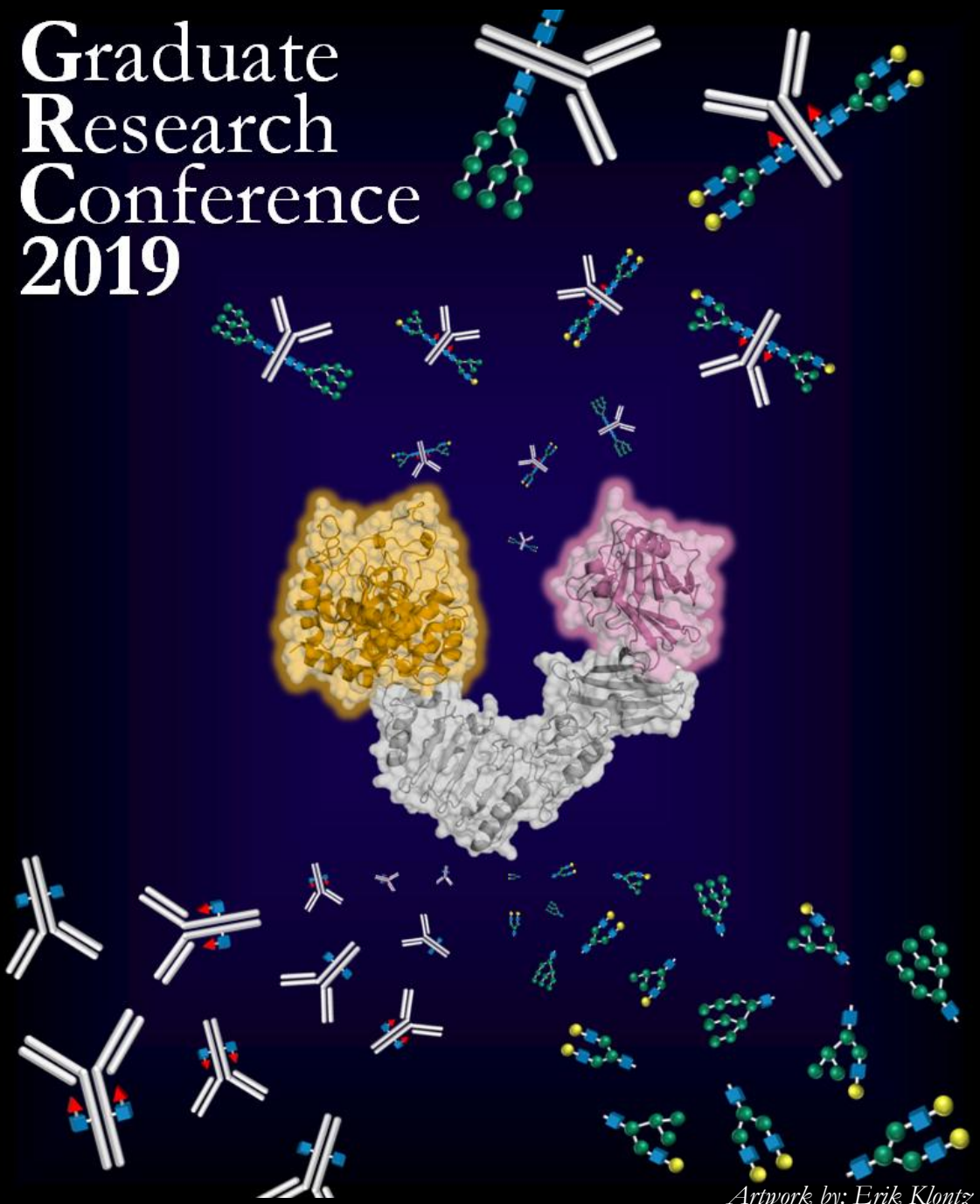
UNIVERSITY of MARYLAND
THE FOUNDING CAMPUS

Graduate Research Conference 2019



Artwork by: Erik Klontz

41st Annual

SMC Campus Center
March 15, 2019
Baltimore, Maryland
Hosted by the Graduate Student Association

GSA graduate student association

Sponsored in part by:
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UNIVERSITY of MARYLAND
THE FOUNDING CAMPUS

41st Annual Graduate Research Conference

Presented by:

GSA graduate student association
UNIVERSITY of MARYLAND

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Contents:

A Message from the President

March 15, 2019

Congratulations on your 2019 Graduate Research Conference. This instinct to share with one another is so important. It's important that each of us understands how our colleagues contribute to our collective mission, and it's important that we consider our work not in isolation but in context.

And that's because the biggest breakthroughs we celebrate in human health and well-being often happen at the intersections—the intersection of scholars and schools and disciplines. When we're eager to talk with one another, to work with one another, to redesign the way we think about the problems that plague us (and the way we imagine their solutions), that's when we see the fire of true creativity and innovation. That's when we see possibilities open up before us, new avenues emerging from dead ends. That's when we dream up new applications for our work, ways to broaden its reach or amplify its impact.

There's another reason I applaud your desire to share today: We need each other. When evidence is degraded and facts are misrepresented and truth is thrown into question, we need passionate, persuasive people like you to fight for the science, scholarship, and service that will lead us to the ideals on which we've staked our careers: health, wellness, equity, opportunity, and justice—for all.

Sincerely,

Jay A. Perman, MD
President

Forward

Welcome to the 41st 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 11th 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. Marey Shriver, a UMB alumna who is now an Assistant Professor in the Department of Biochemistry and Molecular Biology and the Director for the Research Career Development Program in the School of Medicine. 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 President Perman 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. Marey Shriver, 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 41st annual Graduate Research Conference, and we hope you enjoy today's program and events!

<u>GSA Executive Board</u>
Megan Lynch – President
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Janelle Hauserman – Graduate Council Representative
Katie Gwilliam – Public Relations Officer

<u>2019 GRC Organizing Committee</u>
Julia Thayer, Eryn Dixon, Janelle Hauserman, Christine Carney, Talia Guardia, Hadley Bryan, McKayla Mickle, Devin Sharp, and Alyssa Grogan

Student Award Winners

The Graduate Student Association would like to congratulate the students who have won our awards during the 2018-2019 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.

Research Award

Camilo Vanegas
Yanfeng Xu

Travel Award

Sally Hageman, Third Quarter 2018
Eric Lumsden, Third Quarter 2018
Camilo Vanegas, Third Quarter 2018

Sarah Holmes, Fourth Quarter 2018
Rupa Guha, Fourth Quarter 2018
Jordan Pritts, Fourth Quarter 2018
Kiwon Ok, Fourth Quarter 2018
Joel Brandis, Fourth Quarter 2018

Rachel Larson, First Quarter 2018
Kiwon Ok, First Quarter 2018
Alexandra Webster, First Quarter 2018

Sarah Holmes, Second Quarter 2018
Caroline Harmon-Darrow, Second Quarter 2018
Hamzah Alghzawi, Second Quarter 2018
Yanfeng Xu, Second Quarter 2018

Abstract Booklet Image
Erik Klontz

Keynote Speaker Biography

Dr. Marey Shriver

Assistant Professor of Biochemistry and Molecular Biology and Director for the Research Career Development Program, University Maryland Baltimore School of Medicine

Keynote Speaker Dr. Marey Shriver is an alumna from the Program in Molecular Medicine. After receiving her PhD, she completed a Postdoctoral Fellowship at Johns Hopkins University School of Medicine and then served as research administrator in the Office of Research Affairs at UMB. Dr. Shriver is currently an Assistant Professor in the Department of Biochemistry and Molecular Biology and the new Director for the Research Career Development Program in the UMB School of Medicine. In her current position she provides research and professional support for early stage faculty and specializes in early project conception, including developing a clear research question and testable hypothesis. The GSA and student body of UMB would like to welcome Dr. Shriver and express our thanks for her willingness to share her story at our conference.

41st Annual Graduate Research Conference

Schedule of Events

SMC Campus Center
March 15th, 2019

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. Marey Shriver	
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 Kristen Brao), (#2 Justine Yu), (#3 Marie Hanscom), (#4 Gideon Wolf), (#5 Brandi Hobbs) (#6 Elizabeth Robinson)

Session B - Oral Session, 9:00-10:30 am, Elm Ballroom B
(#7 Heather Mutchie), (#8 Nicholas Palmateer), (#9 Tom Jaworek), (#10 Meredid Caves), (#11 Tiffany Owens)

Session C – Poster Session, 10:45-11:45 am, Room 349
(#12 Kelsey DiStefano), (#13 Beth Pruitt), (#14 Denisha Cuffee), (#15 Lanaya Davis), (#16 Courtney Hicks), (#17 Erin Donohue), (#18 Vanessa Hill), (#19 Kelsey Ivusich), (#20 Anju Paudel), (#21 Lindsey Turnbaugh)

Session D – Poster Session, 10:45-11:45 am, Room 349
(#22 Yan Liu), (#23 Brian Johnson), (#24 Aparna Vadlamani), (#25 Sol Baik), (#26 Nicole Viviano), (#27 Jennifer Kirk), (#28 Nimasha Fernando)

Session E – Poster Session, 10:45-11:45 am, Room 349
(#29 Amy Defnet), (#30 Cassandra Jordan), (#31 Chad Johnson), (#32 Kathleen Gwilliam), (#33 Kevin Rose), (#34 Victoria Laye), (#35 Lora Stojanovic), (#36 Olivia Uddin), (#37 Sridevi Ranganath), (#38 Eman Hefni)

Session F – Poster Session, 1:00-2:00 pm, Room 349
(#39 Albert Zhou), (#40 Titilola Akintola), (#41 Raziyeh Baghi), (#42 Kelly Rock), (#43 Emily Stucke), (#44 Haichen Zhang), (#45 Thayana Leao), (#46 Jungmin Yoon), (#47 Matthew Chung)

Session G – Poster Session, 1:00-2:00 pm, Room 349
(#48 Verna Van), (#49 Ashley Lykins), (#50 Tyree Wilson), (#51 Talia Guardia), (#52 Abdulrah Balhaddad), (#53 Dante Johnson), (#54 Nivedita Hegdekar), (#55 Jonelle Lee), (#56 Ebtehal Albeshir), (#57 Perna Singh), (#58 Erica Kundrick)

Session H – Poster Session, 1:00-2:00 pm, Room 349
(#59 Jennifer Spelta), (#60 Katharine Outen), (#61 Ashley Burnham), (#62 Hamzah Alghzawi), (#63 Hyojin Son), (#64 Julie Riggs), (#65 Bianca Zorbach)

Session I – Oral Session, 2:15-3:45 pm, Elm Ballroom A
(#66 Patrick Bailey), (#67 Emily Smith), (#68 Maria Ibrahim), (#69 Anna Dellomo), (#70 Allison Gerber), (#71 Bashayer Baras)

Session J – Oral Session, 2:15-3:45 pm, Elm Ballroom B
(#72 Janelle Geist Hauserman), (#73 Courtney Matson), (#74 Canessa Swanson), (#75 Garrick Centola), (#76 Ava Zapf), (#77 Aksinija Kogan)

Abstracts

1. A NOVEL MODEL FOR CYSTIC FIBROSIS-ASSOCIATED AIRWAY COLONIZATION WITH PSEUDOMONAS AERUGINOSA AND STAPHYLOCOCCUS AUREUS USING B-ENAC MICE

Kristen Brao

Brao, K.J., Harro, J.M., Lieberman, J., Ernst, R.K., and Shirtliff, M.E.

Session A; Oral Presentation; Ballroom A

Cystic fibrosis (CF) is caused by defects in production and function of the cystic fibrosis transmembrane conductance regulator (CFTR) channel, and it is characterized by recurrent and chronic lung infections. Co-infection with Staphylococcus aureus and Pseudomonas aeruginosa is linked to accelerated lung function decline, however, modeling P. aeruginosa infections in mice has been an obstacle in their study. CFTR-knockout mice do not develop pulmonary phenotypes matching cystic fibrosis, and mice typically clear P. aeruginosa from their airways quickly, preventing the study of chronic infections. We are developing a novel murine model for P. aeruginosa and S. aureus lung infections utilizing transgenic mice that over-express epithelial sodium channels (ENaC), driving a CF-like pulmonary pathology. To study how P. aeruginosa and S. aureus colonize CF lungs, we intranasally infected 7-9 week-old mice with P. aeruginosa or S. aureus and collected lungs at 3, 7, 10, and 14 days post-infection for histopathologic and cytokine analysis. We have found that by infecting B-ENaC mice with bacterial aggregates from P. aeruginosa biofilms we are able to produce a pulmonary infection that lasts approximately two weeks, whereas planktonic P. aeruginosa are quickly cleared ($p<.001$, 2-tailed t-test). Additionally, B-ENaC BALB/c mice were generally more likely than their wildtype littermates to remain infected with S. aureus. Cytokines produced in airways during P. aeruginosa infection included IL-17 and IL-22, matching cytokines produced during P. aeruginosa pulmonary exacerbations in CF patients. These results show the promise of B-ENaC mice as a model for early bacterial colonization in the CF airway.

2. LNCRNA-DANCR PROMOTES NSCLC THROUGH ACTIVATION OF WNT/B-CATENIN SIGNALING

Justine Yu

Yu, J.E., Musacchio, N., Vitolo, M.I., and Zhou, Q.

Session A; Oral Presentation; Ballroom A

Non-Small Cell Lung Cancer (NSCLC) comprises 85% of lung cancer cases, which is the leading cause of cancer-related deaths worldwide. Therefore, there is an urgent need to elucidate the mechanisms involved in NSCLC tumorigenesis to define new therapeutic strategies to improve patient outcomes. Differentiation Antagonizing Non-protein Coding RNA (DANCR) is a long non-coding RNA (lncRNA) that regulates cancer cell stemness and invasion. Additionally, Wnt signaling has been shown to promote cancer cell proliferation, stemness, and invasion. Therefore, in this study, we investigate the hypothesis that overexpression of DANCR promotes NSCLC through induction of Wnt/β-catenin signaling. We found that DANCR is highly upregulated in NSCLC tumors and cell lines. Knockdown (KD) of DANCR expression reduced migration, decreased cell viability, and downregulated

the stem cell markers Sox2 and Aldh1/2. Using a β-catenin luciferase reporter, we found that DANCR KD reduces β-catenin signaling activity. Furthermore, DANCR KD reduced Wnt/β-catenin signaling proteins, and reduced expression of Wnt/β-catenin gene targets. One of the best defined functions of lncRNAs is their ability to inhibit miRNA activity by acting as a competing endogenous "miRNA sponge". Through in silico analysis, we found that DANCR was predicted to bind to the tumor suppressor miR-216a. We confirmed this binding through Co-Immunoprecipitation and luciferase reporter assays, and showed that overexpression of miR-216a reduced β-catenin protein expression. Together these data suggest that DANCR may regulate Wnt/β-catenin signaling through miR-216a. Future studies will elucidate the role of miR-216a in the DANCR/Wnt/β-catenin signaling axis in NSCLC tumorigenesis.

3. IMPACT OF SECONDARY INTESTINAL INFLAMMATION ON LONG-TERM NEUROLOGICAL OUTCOMES FOLLOWING EXPERIMENTAL TRAUMATIC BRAIN INJURY IN MICE

Marie Hanscom

Hanscom, M., Aubrecht, T., Molesworth, K., Loane, D. J., Shea-Donohue, T., and Faden, A. I.

Session A; Oral Presentation; Ballroom A

Traumatic brain injury (TBI) often results in secondary complications involving various organ systems including the gastrointestinal track. TBI patients surviving longer than one-year post-injury are 2.5 times more likely to die of digestive disorders. We previously reported that following TBI in mice, pathogenic bacterial infection exacerbated the TBI-associated lesion volume and inflammation. The aim of these studies was to determine the effects of colitis on cognitive function following chronic TBI. Male C576Bl/6 mice were randomized into naïve (anesthetic only), sham (5mm craniotomy), and moderate-to-severe controlled cortical impact (CCI) groups. Twenty-eight days after injury, mice were treated for 7 days with 3% DSS to induce colitis, followed by return to regular water for 7 days. Prior to, during and following induction of colitis, mice were tested on beam walk (BW) and novel object recognition (NOR) to assess motor and cognitive function. Mice were euthanized 7-14 days post-DSS and colons/brains were processed for evaluation of injury. Prior to DSS treatment, only CCI-injured mice exhibited neurobehavioral deficits. Within days of DSS treatment, Sham+DSS mice exhibited persistently impaired deficits in motor (BW) and cognitive (NOR) function, while motor function deficits were exacerbated in CCI+DSS mice. Behavior was unaffected in Naïve+DSS mice. These data show that neither inflammation of the colon alone (Naïve+DSS) nor Sham-injury alone induce neurobehavioral deficits. In contrast, colitis induced significant impairments in behavioral outcomes in both Sham+DSS and CCI+DSS mice indicating that prior brain injury, even when mild, primes the brain for development of neurological deficits in response to gut inflammation.

4. A PARADOXICAL DISPLAY OF EXHAUSTION IMMEDIATELY AFTER INITIAL T CELL ACTIVATION.

Gideon Wolf

Wolf, G., and Singh, N.

Session A; Oral Presentation; Ballroom A

Activated naïve T cells typically acquire effector functions over a 2-3 day period of differentiation in the secondary lymphoid organs, before migrating to the tissue sites to deliver effector functions. If the stimulating antigen is long lasting, as in the case of chronic infections, the T cells shut off by a process known as exhaustion. This involves expression of co-inhibitory receptors such as PD1. Surprisingly, we find that stimulating T cells for even short periods after the initial antigen encounter leads CD4+ T cells to exhibit an exhausted phenotype. This is marked by the loss of proliferative potential and the upregulation of PD1. Naïve TCR-transgenic 5C.C7 T cells stimulated with their cognate peptide, proliferate rapidly between 2-4 days. Re-stimulation of these T cells on the 3rd day however, revealed a profound proliferative arrest accompanied by the rapid re-expression of PD1. The new levels of PD1 was proportional to the dose of re-stimulating antigen. This is consistent with data on effector T cell tuning that has been previously described for cells homing to tissue sites. We are currently examining the molecular machinery underlying this duality to understand why there is a paradoxical loss of T cell responsiveness to antigen during a primary effector response. These studies are expected to develop new approaches to not only improving T cell responses to vaccines and infections, but perhaps also circumventing exhaustion during chronic microbial contagions and tumors.

5. Characterization of Attenuated Francisella tularensis LVS Phagosomal Transporter Mutants

Brandi Hobbs

Hobbs, B. E., and Barry, E. M.

Session A; Oral Presentation; Ballroom A

Francisella tularensis (Ft) is a Gram-negative, facultative intracellular bacterium that is a Tier 1 Select Agent of concern for biodefense. A family of 9 Francisella phagosomal transporter (fpt) genes encoding members of the Major Facilitator Superfamily of transporters has been identified as critical to the pathogenesis of Ft and potential targets for attenuation and vaccine development. The ability of Ft to survive and replicate to high numbers within macrophages is key to pathogenesis. Deletion mutations have been generated in 8 fpt genes in LVS and infection assays within mouse peritoneal macrophages demonstrated altered intracellular replication kinetics by 5/5 fpt mutant strains tested in comparison to parental LVS. Mutant phenotypes varied but included defective intracellular replication, delayed egress, inability to re-infect neighboring cells, and altered host cell death kinetics. Mutations in fptA, fptB, fptE, and fptF resulted in reduced intracellular replication and reduced cytotoxicity, as well as attenuation in the C57BL/6J mouse model of respiratory tularemia. LVSΔfptG exhibited the most significant defect in vitro. It was unable to escape the host cell and re-infect neighboring cells, and induced alterations in host cell cytokine responses. We hypothesize that fptG is essential for the timely escape of Ft from the cell. These results support a fundamental necessity for fpt gene products in the pathogenesis of Ft, and ongoing analysis will further our understanding of these roles.

6. Identification and Characterization of Inhibitors of the Pseudomonas aeruginosa Heme Oxygenase

Elizabeth Robinson

Robinson, E. A., Hom, K., Xue, F., and Wilks, A.

Session A; Oral Presentation; Ballroom A

Iron is necessary for the virulence and survival of many opportunistic and multi-drug resistant pathogens. Many of these pathogenic bacteria have evolved complicated mechanisms to overcome the lack of labile iron in the host system. Pseudomonas aeruginosa, a gram-negative opportunistic pathogen adapts during infection to uptake iron in the form of heme. P. aeruginosa has two main heme uptake systems; one as the main heme transport system and the other as the major extracellular heme sensing system. Both systems consist of transporters and heme-trafficking proteins that chaperone heme through the Pseudomonas outer and inner membranes. Once heme reaches the cytoplasm of the cell it is degraded by heme oxygenase (HemO) to release iron for its own iron containing proteins. This project will i) identify new small molecule inhibitor scaffolds targeting HemO; ii) develop novel in vitro and in-cell assays as a means of more accurately screening small molecule inhibitors of HemO as a means to mitigate bacterial virulence within the host; and iii) characterize the structure-activity relationship between inhibitor and enzyme to further optimize and synthesize lead compounds for further development as inhibitors of P. aeruginosa (HemO). The proposed studies will overcome limitations with the current in vitro and in-cell assays of HemO activity and streamline the identification and characterization of novel scaffolds targeting HemO.

7. FEASIBILITY OF FOUR SQUARE STEP TEST IN HIP FRACTURE PATIENTS

Heather Mutchie

Mutchie, H.L., Orwig, D., Beamer, B., Conroy, V., Guralnik, J., Magaziner, J., and Gruber-Baldini, A.

Session B; Oral Presentation; Ballroom B

The Four Square Step Test (FSST) is a clinical tool testing balance and motor planning for predicting falls in older adults. The FSST has not been widely used in hip fracture patients. The purpose of this study was to assess the feasibility of FSST after hip fracture and consider the impact of cognitive impairment (which is high after hip fracture) on FSST performance. Subjects came from baseline of an ancillary study of a randomized trial, Community Ambulation Project-Mechanistic Pathways (CAP-MP; n=40). Subjects walked between 0.1m/s-0.8m/s by <26wks after surgically repaired hip-fracture and completion of standard rehabilitation. Cognitive measures included the Modified Mini Mental State Examination, Hooper Visual Organization Test, and Trails A&B. Descriptives, bivariate-correlations, and ANCOVA models tested the association of FSST performance with cognitive measures, demographics, physical function, and fracture-side. Only 27 of the 40 CAP-MP participants completed the FSST. Of those who did not attempt, 25%(n=3) refused and 74%(n=9) were deemed unsafe or unable. Participants who did complete had high FSST times (26.85+18.4s), with 74%(n=20)<15seconds. FSST was significantly ($p \leq .05$) correlated with Hooper(r=-0.45), Trails A(r=0.39), gait speed(r=-0.37), fracture-side(r=-0.61), male sex(r=-0.40), and age(r=0.38). In models of FSST, only fracture side remained significant with a borderline interaction with Hooper(p=.07). Those with lower Hooper scores and Left side fracture did worst, while Right side fractures did best (regardless of Hooper). Many CAP-MP hip fracture patients were unable (23%) or failed (50%) the FSST.

The influence of fracture side and cognition merit further exploration to improve FSST testing in hip fracture patients.

8. Characterization of Genetic Variation Between Host-specific Theileria parva Populations

Nicholas Palmateer

Palmateer, N. C., Daubenberger, C. A., Bishop, R. P., and Silva, J. C.

Session B; Oral Presentation; Ballroom B

East Coast Fever (ECF), caused by the parasite Theileria parva, kills more than a million cattle annually in endemic regions of sub-Saharan Africa. The African buffalo is believed to be the natural reservoir of T. parva and rarely exhibits clinical symptoms when infected, but transmits the parasite to cattle via a tick vector. Previous studies based on limited genetic markers have shown that buffalo-derived T. parva populations contain greater antigenic diversity, possibly explaining the failure an ECF vaccine to protect against the more diverse buffalo-derived parasites. Recent studies suggest a degree of T. parva host specificity has occurred. The characterization of genetic variation among and between cattle- and buffalo-derived T. parva strains is critical to shed light on the evolutionary processes that have led to the host specificity, as well as for the design of next-generation vaccines against all strains. We generated whole genome sequence data from cattle- and buffalo-derived T. parva isolates following whole genome DNA capture. Based on genome-wide SNP data, we identified regions of divergence between the cattle- and buffalo-derived T. parva isolates. An FST analysis yielded a genome-wide value of 0.23 between the two sets of strains, revealing strong differentiation. Several known antigens were among the genes with highest FST values, warranting further exploration for vaccine development. We observe a high level of differentiation throughout the genome, demonstrating possible speciation between these two subpopulations, and seek to identify genes with a potential role in infection and transmission, based on the function of the encoded proteins.

9. Polygenic Risk Scores Analysis in Early vs Late Onset Ischemic Stroke

Tom Jaworek

Jaworek, T. J., Gaynor, B., Ryan K., Xu, H., Mitchell, B. D., Kittner, S., and Cole, J.

Session B; Oral Presentation; Ballroom B

Ischemic stroke is a leading cause of mortality and is a collection of heterogeneous disorders. While much of an individual's risk for stroke is mediated by lifestyle, it is also closely associated with other co-morbidities such as CVD, diabetes, and atrial fibrillation. Recent studies have identified several genetic loci that are associated with stroke and have found overlaps between genetic risk factors for stroke and other complex diseases. The distribution of stroke subtypes varies by age and the presence of certain risk factors. A major question in the field is whether these findings are influenced by differences in the genetic architecture between early and late onset strokes. Furthermore, it is unknown to what extent these two categories of stroke have shared biological mechanisms with other disorders. To help answer this question, we used genotype data of from the SiGN stroke genetics consortium (n=15,000) to perform polygenic risk score (PRS) analysis to test whether scores for stroke risk factors are associated with stroke outcomes in early and

late onset cases. Cases were stratified by age 59 into early and late onset categories. In addition, we also examined associations between stroke subtypes and PRSs for both early and late onset cases. These association results may allow us to infer that these traits share a similar genetic etiology, which may advance our understanding of how the genetic architecture of stoke may differ between early and late onset cases.

10. Caregiver Distress and Burden During Outpatient Allogeneic Peri-Hematopoietic Stem Cell Transplantation Period

Meredid Caves

Caves, M.S., Gladstone, D.E., and Krumm, S.

Session B; Oral Presentation; Ballroom B

Problem: Advances in the field of allogeneic hematopoietic stem cell transplantation (HSCT) has allowed inpatient HSCT stays to be replaced by outpatient HSCT in order to improve quality of life for patients and lessen the economic burden on the hospitals. Caregivers are essential to the outpatient HSCT process and lack of having a full-time caregiver limits outpatient HSCT. Because outpatient HSCT transfers the medical care responsibility to the caregiver it can increase burden and distress. Purpose: To examine the trajectory and relationship of caregiver burden and distress during the peri-transplant period. Background: Caregivers are at risk for physical and psychological adverse effects related to caregiving including an increase in mortality. Nearly half of caregivers modified their work schedule in order to provide care. Methods: This single center study employed an observational prospective longitudinal repeated measures design. The target population consists of caregivers of patients undergoing HSCT. The Distress Thermometer Scale and the Caregiver Burden Scale are subjective surveys being used to measure distress and caregiving burden at 3 time points: (1) at the time of bone marrow infusion, (2) when the patient's bone marrow recovers and (3) when the patient is discharged from the clinic. Outcomes Achieved to Date: Internal Review Board Approval was obtained June 2018. To date 37 caregivers have completed the study. Conclusions: This research study could provide novel insights into the trajectory of caregiver distress and burden throughout the peri-transplantation period and refine current research strategies for examining caregiver distress in the HSCT population.

11. Implementing Medicare Annual Wellness Visits (AWV) with a Health Risk Adjustment (HRA) in Primary Care

Tiffany Owens

Owens, T.N.

Session B; Oral Presentation; Ballroom B

Purpose: Within the primary care setting, there is a deficiency of comprehensive, personalized treatment plans that identify modifiable risk factors and endorse preventive care. The Medicare Annual Wellness Visit (AWV) presents an opportunity for patients aged 65 years and older to identify, plan and manage chronic health conditions and increase preventative care. The Health Risk Assessment (HRA) can be utilized to create a personalized prevention plan to reduce risk factors and related diseases. The purpose of this quality improvement doctoral project is to increase the number of Medicare AWVs, which include use of a HRA, in a primary care practice, for Medicare patients aged 65 and older with chronic health conditions.

Methods: The project is being implemented over a 14 week period. Mail and telephonic outreach were conducted to all eligible Medicare patients. HRAs were mailed to the patient and collected during check in for the scheduled AWV appointment. Results: A run chart is being used to track of number of AWVs completed daily. Weekly chart audits will validate completed HRAs in the charts of patients with completed AWVs. An audit tool is being used to track ten variables. Multiple logistic regression models will be constructed for each outcome to determine whether the intervention improved the success. Significance: The results of this project can help identify and decrease health risks, while assisting ageing adults in improving their quality of life. The AWV also has the opportunity to increase the practice's revenue with Medicare reimbursement and increased relative value units (RVU).

12. Implementation and Evaluation of Nurse Mentorship

Kelsey DiStefano

DiStefano, K., and Davenport, J.

Session C; Poster Presentation; Room 349

Nurse retention is a significant problem that currently exists within many healthcare systems today. Specifically, new graduate nurses exist as a vulnerable population to turnover, as they work to fill the nursing shortage, feeling overwhelmed and discouraged secondary to stress, feelings of inadequacy and lack of support. The literature points to the implementation of mentorship for the novice nurse as an intervention to improve satisfaction with work, clinical confidence, and intent to stay; thereby fostering a higher degree of retained nurses who are able to progress from novice to expert in achieving quality patient outcomes. Implementation of a nurse mentorship program targeting nurses with less than one year of clinical experience was conducted as a pilot project on a medical-surgical unit with a high volume of new graduates and subsequent history of high turnover. Mentorship was facilitated through three separate meetings between a paired experienced and novice nurse to discuss gaps in knowledge, professional development, and various topics relevant to self-reflected goals and unit acuity. Data was collected at the end of a 14-week period to evaluate process effectiveness and the relationship had through mentoring as it relates to satisfaction, engagement, and clinical confidence. Initial findings demonstrate mentorship as a meaningful intervention for the novice through providing an intentional mechanism for support to augment the ability for progression from novice to competent, as well as renewed self-fulfillment and engagement in the experienced nurse participating as a mentor.

13. Fall Prevention in Perioperative Units

Beth Pruitt

Pruitt, B. A.

Session C; Poster Presentation; Room 349

In the United States, patient falls have become a critical issue that negatively impacts our healthcare system. According to data from the Agency for Healthcare Research and Quality (AHRQ), falls rates are approximately 3-5 per 1000 bed days, amount to upwards of 1 million falls annually (AHRQ, 2017). Falls are not benign events, and often lead to some level of patient harm or even death. Vulnerable populations including the elderly and those with physical and cognitive

limitations have the highest incidence of falls (AHRQ, 2017). In perioperative units, a highly vulnerable population exists, along with barriers to fall prevention. In a community-based hospital located in a Maryland suburban community, a comprehensive fall prevention plan was initiated to promote safety in this population. Based on the evidence, a fall prevention bundle was initiated on all adult patients in the perioperative units. Bundle compliance was tracked and measured along with calculation of fall rates. Data included bundle compliance audits, and calculation of average compliance rates as well as falls rates per 1,000 bed days. After initiation of the comprehensive fall prevention bundle, staff had a high compliance rate with measures. Furthermore, no falls have occurred since bundle implementation. Based on this data, the successful implementation of a fall prevention bundle has the potential to decrease the number of falls in a vulnerable population.

14. Improving Linkage to Care in the HIV Clinic Setting

Denisha Cuffee

Cuffee, D.

Session C; Poster Presentation; Room 349

Purpose: Linkage-to-care templates (LTCT) within the human immunodeficiency virus (HIV) patient electronic medical records (EMRs) are not all being routinely completed at discharge. Incomplete EMR LTCT compromise follow-up care and result ultimately in poor patient outcomes. The purpose of this Doctor of Nursing Practice (DNP) project is to increase the number of completed LTCT via use of a point-of-care reminder pop- up placed in outlook calendar of case managers treating HIV patients aged 18 and older in an HIV health clinic. Rationale: Linkage-to-care (LTC) is a key determinant in improving outcomes for HIV patients. Studies have demonstrated that any form of a reminder method can aid staff in adhering to the standard of practice. In particular, linkage to a primary care provider reliably improved HIV patient outcomes. Studies also show that thorough LTC provided by an HIV clinic may have a profound positive influence on whether patients follow through with appointments with providers and stay linked to care. Methods: A pre-intervention questionnaire was administered to the clinic staff to assess current barriers to linking patients to care. Staff education and training were conducted on setting outlook calendar reminders for efficiently discharging (linking to care) patients. EMR audits will be conducted to track completed discharges. Implications for practice: The results of this project can help staff efficiently link patients living with HIV to primary care which in return improve patient's overall outcome. Linking patients to care effectively has the opportunity to decrease HIV related complications, comorbidities and mortality.

15. Oral Care Protocol to Prevent Hospital Acquired Pneumonia

Lanaya Davis

Davis, L. M.

Session C; Poster Presentation; Room 349

Hospital acquired pneumonia (HAP) is the second most common hospital acquired infection, and is responsible for 20-33% of mortality rates from infection. Patients with HAP also have higher 30-day hospital readmission rates compared to patients without a hospital acquired infection. Nationwide, HAP accounts for 32.5-35.4

million discharges annually. According to the Centers for Disease Control, 5-7% of hospitalizations due to pneumonia end in death. The oral cavity is a high reservoir for infection, and evidence based practice suggests oral hygiene interventions to prevent HAP. HAP is more common in at risk individuals, and there are four routes of transmission: (1) through aspiration of oral contents (food, oropharyngeal secretions, or gastrointestinal contents), (2) from infectious sites, (3), from inhalation of aerosols that are infected, and (4) from extra-pulmonary sites. Aspiration of infectious organisms remains the number one way to acquire HAP, so reducing oral bacteria is critical in HAP prevention. The purpose of this quality improvement project is to develop and implement the use of an oral care protocol on an acute geriatric inpatient unit in order to decrease HAP incidences. Short-term goals of this project include: implementation of an oral care protocol by September 2018, by November 2018, 50% of patients at risk for aspiration will have documented oral care, and by September 2018, staff knowledge of HAP will be increased by 50% through the use of education and posttests. Long-term goals of this project include: reduction of overall aspiration pneumonia by 90%.

16. Hospital Acquired Pressure Ulcer Prevention Admission Bundle

Courtney Hicks

Hicks, C.

Session C; Poster Presentation; Room 349

The development of a hopsital acquired pressure ulcer (HAPU) is not only detrimental to the patient, but to their family, providers, and hospital-based system as well. HAPU development is not only costly, but they increase patients' morbidity and mortality. HAPUs are prevalent nationally and their incidence is on the rise in the state of Maryland as of 2015. A step-down unit within a community hospital in Maryland is not exempt from this reality. Aims/Objectives: In order to reduce rates of HAPUs and improve patient care, an evidence-based admission bundle will be implemented. The specific aims for this project will include an increase in compliance with aspects of the bundle, and an increase in nurse knowledge and confidence post implementation of the bundle. Methods: After a survey of current practice completed by staff revealed knowledge gaps and specific areas for improvement, an educational online training module was developed and an evidence-based admission bundle was devised. The Plan-Do-Study-Act model was utilized to help facilitate implementation. Results: Implementation is half-way through and there is currently 100% completion of staff education. 47% compliance rate with sacral preventative dressings and 90% compliance rate of low air loss beds utilized for patients with a Braden <16. There is a 52% compliance with turning schedules utilized in all patients' rooms and an 84% two nurse admission skin assessment. Implications: The use of a nurse-driven admission bundle can aim at early identification of risk and lead to early implementation of preventative measures to stop HAPUs from the start.

17. Asthma Clinical Pathway in a Pediatric Emergency Department

Erin Donohue

Donohue, E. K., and Benoff, A.

Session C; Poster Presentation; Room 349

A high prevalence of children with asthma exacerbations seek care in emergency rooms. To better assist emergency personnel on prompt evidence-based (EB) treatment that adheres to the national asthma guidelines, a standardized asthma clinical pathway (ACP) can be utilized. Treatment principles from pathways are associated with increased frequency of appropriate medication, expedited medication administration, decreased hospital admissions, decreased length of stay (LOS), and less return visits. The purpose of this DNP QI project is to standardize asthma treatment for children with moderate to severe exacerbations in a pediatric emergency department (PED) in a Maryland community hospital by implementing a EB ACP and to decrease these patient's LOS. Recommendations from the National Heart, Lung and Blood institute were utilized in addition to the professional input of PED providers, and the DNP student project leader in developing the ACP for the PED. Pre and post data was collected via chart audits to evaluate proper use of the pathway and LOS. A three-question YES/NO post-implementation survey was administered to staff exploring their opinion of the pathway execution. A total of 86 patients qualified for the ACP. The pathway compliance was 80% by staff. The average LOS was 286 minutes, decreasing by 14 minutes pre-implementation. The staff responded 100% YES to pathway ease of use, assist in prompt care, and interest in future treatment pathways. Adherence to a standardized treatment ACP can assist first-line nurses and providers in delivering EB prompt emergent care, and decrease LOS to children in a PED.

18. THE USE OF THE MATERNAL ORAL SCREENING TOOL IN THE ANTENATAL OUTPATIENT SETTING FOR MARYLAND MEDICAID PATIENTS

Vanessa Hill

Hill, V., and Idzik, S.

Session C; Poster Presentation; Room 349

Poor oral health, specifically periodontal disease, is a risk factor for adverse birth outcomes. Additionally, untreated tooth decay in pregnant women elevates dental caries risk of the future child, one of the most common chronic pediatric diseases in the U.S., as caries-causing bacteria are primarily transferred from mother to infant after birth. Maryland Medicaid data show that only 26.1 % of pregnant women covered by Medicaid receive oral health care. Additionally, women who are pregnant are also predisposed to periodontal disease through the hormonal changes that are occurring in their body. Thus, a screening tool for dental problems should be in place during prenatal visits to increase the usage of oral care services—helping both pregnant women and their future children. National guidelines and the Maryland Department of Health Office of Oral Health recommend oral health screening at prenatal visits. The purpose of this quality improvement project is to implement the maternal oral screening tool in the prenatal setting to identify dental needs, specifically in women predisposed to periodontal disease and improve the use of dental referrals in the prenatal setting. This program evaluation will be completed with hopes of becoming a standard of care at the designated prenatal clinic. The potential benefits of this quality improvement project is to: improve utilization of oral health care by women during pregnancy, improve oral health integration in prenatal care, and improve oral health of pregnant women and lower dental caries risk for future infants.

19. The Implementation of Nocturnal Earplugs and Eye Masks to Improve Sleep in the Cardiac Surgery Intensive Care Unit

Kelsey Ivusich

Ivusich, K. S.

Session C; Poster Presentation; Room 349

Background: Sleep deprivation is a concern among intensive care unit (ICU) patients, with noise and light as frequent contributors. The use of nocturnal earplugs (EP) and eye masks (EM) is suggested to increase sleep quality among ICU patients. Purpose: The purpose of this project was to implement and evaluate the usability and feasibility of nocturnal EP and EM in cardiac surgery ICU (CSICU) patients in a large, academic hospital in Maryland. Interventions: Extubated, oriented, non-sedated CSICU patients were asked to wear nocturnal EP and EM, then complete a Patient Usability Survey evaluating the amount and quality of sleep, and comfort of the interventions. Nurses completed a Nursing Questionnaire evaluating the duration of the interventions worn, if EP and EM helped patients sleep through nursing interventions, and their recommendation for EP and EM to future patients. Results: 51% of patients refused participation. Most patients rated they slept "4-6h," with "More than average/normal" sleep quality. EP comfort was described as "Satisfactory" and EM as "Very comfortable." The combination of EP and EM was most popular, with "6-8h" of wear time. Majority of nurses "Agreed" that EP and EM helped patients sleep through interventions and "Agreed" to recommend them. Conclusion: Most patients who accepted EP and EM found them comfortable and beneficial. Nurses believed EP and EM helped patients sleep through interventions and would recommend their use. Despite positive outcomes in those who participated, high refusal rates imply the use of EP and EM may not be suited for the CSICU patient population.

20. Factors Influencing Staff-resident Interactions in Nursing Homes

Anju Paudel

Paudel, A., Galik, E., Resnick., B.

Session C; Poster Presentation; Room 349

Background: Staff-resident interaction is an integral part of daily life of nursing home residents and has an influence on residents' well-being. However, less is known about the factors that influence these interactions. Aim: The purpose of this study was to describe the quality of interaction between staff and residents with dementia in nursing homes, and explore the factors associated with 'positive' and 'negative/neutral' interactions. Method: This cross-sectional analysis utilized baseline data from the first two cohorts in a randomized clinical trial, EIT-4-BPSD, including 338 residents from 35 nursing homes. Generalized linear mixed model (GLMM) was used to explore the factors associated with interactions. It was hypothesized that the resident factors (age, gender, race, marital status, cognition, comorbidities, depressive symptoms, agitation, functional status) and facility factors (facility ownership, facility size, RN hours, LPN hours, CNA hours, and star rating) would be associated with staff-resident interactions. Results: The staff-resident interactions were mostly positive. Overall, the models for 'positive interactions' and 'negative/neutral interactions' correctly classified 82.8% and 85.3% of the cases respectively. Both 'positive' and 'negative/neutral' interactions

were significantly associated with marital status, and profit status of the facility. Being married and living in a not for profit facility was associated with lower odds of positive interaction and higher odds of negative/neutral interaction. Conclusion: There is some evidence that marital status influences staff-resident interactions and that profit status of facilities are associated with staff resident interactions. Future studies could explore staff factors such as consistent assignment, job satisfaction, staff characteristics, and training.

21. Implementation of a Nurse-Driven Nonpharmacological Sleep Bundle to Evaluate the Incidence of Delirium in a Surgical Intensive Care Unit

Lindsey Turnbaugh

Turnbaugh, L. D.

Session C; Poster Presentation; Room 349

The purpose of this quality improvement project is to evaluate the effectiveness of a nurse-driven nonpharmacological sleep bundle in preventing delirium in an adult Surgical Intensive Care Unit (SICU). Several negative outcomes occur in patients diagnosed with delirium in the ICU, including increased mortality, hospital length of stay, cost of care, and long-term cognitive impairment. Sleep, a critical component of health and recovery, is noted to be disrupted in ICU settings resulting in a correlative effect between sleep deprivation and delirium. Multicomponent nonpharmacological interventions are intended to reduce the predisposing factors of this syndrome and have been shown in randomized trials and systematic reviews to be effective in preventing delirium. An evidence-based checklist of nonpharmacological interventions related to reducing noise, light, and patient care interruptions was implemented every night on patients admitted to the SICU over eight weeks. Delirium was measured by the Confusion Assessment Method (CAM-ICU) tool in the electronic health record. The percentage of CAM "positive" delirium scores was compared four weeks pre-implementation and four weeks post-implementation. In the pre-implementation phase, delirium was reported as CAM "positive" 22% of the time versus 51% of the time in the post-implementation phase. A chi-square test determined a statistically significant association between the variables (p=6.25E-25), though an odd's ratio test (OR=0.26) revealed no association between the nonpharmacological sleep bundle and delirium scores. There was an increased awareness in nursing documentation of CAM-ICU scoring after project implementation. Further studies are needed to determine whether multicomponent nonpharmacological sleep bundles can reduce ICU delirium.

22. Asymptomatic Bacteriuria Identification and Management in LTCs

Yan Liu

Liu, Y.

Session D; Poster Presentation; Room 349

Background: Antibiotic treatment for asymptomatic bacteriuria (AB) is one of the key contributors to antibiotic overuse in LTCs. The guidelines from IDSA suggest that antibiotic treatment of AB can only bring harm. However, inappropriate antibiotic treatment for AB in LTCs remains common. The 45-bed unit where the project is implemented is in a city-based LTC facility. A retrospective chart review found that 55% of the patients on the unit with no definitive diagnosis of UTI were placed on antibiotics

without documented reason. To initiate a practice change for proper management of AB is warranted. Objective/Aim: The purpose of this quality improvement project is to develop and implement an evidence-based clinical pathway (CP) based on the modified McGeer Criteria and Loeb Criteria in a 45-bed unit to assist nurses to accurately identify and more effectively manage AB. The anticipated outcomes of the 14-week project are 75% compliance with using CP and 15% decrease in the number of patients treated with antibiotics for UTI. Results: Preliminary results from the data obtained so far revealed that compliance with the pathway was 75% and the percentage decrease in the number of patients treated with antibiotics for UTI was 20% in the first six weeks of the project. The final results are pending the project completion. Conclusion: The evidence based Clinical Pathway for AB has been effective in reducing the number of the patients treated with antibiotics for UTI, and with good compliance. The sustainability of the CP in the facility is likely.

23. Repetitive Acoustic Stimulation Throughout a Daytime Nap to Enhance Non-paretic Arm Skill Performance in Older Adults with Chronic Stroke

Brian Johnson

Johnson, B. P., and Westlake, K. P.

Session D; Poster Presentation; Room 349

Neural replay occurs during sleep to strengthen individual memories and subsequent motor performance. Non-invasive methods of sensory stimulation during sleep have been developed to enhance this process. A widely used method known as targeted memory reactivation (TMR) involves conditioning of an auditory cue paired with task performance during initial skill acquisition, followed by cue replay during sleep. Our previous studies have shown that TMR can enhance sensorimotor skill performance in healthy young adults. What is still unknown is whether TMR can enhance skilled arm performance in individuals with stroke. Older adults (50-80) with a history of stroke performed two sessions of a non-paretic arm throwing task separated by a one-hour period of napping, with half of all participants receiving TMR throughout the hour. The task involved repetitive throwing to targets, each paired with a distinct auditory cue. Participants were divided into groups based on the inter-training interval: Napping+NoTMR (n=8) and Napping+TMR (n=10). Preliminary results demonstrate that a between-group difference was found in throwing accuracy change score ratios between the end of the first session and beginning of the second session, with Napping+TMR demonstrating a decrease in throwing error reduction (-0.089), while Napping+NoTMR did not (0.131). In addition, Napping+TMR demonstrated a greater overall reduction in absolute throwing error (-0.390) than Napping+NoTMR (-0.003) from baseline to post second training session. Further data collection and analyses are currently underway. Further development of a TMR intervention protocol may be able to serve as an adjunct to traditional physical rehabilitation following stroke and other diagnoses.

24. Traumatic Brain Injury Severity is Associated with Increased Risk of Stroke in Older Adults

Aparna Vadlamani

Vadlamani, A., and Albrecht, J. S.

Session D; Poster Presentation; Room 349

Traumatic brain injury (TBI) is a significant public health problem among older adults ≥65 that resulted in 282,000 hospitalizations and 2.5 million emergency department visits in 2013. Stroke risk is increased following TBI and may contribute to increased disability and poorer recovery in older adults. However, the impact of TBI severity on risk of stroke is unknown. This information can inform appropriate care for older adults post-TBI to minimize subsequent stroke occurrence. We linked records of older adults treated for TBI at an urban level 1 trauma center between 2006-2010 to their Medicare administrative claims. Our primary outcome was incident stroke post-TBI, defined by ICD9 codes. TBI severity was obtained from the Abbreviated Injury Scale Head score, ranging from 1 (mild injury) to 6 (fatal injury, excluded), and was dichotomized as low (≤2) and high (>2) severity. The association between TBI severity and stroke was estimated using Cox proportional hazards modeling adjusting for variables associated with stroke. Of 132 subjects with TBI, 67 (51%) had low TBI severity and 65 (49%) had high TBI severity. Absolute risk of stroke following TBI was greater for those in the high TBI severity group vs those with low TBI severity; 25.1 (95%CI 13.4-38.5) vs 3.2 (95%CI 1.3-7.7) stroke cases/100 person-years. High TBI severity was associated with increased risk of stroke compared to low TBI severity (HR 6.68, 95% confidence interval 2.49-17.94), after adjusting for chronic kidney disease. Clinicians should consider close monitoring and prevention efforts for stroke in older adults with severe TBI.

25. Multiple Social Identity Integration and Empowerment of Social Workers on Interprofessional Teams

Sol Baik

Baik, S.

Session D; Poster Presentation; Room 349

Due to the nature of the professional roles and implicit power dynamics in a team, more attention is needed on social workers' identities on interprofessional teams. Considering the interprofessional teamwork, this study focuses on how their multiple social identities, one as a team member and the other as a social worker, are associated with their psychological empowerment. 154 social workers who work on interprofessional teams in US were surveyed and ANOVA and hierarchical multiple regression were used for analyses. Findings indicate that there was a statistically significant association between multiple social identity integration and empowerment of social workers on interprofessional teams. Those who perceived themselves highly as both a social worker and a team member were more empowered than others. This indicates the importance of educating social work students about identity integrity and conflict to foster empowered social workers.

26. Racial Differences in Physical Activity in Nursing Home Residents with Cognitive Impairment

Nicole Viviano

Viviano, N. A., Galik, E., and Resnick, B.

Session D; Poster Presentation; Room 349

INTRODUCTION: Nursing home residents with moderate to severe cognitive impairment are sedentary It is more likely that African-American (AA) older adults tend to be more sedentary than their white counterparts. The purpose of this study was to examine racial

differences in overall time spent in physical activity (PA), time in sedentary, light intensity, and moderate levels of PA, and participation in activities of daily living (ADLs) among cognitively impaired nursing home residents. METHODS: This was a secondary data analysis from the Function and Behavior Focused Care Intervention study. The sample included 336 cognitively impaired residents from 12 nursing homes. RESULTS: The mean age of the residents was 86.2 (SD=10.1) with an average MMSE score of 7.8 (SD=5.0) where 40% were AA and 60% white. White and AA participants engaged in only 50.62 and 46.23 minutes of light and 1.5 and 1.11 minutes of moderate level PA, respectively. There was a significant difference in time spent in light-intensity PA with whites spending more time in this level of activity [$F(4, 1) = 1.261$, $p = .024$]. Conversely, AAs spent more time in functional activities [$F(4, 1) = 4.148$, $p < .001$]. There were no significant racial differences in time in total PA, sedentary, or moderate level physical activity. DISCUSSION: These findings are consistent with prior research showing that AAs had lower PA levels compared to their white counterparts. Future research should focus on increasing physical activity among nursing home residents and consider specific ways to increase activity among AA residents.

27. Hip Fractures in Men without Osteoporosis in the Medicare Current Beneficiaries Survey

Jennifer Kirk

Kirk, J. M.

Session D; Poster Presentation; Room 349

Hip fractures (HF) occur when bones are weak, and they are associated with an increased risk of morbidity and death. Around 150,000 HF occur annually in the United States. While HFs are four times more common in women, there is evidence showing that men have a higher mortality rate after hip fracture compared with women. Bone mineral density (BMD) loss, which is indicative of the development of Osteoporosis, occurs at a younger age in women. As BMD decreases, there is an increased risk of fractures after a fall. As a result, women are being screened more frequently for BMD loss and treated to stave off the development of Osteoporosis, but there is evidence that men are experiencing HF without ever having been screened. This study attempted to fill a gap in the literature regarding clinicians understanding of men's characteristics experiencing HFs without both Osteoporosis treatment. First, the study explored differences in the association between HF and osteoporosis by gender. Second, prevalence odds ratios were calculated to characterize and ascertain significant exposures in a cross-sectional dataset from Medicare Current Beneficiaries Survey from 2013, 2015, and 2016. This study conducted a secondary data analysis of cross-sectional data to answer the following question: Is the association between hip fracture and osteoporosis different by sex? Information gathered in this study contributes to the understanding of hip fractures in men and aided in establishing a proactive assessment of the risks for hip fracture in men over the age of 65.

28. Key Informant Recommendations for Effectively Serving Afghan Refugee and Special Immigrant Visa Holder Patients in Prince George's County, Maryland, U.S.A.

Nimasha Fernando

Fernando, N. B., and Reihani, A.

Session D; Poster Presentation; Room 349

Over 8,000 refugees and special immigrant visa (SIV) holders were resettled in Maryland between fiscal years 2012 and 2016, 14.8% of whom were originally from Afghanistan. Prince George's County is the leading resettlement destination for SIV holders and the second leading county for refugee resettlement in Maryland. This qualitative study aims to identify facilitators and barriers to health for Afghan refugees and SIV holders in Prince George's County, Maryland, U.S.A. In-depth, semi-structured interviews were conducted with five key informants who had direct experience working with Afghan refugee and SIV holders in clinical or community-based settings. Interviews were audio-recorded, transcribed, and thematically analyzed using a grounded theory approach with MAXQDA software. Participants shared their experiences serving this community and provided examples of how providers could effectively help clients from this population overcome the barriers to health they identified. In order to help patients overcome barriers to accessing health care beyond the initial refugee health screening, participants recommended creating more welcoming clinical environments such as by offering appropriate language services, clarifying privacy expectations, and communicating with patients' resettlement teams. To help address patients' barriers to receiving appropriate mental health services, participants recommended providers increase their awareness of patients' pre and post-migration experiences. Identifying key informant recommendations to address the barriers to health for the Afghan refugee and SIV community will help inform service delivery and policies to improve the health of this vulnerable population in Prince George's County and across the U.S.

29. Function Selective ERK Inhibition and Restoration of Retinoic Acid as a Therapeutic Approach to Prevent Airway Smooth Muscle Cell Proliferation in Allergic Asthma

Amy Defnet

Defnet, A.E., Huang, W., Yu, J., Jones, J.W., Deshpande, D.A., Shapiro, P., and Kane, M.A.

Session E; Poster Presentation; Room 349

Hyperproliferation of airway smooth muscle (ASM) cells leads to increased cell mass causing airway obstruction in inflammatory diseases. Currently, there are no effective therapies to stop ASM cell proliferation that leads to debilitating bronchoconstriction. Previous studies suggest that inhibition of the activator protein-1 (AP-1) transcription factor could prevent ASM cell proliferation. The current studies evaluated a novel function-selective extracellular signal-regulated kinase (ERK2) inhibitor, referred to as SF-3-030, which inhibited platelet-derived growth factor (PDGF) induced AP-1 activity and ASM cell proliferation. Additionally, deficiency of vitamin A has been shown to exacerbate allergic asthma. Retinoic acid (RA), an active metabolite of vitamin A and high-affinity ligand for retinoic acid receptor (RAR), is reduced in inflammatory conditions leading to cell hyperproliferation. The current study elucidated the presence and role of retinoids in ASM cells. QPCR of ASM cells identified several receptors and targets including all isoforms of RAR. RA production in ASM cells and lung tissue from a murine model exposed to house dust mite and treated with SF-3-030, was determined using liquid chromatography-multistage tandem mass spectrometry. ASM cells metabolized

holoRBP4-retinol to make all-trans-RA and were capable of storage through retinyl esters. The mouse asthma model lung showed reduced all-trans-RA and retinyl esters with no change upon SF-3-030 treatment confirming a separate mechanism of action. These data suggest two possible therapeutic targets to prevent ASM hyperproliferation associated with allergic asthma; first, the partial inhibition of ERK2 signaling by novel compounds like SF-3-030, and second, the restoration of RA signaling in the asthmatic lung.

30. The Inflammatory Effects of Bordetella pertussis on Human and Mouse cells

Cassandra Jordan

Jordan, C., Skerry, C., Carbonetti, N.

Session E; Poster Presentation; Room 349

Whooping cough, caused by the bacterium Bordetella pertussis, has seen a resurgence in recent years with the most severe cases seen in infants. The use of the original whole-cell pertussis vaccines reduced instances of whooping cough dramatically. After the whole-cell vaccine was replaced with an acellular vaccine, increased incidence of whooping cough was seen, leading to an investigation for alternative methods at combatting the disease. In experimental animal models of pertussis, lung inflammation is a major characteristic of the disease. In this investigational study, we will analyze the inflammatory response of both mouse and human cells in response to B. pertussis bacteria and we will investigate the effects of pertussis toxin (PT), a major virulence factor promoting inflammation in vivo. Mouse and human macrophages as well as human epithelial cells derived from the respiratory tract will be exposed to B. pertussis and inflammatory responses analyzed. We hypothesize that exposure to B. pertussis will result in inflammatory responses in both mouse and human cells and that PT will exacerbate these responses. We will also investigate the effect of sphingosine-1-phosphate receptor targeting drugs on these responses, since these drugs reduce lung inflammation during B. pertussis infection in vivo. This study will further provide data involving host directed therapies for patients affected by B. pertussis.

31. Novel Muscarinic Antagonists with Anti-depressant-like Effects in Rodents

Chad Johnson

Johnson, C., Coop, A., WInger, G., and Woods, J.

Session E; Poster Presentation; Room 349

Scopolamine, a non-selective muscarinic antagonist, is a rapidly effective antidepressant compound in humans likely mediated through an antimuscarinic effect. Unfortunately, scopolamine can produce cognitive impairment including memory disturbances in humans. It is our goal to identify a muscarinic antagonist that may be able to relieve depression without disrupting cognitive effects. The 3-exo-1-azabicyclo[2.2.1]heptane, 1-azabicyclo[2.2.2]octane, and N-methyltetrahydropyidine 3-substituted-1,2,4-oxadiazoles appear to be excellent chemical scaffolds for the generation of potent muscarinic agonists/antagonists. The addition of a methyl group to the 3-position of the 1,2,4-oxadiazole yields some of the most potent muscarinic agonists currently known. Yet, addition of a cyclopropyl group appears

to reduce efficacy and confer antagonist action at muscarinic sites. Herein we show the pharmacological profiles of multiple pairs of methyl/cyclopropyl analogues we have designed in the anticipation of separating antidepressant-like activity from cognitive impairment. (Supported by NIMH Grant 107499).

32. EXPLORING THE ROLES OF RFX 1, 3, AND 7 ALONE AND IN CONCERT IN HEARING AND BALANCE

Kathleen Gwilliam

Gwilliam, K., Milon, B., McMurray, M., Vijayakumar, S., Margulies, Z., Jones, S. M., and Hertzano, R.

Session E; Poster Presentation; Room 349

The regulatory factor X (RFX) family consists of eight transcription factors, RFX1-RFX8, that are divided into four groups based on their functional domains and bind to the X-box promoter motif of genes to regulate transcription. Previous work from our laboratory has found a strong enrichment of the RFX binding motif in the promoter regions of newborn mouse inner ear hair cell-expressed genes. This enrichment suggests a potential role for the RFX family of transcription factors in the development and maintenance of the inner ear hair cells. RFX1 and RFX3 are members of Group 1 of the RFX transcription factors, with RFX3 showing the highest expression out of the RFX members in P1 mouse hair cells. Second highest in expression is RFX7, a member of Group 8. We established a double conditional knockout of Rfx1/3 from hair cells using the Gfi1-Cre mouse. This mouse had profound hearing loss secondary to rapid loss of outer hair cells throughout the length of the cochlear duct following the onset of hearing, between P12-14. Using the Myo15-Cre and PrestinCreERT2 mouse models we showed that conditional deletion of Rfx1/3 up to P4 results in an early profound hearing loss, whereas deletion of these transcription factors from hair cells after P8 does not affect hearing. In addition, conditional knockout mice of Rfx7 alone and in combination with Rfx1 or Rfx3 had normal hearing and vestibular function. Overall, these data support an established role for Group 1 of the RFX transcription factors in hearing.

33. COMPARATIVE ANALYSIS OF THE INNER EAR BETWEEN POSTNATAL DAYS 2 AND 7 USING SCRNA-SEQ

Kevin Rose

Rose, K., Herb, B., Song, Y., Milon, B., Ament, S., and Hertzano, R.

Session E; Poster Presentation; Room 349

Sensory hair cells located in the inner ear are mechanoreceptors essential for hearing and balance. Loss of these sensory hair cells is a final common pathway in most forms of hearing loss and results in permanent hearing impairment in both human and mouse, as they do not spontaneously regenerate in mature mammals. In Contrast, early postnatal inner ear supporting cells are still able to differentiate into new hair cells in mouse but supporting cells lose this ability shortly after birth. Here we aim to better understand the gene expression differences between two postnatal time points (P2 and P7) where supporting cells can and cannot differentiate into hair cells. To obtain a global understanding, we have dissociated sensory epithelia from P2 and P7 wild type mouse cochleae and utricles and profiled gene expression in 445-4813 single-cells using the 10X Genomics Chromium platform. Here we

report our analysis comparing gene expression in the various cell types identified using our approach between P2 and P7 as well as additional downstream gene regulatory analyses. We further provide full access to the analyzed dataset through the gEAR portal (umgear.org).

34. KEY AMINO ACID RESIDUES CONFERRING ENHANCED ENZYME ACTIVITY AT COLD TEMPERATURES IN AN ANTARCTIC POLYEXTREMOPHILIC B-GALACTOSIDASE

Victoria Laye

Laye, V. J., Karan, R. Kim, J.-M., Pecher, W. T., DasSarma, P., and DasSarma, S.

Session E; Poster Presentation; Room 349

The Antarctic microorganism Halorubrum lacusprofundi harbors a model polyextremophilic β-galactosidase that functions in cold, hypersaline conditions. Six amino acid residues potentially important for cold activity were identified by comparative genomics and substituted with evolutionarily conserved residues (N251D, A263S, I299L, F387L, I476V, and V482L) in closely related homologs from mesophilic haloarchaea. Using a homology model, four residues (N251, A263, I299, and F387) were located in the TIM-barrel around the active site in domain A, and two residues (I476 and V482) were within coiled or β-sheet regions in domain B distant to the active site. Site-directed mutagenesis was performed by partial gene synthesis, and enzymes were overproduced from the cold-inducible cspD2 promoter in the genetically tractable Haloarchaeon, Halobacterium sp. NRC-1. Purified enzymes were characterized by steady-state kinetic analysis at temperatures from 0 to 25 °C using the chromogenic substrate o-nitrophenyl-β-galactoside. All substitutions resulted in altered temperature activity profiles compared with wild type, with five of the six clearly exhibiting reduced catalytic efficiency (kcat/Km) at colder temperatures and/or higher efficiency at warmer temperatures. These results could be accounted for by temperature-dependent changes in both Km and kcat (three substitutions) or either Km or kcat (one substitution each). The effects were correlated with perturbation of charge, hydrogen-bonding, or packing, likely affecting the temperature-dependent flexibility and function of the enzyme. Our interdisciplinary approach, incorporating comparative genomics, mutagenesis, enzyme kinetics, and modeling, has shown that divergence of a very small number of amino acid residues can account for the cold temperature function of a polyextremophilic enzyme.

35. DNA METHYLTRANSFERASE INHIBITORS IN COMBINATION WITH PARP INHIBITORS GENERATE SYNTHETIC LETHALITY IN BRCA-PROFICIENT OVARIAN CANCER

Lora Stojanovic

Stojanovic, L.

Session E; Poster Presentation; Room 349

Approximately 10% of Epithelial ovarian cancer (EOC) patients have BRCA mutations and are treated with FDA approved poly (ADP-ribose) polymerase (PARP) inhibitors. In a mechanism known as synthetic lethality, PARPi treatment leads cytotoxic DNA double strand breaks (DSBs) during DNA replication, that cannot be repaired due to key homologous recombination (HR) DSB repair-defective BRCA mutations. However, PARPi therapy has not shown efficacy for the majority of EOC that are BRCA-proficient. These EOC patients are treated with platinum-based chemotherapies which often lead to resistance

to these treatments, and relapse. Therefore, new therapies are essential for the improvement of EOC treatment. In recently published and preliminary data, our laboratory has shown that when PARPi (Talazoparib) is used in combination with a low dose epigenetic drug (Azacytidine, 5-AZA), increased PARP trapping and cytotoxic DSBs are observed in multiple cancer models, including EOC. In addition, our in vivo studies showed that this low dose combination therapy decreased tumor volume, increased survival and was non-toxic to mice, suggesting that this could potentially be a novel strategy in treatment of BRCA-proficient cancers. In this study we will investigate the role of low-dose epigenetic therapy in EOC, in reprograming the DSB repair response, to potentially induce a "BRCAness" effect that sensitizes cells to PARPi. We show that 5-AZA reprograms epigenome by changing the gene expression in DNA repair genes, including, Fanconi Anemia (FANC) and other homologous recombination (HR) genes, which lead to BRCAness and results in impaired HR-mediated repair.

36. Role of the Parabrachial Nucleus in Migraine

Olivia Uddin

Uddin, O., Anderson, M., Smith, J., and Keller, A.

Session E; Poster Presentation; Room 349

Migraine headaches affect 13% of the USA population. These headaches cause significant disability and contribute heavily to healthcare costs. Despite this severity, there is a relative lack of effective drugs to prevent and treat migraines. It is thought that migraine pathology includes irritation of the dura (the outermost layer of the meninges), and transmission through the trigeminal pathway, which relays sensory information from the head, face, and dura to central centers. However, we have not elucidated the central changes that underlie migraines. Clarifying these pathways could provide new targets for migraine management and prevention. One central nucleus receiving input from the trigeminal pathway is the Parabrachial Nucleus (PB). PB is involved in pain transmission, and we have shown previously that its activity is amplified in a rat model of trigeminal neuropathic pain. Using in vivo extracellular recordings, we have identified for the first time a subset of PB neurons that respond directly to electrical stimulation of the dura (36 cells from 13 rats). We hypothesize that in a rat model of migraine, hyperactivity of dural-stimulus-responsive PB neurons underlies migraine headache pain. We predict that if we apply low pH solution to the dura (a commonly used rodent migraine model), firing rates for PB neurons of interest will increase. In preliminary experiments measuring PB activity several hours after applying low pH to the dura, we have identified two dural-stimulus-responsive PB neurons in which either receptive field or neural activity is increased compared to baseline.

37. Establishment of a human colonoid model to study Shigella pathogenesis and evaluate vaccine candidates

Sridevi Ranganathan

Ranganathan, S., Doucet, M., Grassel, C. L., Delaine-Elias, B., Zachos, N. C., and Barry, E. M.

Session E; Poster Presentation; Room 349

The enteric pathogen, Shigella, is one of the leading causes of moderate-to-severe diarrhea

and death in young children in developing countries. Transformed cell lines and animal models have been widely used to study Shigella pathogenesis. In addition to altered physiology, transformed cell lines are composed of a single cell type that does not sufficiently represent the complex multi-cellular environment of the human colon. Most available animal models do not accurately mimic human disease. The human intestinal enteroid model, derived from LGR5+ stem cell-containing intestinal crypts from healthy subjects represents a technological leap in human gastrointestinal system modeling and provides a more physiologically relevant system that includes multiple cell types and features of the human intestine. We established the utility of this model for studying basic aspects of Shigella pathogenesis and host responses. In this study, we show that S. flexneri is capable of infecting and replicating intracellularly in human enteroids derived from different segments of the intestine. Apical invasion by S. flexneri is very limited but increases ~10-fold when enteroids are differentiated to include M cells. Invasion via the basolateral surface was at least 2-log10 more efficient than apical infection. Increased secretion of Interleukin-8 and higher expression of the mucin glycoprotein Muc2 was observed in the enteroids following S. flexneri infection. Ongoing studies are aimed at evaluating the usefulness of human enteroids as a pre-clinical model system to evaluate live attenuated S. flexneri vaccine strains.

38. Role of Angiopoietin-Like 4 In the Progression And Dissemination Of Head And Neck Squamous Cell Carcinomas (HNSCCS)

Eman Hefni

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

Session E; Poster Presentation; Room 349

Oral cavity or oropharyngeal cancer one of the leading causes of death in men in the United States. 51,540 patients in the United States will be diagnosed with oral cancer in 2018, and 10,030 deaths are expected to occur. The most common cancer of the oral cavity is head and neck squamous cell carcinoma (HNSCC) which accounts for approximately 80% of the cases. It is reported that HNSCC metastasizes to the regional lymphatic nodes. Lymph node involvement is considered as a strong prognostic factor for the development of distant metastases in HNSCCs. Cancer cell releases different lymphangiogenesis factors such as ANGPTL4 that induces cancer cell escape into the lymphatic system. Metastatic HNSCC breaks free from the primary tumor and escapes toward the lymphatic vessels. ANGPTL4 (Angiopoietin-like 4) is a secretory glycoprotein, highly expressed in adipose tissue, liver, and placental tissue as well as ischemic tissues. It is important for angiogenesis and metabolism regulation. ANGPTL4 increased expression has been reported in different types of human cancers, including prostate cancer, tongue and esophageal SCC. However, the role of ANGPTL4 in promoting HNSSC metastasis through the promotion of lymphangiogenesis is not well understood. We found that expression and secretion of ANGPTL4 is elevated in premalignant and malignant oral squamous cell carcinoma cell lines. As we expected, hypoxia increased ANGPTL4 expression. Furthermore, inhibition of ANGPTL4 in oral malignant cell lines blocked cell proliferation and migration. Collectively, these preliminary findings suggest that ANGPTL4 may play an important role in promoting HNSSC metastasis.

39. Semi-conserved Domains of RIFINs and STEVORs Associated with Severe Malaria Vulnerability Harbor Peptides Reflecting Malaria Exposure

Albert Zhou

Zhou, A.E., Berry, A.A., Bailey, J.A., Pike, A., Dara, A., Agrawal, S., Stucke, E.M., Ouattara, A., Coulibaly, D., Lyke, K.E., Laurens, M.B., Adams, M., Takala-Harrison, S., Pablo, J., Jasinskas, A., Nakajima, R., Niangaly, A., Kouriba, B., Kone, A.K., Rowe, A., Doumbo, O.K., Thera, M.A., Patel, J.J., Tan, J.C., Felgner, P.L., Plowe, C.V., and Travassos, M.A.

Session F; Poster Presentation; Room 349

Repetitive interspersed family (RIFIN) and subtelomeric variable open reading frame (STEVOR) represent two of three major Plasmodium falciparum variant surface antigen families involved in malaria pathogenesis and immune evasion, and are potential targets in the development of natural immunity. Protein and peptide microarrays populated with RIFINs and STEVORs associated with severe malaria vulnerability in Malian children were probed with adult and pediatric sera to identify epitopes that reflect malaria exposure. Adult sera recognized and reacted with greater intensity to all STEVOR proteins than pediatric sera. Serorecognition of and seroreactivity to peptides within the semi-conserved domain of STEVORs increased with age and seasonal malaria exposure, while serorecognition and seroreactivity for the semi-conserved and second hypervariable domains of RIFINs increased only with age. Serologic responses to RIFIN and STEVOR peptides within the semi-conserved domains may play a role in natural immunity to severe malaria.

40. Novel Race Effects on Expectancy-Induced Analgesia in Temporomandibular Joint Disorder

Titilola Akintola

Akintola, T., Haycock, N., Okusogu, C., Thomas, S., Corsi, N., Schenk, L., Blasini, M., Nandini, R., Wang, Y., Phillips, J., and Colloca L.

Session F; Poster Presentation; Room 349

Chronic pain (CP) is a major US public health issue costing an estimated $600 billion annually. Temporomandibular joint disorder (TMD) is the 2nd most common cause of chronic orofacial pain affecting at least 20% of adults. Differences in pain sensitivity and treatment effectiveness continually pose challenges to CP therapy development. Furthermore, ethnic minorities report more clinical, experimental pain sensitivity and severity. Studies show that African Americans (AA) and other minorities experience more pain and less pain relief than Whites. Expectancy-Induced Analgesia (EIA) is a form of endogenous pain modulation that depends on the activation of descending pain inhibitory systems. This study examined the effects of race on EIA in a multi-ethnic population of TMD and healthy control participants. 490 participants (152 TMD and 338 controls) were recruited for this study. Race was measured via self-report using the National Institutes of Health Collaboratory Race/Data Standard. EIA was then established through a behavioral pain modulation task in which participants underwent a 2-trial conditioning paradigm to learn to associate visual cues with high and low-pain heat stimulations. A final test-session was performed to determine EIA. Univariate analyses showed a significant main effect of

race on pain tolerance (F=6.62, p=0.002) and placebo analgesia (F=5.89, p=0.03) but not on pain thresholds in both TMD and healthy participants. These findings suggest that race may affect EIA in chronic pain participants. Further research with larger databases is needed to fully understand how ethnicity, race and cultural elements shape the formation of placebo effects.

41. ULTRASONOGRAPHIC MEASUREMENT OF GASTROCNEMIUS BIOMECHANICAL PROPERTIES DURING STEPPING ON THE ELLIPTICAL TRAINER: A CASE STUDY

Raziyeh Baghi

Baghi, R.,Oppizzi, G., Koh, K., Kim, D., Lo, L-C., and Zhang, L-Q.

Session F; Poster Presentation; Room 349

Elliptical training has recently become a popular device in training and rehabilitation of musculoskeletal injuries. However, there is lack of evaluations on muscle biomechanical properties during this exercise. We measured the elasticity, thickness and fascicle length of medial gastrocnemius muscle (MG) of a healthy subject using shear wave elastography and ultrasonography during stepping on an elliptical trainer. The subject was asked to perform stepping paced with a metronome set at 60bpm for 30 seconds while by hearing each beat, one foot was in the midstance and the other foot was in mid- swing phase. An ultrasonography video was captured during stepping. Considering that stance phase constitutes 50% of gait cycle on the elliptical and swing phase constitutes the remaining 50%, each second was corresponding to midstance or mid-swing phase. The elasticity, thickness and fascicle length of MG were measured in every second of the movement. Elasticity and ultrasonography measurements showed changes in the MG elasticity, thickness and fascicle length during stepping on the elliptical trainer. Muscle elasticity, thickness and fascicle length range were 10.10-59.40 Kpa, 1.65-1.95 cm, 7.78-10.31 cm during stance phase and 7.40-59.40 Kpa, 1.61-1.95 cm, and 8.66-10.52 cm during swing phase, respectively. There was a moderate correlation between muscle thickness and elasticity (P=.018). In this study it's been shown that elasticity, thickness and fascicle length of medial gastrocnemius varied systematically during stepping, which can be used to evaluate muscle impairments and effect of elliptical training on the lower limb muscles.

42. EXPLORING POSTURAL CONTROL DURING WALKING AND RUNNING IN ACUTE LYMPHOBLASTIC LEUKEMIA CHILDHOOD CANCER SURVIVORS

Kelly Rock

Rock, K., Creath, R., and Marchese, V.

Session F; Poster Presentation; Room 349

Acute lymphoblastic leukemia (ALL) is the most common childhood cancer in the United States. Advancements in medical treatments have resulted in up to 90% five-year survival rates, but not without secondary effects from chemotherapeutic agents. ALL childhood cancer survivors (ALL CCS) are known to present with decreased range of motion, strength, and impaired physical performance including balance, gait characteristics, and running speed and agility. Postural control in walking and running have not yet been explored in ALL CCS. The purpose of this pilot study is to compare postural control during walking and running between ALL CCS and age- and sex-matched peers with typical development (TD). This study

included six ALL CCS (6-17 years) and six age- and sex-matched peers with TD. Gait and kinematic measurements were obtain through GaitRite pressure walkway and Vicon motion capture systems. Clinical measures included ankle active range of motion (ROM), ankle proprioception, Bruininks-Oseretsky Test of Motor Proficiency (BOT-2) and the timed up and go (TUG). ALL CCS compared to peers with TD demonstrated differences in clinical measures with identified deficiencies in ROM, BOT-2 balance score, and TUG performance. Additionally, ALL CCS displayed greater trunk angle variability during walking. Correlations between ROM, BOT-2 balance score, and TUG time with walking and running measures suggest ALL CCS have dynamic balance deficiencies affecting postural control during walking and running. In conclusion, we recommend that physical therapy interventions include exercises to improve dynamic balance in children with ALL CCS.

43. A Novel Method for Identifying Parasite Erythrocyte Membrane Antigens from Whole Blood Clinical Samples

Emily Stucke

Stucke, E. M., Dara, A., Dwivedi, A., Hodges, T., Coulibaly, D., Kone, A. K., Traore, K., Guindo, B., Tangara, B. M., Niangaly, A., Daou, M., Tolo, Y., Sissoko, M., Laurens, M. B., Ouattara, A., Kouriba, B., Duombo, O. K., Takala-Harrison, S., Thera, M. A., Plowe, C. V., Travassos, M. A., and Silva, J. C.

Session F; Poster Presentation; Room 349

Plasmodium falciparum is the parasite that is responsible for nearly all cases of malaria in Africa. Plasmodium falciparum erythrocyte membrane protein-1 (PfEMP1) antigens, expressed on the surface of parasite-infected erythrocytes, play a critical role in immune evasion by mediating cytoadhesion and sequestration in host capillaries. Var genes encode 40-60 PfEMP1 antigens per P. falciparum genome, yet each parasitized erythrocyte displays only one PfEMP1. Studies of var expression using non-leukocyte-depleted blood are challenging due to the predominance of host genetic material and lack of var reference sequences to guide read recruitment and assembly. To address these barriers, we compared the following mRNA library preparation and var transcript enrichment methods to generate assembled var transcripts using RNA extracted from whole peripheral blood samples: (1) depletion of globin transcripts and (2) both depletion of globin transcripts and polyA selection. cDNA was generated via reverse transcription and libraries were sequenced using an Illumina platform. De novo transcript assemblies were generated and vars as long as 10,000 bp identified. To assess sensitivity, we compared the de novo var transcripts to the known var repertoires. Results will facilitate var expression comparative analyses in severe malaria, uncomplicated malaria, and asymptomatic parasitemia to illuminate if var expression is associated with different malaria syndromes.

44. Cascade Testing of Personalized Diabetes Medicine Program (PDMP) Probands is Efficient in Diagnosing At-Risk Individuals of Monogenic Diabetes

Haichen Zhang

Zhang, H., Kleinberger, J.W., Mathias, T.J., Guan, Y., Maloney, K.A., Streeten, E.A., Blessing, K., Snyder, M.N., Bromberger, L., Goehringer, J., Kimball, A., Ferguson, M., Billiet, J., Damcott, C.M., Taylor, C.O.,

Nicholson, M., Nwaba, D.C., Palmer, K., Ambulos, N., Shuldiner, A.R., Jeng, L.J.B., Levin, P., Carey, D.J., and Pollin, T.I.

Session F; Poster Presentation; Room 349

Approximately 1-2% of all diabetes is monogenic in nature but is usually misdiagnosed as type 1 or type 2 diabetes, leading to sub-optimal treatment. The Personalized Diabetes Medicine Program (PDMP) was designed to implement, disseminate and evaluate a comprehensive approach for identifying, genetically diagnosing and promoting individualized therapy of monogenic diabetes in individuals ascertained in diabetes clinics and their relatives. The PDMP screened 2,522 diabetic individuals and tested 312 individuals suspected of having monogenic diabetes from four different sites. Participants enrolled into the PDMP underwent targeted next-generation sequencing. Variants classified as pathogenic or likely pathogenic were confirmed and disclosed. PDMP staff developed letters describing the study and explaining cascade genetic testing for the probands to distribute to certain relatives. Interested relatives were tested for the familial variant. Results of cascade genetic testing were disclosed. The PDMP identified pathogenic or likely pathogenic mutations in 36 of the 312 individuals suspected of monogenic diabetes. To date, variants in seven genes have been disclosed results to 27 participants. PDMP staff recommended 95 relatives of these individuals be invited for genetic testing, 36 of which were known to be diabetic. Twenty-two relatives of 9 probands were tested. Twelve of 22 tested relatives from 8 families tested positive for familial variants for a diagnosis rate of 81.8% in diabetic/prediabetic individuals and 30.6% in non-diabetic relatives. Previous diagnoses in the 9 mutation-positive diabetic/prediabetic individuals were MODY, type 1 diabetes, type 2 diabetes, or mild hyperglycemia. At least 5 relatives had not been receiving optimal treatment.

45. TOOTH LOSS IS INDEPENDENTLY ASSOCIATED WITH CAROTID ATHEROSCLEROTIC BURDEN AND WORSE NEUROLOGICAL DEFICIT AMONG ISCHEMIC STROKE PATIENTS

Thayana Leao

Leao, T.S.S., Tomasi, G.H., Ibrahim, M.S., Conzatti, L.P., Marrone, L.C.P., Reynolds, M.A., and Gomes, M.S.

Session F; Poster Presentation; Room 349

This study aimed (I) to test the hypothesis that tooth loss (TL) is independently associated with the carotid atherosclerotic burden (CAB) among individuals with ischemic stroke (IS) or transient ischemic attack (TIA) and (II) to test the association between TL and disability after the occurrence of cerebral ischemia. This cross-sectional observational study included 418 hospitalized patients with the diagnosis of IS or TIA, in the period between January 2015 to December 2017. TL and CAB were measured through a head and neck Multidetector Computed Tomography Angiography (MDCTA). Poisson regression with robust variance was carried out to analyze the association between CAB and TL, and to identify the correlation between TL and the subtypes of cerebral ischemia. CAB was analyzed in both common, internal and external carotid arteries. Socio-demographic and medical confounding variables were collected from patients' charts. Cox regression was used to evaluate the level of disability at patient discharge using the modified Rankin scale (mRS). Mean age was 65.61 ±13.8 years, with 52.4% males. Multivariate

analyses revealed that severe tooth loss (number teeth (NT) ≤5) was independently associated with CAB ≥ 50% (PR= 2.86, 95% CI= 1.19- 6.89) and worse mRS scores (>2) (HR= 1.97, 95% CI= 1.10- 3.75). Moderate tooth loss (NT ≥ 6 & NT≤ 19) increased the risk of IS due to embolic causes (PR= 1.90, 95% CI= 1.01- 3.57). The number of permanent natural teeth is inversely and independently associated with the CAB and worse neurological deficit among IS and TIA patient.

46. USE OF HEALTH INFORMATION TECHNOLOGIES FOR CANCER SURVIVORSHIP CARE: A COMPREHENSIVE REVIEW OF THE LITERATURE

Jungmin Yoon

Yoon, J., Son, H., La, I.S., Hertsenberg, L.A., Powell, K., Nahm, E.-S., Corbitt, N., McQuaige, M., Jaidar, N., and Ronseblatt, P.

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Background: There has been a rapid growth in the cancer survivor population, which has reached 15.5 million in the U.S. Survivors who transition from active treatment to a new normal life require continued support to manage various care needs; however, these individuals are often lost in the current fragmented healthcare delivery system. Objective: To examine the current status of health IT program use to provide continued supportive care to survivors who are in transition through a comprehensive literature review. Interventions/Methods: The review was conducted using the preferred reporting items for systematic reviews and meta-analyses (PRISMA) approach through an iterative processes. Terms in the following two categories were linked together with the AND operator: (1) cancer survivor terms and (2) technology-based intervention terms (e.g., eHealth, mHealth, EHR, and patient portal [PP]). Results: The review included a total of 28 articles including 13 in eHealth and 9 in mHealth. Only a few studies discussed the use of EHRs and PPs. The findings suggest that various health IT programs can help deliver continued support to cancer survivors in the transition phase to manage symptoms and maintain a healthier lifestyle. However, the results were inconclusive. Conclusions: Provision of needed support to cancer survivors in each phase of survivorship is vital. Further research is needed to investigate the effectiveness of those programs using more rigorous randomized trials and with diverse samples. Implications for Practice: Health IT-based interventions can be helpful to deliver continued follow-up care to survivors who are in the transition phase.

47. DISCOVERY OF A POTENTIAL NOVEL THERAPEUTIC FOR LYMPHATIC FILARIASIS GUIDED BY MULTI-SPECIES TRANSCRIPTOMICS

Matthew Chung

Chung, M., Teigen, L.E., Libro, S., Bromley, R.E., Olley, D., Kumar, N., Sadzewicz, L., Tallon, L.J., Mahurkar, A., Foster, J.M., Michalski, M.L., and Dunning Hotopp, J.C.

Session F; Poster Presentation; Room 349

Most of the current anti-helminthic treatments for filarial disease have limited macrofilaricidal efficacy. To identify and test potential repurposed drugs to target adult nematodes, we conducted a multi-species RNA-Seq on the filarial nematode Brugia malayi, its Wolbachia endosymbiont wBm, and its laboratory vector A. aegypti across the entire B. malayi life cycle. We find little evidence for clusters of gene expression

correlated with specific life stages in the bacterial endosymbiont wBm, but the noncoding 6S RNA levels correlate with bacterial replication rates, rising as the nematode matures from L3 to adult life stages before plummeting in microfilariae. For A. aegypti, the transcriptional response reflects the stress B. malayi infection exerts on the mosquito with indicators of increased energy demand and decreased fitness observed at 18 hpi. Mosquito stress proteins are upregulated as the nematodes mature to their L3 life stage. In the mammalian stages, B. malayi has male-specific kinase signaling cascades, while the transcription profile of adult females, embryos, and microfilariae includes a significant number of chromatin remodeling proteins. The B. malayi genes upregulated in adult females, embryos, and microfilariae include those for 15/18 bromodomain-containing proteins, which are involved in chromatin remodeling, including 2 members of the bromodomain and extra-terminal (BET) protein family. The BET inhibitor JQ1(+), which was originally developed as a cancer therapeutic, caused lethality and sterility of adult worms in vitro suggesting it may be a potent adulticidal drug and novel treatment for lymphatic filariasis.

48. Crystallization and biophysical characterization of Saccharomyces cerevisiae arginine tRNA transferase 1 (ATE1)

Verna Van

Van, V., Mohamed, I. R., Bui, T. S., and Smith, A. T.

Session G; Poster Presentation; Room 349

The eukaryotic arginine tRNA transferases (ATE1s) are essential enzymes that catalyze arginylation, the posttranslational attachment of L-Arg to a polypeptide in order to control its in vivo degradation. Despite the involvement of this process in general homeostasis of most eukaryotes via processes such as embryogenesis, cell migration, and aging, there is a deficit in structural and regulatory information on ATE1s. The goal of this project is to define the structure and the mechanism of ATE1-mediated arginylation in order to garner insight into this essential biological posttranslational modification. To that end, we have made significant progress in the structural determination of Saccharomyces cerevisiae ATE1 (ScATE). Sitting-drop vapor diffusion trays of ScATE1 have yielded cubic-shaped protein crystals that diffract isotropically to approximately 5Å, and these crystals are being optimized by iterative fine-screening. In addition, structural modeling and small-angle X-ray scattering (SAXS) are being used to complement our crystallization efforts. Finally, we have recently discovered that ScATE1 binds an Fe-S cluster, and we are exploring the composition, the structure, and the regulatory nature of this cluster. Combined, these studies will reveal structural, mechanistic, and regulatory aspects of ATE1s that may be targeted by therapeutics to control posttranslational arginylation.

49. PrrF-Mediated Iron Regulation of a Putative Iron Storage Protein Pseudomonas aeruginosa

Ashley Lykins

Lykins, A.T., Djapne, L., and Oglesby-Sherrouse, A. G.

Session G; Poster Presentation; Room 349

Pseudomonas aeruginosa is an opportunistic pathogen that causes acute and chronic infections in immunocompromised individuals. Iron acquisition in P. aeruginosa

is necessary for pathogenesis. As cytosolic iron levels increase, the ferric uptake regulator (Fur) protein blocks transcription of iron uptake genes to prevent iron-mediated toxicity. Fur regulates the PrrF small regulatory RNAs (sRNAs), which post-transcriptionally repress the expression of nonessential iron-containing proteins when iron is limited. Our laboratory has previously shown PrrF sRNAs are required for iron homeostasis and virulence. One probable PrrF target in the PAO1 laboratory strain is the putative bacterioferritin PA4880, which is conserved amongst Pseudomonads. PrrF shares complementarity with the 5' untranslated region (UTR) of PA4880, suggesting that PrrF interacts with PA4880 mRNA. Sequence analysis of the promoter and UTR from PA4880 homologs indicates that PrrF regulation of PA4880 is widespread amongst clinical isolates of P. aeruginosa. Real time PCR analysis of PAO1 and an isogenic prrF mutant confirmed that PA4880 mRNA levels are negatively affected by PrrF small RNAs. Analysis of a reporter fusion further demonstrated that PA4880 expression was increased upon iron supplementation in both PAO1 and PA14. Additionally, in PAO1 ΔprrF, expression was de-repressed in low iron conditions compared to wild type PAO1. Analyses are underway to determine the genetic basis of PrrF-regulated expression of PA4880 in PAO1 and PA14, and to investigate this regulatory pathway in clinical isolates of P. aeruginosa. These studies will provide the basis for determining how PrrF-regulated expression of PA4880 impacts P. aeruginosa iron homeostasis and virulence.

50. Determining the Role of PhuS in the sRNA PrrF/PrrH Regulatory Network in Pseudomonas aeruginosa

Tyree Wilson, T., Mourino, S., and Wilks, A.

Session G; Poster Presentation; Room 349

Pseudomonas aeruginosa is a gram-negative opportunistic pathogen that requires iron for survival and virulence. P. aeruginosa can acquire iron through several mechanisms which include heme uptake and metabolism. P. aeruginosa 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. Heme flux through the iron-regulated HemO to release iron and biliverdin IX-beta/delta is regulated by the cytoplasmic heme binding protein, PhuS. In addition to its role in regulating heme flux through HemO, we have uncovered a link between PhuS and the iron-regulated sRNAs, PrrF1 and PrrF2. These sRNAs are arranged in tandem arrangement upstream of the phu operon. This arrangement is only found in pathogenetic P. aeruginosa strains that also encode PhuS. Furthermore, the tandem arrangement allows for heme-dependent read through of prrF1/2 to give PrrH. This led us to hypothesis 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. Through pull down assays of iron-restricted P. aeruginosa WT and delta-phuS cultures we show that PhuS binds specifically to the prrF1 promoter. Following identification of the PhuS-protected sequence, we performed EMSAs with a 50 bp fragment showing that Holo-PhuS does not bind to DNA, whereas addition of apo-PhuS induced a concentration dependent increase in low mobility complexes. Further studies are underway to delineate the role of PhuS in integrating heme uptake and metabolism in regulating PrrF1 and/or PrrH.

51. INTERROGATING THE TUMOR SUPPRESSOR FUNCTION OF OBSCURINS IN BREAST CANCER

Talia Guardia

Guardia, T., and Kontrogianni-Konstantopoulos, A.

Session G; Poster Presentation; Room 349

Obscurins are giant modular proteins that were originally discovered and primarily studied in striated muscles. Recently, alterations in obscurin expression have been linked to cancer formation and progression. Obscurins are abundantly expressed in normal breast epithelial cell lines and tissue, however their expression is decreased in breast cancer cell lines and advanced grade breast cancer biopsies. Consistent with this, down-regulation of obscurins in normal breast epithelial cells results in increased tumorigenicity and metastasis. Giant obscurins bind directly to the PI3K/p85 regulatory subunit, and loss of obscurins in "normal" breast epithelial cells results in increased PI3K pathway activity, which occurs commonly in breast cancer and is linked to therapy resistance. Our analysis of Kaplan-Meier-Plotter data sets revealed that low obscurin levels significantly correlate with reduced relapse-free survival (RFS) in breast cancer patients independently of molecular subtype, and in patients with Luminal B (ER+PR+Her2+) breast cancer. Collectively these findings implicate obscurins' loss in tumor potentiation, metastasis and reduced treatment response. In order to interrogate these roles, we are utilizing two complementary approaches: CRISPR-Cas9 mediated activation (overexpression) and deletion of obscurins in breast cancer cell lines. In the activation cell lines, I aim to assess whether restoration of obscurin expression results in reduced growth, motility and invasion in vitro and in vivo. Conversely, in the deletion cell lines I aim to assess if loss of obscurins further potentiates tumorigenicity and metastasis and results in reduced treatment response. Taken together, these experiments will advance our knowledge on obscurins' function in breast cancer.

52. CONTACT KILLING AND ACID NEUTRALIZING DENTAL COMPOSITE AGAINST IN VITRO DENTAL PLAQUE

Abdulrahman Balhaddad

Balhaddad, A., Weir, M.D., Xu, H.H.K., and Melo, M.A.S.

Session G; Poster Presentation; Room 349

A recent promising approach to combat surface microbial contamination is the development of antibacterial materials that integrate contact-active biocidal and acid-neutralizing properties. The combination of 3% Dimethylaminohexadecyl Methacrylate (DMAHDM) and 20% amorphous calcium phosphate (NACP) into a dental composite formulation has previously reached a great bacterial reduction against caries-related mono-species in vitro. The rational of using the combined agents is based on their bioactive benefits, including less accumulation of bacteria over the composite surface and the release of calcium and phosphate ions for acid neutralization. For that, DMAHDM, a recent synthetized antibacterial monomer, was incorporated into dental composite at 0%, 3% and 5% mass fraction with 20% NACP. To assess the antibacterial effect of these formulations, a complex diverse microcosm biofilm model using human saliva as inoculum was performed. Microcosm is defined as a microbiological model that represents the natural in vitro dental plaque.

This was used to measure the metabolic activity via colorimetric assay and the biofilm formation via colony-forming units (CFU) on composites containing both agents in its formulations. Adding DMAHDM and NACP in composite for Class V restorations had stronger antibacterial activities against microcosm biofilms compared to the control composite. The composite with DMAHDM and NACP reduced the metabolic activity and the CFU by an order of magnitude. DMAHDM-NACP composites are promising to combat residual bacteria in tooth cavity and invading bacteria at the margins, thereby inhibiting root caries. DMAHDM and NACP incorporation may have a wide applicability to other resin-based restorative materials.

53. Innovation, Assembly, and Optimization of a Novel Pulse-Chase In Cell Footprinting Method for the Study of Protein Folding

Dante Johnson

Johnson, D.T., Smith, B.P., Gershenson, A., and Jones, L.M.

Session G; Poster Presentation; Room 349

Traditionally, protein folding has been observed in vitro using full length protein sequences, but folding in the cell is quite different from folding studies in an isolated environment due to the interactions of chaperones and modifying enzymes. To overcome these limitations, our lab has begun development of a new method for protein folding studies. This method, pulse chase in-cell fast photochemical oxidation of proteins (pcIC-FPOP), couples pulse-chase technology with mass spectrometry-based in-cell footprinting which will allow for quick analysis of short lived protein folding intermediates. While studies are ongoing, the development of this method would fill gaps in knowledge on protein folding and its role in disease. The new platform includes the incubation system, the stage, controllers the peristaltic pumps, the 248nm KrF excimer laser, and the optics/lens. First, the incubation system which included a temperature unit, humidifier, and monitoring system was assembled. Next was the assembly of the custom made 6 well plate incubator Nanopositioning and XY Madmotor drives. Perfusion line tubing were placed flushed against the walls of each well with robust 3D printed rings that secure the tubing without disturbing the cells or getting in the way of the laser beam pulse. Transient transfections were performed to assess and compare cell culture quality under standard incubator and stage top incubator conditions. A luciferase assay was performed to quantitate transfection efficiency. This method will become a powerful tool in probing protein folding and misfolding in the native cellular environment.

54. Crosstalk between Autophagy and Neuroinflammation following Traumatic Brain Injury

Nivedita Hegdekar

Hegdekar, N., Sarkar, C., Ritzel, R., Ravishankar, P., Philkana, D., Loane, D., and Lipinksi, M.M.

Session G; Poster Presentation; Room 349

The autophagy-lysosomal pathway serves an important role in cellular homeostasis and protection against neurodegeneration. Recently autophagy has been also implicated in regulation of immune and inflammatory responses. Specifically, high levels of autophagy flux are generally associated with anti-inflammatory, and inhibition of flux with pro-inflammatory phenotypes. To determine if

autophagy may be involved in modulation of neuroinflammation after TBI, we assessed the levels of autophagy in resident microglia and infiltrating macrophages following moderate controlled cortical impact (CCI) in C57Bl/6 mice. We observed accumulation of autophagosomes and inhibition of autophagy flux specifically in the activated microglia/macrophages. Our studies using transgenic reporter mice demonstrated that infiltrating macrophages are affected by the block of autophagy flux to a higher degree than activated resident microglia. Autophagy impairment in the activated cells of the microglia/macrophage lineage peaked at day 3 post-CCI and persisted at least through day 7. At day 3 after CCI, the cells with inhibited autophagy reveal a mixed (transitional) inflammatory phenotype, characterized by expression of both pro- and anti-inflammatory polarization markers. We hypothesize that inhibition of autophagy within these cells could promote their pro-inflammatory polarization after TBI. Our in vitro experiments demonstrate that inhibition of autophagy can potentiate pro-inflammatory activation induced by LPS treatment of BV2 microglial cells and in vivo data showing altered expression of inflammatory markers in autophagy hypomorph Becn1+/- mice after injury. Furthermore, Becn1+/- mice performed worse than C57Bl/6 mice on behavioral tasks after injury. These findings provide insights into the molecular crosstalk between autophagy and neuroinflammation following brain injury.

55. CONCURRENT FLT3 AND PIM KINASE INHIBITION POST-TRANSLATIONALLY DOWNREGULATES C-MYC IN CELLS WITH FLT3-ITD

Jonelle Lee

Lee, J. K., Scarpa, M., Kapoor, S., and Baer, M. R.

Session G; Poster Presentation; Room 349

Acute myeloid leukemia (AML) is the common form of acute leukemia in adults. Approximately 30% of AML patients have somatic internal tandem duplications (ITD) in the fms-like tyrosine kinase 3 (FLT3) receptor, causing constitutive and aberrant receptor signaling. FLT3 inhibitors are being developed but have limited clinical activity, with rapid onset of resistance. Pim-1 kinase is an oncogenic serine/threonine kinase transcriptionally upregulated downstream of FLT3-ITD; it directly increases proliferation and inhibits apoptosis, and also phosphorylates FLT3-ITD, enhancing its stability. Dual inhibition of FLT3 and Pim kinases is a promising treatment strategy for AML with FLT3-ITD. The proto-oncogene c-Myc drives proliferation and causes resistance to apoptosis in many cancer types. We previously showed that concurrent FLT3 and Pim inhibition increases apoptosis in cells with FLT3-ITD through downregulation of the anti-apoptotic protein Mcl-1. Here we demonstrate downregulation of c-Myc upstream of Mcl-1. Ba/F3-ITD and MV4-11 cells, with FLT3-ITD, were cultured with the FLT3 inhibitors gilteritinib or quizartinib and/or the pan-Pim inhibitor AZD1208. FLT3 and Pim inhibitor co-treatment decreased c-Myc protein expression within 30 minutes, while Mcl-1 protein levels decreased later. While c-Myc mRNA levels did not decrease with combination treatment, c-Myc protein half-life decreased, and this decrease was abrogated by proteasome inhibition. Treatment with the c-Myc inhibitor 10058-F4 decreased Mcl-1 expression and increased apoptosis induction. Conversely, apoptosis induction by co-treatment decreased by 20% in Ba/F3-ITD cells infected with retrovirus

overexpressing c-Myc. Thus, FLT3 and Pim inhibitor co-treatment increases apoptosis via c-Myc downregulation and c-Myc is a therapeutic target in FLT3-ITD AML.

56. IMPACT OF MOUTHRINSES ON FLUORIDE DENTIFRICES EFFICACY PREVENTING ENAMEL AND DENTIN EROSION/ABRASION

Ebtehal Albeshir

Ebtehal, G., Albeshira Norman, B., Cookb George, J., Eckertc Anderson, T., and Lipperte, H.

Session G; Poster Presentation; Room 349

The aim of this in vitro study was to investigate and compare the impact of chlorhexidine (CHX), essential oils (EO) and cetylpyridinium chloride (CPC) mouthrinses on erosive tooth wear protection afforded by conventional fluoride toothpastes. Methodology: The following experimental factors were considered: five rinses: CHX, EO, CPC, a fluoride rinse, and deionized water, two fluoride toothpastes: stannous fluoride (SnF2), sodium fluoride (NaF) and two models: erosion only and erosion + abrasion. Slabs of bovine enamel and dentin were embedded in resin blocks (n=8 per group). Specimens were subjected to a five-day cycling regimen consisting of twice-daily treatments, with or without abrasion, with fluoride toothpaste (1 min) followed by mouthrinse exposure (1 min). Erosion (0.3% citric acid, pH 2.6) was performed 5×/d. Specimens were exposed to artificial saliva during remineralization periods. Surface loss (SL) was determined using profilometry. Data were analyzed using ANOVA (□=0.05). Results: There was no interaction among the three factors (type of toothpaste, mouthrinse and abrasion or not (dentin p=0.0520, enamel p=0.4720). There were no significant two-way interactions as SL was only affected by toothpaste and mouthrinse. NaF caused less SL than SnF2 (4.60 vs. 5.83 µm; p<0.0001) in dentin, whereas the opposite was found in enamel (5.20 vs. 3.56 µm; p<0.0001). Erosion + abrasion caused comparatively more SL than erosion only in both enamel (6.53 vs. 2.23 µm; p<0.0001) and dentin (6.06 vs. 4.38 µm; p<0.0001). None of the tested mouthrinses affected SL. Conclusion: Commonly used mouthrinses do not impair the erosion/abrasion protection afforded by fluoride toothpastes.

57. HYPERTHERMIA WITH PROTON BEAM RADIATION THERAPY ON CHORDOMA CELL LINES

Prerna Singh

Singh, P., Mahmood, J., Eley, J., Bentzen, S., Malyapa, R., and Vujaskovic, Z.

Session G; Poster Presentation; Room 349

Chordomas are rare malignant tumors with a median survival in the United States of 7 years. The current standard of care is limited to en-bloc resection followed by adjuvant Radiotherapy (RT). However, chordoma is highly radioresistant and novel strategies to improve the response of RT are warranted. Tumor targeted Hyperthermia (HT) acts as a potent radiosensitizer. Proton beam therapy (PBT) is a state-of-the-art RT technology with its spread of Bragg-peak (SOBP). We investigated whether PBT with HT can act as a radiosensitizer and tumor cell killing at the end of the SOBP compared to the middle of the SOBP with HT. Method: Human Chordoma cell lines, U-CH2 and Mug-chor1 were treated with HT (43oC for 1 hour) followed by PBRT at both middle and distal SOBP with the dose of 4, 8, 12 and 16Gy for U-CH2 and 1, 2, 4, and 8Gy for Mug-chor1.

Colony forming assay was performed for 2 weeks. Results: HT significantly ($p<0.05$) decreased colony survival in combination with PBT at both middle and the distal SOBP for both cell lines. In U-CH2, HT with PBT significantly killed ($p<0.05$) cells at doses 4 and 8Gy and for Mug-Chor1 ($p<0.05$) at 1, 2 and 4Gy at both middle and distal SOBP. We also found that Mug-chor1 is more heat-sensitive and radiosensitive while U-CH2 is heat-resistant and radioresistant. Conclusions: Our results provide the first-time in vitro evidence about the effects of HT as a novel additive treatment to increase PBT effectiveness in Chordoma cell lines.

58. DELAYED TREATMENT WITH MIDAZOLAM INCREASES SURVIVAL BUT IS NOT FULLY PROTECTIVE AGAINST SOMAN-INDUCED EPILEPTOGENESIS AND NEUROPATHOLOGY IN MALE AND FEMALE CARBOXYLESTERASE KNOCKOUT MICE

Erica Kundrick

Kundrick, E., Marrero-Rosado, M., de Araujo Furtado, M., Stone, M., Schultz, C., Walker, K., O'Brien, S., Lee, R., and Lumley, L.

Session G; Poster Presentation; Room 349

Chemical warfare nerve agents (CWNA) are inhibitors of acetylcholinesterase and lead to status epilepticus (SE), spontaneous recurrent seizures (SRS) and severe neuropathology when treatment is delayed. In addition to acetylcholinestesterase inhibition, the CWNA soman also inhibits carboxylesterase, and can greatly affect soman toxicity in rodents, which unlike humans, have plasma carboxylesterase activity. The carboxylesterase knockout (ES1-/-) mouse specifically lacks plasma carboxylesterase and might better model human soman exposure compared to wildtype rodents. Since delayed midazolam treatment leads to benzodiazepine-refractory SE, we characterized the dose-response effects of delayed midazolam in male and female ES1-/- mice, for use as a model to evaluate adjunct therapies. In Exp. 1 the 24h lethality dose-response curve of GD was determined in both sexes and across the estrous cycle. In Exp. 2, mice exposed to a toxic dose of GD were treated with an admix (ip) of atropine sulfate and HI-6 1 min after exposure, and with a dose range of midazolam at 40 min after seizure onset. Electroencephalography was continuously recorded to evaluate initial seizure duration and SRS, and mice were euthanized 2 weeks after exposure for neuropathology assessment. Mice in estrus were the least susceptible to soman lethality. Delayed midazolam treatment increased survival in a dose-dependent manner in both sexes, but was unable to rapidly terminate seizure activity and did not prevent SRS or neuronal loss following soman exposure. This study demonstrates that delayed midazolam treatment of SE does not protect against soman-induced epileptogenesis and neuropathology, exemplifying the need for adjunct treatment to midazolam.

59. IMPLEMENTATION OF A TRANSITION OF CARE PROCESS TO REDUCE PATIENT/FAMILY RELOCATION STRESS/ANXIETY

Jennifer Spelta

Spelta, J.M.

Session H; Poster Presentation; Room 349

Transitions of care are processes patient's encounter frequently, particularly intensive care unit (ICU) patients. ICU's aim to minimize disruption; however, patients/families still experience stress/anxiety, and support processes for

transitions have demonstrated effectiveness in reducing patient/family relocation stress/anxiety. A quality improvement project was completed in a 24-bed surgical intensive care unit (SICU). A pre-post design was used with separate adult populations transitioning to the surgical intermediate care unit (SIMC). The new transition process included a nurse checklist including unit information, information about decreased patient monitoring, family visiting, patient safety, and expectations. SICU nurses collected self-reported post-transition data within 48 hours in the SIMC. Data composed of the faces anxiety scale (FAS), brochure feedback, and staff compliance was collected. The FAS scale included an anxiety range from none, just a little, little bit more, to most ever. The pre-group provided baseline data. Pre- FAS data (N=6), included 33% of patients rated a little bit more stress/anxiety with transitions and 50% indicating a bit more. Post-implementation, 24 patients were surveyed with 42% indicating no stress/anxiety and 37% just a little. Seventy-five percent of data collected were patients and 25% family. Post-implementation, SICU nurses (N=15) completed the transition of care-system usability survey with a 97% positive rating to continue the process. The transition of care process demonstrated success in decreasing transition stress/anxiety, and SICU nurses indicated support for the process. This transition of care process can provide a model to enhance patient and family support in other settings.

60. Implementation of the Confusion Assessment Method on a Medical Intermediate Care Unit

Katharine Outen

Outen, K.A.

Session H; Poster Presentation; Room 349

BACKGROUND: Developing delirium in the hospital leads to an increased length of stay in an intensive care unit (ICU), length of overall hospital stay, likelihood of requiring nursing home care after discharge, and risk of mortality following hospitalization. Longer periods of delirium worsen cognition, executive functioning, and sensory-motor functioning. PURPOSE: The purpose of this quality improvement project was to assess the nurse-perceived usability of the Confusion Assessment Method (CAM) delirium screening tool for patients on a medical intermediate care unit (MIMC) of a large, urban academic medical center. INTERVENATIONS: Eligible patients had a CAM screening completed once per shift by the primary nurse. The nurse was also asked to complete a System Usability Scale (SUS) survey, a Likert-style questionnaire, to evaluate the usability of the CAM for this patient population. RESULTS: There were 329 eligible patient encounters with 183 CAM screenings completed. Compliance rate with completing the CAM screening was 55.6%. Of the completed CAM screenings 16 were "positive," or suggestive that a diagnosis of delirium was present, for a point incidence of 8.7%. 181 SUS surveys were completed by the nursing staff with scores ranging from 35 to 100. The mean score was 77.94 (SD ±12.21). According to the SUS survey, scores over 68 indicate above average usability. CONCLUSIONS: This quality improvement project provides initial support regarding the usability of the CAM screening tool for non-critically ill patients on a MIMC. Integration of delirium screening tools into the electronic medical records may improve compliance with screening.

61. Interunit Implementation of a Standardized Nurse Handoff Method in Cardiac Surgery

Ashley Burnham

Burnham, A. M.

Session H; Poster Presentation; Room 349

Background: Handoff is inevitable and creates the potential for error or injury. Communication errors have been associated with hundreds of patient deaths and upwards of one billion dollars in cost annually. A method accounting for illness severity, patient summary, action list, situational awareness and contingency plans, and synthesis by receiver, called I-PASS, was developed to provide a handoff framework resulting in improved communication, reduced errors, and improved patient safety. Purpose: Evaluate the effect of the I-PASS method on the nurse satisfaction, quality, handoff duration, and usability during nurse handoff between the Cardiac Surgery Intensive Care Unit and Telemetry units. Methods: A 13-week multi-unit quality improvement project using the Plan-Do-Study-Act framework was implemented at a tertiary academic medical center. Inclusion criteria included patients selected for unit transfer pre or post-intervention. Exclusion criteria included rapid response or emergent patient transfer. Interventions: The I-PASS method was adapted for cardiac surgery. Staff education occurred during huddles. A resource sheet, modified system usability score and nurse satisfaction surveys were distributed to transferring and receiving nurses. Surveys were collected from each nurse and handoff duration documented. Outcomes: The I-PASS method was liked by 39.5% of nurses. I-PASS reduced unnecessary or erroneous information reported by 41.7% of nurses. Longer handoff duration was perceived by 41.7% of nurses. I-PASS averaged a mean usability score of 59.36 and a mean handoff duration of 11 minutes. Conclusion: The current I-PASS method cannot be recommended. Modifications should be made to the nurse handoff method. Additional studies are recommended to further evaluate the impact of the I-PASS method.

62. GENDER DIFFERENCES IN THE INTERRELATIONS AMONG SOCIAL SUPPORT, STRESSFUL LIFE EVENTS, AND SMOKING CESSATION IN PEOPLE WITH SEVERE MENTAL ILLNESSES

Hamzah Alghzawi

Alghzawi, H., Zhu, S., Trinkoff, A., Wagner, F., and Storr, C.

Session H; Poster Presentation; Room 349

Objective: Severe mental illness is associated with less success in quitting and maintaining abstinence. Social support and stressful life events (SLEs) have been found to be influential factors for smoking cessation in the general population, but little is known about these factors among smokers with mental illnesses. Methods: A population sample of 4,610 American lifetime adult smokers with schizophrenia, bipolar disorder, or major depressive disorder were identified in a limited public use dataset of the 2012-2013 National Epidemiologic Survey on Alcohol and Related Conditions (NESARC-III). Four mediation and moderated mediation models were used to examine gender differences in the interrelations among social support, SLEs, and smoking status in the prior year. Results: Analyses indicated that total, appraisal, and tangible support in females exerted indirect effects on smoking cessation via decreased SLEs (indirect effects: total= .0094, LLCI = .0054, ULCI = .0136; appraisal = .0229, LLCI = .0137, ULCI = .0338; tangible = .0298, LLCI = .0190, ULCI = .0416). That is, higher

total, appraisal, and tangible support were associated with lower SLEs, which in turn were associated with higher smoking cessation. In males, only belonging support exerted an indirect effect on smoking cessation via increased SLEs (indirect effect = -.0107, LLCI = -.0214, ULCI = -.0008). Specifically, higher belonging support was associated with higher SLEs in males, which in turn were associated with lower smoking cessation. Conclusions: The current study suggests that interventions focusing on improving social support should be a priority for those working with female smokers with SMI.

63. Examining the Factors Influencing Older Adults' Patient Portal Use Using Structural Equation Modeling

Hyojin Son

Son, H., Zhu, S., and Nahm, E-S.

Session H; Poster Presentation; Room 349

Background: Patient portal (PP) can benefit older adults in managing their health, but low adoption has been a concern. There is a limited understanding of how potential factors influence older adults' PP use, and few studies have been conceptually based. Objective: Technology Acceptance Model (TAM) describes that perceived usability influences person's technology adoption behaviors. The purpose of this study is to test whether TAM model can explain the relationship between older adults' PP use and the influential factors including perceived PP usability and PP self-efficacy. Method: This was a model testing using the baseline data from a trial that tested a PP eLearning program. Data from 194 older adults with PP accounts were analyzed. Structural equation modeling was applied. Results: Perceived PP usability was: PP ease of use 4.9±1.66; PP usefulness 4.6±1.84 (range: 1-7). Self-efficacy for using PP was 28.8±11.47 (range: 0-40). The initial model was revised, and the final model revealed a good fit (□2/df, 1.089; RMSEA, 0.021; CFI, 0.993). Age and eHealth literacy influenced PP ease of use. Gender, eHealth literacy, and PP ease of use influenced PP usefulness. Education and PP usefulness influenced PP self-efficacy. PP self-efficacy influenced PP use. PP ease of use indirectly influenced PP self-efficacy via PP usefulness. PP usefulness indirectly influenced PP use, mediated by PP self-efficacy. Discussion: Raising perceived PP usability may help improve older adults' PP use by enhancing PP self-efficacy. Further investigation is needed to examine the influence of perceived PP usability on PP use among various older adult populations.

64. Early Hearing Detection: Using Family Education and Pre-Discharge Referrals to Reduce Infant Lost to Follow-Up Rates

Julie Riggs

Riggs, J. M.

Session H; Poster Presentation; Room 349

Background There are lags in ensuring that infants who do not pass their hospital newborn hearing screens receive the follow-up testing they need by the recommended three-month benchmark. The purpose of this project is to address disparities in infants lost to follow-up (LTF) by piloting a program for pre-discharge education and referrals to free follow-up care at a suburban hospital in Prince George's County, Maryland. Intervention A partnership between the state department of health and a local university audiology program provided education and free follow-up testing of infants who do not pass the

newborn hearing screen. Audiology technicians provided a screening results card to families, which also included hearing developmental milestones. Families received brief verbal education about the test result and the urgent need for a retest for those who did not pass. Infants requiring follow-up received appointments with the partner audiology clinic for a free evaluation. Results 216 infants were born at the site and 214 babies received the in-hospital hearing screens. All 214 babies passed the in-hospital screens and did not require referral. An additional three babies were referred to the university clinic from other sites. Conclusion This project did not yield opportunities for evaluation of LTF due to low birth volume during the short data collection period. However, this project indicated future potential for positive change. Families responded well to the cards and engaged with the education. This partnership provided opportunities for follow-up of at-risk infants in the region and is likely a model worth expanding.

65. Evaluation of a Terminal Weaning Protocol in a Critical Care Unit

Bianca Zorbach

Zorbach, B.

Session H; Poster Presentation; Room 349

Background Withdrawal of life support can be a traumatic experience for patients, their relatives and medical staff. Terminal weaning from mechanical ventilation and administration of medications are associated with less respiratory distress and increased comfort in patients when compared to single-step extubation (Robert et al., 2017). Also, an evidence-based scale, known as the Respiratory Distress Observation Scale (RDOS) effectively identifies respiratory distress in patients who cannot self-report dyspnea (Campbell, Kero & Templin, 2017). The purpose of this project was to implement and evaluate a terminal weaning protocol using the RDOS to properly manage end-of-life symptoms of terminally-ill patients in a critical care unit at a rural community hospital. Methods A literature review was completed focusing on implementation of terminal weaning instead of immediate extubation and use of the RDOS. A terminal weaning protocol, algorithm, and Likert-style nursing survey were implemented. Descriptive statistics was used to evaluate protocol compliance, nursing satisfaction, and RDOS scores before, during and after terminal weaning. Results After eight weeks, five patients were enrolled in the project and five surveys were completed. Strict protocol adherence was evident with three patients (60%). The average RDOS scores for the entire sample before, during and after terminal weaning were 3, 3.5 and 2. Furthermore, 80% of nurses were “very satisfied” with terminal weaning and “satisfied” with the usability of the RDOS. Conclusion Implementation of a terminal weaning protocol using the RDOS can improve nursing satisfaction with end-of-life care and respiratory distress experienced by patients requiring withdrawal of life support.

66. Single cell tracking eliminates mammosphere aggregation and allows highly accurate prediction of sphere formation

Patrick Bailey

Bailey, P.C., Lee, R.M., Bhandary, L., Mathias, T. and Martin, S.S.

Session I; Oral Presentation; Ballroom A

The mammosphere assay purports to identify the fraction of stem-like cells in a population by quantifying the number of spheroids that

grow from single cells after culture in suspension. There is no consensus protocol in the field regarding seeding densities however. Densities of up to 100,000 cells/mL have been reported. This leads to cellular aggregation over time, increasing the survival of suspended cells yet decreasing calculated sphere forming efficiencies (SFE). Drugs which reduce the sphere forming efficiency of a population are assumed to have decreased the quantity of stem-like cells. This interpretation is problematic when viewed in terms of aggregation. Changes in sphere forming efficiency could be due in large part to changes in aggregation. We have addressed this with single cell tracking. We found that SFEs in multiple cell lines were over 30 times higher than commonly reported. We also used tracking data to predict day 14 sphere formation after only 24 hours post seeding with a high degree of accuracy. To make the assay more high-throughput we have developed a cell tethering technology that keeps cells anchored in space yet forces them to maintain a suspended-cell morphology. This procedure significantly reduces aggregation and increases the throughput by tenfold.

67. The Role of Colonization Factors CFA/I and CS21 in ETEC Pathogenesis in the Human Enteroid Model

Emily Smith

Smith, E. M., and Barry, E. M.

Session I; Oral Presentation; Ballroom A

Lymphotoxin 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 the intestinal epithelium and secrete heat-stable toxin (ST) and/or heat-labile toxin (LT), causing dysregulation of 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 pathogenesis. Clinical strains harboring genes encoding CFA/I and/or CS21 were used to investigate CF expression and function. After growing clinical strains in differential media, we determined that CFA/I expression was restricted to CFA agar plate conditions whereas CS21 was expressed in all growth conditions. Adherence assays indicated that ETEC strains H10407, CVD19, and CVD30 adhere to nonpolarized and polarized T84 monolayers as well as differentiated enteroid monolayers in a CFA/I-dependent manner. Interestingly, CVD30 that expresses high levels of both 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. Delivery of purified LT induced a concentration- and time-dependent increase in cAMP in T84 cell monolayers and ileal enteroid monolayers. Infection of T84 cell monolayers with H10407 or CVD19 demonstrated that ETEC delivers LT in a CFA/I-dependent manner. These data suggest that CFA/I and CS21 can be expressed simultaneously. This supports the role of multiple CFs in ETEC pathogenesis and proposes new targets for consideration in vaccine development.

68. Antibacterial Monomer in Dental Sealant Formulation Alters Cariogenic Pathogenicity of Streptococcus mutans Biofilm

Maria Ibrahim

Ibrahim, M. S., Ibrahim, A. S., Weir, M. D., Xu, H. H. K., and Melo, M. A. S.

Session I; Oral Presentation; Ballroom A

Cariogenic oral biofilms are strongly linked to dental caries around dental sealants. This may hinder the preventive effect of sealants in protecting the posterior teeth from cavitation, especially in high-caries risk children. Quaternary ammonium monomers that can be copolymerized with the existing dental resin systems have been increasingly explored for modulation of dental plaque biofilm growth over dental composite surfaces. Here, we investigated the effect of dimethylaminohexadecyl methacrylate (DMAHDM) on cariogenic pathogenicity of Streptococcus mutans. The inhibitory effects of the novel sealants containing 5% DMAHDM and 20% nanoparticles of amorphous calcium phosphate (NACP) against S. mutans and its virulence properties were assessed by determining the acid neutralizing activities, the metabolic activities, the lactic acid production, the exopolysaccharides (EPS) production, the colony-forming unit counts and acid and hydrogen peroxide stress tolerance. Our findings suggest that (1) 5% DMAHDM and 20% NACP sealant was able to impart detrimental biological effect on S. mutans by inhibiting approximately 50-90% of the biofilm formation, metabolic and EPS responses; (2) 5%DMAHDM and 20%NACP sealant in contact with S. mutans was also able to significantly reduce the aciduricity and the tolerance to oxygen stress; the two major virulence factors of this microorganism, which are linked to its cariogenic pathogenicity. These results provide a view on the significance of integrating bioactive dental materials with the traditional caries prevention protocols. The strategy of contact-killing via monomers such as DMAHDM seems to reduce high numbers of S. mutans and may be considered as a promising approach for high-caries risk patients.

69. PARP Inhibitor Resensitization of FLT3 Inhibitor-Resistant AML

Anna Dellomo

Dellomo, A. J., Baer, M. R., and Rassool, F. V.

Session I; 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 FLT3 receptor and signals through signal transducer and activator of transcription (STAT) 5. FLT3-specific tyrosine kinase inhibitors (TKI) have clinical effects in FLT3-ITD AML but efficacy is limited and transient due to the development of resistance through various means including point mutations within the tyrosine kinase domain (TKD) of FLT3. Novel therapies are therefore required for TKI-resistant AML. Poly (ADP-ribose) polymerase inhibitors (PARPi) are effective in cancers with impaired homologous recombination due to BRCA mutations but have not been fully explored in BRCA-proficient cancers such as AML. Although PARP1 is primarily known for poly-ADP-ribosylating (PAR) itself and other proteins to catalyze DNA repair, PARylation can also regulate the function of proteins involved in many other processes. We have found that, compared to TKI-sensitive counterparts, TKI-resistant TKD-mutated forms of FLT3-ITD AML have elevated levels of ROS, PARP1, and activated STAT5 (pSTAT5). Notably, we show for the first time that loss of PARP1

leads to decreased pSTAT5 and this regulation may occur through PARylation of STAT5. Importantly, we found that use of the PARPi, talazoparib, in combination with the TKI, quizartinib, is synergistically lethal in these otherwise TKI-resistant cells suggesting that talazoparib is resensitizing the cells to quizartinib. This leads us to believe this combination therapy may be important for treatment of TKI-resistant AML.

70. Dendritic Cell Derived IL-12p40 Binds Extracellular Proteins to Make Heterodimeric Cytokines

Allison Gerber

Gerber, A.G., Abdi, K., and Singh, N.J.

Session I; Oral Presentation; Ballroom A

Upon infection, naïve T cells differentiate into effector subsets to generate an appropriate response. In order to skew T cells into the proper effector response, dendritic cells (DC) release specific cytokines. IL-12 and IL-23 are heterodimeric cytokines which share a common subunit, p40. Binding of p40 to p35 results in IL-12, while binding to p19 generates IL-23. Despite this shared subunit, these two cytokines lead to very different effector T cell responses – IL-12 leads to IFNγ producing effectors while IL-23 gives rise to IL-17 producing effectors. Assembly of these cytokines 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 (or p19) 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. Chimeras infected with Leishmania major were able to induce IFNγ production by T cells. These results suggest that functional IL-12 assembly can occur in the extracellular milieu from component peptides. Importantly, this mechanism may allow even non-hematopoietic tissues to direct T cell differentiation by releasing proteins capable of binding to DC-derived p40.

71. Developing a Novel Root Canal Sealer with Dual Antibiofilm Strategies of Dimethylaminohexadecyl Methacrylate and Nanoparticles of Silver to Inhibit Root Canal Biofilms

Bashayer Baras

Baras, B. H., Melo, M.A.S., Sun, J., Oates, T.W., Weir, M.D., Xie, X., Bai, Y., and Xu, H.H.K.

Session I; Oral Presentation; Ballroom A

Objectives: (1) Develop a new root canal sealer with potent and long-lasting antibiofilm effects using dimethylaminohexadecyl methacrylate (DMAHDM) and nanoparticles of silver (NAg); (2) determine the effects of incorporating DMAHDM and NAg each alone versus in combination on biofilm inhibition efficacy; and (3) determine the effects on sealer paste flow, film thickness and sealing ability, compared to a commercial control sealer. Methods: Dual-cure endodontic sealers were formulated using DMAHDM mass fractions of 0%, 2.5% and 5%, and NAg mass fractions of 0.05%, 0.1% and 0.15 %. The sealing ability of the sealers was measured using linear dye penetration method. Colony-forming units (CFU), live/dead assay, and polysaccharide production of biofilms on sealers were determined. Results: The sealer with 5% DMAHDM and 0.15% NAg yielded

a flow of (22.18±0.58) which was within the range of ISO recommendations and not statistically different from AH Plus control (23.3±0.84) ($p>0.05$). Incorporating DMAHDM and NAg did not negatively affect the film thickness and sealing properties ($p>0.05$). The sealer with 5% DMAHDM and 0.15% NAg greatly reduced polysaccharide production by biofilms, and decreased the biofilm CFU by nearly 6 orders of magnitude, compared to AH plus and experimental controls ($p<0.05$). Significance: A therapeutic root canal sealer was developed through the addition of 5% DMAHDM with biofilm-inhibition through contact-meditated mechanisms and 0.15% NAg to release silver ions into the complex and difficult-to-reach root canal environment. The novel root canal sealer exerted potent antibiofilm effects and reduced biofilm CFU by 6 orders of magnitude without compromising needed properties.

72. IMPLICATIONS OF NOVEL TREMOR MUTATIONS IN MYOSIN BINDING PROTEIN-C SLOW (SMYBP-C)

Janelle Geist Hauserman

Geist Hauserman, J., Stavusis, J., Lace, B., Wright, N., Bonneman, C., Ward, C., and Kontrogianni-Konstantopoulos, A.

Session J; Oral Presentation; Ballroom B

Myosin Binding Protein-C (MyBP-C) comprises a family of proteins with structural and regulatory roles in striated muscles. The slow (s) skeletal isoform is understudied, yet has been associated with severe and lethal forms of distal arthrogryposis. More recently, our studies causatively linked sMyBP-C to a new form of myopathy characterized by muscle weakness, hypotonia, facial/body deformities, and tremor. Two novel autosomal dominant mutations, Y247H and E248K, were found to co-segregate with the myopathic phenotype in all carriers. Both mutations are in a MyBP-C specific motif, termed M-motif, within the NH2-terminus of the protein, which has been shown to regulate actomyosin crossbridges. In vitro binding studies showed that the Y247H and E248K mutations result in enhanced binding to myosin. Moreover, molecular dynamic simulations demonstrated that the Y247H and E248K mutations increase the number of favorable electrostatic interactions with myosin. To begin deciphering the molecular, cellular, and functional alterations underlying this new form of myopathy in vivo, we generated an E248K knock-in (KI) model. Homozygous KI mice exhibit neonatal lethality, while heterozygous KI mice are significantly smaller, develop severe tremor, and display behavioral, locomotion and strength deficits compared to their wild type littermates throughout postnatal life and in adulthood. Taken together, my studies reveal the presence of novel mutations in sMyBP-C that co-segregate with a new form of myopathy characterized by muscle weakness and tremor that is potentially of myogenic origin.

73. THE SELF-REACTIVITY INTRINSIC TO ALL T CELLS INVOLVES THE CD5-DEPENDENT MODULATION OF NFKB

Courtney Matson

Matson, C.A., Love, P.E., Szeto, G.L., and Singh, N.J.

Session J; Oral Presentation; Ballroom B

A cornerstone of immunity is that T cells respond to pathogens while avoiding autoimmunity. Yet, all peripheral T cells are intrinsically self-reactive because they undergo selection on self-peptides during

development. These cells do not all cause fulminant autoimmunity because signaling alterations downstream of T cell receptors (TCRs) after development prevent peripheral activation from these self-peptides. One alteration involves CD5, an inhibitory molecule, upregulated proportional to self-signals during development. Recent studies have examined whether self-reactivity in T cells, as indicated by CD5 levels, plays a role in protective immunity. Surprisingly, CD5-hi (and by extension, more self-reactive) T cells were found to dominate the pathogen specific response. It is unclear if this is from CD5 expression or TCR self-reactivity. The precise signaling networks that enable the CD5-hi T cells to respond better to pathogens is also not known. We find that peripheral T cells express intracellular IκBα, a component of the NFκB signaling pathway, proportional to the levels of CD5. To examine whether this is an independent indicator for high self-reactivity, we used CD5-knockout (CD5-KO) mice. CD5-KO T cells expressed lower IκBα than wild-type suggesting that IκBα regulation was downstream of CD5 not directly the TCR. This was validated using an inducible knock-out of CD5 (by tamoxifen administration) suggesting that continuous CD5 expression is required. Taken together our data suggest that CD5 is an active mediator of a TCR's intrinsic self-reactivity, rather than a passive marker for it. Understanding this axis may provide insight into improving vaccination strategies and cellular immunotherapy.

74. THE STRUCTURAL BASIS AND MECHANISM OF HIV-1 GENOME PACKAGING

Canessa Swanson

Swanson, C. J., and Summers, M. F.

Session J; Oral Presentation; Ballroom B

Globally, nearly 40 million people are HIV-positive, those that are receiving therapeutic treatment can often develop drug toxicity and viral resistance. Mainly due to antiretroviral drugs targeting proteins which are susceptible to mutation rendering therapeutics inefficient, and highlighting the need for the discovery of conserved drug targets for pharmaceutical development. Despite this high mutation rate, sequence analysis of the viral genome revealed that the 5′-Leader is not only the most highly conserved but also the most structured, suggesting the physiological importance of the 5′-Leader in the propagation of virus production. Previous studies have shown that genome recognition is mediated by an intermolecular interaction between the nucleocapsid (NC) domain the Gag polyprotein and a conserved stretch of nucleotides within the 5′-Leader, termed the Core Encapsidation Signal (CES). Structural evaluation of the NL4-3 strain CES, revealed a unique tandem three-way junction which has been hypothesized to serve as a mechanism, for the viral genome to outcompete cellular RNAs for packaging. Unfortunately, the three-way junctions exhibit a flexible nature which causes conformational heterogeneity and signal broadening within nuclear magnetic resonance (NMR) spectroscopy. Sequence alignment and Mfold predictions of the 5′-Leader from another HIV-1 strain (MAL) revealed that the proposed tandem three-way junction structure may exhibit more rigidity afforded by stabilizing mutations in

comparison to NL4-3. NMR data of the MAL strain showed sharper signals than NL4-3, a spectral feature which could allow for more thorough evaluation of the CES structure and facilitate in the identification of conserved structural components utilized in genomic recognition.

75. IRON(III)-SALOPHEN COMPOUNDS INHIBIT HEME SENSING IN PSEUDOMONAS AERUGINOSA

Garrick Centola

Centola, G. A., Jiang, W., Yu, W., Hom, K., Mackerell, A.D., Wilks, A., and Xue, F.

Session J; Oral Presentation; Ballroom B

Iron is an essential nutrient for bacterial virulence, with several bacterial species expressing specific and highly-tunable systems for extracellular iron sensing and uptake. Pseudomonas aeruginosa, a gram-negative opportunistic pathogen, acquires iron predominantly in the form of heme through the Pseudomonas heme uptake (Phu) system, and a non-redundant heme acquisition system (has) which serves to sense and respond to extracellular heme availability. The Has system relies on a secreted hemophore, HasA, to scavenge for heme in a host and delivers it to the outer-membrane receptor HasR, initiating an Extra Cytoplasmic Function signaling cascade leading to the downstream upregulation of the Has system. Since this system is highly expressed in infection models and genetic deletion attenuates virulence, it is proposed that the inhibition of this system could lead to a new therapeutic strategy that is slower to develop drug resistance. Additionally, targeting a protein-protein interaction (PPI) on the outer membrane circumvents potential pitfalls of efflux pumps and other drug-resistance mechanisms. To accomplish this, we have shown that synthetic iron complexes can act as heme mimics, interrupting the signaling pathway in bacterial culture. Additional compound libraries will be screened for activity in P. aeruginosa cultures based on a computationally-predicted binding site of HasA. Long-term, we aim to generate bifunctional molecules capable of targeting both the protein-protein interaction region and the heme-binding site to generate specifically targeted molecules with increased affinity. Through these aims, we intend to identify and develop novel antivirulent compounds capable of targeting the heme-sensing abilities of P. aeruginosa.

76. PARACRINE COMMUNICATION LINKS SODIUM CHLORIDE COTRANSPORTER ACTIVITY IN THE DISTAL CONVOLUTED TUBULE TO REMODELING OF THE ALDOSTERONE-SENSITIVE DISTAL NEPHRON

Ava Zapf

Zapf, A., Grimm, P.R., Delpire, E., and Welling, P.A.

Session J; Oral Presentation; Ballroom B

We recently discovered that cell-specific expression of constitutively active SPAK (CA-SPAK) in the early distal tubule is sufficient to drive a remodeling process of the entire distal nephron that includes structural dystrophy of the aldosterone-sensitive distal nephron and inhibition of ROMK and ENaC. Here, we tested the hypothesis that SPAK-activation of NCC stimulates the release of

paracrine or autocrine factors that cause the dystrophic response in the connecting tubule (CNT). We found increased levels of PGE2 in kidney cortical homogenates of CA-SPAK mice compared to control mice. Comparable elevation of PGE2 was also observed when NCC was physiologically activated by feeding wild-type mice (WT) a low potassium diet (LKD). Administration of the NCC-blocking diuretic, hydrochlorothiazide, to either CA-SPAK or WT mice on LKD, restored PGE2 to control levels. PGE2 synthesis is mediated by prostaglandin E synthase isoforms. Western blot analysis revealed microsomal prostaglandin E synthase-1(mPGES1) was elevated in the kidney cortex of CA-SPAK mice and WT mice on LKD compared to control mice. Quantitative microscopy of mPGES1 revealed localization of mPGES1 was confined to the CNT and CCD of CA-SPAK and LKD treated mice. In conclusion, these studies identify PGE2 as a potential remodeling autocrine that is released from the CNT and CCD in response to activation of NCC. We speculate that decreased sodium delivery to the CNT and CCD when NCC is activated drives this response. The autocrine pathway provides a novel means to communicate potassium sensing in the DCT to potassium secretion in the ASDN.

77. THE COMBINATION OF PARP INHIBITORS AND DNMT INHIBITORS MODULATES IMMUNE ACTIVITY AND SUGGESTS A ROLE FOR IMMUNE THERAPY IN AML

Aksinija Kogan

Kogan, A.A., Topper, M., Shissler, S.C., Lee, M.S., Bollino, D.R., Choi, E.Y., Lapidus, R.G., Li, L., Small, D., Baer, M.R, Webb, T.J., Baylin, S.B., and Rassool, F.V

Session J; Oral Presentation; Ballroom B

Acute myeloid leukemia (AML) is a genetically heterogeneous disease where malignant clonal proliferation of immature myeloid cells in the bone marrow leads to disruption of normal hematopoiesis and bone marrow failure. Most treatment improvements have consisted of limited chemotherapeutic interventions, and morbidity and mortality remain unacceptably high. While patients unfit for intensive chemotherapy have the options of epigenetic treatments with DNA methyltransferase inhibitors (DNMTis), and the preclinical research underpinning these treatments is robust and promising, clinical response rates have been poor. Therefore, we have derived a unique treatment strategy combining poly-ADP ribose polymerase inhibitors (PARPis) with DNMTis, and we have previously demonstrated efficacy of this combination in AML in both in vitro and in vivo models. To identify molecular pathways underpinning this combination, genome-wide expression microarray analysis was performed. Interestingly, combination drug treatment, more than either single treatment alone, up regulated genes in immune response pathways. Interferon-inducible genes were increased in selected AML samples post combination treatment. To functionally validate this immune involvement in vivo, we use an immune competent mouse model that spontaneously develops AML. We found that mice in the combination therapy group had increased T cell populations with increased PD1, CD28 and 4-1BB expression. These results indicate that our combination therapy results in immune activation, and suggest the potential to target the immune system in order to induce anti-tumor effects, enhance efficacy of our combination treatment and improve clinical outcomes in AML.

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