sequence alignment of the sclerostin amino acid sequence across different species revealed multiple conserved lysosomal signal sequences. Importantly, exogenously expressed sclerostin is degraded on the same time scale through the lysosome, indicating that sclerostin is post-translationally modified to control abundance. Using a mouse ulnar load model to stimulate mechano-activated bone formation, treatment with Bafilomycin A1, a lysosome inhibitor, decreased bone formation rate, a measure of osteoblast activity, following ulnar loading. Together, these discoveries provide key insights into the control of sclerostin and reveal new therapeutic targets that can be exploited to improve bone mass in conditions such as osteoporosis.

73. CAPABILITIES OF AN AEROSOLIZATION MACHINE FOR ELECTRONIC NICOTINE DELIVERY SYSTEMS

Angela Lee

Lee, A., Eng, B., Liu, T., Brandis, J., Ma, T., Schneider, A., Michel, S. L. J., Kane, M. A., & Dalby, R. N.

Session J; Oral Presentation; Ballroom B

Health consequences of inhaling aerosols from electronic nicotine delivery systems(ENDS) remains uncertain. To better understand these products requires the development of a machine to generate and capture generated aerosols to evaluate their chemical constituents and effects on biological systems.

We built an affordable and flexible machine augmenting practices well-established for pharmaceutical inhaler testing. Airflow, generated by vacuum pump and controlled by needle valve, is switched through an e-cigarette or bypass. Valve opening, heating coil activation, and voltage are controlled using an Arduino microcontroller running custom code. The machine design permits capture of the aerosol in various collection systems suited for detection of harmful and potentially harmful constituents including carbonyls and metals and exposure of cultured cells, so biological effects can be assessed.

Employing user-refillable ENDS, the machine can generate aerosols from custom e-liquids to test hypotheses concerned with metal ions and carbonyl generation into aerosols. These collection tools combined with control of puff duration, inter-puff interval, number of puffs, airflow rate, and coil voltage have been used to conduct various studies. We are able to quantify carbonyls, such as formaldehyde, acetaldehyde, acetone, and acrolein using an LC-MS/MS method. Similarly, metals such as lead, chromium, and nickel from the aerosol have been quantified via ICP-MS.

The aerosolization machine is a versatile tool that permits testing of various ENDS with numerous aerosol capture systems. Studies using our aerosolization machine revealed the presence of carbonyl compounds and heavy metals, and further studies are underway to determine biological effects on various cell culture systems.

74. SEX-SPECIFIC TRANSCRIPTIONAL NETWORKS IN THE MEDIAL AMYGDALA UNDERLIE DIFFERENCES IN EXPRESSION OF JUVENILE SOCIAL PLAY

Ashley Marquardt

Marquardt, A.E., Shetty, A.C., Ament, S.A., & McCarthy, M.M.

Session J; Oral Presentation; Ballroom B

Social play, or rough-and-tumble play, is a characteristic pattern of behavior exhibited by most juvenile mammals, believed to contribute to the development of social and emotional skills needed throughout life. Importantly, there is a sex difference in expression of play, with males exhibiting greater intensity and frequency of play than females. To explore whether play is associated with similar or different transcriptional signatures in males compared to females, we performed RNA-sequencing (RNA-seq) of the medial amygdala (MeA), the brain region known to drive masculinization of play, in high- and low-playing juvenile rats of both sexes. As play is a dynamic behavior likely produced by complex interactions among many genes, we then utilized a network approach, Weighted Gene Co-expression Network Analysis (WGCNA), to analyze the results, focusing on the 4,261 genes that showed nominal differences in expression related to sex or play. From these data, we identified 22 gene co-expression modules. Surprisingly, 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. This novel finding suggests that there is a distinct profile associated with playfulness in males compared to females. Here, we present these modules and discuss plans for future experiments to assess their functional relevance in driving sex differences in juvenile play and later-life sex-typical social behaviors. Together, these novel analyses will greatly improve our understanding of how differential transcriptomic regulation in the medial amygdala drives sex differences in MeA circuitry and social play.

75. RECEIPT OF TREATMENT FOR DEPRESSION AFTER TRAUMATIC BRAIN INJURY IN OLDER ADULTS IS ASSOCIATED WITH INCREASED HEALTH CARE UTILIZATION

M. Doyinsola Ismail

Ismail, M. D., & Albrecht, J. S.

Session J; Oral Presentation; Ballroom B

Depression is common among older adults following traumatic brain injury (TBI). Evidence suggests that older adults diagnosed with depression following TBI are less likely to receive antidepressants compared to those without TBI. This may be due to concerns about increased risk of adverse events. To understand this better, we estimated the effect of treatment of depression (antidepressants or psychotherapy) on health care utilization (HCU) among older adults newly diagnosed with depression following TBI.
We conducted a retrospective cohort study among adults ≥65 years, diagnosed with TBI 2009-2012 using administrative claims data for privately insured and Medicare Advantage enrollees. We searched for depression diagnoses and psychotherapy claims using diagnostic and health care procedure codes and obtained antidepressant prescription fills in the drug file. Enrollees were excluded if they received a diagnosis or treatment for depression prior to TBI. We operationalized HCU as counts of inpatient, outpatient, emergency department or medication claims

per month following depression diagnosis. Rate ratios (RR) were estimated using generalized estimating equations, controlling for demographic factors and pre-existing comorbidities.
We included 6,238 enrollees. Of these, 66% received ≥1 fill for an antidepressant or ≥1 psychotherapy claim. Among the treated, 79% received ≥1 antidepressant. Compared to those not receiving treatment, receiving treatment for depression was associated with higher outpatient (RR 1.32; 95% CI 1.25 1.39), emergency (RR 1.18; 95% CI 1.06, 1.31) and medication use (RR 1.62; 95% CI 1.58, 1.67).
Treatment of depression was associated with increased emergency department utilization. This should be further explored in future work.

75.THE ASSOCIATION BETWEEN CLINICAL MALARIA IN THE FIRST SIX MONTHS OF LIFE AND SUBSEQUENT DISEASE AMONG CHILDREN UNDER 24 MONTHS IN MALAWI, 2016-2018

Liana Andronescu

Andronescu, L.R., Buchwald, A.G., Kachingwe, M., Kachepa, W., Bauleni, A., Mawindo, P., Gutman, J.R., Mathanga, D.P., & Laufer, M.K.

Session J; Oral Presentation; Ballroom B

In the first six months of life, variables that impact an infant's malaria risk include maternally-derived immunity, health, background malaria exposure, season, and maternal age. Despite high prevalence of malaria in infants, the impact of early-life malaria on subsequent disease risk is unclear. We aimed to determine if clinical malaria in the first six months of life is associated with risk of subsequent disease. Infants were recruited at two antenatal clinics, either as a continuation of an ongoing trial or in a separate study that enrolled infants at birth. Participants were followed quarterly from birth and asked to visit the clinic in the event of any illness. Clinical malaria was defined as fever >37.5°C, or other malaria-associated symptoms, combined with positive RDT. Mean follow-up time was 16.8 (SD: 4.8) months among 437 infants. . There were 68 clinical malaria cases among 49 infants in the first six months of follow-up (incidence rate: 0.40 cases/person-year), and 373 cases in the following 18 months (incidence rate: 0.95 cases/person-year). In Poisson analysis birth season and sex were not associated with malaria during follow-up. Maternal age and study site were associated with reinfection and included in the final model. Having clinical malaria before six months was associated with a 44% increase (RR: 1.44; 95%CI 1.25, 1.66) in risk of subsequent clinical malaria. This may reflect background exposure to P. falciparum or indicate that infants infected in the first six months of life have altered risk to later disease.

77. DELETION OF OBSCURIN IMMUNOGLOBULIN DOMAINS IG58/59 LEADS TO MALADAPTIVE RESPONSES IN THE HEART

Alyssa Grogan

Grogan, A., Coleman, A., Joca, H., Granzier, H., Russell, M., Ward, C., & Kontrogianni-Konstantopoulos, A.

Session J; Oral Presentation; Ballroom B

Obscurin comprises a family of giant modular proteins that play key structural and regulatory roles in striated muscles. Immunoglobulin domains 58/59 (Ig58/59) of obscurin mediate binding to diverse proteins that are essential for normal muscle structure

and function, including canonical titin, a splice variant of titin, termed novex-3, and phospholamban (PLN). Missense mutations localized within the obscurin Ig58/59 module that affect binding to titins and/or PLN have been linked to the development of myopathies in humans. To elucidate the pathophysiological role of these domains, we generated a constitutive deletion mouse model, Obscn-ΔIg58/59, that expresses obscurin lacking Ig58/59, and determined the consequences of this molecular manipulation on cardiac morphology and function. Our studies demonstrate that young Obscn-ΔIg58/59 mice are susceptible to acute β-adrenergic stress. Moreover, sedentary Obscn-ΔIg58/59 mice develop compensatory left ventricular (LV) hypertrophy that progresses to maladaptive ventricular dilation, contractile impairment, atrial enlargement, and severe arrhythmia as a function of aging with male mice being more affected than female. Experiments in isolated LV cardiomyocytes revealed altered Ca2+ cycling in male Obscn-ΔIg58/59 mice associated with changes in the expression and/or phosphorylation levels of major Ca2+ cycling proteins including PLN, the sarcoendoplasmic reticulum Ca2+ ATPase 2 (SERCA2) and ryanodine receptor 2 (RyR2). Taken together, our work demonstrates that obscurin Ig58/59 is an essential regulatory module in the heart and its deletion leads to cardiac remodeling, ventricular dilation, and arrhythmia due to deregulated Ca2+ cycling in response to aging in a sex-dependent manner.

78. EVALUATION OF PEDESTRIAN-TRAIN FATALITIES IN THE STATE OF MARYLAND: A FIVE-YEAR RETROSPECTIVE STUDY OF FORENSIC AUTOPSY CASES.

Elvira N. Carias, Claire Hammerschmidt, & Taylor Hall.

Carias, E.N., Hammerschmidt, C., Hall, T., Ripple, M., & Li, L.

Few studies have been done on the incidences of train-related pedestrian fatalities throughout the United States, with no previous studies reported in the State of Maryland. A retrospective study was conducted at the statewide medical examiner's office in Maryland to evaluate the characteristics of train-related pedestrian fatalities in the past five years from 2014 to 2018. The aim of the study was to analyze circumstances of deaths through the medicolegal death investigation and postmortem examination findings including toxicological study and to help identify future safety measures.

A total of 48 cases were identified. Of the 48 deaths, 21 deaths (43.7%) were determined to be accident, 20 deaths (41.7%) were suicide, and 7 deaths (14.6%) whose manner of death could not be determined. Of the 21 accidental victims, 17 were males and 4 female (M: F ratio = 4:3:1), 15 (71.4) were white and 6 (28.6%) with age ranging from 16 to 58 years (mean age = 35). While the 20 suicide victims, 17 were males and 3 females (M: F ratio = 5.7:1), 18 (90%) were white and 2 (10%) African American, with age ranging from 22 to 60 years (mean age: 40). The majority of accidents occurred during weekday evening rush hours between 4pm and 9pm while the suicides showed no specific time frames. No specific peak for seasons of year was found in suicides nor accidents. Postmortem toxicological study showed that accidental victims were 57.1% (12/21 cases) positive for alcohol and the suicide victims were 30% (6/20 cases) positive for alcohol. Manner of death could not be determined in 7 cases because unclear circumstances of death. Thorough death scene investigation and complete postmortem examination including comprehensive toxicological testing is very

important in all train-related pedestrian fatalities to accurately determine the manner of death because accident vs suicide can directly affect the outcome of civil ligation and dispersal of insurance benefits. The characteristic profiles of train-related pedestrian fatalities can also assist effective preventive measures on of railway suicides and accidents.

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NASW-MD would like to congratulate the social work students presenting at today's event:

Ivana Alexander, Todd Becker, Ji Hyang Cheon, Nancy Franke, Kimberly Leffler, Shawna Murray-Brown, Eusong Park, Danielle Phillips, and Yao Wang.


Phyo Nay Lin