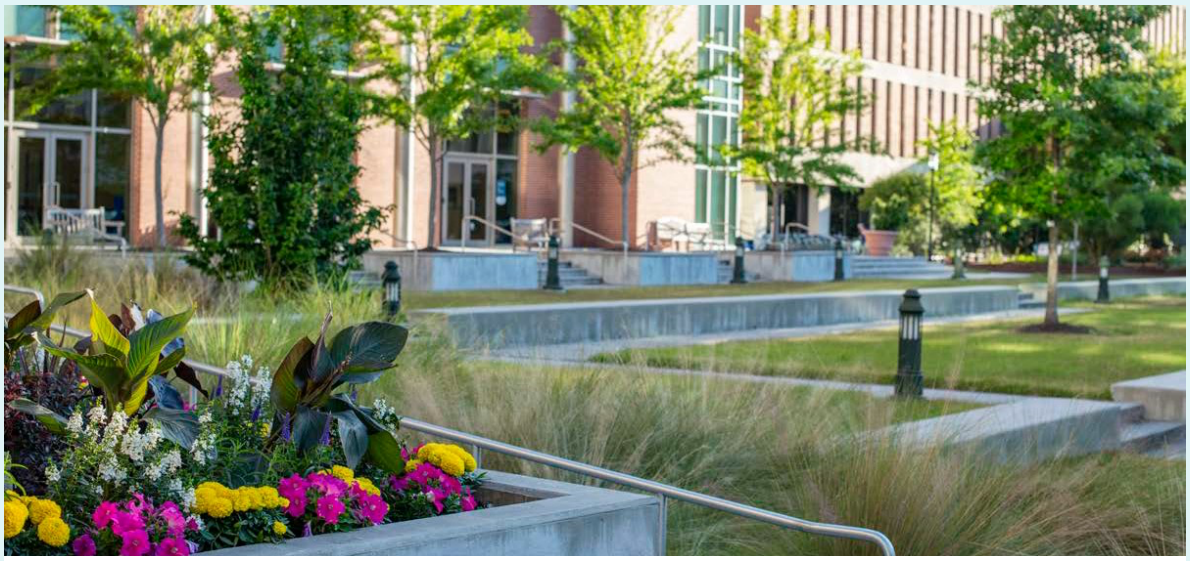
MUSC
Medical University
of South Carolina

Perry V. Halushka 56th Annual Research Day 2021



K-Awardee & Predoctoral Trainee Collaborative Grant RFA

This new grant mechanism seeks to promote a team-based collaborative translational research project between a predoctoral trainee and a current or recently graduated K-awardee* while enhancing team science and mentoring. The project could involve basic research, clinical research, and/or community/population health research approaches for the purposes of collecting critical preliminary data for submission of extramural grant applications, fellowship applications and to publish, disseminate and/or implement research findings.

Budget: $50,000; 2 years

View the ***RFA** to learn more about eligibility requirements.

Key Dates:

RFA Release Date: Wednesday, October 13, 2021
Pre-application Due (REQUIRED): Friday, November 19, 2021, by 5 pm EST
Full Application Due (by Invitation): Friday, January 21, 2022, by 5 pm EST
Earliest Anticipated Project Start Date: March 1, 2022

Contact: Dayan Ranwala
SCTR Pilot Project Program

MUSC Medical University of South Carolina | South Carolina Clinical & Translational Research Institute

Sigma Xi, The Charleston Chapter

WANTS YOU TO JOIN AS A NEW MEMBER OR AS A RENEWED MEMBER

Sigma Xi, The Scientific Research Society, is the international society of science and engineering. In addition to all of the national and international efforts of the Society, your membership will afford you immediate local benefits. The Charleston Chapter is comprised of members from the Medical University of South Carolina, The College of Charleston, The Citadel, Trident Tech, Bayer Corporation, NOAA, SCDNR as well as other science and education based institutions. Membership in the Charleston Chapter brings you into immediate contact with scientists from all disciplines and in all work environments in our area.

Please consider nominating yourself for membership or renewing your membership and then enjoy the benefits:

- **Subscription to the *American Scientist***. The American Scientist, published bimonthly since 1913, contains articles to inform scientists and engineers about developments outside of their own fields.
- **Grants-in-Aid of Research**. Small grants to encourage the professional development of new scientists.
- **Support of Charleston Area Schools**. Our Chapter members serve as consultants for local teachers, give classroom presentations to encourage student interest in science, judge science fair projects, host classes for field trips to professional sites, and much more.
- **Support of Charleston Area Undergraduate and Graduate Research**. Our Chapter sponsors awards for Outstanding Research Presentations by students at MUSC's Student Research Day, CofC's Marine Biology Colloquium, The Citadel's Undergraduate Research Conference and the Annual Meeting of the South Carolina Academy of Sciences.
- **Local Professional Talks**. Throughout the year our Chapter sponsors research seminars and field activities featuring our own members and their broad range of scientific disciplines.
- **National Speakers**. At least once a year, we bring in a Sigma Xi National Distinguished Lecturer. In recent years, the visit of our National speaker has been the highlight of Darwin Week.
- **Annual Banquet**. Each spring we recognize the outstanding accomplishments of scientists and teachers in our Chapter with a banquet and a keynote address of particular scientific or policy interest.
- **Chapter Listserver.** Our chapter sponsors Chs-Sci-Net, the best way to stay informed about all manner of science activities in the Lowcountry and throughout South Carolina.

To join, go to https://www.sigmaxi.org/members/becoming-a-member for additional details. Simply download and complete the nomination form for becoming a member through a local Sigma Xi chapter. We can provide nomination signatures if you do not know other Sigma Xi members.
New member dues: $125 (students $40) + one time $20 initiation fee (chapter dues waived).
Transitional dues for recent graduates (e.g. postdocs): $55.00 + $20 initiation fee.

Send the completed form to:
Dr. Karen Burnett, President
Charleston Chapter of Sigma Xi
Grice Marine Laborratory
Charleston, SC 29412
Phone: 843-709-4122
E-mail: burnettk@cofc.edu

Questions? Contact:
Dr. Jessica McCoy, Secretary
Charleston Chapter of Sigma Xi
Dept. of Biology, College of Charleston
66 George Street
Charleston, SC, 29424
Phone: (843) 830-0434; E-mail: mccoyja@cofc.edu

Poster and Oral Presentation Program

POSTER PRESENTATIONS

9:00 am - 12:00 pm		Abstracts
Session 1:	High School	001-012
Session 2:	Clinical / Professional / Masters I	013-022
Session 3:	Clinical / Professional / Masters II	023-032
Session 4:	Clinical / Professional / Masters III	033-043
Session 5:	Clinical / Professional / Masters IV	044-053
Session 6:	Clinical / Professional / Masters V	054-064
Session 7:	PhD – I	065-074
Session 8:	PhD – II	075-084
Session 9:	Postdoc / Resident / Fellow / Staff Scientist	085-095
Session 10:	Research Specialist / Technician	096-103

ORAL PRESENTATIONS

1:00 pm - 4:00 pm		Abstracts
Session 11:	Clinical / Professional / Masters I	104-114
Session 12:	Clinical / Professional / Masters II	115-124
Session 13:	Clinical / Professional / Masters III	125-134
Session 14:	Clinical / Professional / Masters IV	135-144
Session 15:	Clinical / Professional / Masters V	145-154
Session 16:	PhD I	155-164
Session 17:	PhD II	165-174
Session 18:	PhD III	175-184
Session 19:	Postdoc / Resident / Fellow / Staff Scientist	185-195
Session 20:	Research Specialist / Technician	196-203

SPECIAL AWARD PRESENTATIONS

Sigma Xi:	Poster & Oral
Interprofessional:	Poster
Interprofessional:	Oral
Ralph H Johnson VA Medical Center:	Poster
Ralph H Johnson VA Medical Center:	Oral
John Vournakis Innovation:	Poster & Oral
Health Humanities:	Poster & Oral
Center on Aging:	Poster
Center on Aging:	Oral
TACHL (Technology Applications Center for Healthful Lifestyles)	Poster
TACHL (Technology Applications Center for Healthful Lifestyles)	Oral

Session Guide

Session 1	Undergraduate	POSTER

09:00

1 **Sourcing Real-World Data to Build the Determinants of Health Ontology of Mappable Elements (DHOME) to Understand Disparities**

Lauren Cuppy, Alexander Alekseyenko, Tami Crawford, College of Medicine, MUSC

09:15

2 **An Investigation of the Relationship between Cortico- Cortical Connectivity and Upper Limb Motor Function in Stroke Survivors**

MiLana Wiltshire, Na Jin Seo, Christain Schranz PhD, College of Health Professions/ College of Graduate Studies(SURP), MUSC

09:30

3 **Cochlear lateral wall degeneration in a mouse model of complement Factor B Deficiency**

Shabih Jafri , Hainan Lang , Brown, Shardai, Barth, Jeremy, Atkinson, Carl, Department of Pathology and Laboratory Medicine , MUSC

09:45

4 **Bidirectional modulation of reward seeking behavior using cell type specific optogenetic control in the nucleus accumbens**

Camille Carthy, Peter Kalivas, Reda Chalhoub, Drew Kalasky, Stephen Walterhouse, Michael Mayerink, Eric Dereschewitz, College of Medicine (MD, PhD), MUSC

BREAK

10:05

5 **Opacification of Sino-Nasal Imaging Correlates with SNOT22 Scores in Patients with Chronic Rhinosinusitis**

Jacob Snyder, Rodney Schlosser, Matthew Germroth, Michael Shih, Thomas Edwards, Department of Rhinology, College of Medicine, MUSC

10:20

6 **Roles of Hydrogen Bond Interaction for Ca2+-Dependent Regulation of Ryanodine Receptor Calcium Release Channel**

Millar Elferdink, Naohiro Yamaguchi, Savannah Heitmann, Venkat R. Chirasani, Gerhard Meissner, Department of Regenerative Medicine and Cell Biology, College of Medicine, MUSC

10:35

7 **The effects of using a novel device for the symptomatic treatment of sinus headaches**

Matthew Germroth, Ted Meyer, Craig Salvador, BS; Shaun A. Nguyen, MD FAPCR, Department of Otolaryngology, College of Dental Medicine, MUSC

10:50

8 **Defining the importance of proline residues in the hypervariable region of HRAS for interaction with RAF**

Megan Mazzei, John O'Bryan, Imran Khan, Department of Pharmacology, College of Graduate Studies, MUSC

BREAK

11:10

9 **Protein Tyrosine Phosphatase Inhibition for Melanoma Therapy**

Amanda Manea, Haizhen Wang, Tiffany T. Penaloza, Xueliang Gao, Department of Cell and Molecular Pharmacology and Experimental Therapeutics, College of Medicine, MUSC

11:25

10 **Novel Gal-3 Macrophage Interactions in a Murine Presbycusis Model**

Rachel Eisenhart, Cynthia Wright, Department of Pathology and Laboratory Medicine, College of Graduate Studies, MUSC

11:40

11 **Motor Activated Auricular Vagus Nerve Stimulation (MAAVNS) Facilitates Upper Extremity Functional Recovery After Stroke**

Ellen Kitchens, Bashar Badran, Brenna Baker-Vogel, Kelly Rishe, Andrew Fortune, Scott Hutchinson, Christian Finetto, Gabrielle Walker, Steve Kautz, Mark S. George, College of Medicine, MUSC

11:55

12 **The Relationship Between LINE-1 and Inflammation in High Grade Serous Ovarian Cancer**

Savannah Stockton, Joseph Delaney, College of Graduate Studies, MUSC

Session 2 Clinical/Professional/Masters I POSTER

09:00

13 **RNAi regulation of virulence in the human oral pathogen Candida albicans**

Gurbir Malhi, Andrew Jakymiw, Evan Biles, Dong Phan, Janessa Montefalco, Caroline Westwater, Department of Oral Health Sciences, College of Dental Medicine, MUSC

09:15

14 **Inhibition of Sphingosine-1-Phosphate Receptor 2 by JTE013 Promoted Osteogenesis by Increasing Vesicle Trafficking, Wnt /Ca2+, and BMP/Smad Signaling**

Simon Lin, Hong Yu, Pandruvada Subramanya, Department of Oral Health Science, College of Dental Medicine, MUSC

09:30

15 **UTILITY OF DRIVE THRU HEALTH SCREENINGS WITH THE ONSET OF COVID-19**

Kasparas Zilinskas, Anita Ramsetty, Almeera Lateef, College of Medicine, MUSC

09:45

16 **Reduced antitumor immunity in colorectal cancer tissues of African Americans compared to Caucasian Americans**

Lauren Fanning, Kristin Wallace, Silvia Guglietta, Alexander Alekseyenko, Kent Armeson, Grant Brazeal, David Lewin, Alexandria Cousart, Department of Public Health Sciences, College of Health Professions, MUSC

BREAK

10:05

17 **The role of P-selectin and Complement in the Pathogenesis of Germinal Matrix Hemorrhage-Induced Secondary Injury in a Neonatal Model**

Devin Hatchell, Stephen Tomlinson, Mohammed Alshareef, Chunfang Guo, Aakash Shingala, Ramin Eskandari, Department of Microbiology and Immunology, College of Medicine, MUSC

10:20

18 **Adolescent Alcohol Use is Related to Alcohol Demand**

Helen Liu, Lindsay Squeglia, Anna Kirkland, Brittney Browning, Samuel Acuff, Cori Herring, Kevin Gray, Department of Psychiatry and Behavioral Science, College of Medicine, MUSC

10:35

19 **The impact of restoring insulin receptor endocytosis on brain insulin transport and cognitive impairment.**

Alexus Williams, Catrina Robinson, Luke Watson, Crystal Smith, Stephanie Dilucia, Department of Neuroscience/Neurology, College of Graduate Studies, MUSC

10:50

20 **Red Algae Extracts Containing Mycosporine-like Amino Acids (MAAs) may Treat Non-Healing Pathological Wounds**

Menny Benjamin, Russell Norris, Dr. Mark Hamann, Dr. Rupak Mukherjee, Dr. Amy Bradshaw, George Hanna, Department of Drug Discovery and Regenerative Medicine, College of Medicine, MUSC

BREAK

11:10
21 **Predictors of abstinent smoking status at 6-months after baseline tobacco treatment in Hollings Cancer Center patients**
Alexandria Cousart, Alexandria Cousart, Benjamin Toll, Kenneth Cummings, Amanda Palmer, Department of Public Health Sciences, College of Medicine, MUSC

11:25
22 **Attitudes Toward COVID-19 in South Carolina at Height of Pandemic**
Almeera Lateef, Mahsa Javid, Parker McDuffie, College of Medicine, MUSC

Session 3 Clinical/Professional/Masters II POSTER
09:00
23 **Getting Kids Moving: Identifying the Need for Increasing Inclusive Youth Physical Activity Resources**
Allison Farrell, Amanda Giles, Department of Occupational Therapy, College of Health Professions, MUSC

09:15
24 **The A.B.L.E. Program: A Specially Designed Adaptive Sports Program for Youth with Moderate to Severe Disabilities**
Sarah Grace Lindsey, Patty Coker-Bolt, PhD, OTR/L, FAOTA; Shelli Davis, MS, College of Health Professions, MUSC

09:30
25 **Preventing Pediatric Post-Intensive Care Syndrome: The New MUSC Sleep, Play, Heal Program**
Kaitlyn Schultz, Lindsay Davies, MS, OTR/L, Patty Coker-Bolt, PhD, OTR/L, FNAP, FAOTA, Department of Occupational Therapy, College of Health Professions, MUSC

09:45
26 **Supporting Families of Children with Cerebral Palsy: Parent Training Resources to Increase Compliance with Home Based Constraint-Induced Movement Therapy**
McRae Lawrence, Liz Humanitzki, MS, OTR/L, C/NDT, Patty Coker Bolt PhD OTR/L FAOTA, College of Health Professions, MUSC

BREAK

10:05

27 **Identifying the Need for Student Education on the Scope of Occupational Therapy in Addressing Sexuality and Intimacy**

Jennifer Barnett, Amanda Giles, Department of Occupational Therapy, College of Health Professions, MUSC

10:20

28 **Assessing the Impact of Learning Tools on Fieldwork Preparedness of Occupational Therapy Students**

Kirsten Temple, Amanda Giles, Department of Occupational Therapy, College of Health Professions, MUSC

10:35

29 **Effects of a Transfer Package on Upper-Extremity Use at Home for Stroke Patients**

Corinne Gillion, Na Jin Seo, Gabrielle Scronce, PT, PhD, Kristen Coupland, MS, OTR/L, Adam Baker, B.S., Viswanathan Ramakrishnan, PhD, Department of Rehabilitation Sciences, College of Health Professions, MUSC

10:50

30 **Social-emotional Services for Brain Injury Survivors Post Insurance Discharge**

Kelsey Reilly, Amanda Giles, Department of Occupational Therapy, College of Health Professions, MUSC

BREAK

11:10

31 **Exploring Health Care Students' Perceptions about Race and Privilege: A Case Study of a Peer Education Program**

Chinieka Jackman, Madison Kimmell, Kristina Stepanova, Amy Payne, Dante Pelzer, PhD, Elizabeth Brown, PhD, Department of Clinical Sciences, College of Medicine, MUSC

11:25

32 **Regional Socioeconomic Disadvantage is Associated with Attenuation of Amygdala Responsivity to Threat in a Community Sample of School-Aged Children**

Rachel Polcyn, Lisa McTeague, Ashley A. Huggins, Casey Calhoun, Curtisha Shacklewood, Alison Line, Laura Carpenter, Zachary Adams, Colleen Halliday-Boykins, Greg Hajcak, Jane Joseph, Carla Kmett Danielson, Department of Psychiatry & Behavioral Sciences, College of Medicine, MUSC

Session 4 Clinical/Professional/Masters III POSTERr

09:00
33 **WITHDRAWN**

09:15
34 **Cellular Viability of Partial Heart Transplant Grafts in Cold Storage**
Morgan Hill, Taufiek Rajab, Jennie H. Kwon, Brielle Jerry, Jordan Morningstar, Minoo N. Kavarana, Satish N. Nadig, Department of Surgery, College of Medicine, MUSC

09:30
35 **Creating an Evidence-Based High-Fidelity Simulation Crisis Scenario for the Anesthesia Provider**
Shannon McDermott, BSN, RN, Michele Ballister, DNP, APRN, CRNA, CHSE, Monica Karlen, BSN, RN, Chloe Urig, BSN, RN, Lester Kitten, MHS, CRNA, Joey Seymour, MSN, CRNA, Lisa Rogers, DNAP, APRN, CRNA, Anesthesia for Nurses, College of Health Professions, MUSC

09:45
36 **CD8+ T-cells Recruit Macrophages Following a Myocardial Infarction**
Gualberto Munoz, Kristine Deleon-Pennell, Hallie Roerden, Penny Huebsch, Department of Cardiology, College of Medicine, MUSC

BREAK
10:05
37 **Quality Improvement Study in Patients with Epilepsy treated with Epidiolex®: Retention Rate and Barriers to Patient Compliance**
Chanbormey Leatheng, Karla A. Mora Rodriguez, Sonal Bhatia, Leah Horstemeyer Cobb, Gustavo Carmen-Lopez, Ekrem Kutluay, Department of Neurology, College of Medicine, MUSC

10:20
38 **Physiological effects of histamine 2 receptor inhibition in salt sensitive hypertension**
Samantha Perez, Daria Ilatovskaya, Mark Domondon, Callie Clarke, Ryan Schibalski, Thelma Amoah, Denisha Spires, College of Medicine, MUSC

10:35
39 **Growth of the gender dysphoric transgender population in the MUSC Pediatric Endocrinology Clinic**
Thomas Agostini, Deborah Bowlby, Terry Headley, College of Medicine, MUSC

10:50
40 **Anesthetic Management of Post-Thoracotomy Pain Syndrome**
Courtney Williams, Angela Mund, Department of Anesthesia for Nurses, College of Health Professions, MUSC

BREAK

11:10
41 **Substance Use Disorder Education and its Effect on Stigma in the CRNA Population**
Michael Martz, Angela Mund, Department of Anesthesia for Nurses, College of Health Professions, MUSC

11:25
42 **Concomitant Spinal Deformities in Patients with Congenital Heart Defects**
Ngozi Ogburu-Ogbonnaya Ogburu-Ogbonnaya, Liz L. Boyle, DRr. William R. Barfield, Dr. John Costello, Dr. Robert F. Murphy, Departments of Cardiology and Orthopedics, College of Medicine, MUSC

11:40
43 **Factors Contributing to Prolonged Ventilation in Blunt Chest Trauma and Minimal Brain Injury**
Danielle Lefebvre, Evert Eriksson, William B DeVoe MD, College of Medicine, MUSC

Session 5 Clinical/Professional/Masters IV POSTER

09:00
44 **Varying Metatarsophalangeal Arthrodesis Outcomes Between Hallux Valgus and Hallux Rigidus Cohorts**
Warren Roth, Daniel Scott, Caroline Hoch, Christopher Gross, College of Medicine, MUSC

09:15
45 **Pediatric Firearm Injury Mortality Epidemiology**
Xzavier Killings, Annie Andrews, Elizabeth Oddo, Kelsey Gastineau, Ashley Hink, College of Medicine, MUSC

09:30
46 **Analysis of Author Gender in the Pediatric Orthopaedic Literature from 2011-2020**
Anjali Prior, Robert Murphy, Ngozi Ogburu-Ogbonnaya BA MS, William R. Barfield PhD, James F. Mooney III MD, Sara Van Nortwick MD, College of Medicine, MUSC
09:45
47 **Investigating the mechanisms underlying secondary injury following germinal matrix hemorrhage**
Aakash Shingala, Stephen Tomlinson, Mohammed Alshareef, Rosy Guo, Devin Hatchell, Ramin Eskandari, College of Medicine, MUSC

BREAK

10:05
48 **Feasibility of resource-limited 3D imaging of the esophagus in cadaveric specimens**
Jason Erno, Steven Kubalak, Joe Carson, College of Medicine, MUSC

10:20
49 **Identification of facilitators and barriers to cochlear implant uptake in adult candidates**
Gabriel Brandner, Theodore McRackan, Cheng Ma, David Aamodt, Judy Dubno, College of Medicine, MUSC

10:35
50 **Autoantibodies Unique to Lupus Nephritis**
Ansley DeVore, Jim Oates, Rachael Werner, College of Medicine, MUSC

10:50
51 **The Effect of Acetaminophen on Delirium Outcomes in Cardiovascular Surgical Intensive Care Unit patients: A Retrospective Chart Review**
Kaitlyn Monahan, Kaitlyn Monahan, College of Health Professions,-DNAP AFN, MUSC

BREAK

11:10
52 **Stress Among Student Registered Nurse Anesthetists and Its Impact on Wellness**
Esther Odeghe, Esther Odeghe, Dr. Ballister Michelle, College of Health Professions, AFN, MUSC

11:25
53 **Interpreting the Mini-Cog: A postoperative cognitive dysfunction screening tool**
Alyssa Farber, College of Health Professions, MUSC

Session 6 Clinical/Professional/Masters V POSTER

09:00
54 **Current Adhesion Barriers in Cardiac Surgery: An Assessment of Safety and Efficacy**
William Head, Taufiek Rajab, Namrata Paladugu, Hyejin Kwon, Department of Surgery, College of Medicine MUSC

09:15
55 **The COVID-19 Vaccine Outreach Initiative: A Student's Response to Vaccine Hesitancy**
India Robinson, Danielle Scheurer, Alan Snyder, MD, MSCR; Lancer Scott, MD; Dirk Elston, MD; Leslie Lenert, MD, Department of Dermatology, College of Medicine, MUSC

09:30
56 **Variability and Reliability of 2 Dimensional Versus 3 Dimensional Glenoid Version Measurements with 3 Dimensional Preoperative Planning Software**
Jared Reid, Richard Friedman, Bryce Kunkle, Alexander Greene, Josef Eichinger, Department of Orthopaedics, College of Medicine, MUSC

09:45
57 **Characterizing Retinal Dystrophy in South Carolina**
Joseph Griffith, Mae Millicent Winfrey Peterseim, Kareem Sioufi, George Magrath, Michael Lyons, College of Medicine, MUSC

BREAK

10:05
58 **SHP2-dependent Signaling Pathways Programming the Oral Cancer Cell Secretome**
Merrell Still, Subramanya Pandruvada, Jack Goertzen, Nico Farrar, Brad Neville, Besim Ogretmen, Department of Oral Health Sciences, College of Dental Medicine, MUSC

10:20
59 **Treating Congenital Cutaneous Candidiasis in a Preterm Infant**
Chelsea Shope, Lara Wine Lee, Samantha Karlin, Alexandra Ritter, Colleen Cotton, College of Medicine, MUSC

10:35
60 **Acute Onset Esotropia with Increased Screen Time: a case series**
Jared Tallo, Edward Cheeseman, Anastasia Alex, MD, Mae Millicent Peterseim, MD, James Bowsher, MD, College of Medicine, MUSC

10:50
61 **Evaluating the Role of IFNLR1 Receptor Dynamics and Plasticity in Regulating Cellular Response to Interferons**
John Evans, Eric Meissner, Laura Novotny, College of Medicine, MUSC

BREAK

11:10
62 **Identifying Quality Improvement Opportunities in Efforts to Reduce Racial and Ethnic Disparities that Persist Among the Management of Anemia in Pregnancy**
Latyra Gibbs, College of Medicine, MUSC

11:25
63 **Validation of a Highly Accelerated Flow Technique for the Simultaneous Evaluation of Flow in the True and False Lumens in Thoracic Aortic Dissection**
Gabrielle Young, Akos Varga-Szemes, Tilman Emrich, MD U. Joseph Schoepf, MD Fei Xiong Akos Varga-Szemes, MD PhD, College of Medicine, MUSC

11:40
64 **Chronic Kidney Disease and in-hospital outcomes among patients treated with thrombolysis for acute ischemic stroke**
Henry Best, Erin Weeda, Dr. Erin Weeda Shayma Al Zaidi, College of Pharmacy, MUSC

Session 7 PhD I POSTER

09:00
65 **Sex divergent effects of lofexidine on heroin seeking in male and female rodents**
Jordan Carter, Carmela Reichel, Angela Kearns, Michael Kong, Department of Neuroscience, College of Graduate Studies (MSTP), MUSC

09:15
66 **Heat Shock Protein 27 is an Important Early Regulator and Platform Molecule in P. gingivalis-Driven Selective Autophagy**
Bridgette Wellslager, Özlem Yilmaz, Nityananda Chowdhury, Department of Oral Health Sciences, College of Graduate Studies, MUSC

09:30
67 **The importance of hand function for stroke survivors' quality of life**
Corey Morrow, Kit Simpson, Michelle Woodbury, Department of Health Sciences and Research, College of Health Professions, MUSC

09:45
68 **Cadherin complexes recruit PIWIL2 to suppress transposons and pro-tumorigenic transformation**
Alyssa Risner, Antonis Kourtidis, Joyce Nair-Menon, Colin McDowell, Vamsi Gangaraju, Department of Regenerative Medicine and Cell Biology, College of Graduate Studies, MUSC

BREAK

10:05
69 **Kv3 channel positive modulation decreases ethanol binge drinking**
Kathy Lindquist, Patrick Mulholland, Reginald Cannady, Jennifer A. Rinker, Department of Neuroscience, College of Graduate Studies, MUSC

10:20
70 **Exploring the Impact of Advanced Glycation End Products on Macrophages Polarization in the Mouse Mammary Gland**
Kendell Peterson, Victoria Findlay, Bradley A Krisanits, Lourdes M Nogueira, David P Turner, Department of Molecular and Cellular Biology and Pathobiology, College of Graduate Studies, MUSC

10:35
71 **Proteasome-mediated protein catabolism fuels antitumor immunity**
Megan Tennant, Jessica Thaxton, Katie Hurst, Brian Riesenberg, Alex Andrews, Lee Leddy, David Neskey, Guillermo Rangel Rivera, Chrystal Paulos, Elizabeth Hill, Peng Gao, Lauren Ball, Department of Microbiology and Immunology, College of Graduate Studies, MUSC

10:50
72 **GABA Concentrations in the Anterior Cingulate Cortex are Associated with Impulsivity Scores in Adolescent Heavy Drinkers: A 1H-magnetic Resonance Spectroscopy Study**
Brittney Browning, Lindsay Squeglia, Anna Kirkland, Helen Liu, Cori Herring, Department of Neuroscience, College of Graduate Studies, MUSC

BREAK

11:10
73 **Gene and Environmental Interaction for the Pathogenesis of Cardiac Alzheimer's**
Helen Butler, Federica del Monte, Marice McCrorey, Stephanie Dilucia, Gianlorenzo Daniele, Amy Mackos, Loren Wold, Department of Cardiology (MCBP), College of Medicine and Graduate Studies, MUSC

11:25
74 **Determining the Role of Skeletal Muscle Ceramides in the Pathology of Cancer Cachexia**
Victoria Spadafora, Denis Guttridge, Erin Talbert, Besim Ogretmen, Natalia Oleinik, Department of Biochemistry, College of Graduate Studies (MSTP), MUSC

Session 8 PhD II POSTER

09:00

75 **Role of Porphyromonas gingivalis in mediating ceramide-dependent mitophagy in oral squamous cell carcinoma**

Megan Sheridan, Besim Ogretmen, Nityananda Chowdhury, Han Lee, Zdzislaw Szulc, Mohamed Kassir, Subramanya Pandruvada, Özlem Yilmaz, Department of Biochemistry and Molecular Biology, College of Graduate Studies, MUSC

09:15

76 **Inhibition of ferroptosis using UAMC-3203 in the post stroke period does not impact cognitive outcomes in diabetic rats**

Mia Edgerton, AdviyeErgul, Ashley Phoenix, Raghavendar Chandran, Victoria Wolf, Yasir Abdul, Sarah Jamil, Weiguo Li, and Adviye Ergul, Department of Pathology and Laboratory Medicine, College of Graduate Studies, MUSC

09:30

77 **Understanding the role of the insulin receptor during transport and signaling in post stroke cognitive impairment.**

Crystal Smith, Catrina Robinson, Department of Neurology, College of Graduate Studies, MUSC

09:45

78 **Identifying aMCI network models of cognitive domains via functional connectomics**

Duncan Nowling, Jane Joseph, Graham Warner, Nicholas Bustos, Katherine Barlis, College of Neuroscience, College of Graduate Studies, MUSC

BREAK

10:05

79 **Severe Post-Stroke Gait Impairments: Rancho Los Amigos Observational Gait Analysis vs. Quantitative Analyses**

Jasmine Cash, Mark Bowden, John Kindred, Department of Health Sciences and Research, College of Health Professions, MUSC

10:20

80 **Drinking Frequency Modulates Functional Brain Activity in Chronic Alcohol Abusers During 2-Back Spatial Working-Memory Task**

Graham Warner, Jane Joseph, Flanagan J, Benitez A, Barlis K, Richardson J, Stomberg-Firestein, Bustos N, Lawson A, College of Graduate Studies, MUSC

10:35
81 **Regulatable complement inhibition of the alternative pathway mitigates age-related macular degeneration pathology in a mouse model**
Nathaniel Parsons, Bärbel Rohrer, Department of Ophthalmology, College of Graduate Studies, MUSC

10:50
82 **The effects of COVID-19 on the Medical University of South Carolina's Presidential Scholars Program**
Parker Rhoden, Parker Rhoden, Dustin Mueller, Grant Brazeal, Kristin Wallace, Jillian B. Harvey, Department of Healthcare Leadership and Management, College of Health Professions, MUSC

BREAK

11:10
83 **Considerations in the Use of the Presenilin-2 Haploinsufficient Murine Model**
Stephanie DiLucia, Federica del Monte, Sophia Emetu, Kennedy Simmons, Catrina Sims-Robinson, Department of Cardiology, College of Medicine and Graduate Studies (MSTP), MUSC

11:25
84 **Catalytic Modulation of Receptor Protein Tyrosine Phosphatases by the Inactive D2 Domain**
Colin Welsh, Lalima Ahuja, Preeti Pandey, Department of Pharmacology, College of Graduate Studies, MUSC

Session 9 Postdoc/Resident/Fellow/Staff Scientist POSTER

09:00
85 **Effect of Self-Directed Home Therapy Adherence combined with TheraBracelet on Post-Stroke Hand Recovery**
Gabrielle Scronce, Na Jin Seo, Viswanathan Ramakrishnan, Amanda Vatinno, Corey Morrow, Allison Pennington, Department of Health Sciences and Research, College of Health Professions, MUSC

09:15
86 **The Impact of Intranasal Administration of BDNF on Functional Recovery in a Neonatal Mouse Model of Hypoxic Ischemia**
Serena-Kaye Sims, Catrina Robinson, Taylor Lowry, Lilly McGonegal, Madelynne Saddow, Department of Neurology, College of Medicine, MUSC

09:30
87 **ISMN and Cilostazol Treatment Prevents Temporal Changes in the Brain Microstructure of Diabetic Rats following Microemboli Injection: Relevance to Vascular Cognitive Impairment and Dementia (VCID)**
Raghavendar Chandran, Adviye Ergul, Weiguo Li, Xingju Nie, Joshua Voltin, Lianying He, Sarah Jamil, Maria Fatima Falangola, Department of Pathology and Laboratory Medicine, College of Medicine, MUSC

09:45
88 **Linking Structural and Functional Connectivity for Upper Extremity Motor Recovery after Stroke**
Adam Baker, Na Jin Seo, Christian Schranz, Ph.D., Janina Wilmskoetter, Ph.D., Jens Jensen, Ph.D., Department of Health Sciences and Research, College of Health Professions, MUSC

BREAK

10:05
89 **Can Transcutaneous Auricular Vagus Nerve Stimulation (taVNS) Attenuate Increases in Heart Rate Associated with the Cold Pressor Test?**
Christopher Austelle, Mark George, Christopher T. Sege, Danielle L. Taylor, Lisa M. McTeague, E. Baron Short, Bashar W. Badran, Department of Psychiatry, College of Medicine (MD, PhD), MUSC

10:20
90 **3D Mandibular Kinematic Analysis of the Temporomandibular Joint**
Cherice Hill, Hai Yao, Feng Wei, Shuchun Sun, Nadine Almpani, Marshall Wilson, Brooke Damon, Michael Lecholop, Martin Steed, Janice Lee, Clemson-MUSC Bioengineering Program, Department of Oral Health Sciences, College of Dental Medicine, MUSC

10:35
91 **Immune response modulation in post myocardial infarction**
Toolika Singh, Donald Menick, Tajinder Dhammu, Miller W. Shealy, Rajendran JC Bose, Jason R. McCarthy, College of Medicine, MUSC

10:50
92 **Central Amygdala Dynorphinergic Neuron Activity in a Mouse Model of Voluntary Alcohol Drinking**
Christina Lebonville, Patrick Mulholland, Harold Haun, William Griffin, Jennifer Rinker, Howard Becker, Department of Psychiatry and Neuroscience, College of Medicine, MUSC

BREAK

11:10
93 **Novel P-selectin targeted complement inhibitors reduce limb injury following ischemia/reperfusion and vascularized composite graft transplantation**
Chaowen Zheng, Stephen Tomlminson, Jerec Ricci, Qinqin Zhang, Satish Nadig, Pablo Engel, Junfei-Jin, Carl Atkinson, Department of Microbiology and Immunology, College of Medicine, MUSC

11:25
94 **Impact of IFNLR1 expression and engagement with lambda interferons on hepatitis B infection**
Laura Novotny, Eric Meissner, Gray Evans, Sarah Stephenson, Department of Infectious Diseases, College of Medicine, MUSC

11:40
95 **All the Risk, None of the Reward: An Analysis of the Reward Response in Depressed Youth**
Robert James, Carla Danielson, Christopher Sege, Greg Hajcak, Lisa McTeague, Department of Psychiatry and Behavioral Sciences, Medicine (MD, PhD), MUSC

Session 10 Research Specialist/Technician POSTER

09:00
96 **Examining the association between pre-adolescent mental health and caffeine consumption in the Adolescent Brain and Cognitive Development (ABCD) Study**
Dominique Black, Squeglia Lindsay, John Redhead, B.S., & Alexis Garcia, Ph.D, Department of Addiction Sciences, College of Medicine (MD, PhD), MUSC

09:15
97 **Oral bacteria Porphyromonas gingivalis spreads intercellularly through gingival epithelium using ER autophagic vesicles**
Ayana Paul, Ozlem Yilmaz, Bridgette Wellslager, Department of Oral Health Sciences, College of Graduate Studies, MUSC

09:30
98 **Molecular Choreography of Vaccinia Virus Genome Encapsidation**
Esteban Castro, Paula Traktman, Matthew Greseth, Paula Traktman, Department of Biochemistry and Molecular Biology, College of Graduate Studies, MUSC

09:45
99 **Subcellular Targeting of Induced CYP2E1 in the Brain During Alcohol Use**
Hyland Gonzalez, Jessica Hartman, Baylee Westbury, Patrick Mulholland, College of Graduate Studies, MUSC

BREAK

10:05
100 **In Vivo Two-Photon Imaging of Prelimbic Cortex during Alcohol Seeking in Mice**
Kion Winston, Jim Otis, Jen Rinker, Department of Neuroscience, College of Graduate Studies, MUSC

10:20
101 **Accelerated rTMS for Cognitive Rehabilitation in Chronic Stroke: A Safety and Feasibility Study**
Bridgette Holland, Lisa McTeague, Holly H. Fleischmann, James W. Lopez, Kevin A. Caulfield, Stephanie Fountain-Zeragoza, Michael U. Antonucci, Andreana Benitez, Mark S. George, Department of Psychiatry & Behavioral Sciences, College of Medicine, MUSC

10:35
102 **Low nutrient availability drives increased macropinocytosis and MEK inhibitor resistance in KRASG12R-mutant Pancreatic Ductal Adenocarcinoma**
Amanda Linke, Aaron Hobbs, Rachel Burge, Department of Pharmacology, College of Graduate Studies, MUSC

10:50
103 **Understanding the Role of microRNA-204 in Driving Neuroendocrine Differentiation During Prostate Cancer Progression**
Deavian Harvin, Victoria Findlay, Pathology and Laboratory Medicine, Graduate Studies, MUSC

BREAK FOR LUNCH

Session 11 Clinical/Professional/MastersI ORAL

01:00
104 **Midfoot Charcot Deformity Correction is Well Maintained with Beam Fixation**
Alexander Guareschi, Christopher Gross, Andrew Moore, Caroline Hoch, J. Brett Goodloe, Daniel Scott, College of Medicine, MUSC

01:15
105 **Risks of Preoperative Opioid Therapy on Forefoot and Hindfoot Surgery Success**
Kevin Shrake, Christopher Gross, William Newton, BS; Caroline Hoch, BS; Daniel Scott, MD, MBA, College of Medicine, MUSC

01:30
106 **Predicting Vitamin D Status: Post-hoc Analysis of Traditional Biochemical Safety Measurements in Infants Less than Seven Months**
Grace Pouch, Carol Wagner, Authors: Myla Ebeling (2), Judy R. Shary (2), Bruce W. Hollis PhD (2), Cynthia R. Howard MD (3) Affiliations: (2) Division of Neonatology, Department of Pediatrics, Shawn Jenkins Children's Hospital, Charleston, SC 29425 (3) Department of Pediatrics, University of Rochester, Rochester, NY 14620 ,

01:45
107 **A novel Thioredoxin protein of Porphyromonas gingivalis is important for intracellular survival in human gingival epithelial cells**
Danielle Vines, Özlem Yilmaz, Kayla Anderson, Casey Derieux, Bridgette Wellslager, Nityananda Chowdhury, Department of Oral Health Sciences, College of Dental Medicine, MUSC

BREAK

02:10
108 **The Role of Complement C3a/C3aR in Commensal Gut Microbiota Actions on Osteoclastogenesis**
Hayden VandenBerg, Chad Novince, Megan B. Kuhn, Amy J. Warner, Matthew D. Carson, Jessica D. Hathaway-Schrader, Chad M. Novince, College of Dental Medicine, MUSC

02:25
109 **Optimizing Glioblastoma Mouse Models to Provide an Accurate Framework for Differentiating Tumor Recurrence, Acute Radiation Necrosis, and Chronic Radiation Necrosis with Diffusion Kurtosis Imaging**
Connor Stephenson, Arabinda Das, Scott M. Lindhorst M.D Arunprasad Gunasekaran M.D. Milad Yazdani M.D Daniel G. McDonald MS Libby Kosnik Infinger MD, MPH Abhay K. Varma M.D. William A. Vandergrift III M.D. Sunil J. Patel M.D. Pierre Giglio, M.D. David Cachia M.D., College of Medicine, MUSC

02:40
110 **Subdural Evacuation Port System and Middle Meningeal Artery Embolization for the Treatment of Chronic Subdural Hematoma: A Single Center Experience**
Craig Salvador, Alejandro Spiotta, Brian Saway, Warren Roth, Guilherme Porto, College of Medicine, MUSC

BREAK

03:05

111 **Addressing Racial Disparities in Hypertension Control through Implementation of a Telephone-Based Outreach Intervention at a Federally Qualified Health Center**

Rohith Raman, Bradi Granger, Holly Biola, Melanie Bakovic, Tiffany Hayes, Colette Whitney, Dominique Bulgin, Yunah Kang, Cameron Eck, L'Tanya Gilchrist, Awanya Caesar, Joan Chaplin, College of Medicine, MUSC

03:20

112 **Hyperemesis Gravidarum induced Wernicke's Encephalopathy: An Unusual Presentation of Altered Mental Status**

Caroline Brailsford, Caroline Brailsford, Dr. Jordan M. Spencer DO, Sophia S. Urban, MD, MPH, George Book, MD, College of Medicine, MUSC

113 **WITHDRAWN**

03:35

114 **Collagen Hydroxyproline Analysis of Colon Cancer Polyps in Patients within the Appalachian Mountain Region.**

Alexander Sougiannis, Peggi Angel, College of Medicine, MUSC

Session 12 Clinical/Professional/Masters II ORAL

01:00

115 **Helping Infants with Congenital Heart Defects: Enhancing Parent and Therapist Engagement Through Infant Massage**

Catherine Flynn, Catherine Flynn, Courtney Jarrard, OTR/L, C/NDT, Patty Coker-Bolt, PhD, OTR/L, FAOTA, Department of Occupational Therapy, College of Health Professions, MUSC

01:15

116 **How to Address Challenges with Early Intervention for Infants of Underrepresented Families: Helping the Babies at MUSC High Risk Clinic**

Daijah Washington, Daijah Washington, Amy Ruddy-Humphries CNP, Dr.Patricia Coker-Bolt PhD, OTR/L, FNAP, FAOTA, Department of Occupational Therapy, College of Health Professions, MUSC

01:30

117 **Coming Home: Improving Post-Adoption Adjustment for Families at the MUSC International Adoption Clinic**

Brittany Randall, Brittany Randall, Patty Coker-Bolt PhD, OTR/L, FNAP, FAOTA, Angela LaRosa M.D. MSCR, Shannon Hemberger MOT, OTR/L, CSRS, College of Health Professions, MUSC

01:45
118 **Effects of Dry Needling on Spinal Reciprocal Inhibition**
Anna Zuloaga, Gretchen Seif, Alan Phipps, Anna Zuloaga, Rachel (Abby) McLaughlin, Blair Dellenbach, and Aiko Thompson, Department of Physical Therapy, College of Health Professions, MUSC

BREAK

02:10
119 **Clinical and Radiographic Outcomes Following Reverse Total Shoulder Arthroplasty in Patients 60 Years of Age and Younger**
Garrett Neel, Richard Friedman, Marissa Boettcher, Josef Eichinger, College of Medicine, MUSC

02:25
120 **Quality of Care in US Critical Access Hospitals: A Systematic Review**
Olivia Reszczynski, Paula Chatterjee, College of Medicine, MUSC

02:40
121 **Electrical Stimulation of the Trigeminal Nerve Improves Olfactory Sensitivity in Healthy Individuals: A Randomized, Sham-Controlled Trial**
Elise Gruber, Bashar Badran, Georgia O'Leary, Chris W. Austelle, Sarah Huffman, Alex Kahn, Lisa McTeague, Thomas Uhde, and Bernadette Cortese, Department of Psychiatry, College of Medicine, MUSC

BREAK

03:05
122 **An Exploration of Curricular Needs for Entry Level Occupational Therapy Doctoral Students to Increase Cultural Responsiveness and Communication with Clients from Diverse and Underserved Communities**
Nikki Kardouni, Cristina Smith Reyes, Department of Occupational Therapy, College of Graduate Studies, MUSC

03:20
123 **Carbohydrate-Binding Protein Galectin-3 and its Role in Age-Related Hearing Loss**
Blake Howard, Hainan Lang, College of Medicine, MUSC

03:35
124 **Adverse outcomes comprehensively worse among children and transition-aged youth with comorbid Autism Spectrum Disorder (ASD) and Disruptive Behavior Disorders (DBD) across lifespan**
Nicole Vonada, Andrea Boan, Catherine C Bradley, PhD; Rosmary Ros-Demarize PhD, Laura A Carpenter, PhD, College of Medicine, MUSC

Session 13 Clinical/Professional/Masters III ORAL

01:00

125 **Impact of gestational age on glucose tolerance test and risk of fetal overgrowth**

Haley Hopkinson, Matthew Finneran, Ralitza Peneva, Ryan Cuff, Department of OB/GYN, College of Medicine, MUSC

01:15

126

Verbal Autopsy: A systematic literature review for data acquisition methods to determine under-5-mortality and causes of death in low resource settings

Stiles Harper, Tram Jones, Dr. Nancy Hagood, MD, Department of Global Health, College of Medicine, MUSC

01:30

127 **Diversity in the Pediatric Heart Transplant Surgeon Workforce Between 2000 and 2020**

Olivia Walkowiak, Taufiek Rajab, William Hardy, Lauren V. Huckaby, Morgan Hill, Suyog Mokashi M.D., Minoo N. Kavarana M.D., College of Medicine, Department of Surgery, College of Medicine, MUSC

01:45

128 **The Role of Prostaglandin E2 in PD-1 Expression on THP-1-derived Macrophages and Mouse CD8+ T-cells**

David Wilson, Raymond DuBois, Dingzhi Wang, Jie Wei, and Bo Cen, College of Medicine, MUSC

BREAK

02:10

129 **Single incision latissimus dorsi surgical technique: a three button repair**

John Pike, Josef Eichinger, Brett Goodloe, Kirsi Oldenburg, College of Medicine, MUSC

02:25

130 **Provider Perception of Risk as a Barrier to Implementation of a High-Sensitivity Troponin Accelerated Diagnostic Protocol**

John Hall, Andrew Matuskowitz, MD, Mathew Gregoski, PhD, Steven Saef, MD, College of Medicine, MUSC

02:40

131 **Cost Analysis of Procedure Delays in the MUSC Vascular/Interventional Radiology Department among Floor and ICU Patients for December 2020**

Nathan Leaphart, Marcelo Guimaraes, Kirkpatrick Gillen, Matthew Bridges, Anand Mulji, Kelsey Duckett, Department of Vascular/Interventional Radiology, College of Medicine, MUSC

BREAK

03:05

132 **Is There a Psychiatric Diagnosis in Chronic Ankle Instability Patients?**

John Allen, Christopher Gross, Caroline Hoch, Daniel Scott, Christopher Gross, Department of Orthopedics, College of Medicine, MUSC

03:20

133 **Factors associated with caregiver adherence to mobile health interstage home monitoring in infants with single ventricle heart disease**

Sydney Reed, Sinai Zyblewski, Shahryar Chowdhury, Frances Woodard, College of Medicine, MUSC

03:35

134 **COVID-19 Modifications of Offseason and Preseason Training for NFL Athletes Are Associated with Increased Risk of Regular Season Injuries**

Evan Bailey, Harris Slone, J. Brett Goodloe, College of Medicine, MUSC

Session 14 Clinical/Professional/Masters IV ORAL

01:00

135 **Effects of body positioning on laryngeal penetration and aspiration in children with unilateral vocal cord paralysis.**

Neil Monaghan, Clarice Clemmens, Heather McGhee, Erick Yuen, Shaun Nguyen, College of Medicine, MUSC

01:15

136 **The Impact of Changes in Renal Function During Waitlist Time on Outcomes after Heart Transplantation**

Paul Brocklebank, Arman Kilic, Jennie H. Kwon, MD, Z. A. Hashmi, MD, Chakradhari Inampudi, MBBS, Brian A. Houston, MD, Lucas J. Witer, MD, Ryan J. Tedford, MD, College of Medicine, MUSC

01:30

137 **Fall Prevention Deserves Your Attention: Analysis of MUSC In-Patient Fall Events in 2020 with Emphasis on Drug Interventions**

Bethany Burnette, Nicole Pilch, Michael Duong, Shelby Kolo, College of Pharmacy, MUSC

138 **WITHDRAWN**

01:45
139 **Effects of Dry Needling on Spinal Reflexes**
Rachel McLaughlin, Gretchen Seif, Alan Phipps, Anna Zuloaga, Blair Dellenbach, and Aiko Thompson, College of Health Professions, MUSC

BREAK

02:10
140 **Post-hemorrhagic Hydrocephalus and Ventricular Tapping: Weaning Protocols and Factors Affecting Success**
Christopher Litts, Thomas Larrew, MD, Pearce Jackson, Tyler Vasas, Mohammed Alshareef, MD, Libby Infinger, MD, MPH, Ramin Eskandari, MD, MS, College of Medicine, MUSC

02:25
141 **Step 1 is Pass/Fail, Now What? Can clinical clerkship grades be used as a reliable metric to screen General Surgery residency applicants?**
Laura Campbell, Christian Streck, Kristen Quinn, Laura Campbell, Andrea Abbott, College of Medicine, MUSC

02:40
142 **Resilience culture in healthcare teams during COVID-19**
John Ambrose, John Ambrose, Diana M. Layne, Ken Catchpole, Heather Evans, and Lynne S. Nemeth, College of Nursing, MUSC

BREAK

03:05
143 **Effect of Preexisting Hypertension on Pregnancy Outcomes among Women with Systemic Lupus Erythematosus (SLE)**
Azalfa Lateef, Diane Kamen, Dulaney Wilson, Jim Oates, Gary Gilkeson, College of Medicine, MUSC

03:20
144 **Complement peptide C3a interacts with Candida cell wall components to mediate antifungal activity**
Janessa Montefalco, Caroline Westwater, Silvia Vaena, Jessica Dinh, Department of Oral Health Sciences, College of Dental Medicine, MUSC

Session 15 Clinical/Professional/Masters V ORAL

01:00

145 **Tranexamic Acid Associated with Less Wound Complications in Hindfoot Surgery**

Andrew Moore, Daniel Scott, Ryan O'Leary, Benjamin Smith, Caroline Hoch, Christopher Gross, Department of Orthopaedics, College of Medicine, MUSC

01:15

146 **Preventing central venous catheter (CVC) associated venous thromboemboli (VTE) among pediatric patients**

Ingrid Bonilla, Elizabeth Mack, Stephanie Santana, Riley Dunnam, Corinne Corrigan, Department of Pediatrics, College of Medicine (MD, PhD), MUSC

01:30

147 **Host-adaptive Porphyromonas gingivalis targets pro-inflammatory Interleukin-6 trans-signaling in epithelial cells**

Jaden Lee, Ozlem Yilmaz, Nityananda Chowdhury, College of Dental Medicine (DMD, PhD), MUSC

01:45

148 **CD26 defines responsiveness to neoadjuvant checkpoint blockade**

Hannah Knochelmann, David Neskey, Amalia Rivera-Reyes, Joshua Horton, Michael Bobian, Megan Wyatt, Carsten Krieg, Kent Armeson, Mark Rubinstein, Chrystal Paulos, Department of Microbiology & Immunology, College of Medicine (MD, PhD), MUSC

BREAK

02:10

149 **Association between nailfold capillaroscopy abnormalities and autoimmune disease in pediatric populations**

Andraia Li, Lara Wine Lee, Connor Burke, Colby Purvis, Department of Dermatology & Dermatological Surgery, College of Medicine, MUSC

02:25

150 **Enhancing the efficacy and safety of a human complement inhibitor for treating post-transplant cardiac ischemia reperfusion injury by targeting to a graft-specific neoepitope**

Mohamad Mahdi Sleiman, Stephen Tomlinson, Chaowen Zheng, Xiaofeng Yang, Songqing He, Carl Atkinson, Department of Microbiology and Immunology, College of Medicine (MD, PhD), MUSC

02:40

151 **The Role of Complement in Propagating Neuroinflammation in Chronic Traumatic Brain Injury - A Transcriptomic Analysis**

Amer Toutonji, Stephen Tomlinson, Mamatha Mandava, Silvia Guglietta, College of Medicine(MD, PhD), MUSC

BREAK

03:05

152 **ADAMTS5 is Required for Subchondral Bone Formation in the Mandibular Condyle**

Alexandra Rogers-DeCotes, Christine Kern, Sarah E. Porto, College of Dental Medicine (DMD, PhD), MUSC

03:20

153 **Rib Construct for Early-onset Spinal Deformity (EOSD)**

Daniel Bonthius, Hai Yao, Richard Gross, MCBP, College of Graduate Studies (MSTP), MUSC

03:35

154 **Risk Prediction By Quantitative Analysis Of Pre-Procedural CTA Provides Superior Prediction Of Mortality Compared To Conventional Risk Scores In Transcatheter Aortic Valve Replacement**

Franco Godoy, Uwe Schoepf, Tilman Emrich, Gilberto Aquino, Josua Decker, Moritz Halfmann, Landin Carson, Akos Varga-Szemes, Department of Radiology and Radiological Science, College of Medicine, MUSC

Session 16 PhD I ORAL

01:00

155 **RIDD is required for the prevention of chronic GVHD by targeting IRE-1α/XBP-1s signaling**

Hee-Jin Choi, Xue-Zhong Yu, Chih-Hang Anthony Tang, Linlu Tian, Yongxia Wu, M. Hanief Sofi, Taylor Ticer, Steven D. Schutt, Chih-Chi Andrew Hu, Department of Microbiology and Immunology, College of Medicine (MD, PhD), MUSC

01:15

156 **Antibiotic Disruption of the Gut-Liver-Bile Acid Axis Impairs Late Skeletal Maturation through Suppressed Osteoblastogenesis**

Matthew Carson, Chad Novince, Amy Warner, Jessica Hathaway-Schrader, Brooks Swanson, Joy Kirkpatrick, Dmitry Kondrikov, William Hill, John Lemasters, Alexander Alekseyenko, Yongren Wu, Hai Yao, Jose Aguirre, Caroline Westwater, Department of Oral Health Sciences, College of Graduate Studies, MUSC

01:30
157 **Sex differences in CD8+ T-cells in Response to Male DAMPs.**
Alexa Corker, Kristine Deleon-Pennell, Philip Broughton, Kimberly Oviedo, Department of Cardiology, College of Graduate Studies, MUSC

01:45
158 **Essential role for the neurodevelopmental disorder-linked gene, MEF2C, in inhibitory neuron function and neurotypical behaviors**
Yongjoo Cho, Christopher Cowan, Ahlem Assali, Evgeny Tsvetkov, Department of Neuroscience, College of Graduate Studies (MSTP), MUSC

BREAK

02:10
159 **Vascular Cognitive Impairment: Novel Endothelial Mechanisms and the Impact of Mediterranean Diet**
Jensen Tomberlin, Adviye Ergul, Onder Albayram, John Kurtz, Department of Neuroscience, College of Graduate Studies, MUSC

02:25
160 **The Role of Extracellular Vesicles in the Propagation of Scleroderma-Associated Lung Fibrosis.**
Joe Mouawad, Carol Feghali-Bostwick, College of Medicine (MD, PhD), MUSC

02:40
161 **STAT3 in cancer-associated fibroblasts promotes an immunosuppressive tumor microenvironment**
Julia Lefler, Michael Ostrowski, Katie MarElia-Bennett, Department of Biochemistry and Molecular Biology, College of Graduate Studies, MUSC

BREAK

03:05
162 **Using hepatocytes derived from PNPLA3 I148M iPSCs to model Nonalcoholic Fatty Liver Disease (NAFLD)**
Caren Doueiry, Stephen Duncan, Department of Regenerative Medicine, College of Graduate Studies (MSTP), MUSC

03:20
163 **Proteomic analysis for potential therapeutics in treating osteoarthritis**
Jen Xu, Patrick Woster, Leticia Reyes, Department of Drug Discovery, College of Medicine (MD, PhD), MUSC

03:35

164 **Optimized Transcranial Direct Current Stimulation (tDCS) For Higher and More Focal Cortical Electric Fields**

Kevin Caulfield, Mark George, Department of Neuroscience, College of Graduate Studies, MUSC

Session 17 PhD II ORAL

01:00

165 **Priming Upper Extremity Motor Practice with Aerobic Exercise (PUMP-Ex) - A Preliminary Report on Feasibility and Efficacy**

Emerson Hart, Ryan Ross, Michelle Woodbury, Chris Gregory, Department of Health Sciences and Research, College of Health Professions, MUSC

01:15

166 **Investigating the redox regulation of histone deacetylase 5 in drug-seeking behavior**

Daniel Wood, Christopher Cowan, Ethan Anderson, Makoto Taniguchi, Department of Neuroscience, College of Graduate Studies (MSTP), MUSC

01:30

167 **Synthesis and evaluation of novel, small molecule inhibitors of spermine oxidase as neuroprotective agents**

Amelia Furbish, Patrick Woster, Seth Ruimveld, Department of Drug Discovery and Biomedical Sciences, College of Pharmacy, MUSC

01:45

168 **Mechanisms Controlling Regression of Cardiac Fibrosis by Removal of Pressure Overload**

Lily Neff, Amy Bradshaw, An O. Van Laer, Catalin F. Baicu, Michael R. Zile, College of Medicine and Graduate Studies, MUSC

BREAK

02:10

169 **Modulating anti-tumor reactive T cells with hydrogen sulfide**

Nathaniel Oberholtzer, Shikhar Mehrotra, Department of Surgery, College of Graduate Studies (MSTP), MUSC

02:25
170 **Kinematic Motion Analysis of Healthy and Osteoarthritic Human Thumb Basal Joints**
Mary Walker, Yongren Wu, Shuchun Sun, Daniel Gordon, Nicholas Bain, Alex Chiaramonti, Elizabeth Nadeau, Dane Daley, Thierry Bacro, Hai Yao, Department of Bioengineering, College of Graduate Studies, MUSC

02:40
171 **Advancing peptide siRNA-carrier designs through stereochemistry and D-amino acid modifications to enhance gene silencing**
Charles Holjencin, Andrew Jakymiw, Colton Feinberg, Travis Hedrick, Gregory Halsey, Robert Williams, Priya Patel, Evan Biles, James Cummings, Chance Wagner, Naren Vyavahare, Department of Oral Health Sciences, College of Dental Medicine (DMD, PhD), MUSC

BREAK

03:05
172 **A Novel Regional Target for studying a mouse model of PTSD: The Dorsal Peduncular Cortex**
Krysten O'Hara, Patrick Mulholland, Dr. Jen Rinker, Heyam Saleh, Christina Lebonville, Dr. Howard Becker, Department of Neuroscience, College of Graduate Studies, MUSC

03:20
173 **Neuronal Signature of Cocaine Seeking Behavior in the Nucleus Accumbens Core**
Reda Chalhoub, Peter Kalivas, Camille Carthy, Drew Kalasky, Stephen Walterhouse, Constanza Garcia-Keller, Department of Neuroscience, College of Graduate Studies (MSTP), MUSC

03:35
174 **The osteogenic and antimicrobial effects of strontium and chloride-containing bioactive glasses**
Dustin Mueller, Hai Yao, Daniel Bonthius, Xiaojing Chen, Department of Oral Health Sciences and Clemson-MUSC Bioengineering Program, College of Dental Medicine (DMD, PhD), MUSC

Session 18 PhD III ORAL

01:00

175 **TLR9 activation bolsters B cell - T cell interactions and expands potent antitumor CD8+ T cells**

Aubrey Smith, Chrystal Paulos, Hannah M. Knochelmann, Megan M. Wyatt, Amalia M. Rivera-Reyes, Guillermo O. Rangel Rivera, Michael B. Ware, Anna C. Cole, Connor J. Dwyer, David M. Neskey, Mark P. Rubinstein, Bei Liu, Jessica E. Thaxton, Eric Bartee, Department of Microbiology and Immunology, College of Graduate Studies, MUSC

01:15

176 **Immunostimulatory effects of a novel small molecule CD38 inhibitor and application for treatment of neuroblastoma**

Catherine Mills, Patrick Woster, Thomas Benton, Megan Francis, Dalan Soloman, Ivett Pina Gomez, Yuri Peterson, Department of Drug Discovery and Biomedical Science, College of Graduate Studies, MUSC

01:30

177 **The effect of non-invasive transcutaneous auricular vagus nerve stimulation (taVNS) on hypoxic-ischemic injury in newborn rats**

Melanie Wiley, Mark George, Catrina Sims-Robinson PhD, Heather A. Boger PhD, Dorothea D. Jenkins MD, Department of Neurosciences, College of Medicine (MD, PhD), MUSC

01:45

178 **The Role of MyoD as a Promoter of Cell Survival in Rhabdomyosarcoma**

Alexander Oles, Denis Guttridge, Peter Yu, Sudarshana Sharma, Priya Londhe, Eric Hill, Ryan D. Roberts, David J. Wang, Department of Pediatrics, College of Graduate Studies (MSTP), MUSC

BREAK

02:10

179 **Interaction Between Fam3c And Lifr Regulates Self-Renewal In Mammary Epithelial Cells**

William Streitfeld, Philip Howe, Annamarie Dalton, Breege Howley, Department of Biochemistry and Molecular Biology, Department of Graduate Studies, MUSC

02:25

180 **Epithelial adherens junctions regulate ECM remodeling via miRNAs**

Amanda Daulagala, Antonis Kourtidis, Catherine Bridges, Joyce Nair-Menon, Department of Regenerative Medicine and Cell Biology, College of Graduate Studies, MUSC

02:40
181 **Regionally specific losses in gray and white matter in Alcohol Use Disorder: Implications for non-invasive brain stimulation**
Daniel McCalley, Colleen Hanlon, Department of Neuroscience, College of Graduate Studies, MUSC

BREAK

03:05
182 **Conditioning hPSC-Derived Cardiac Fibroblasts for Isogenic Cardiac Organoid Development**
Charles Kerr, Ying Mei, Department of Regenerative Medicine, College of Graduate Studies, MUSC

03:20
183 **Treatment with a site-targeted complement inhibitor reduces visual deficits following traumatic brain injury**
Davis Borucki, Stephen Tomlinson, Wenxue Wang, Shahid Husain, Baerbel Rohrer, Department of Neuroscience, College of Graduate Studies (MSTP), MUSC

03:35
184 **PI3K inhibition promotes levels of stemness in a dose dependent manner and enhances their mitochondrial fitness**
Guillermo Rangel Rivera, Chrystal Paulos, Dwyer Connor Jude, Knochelmann Hannah Marie, Smith Aubrey, Ware Brandon Michael, Cole Anna Camille, Wyatt Megan, Department of Microbiology and Immunology, College of Graduate Studies (MSTP), MUSC

Session 19 Postdoc/Resident/Fellow/Staff Scientist ORAL

01:00
185 **Combined primary and secondary ocular blast injury model for translational research**
R. Glenn Hepfer, Hai Yao, Peng Chen, Jie Fan, Craig Crosson, Department of Oral Health Sciences, College of Dental Medicine (DMD, PhD), MUSC

01:15
186 **lncRNA Neat1/hemoglobin subunit beta axis regulates neuronal dysfunction in sepsis-associated encephalopathy**
Yan Wu, Hongkuan Fan, Department of Pathology and Laboratory Medicine Research, College of Medicine, MUSC

01:30
187 **Comparison of chemotherapy agents for delivery by thermosensitive liposomes in a computational model**
Krishna Ramajayam, Dieter Haemmerich, Department of Pediatrics, CRI, College of Medicine, MUSC

01:45
188 **Frontal lobe neurometabolite alterations associated with heavy alcohol use: A meta-analysis of proton magnetic resonance spectroscopy studies**
Anna Kirkland, Lindsay Squeglia, Brittney Browning, Lorenzo Leggio, Dieter Meyerhoff, Department of Psychiatry and Behavioral Sciences, College of Medicine, MUSC

BREAK

02:10
189 **The perioperative patient experience during COVID-19**
Kristen Quinn, Andrea Abbott, Andrew Dippre, Melinda Ryan, Rupak Mukherjee PhD, Prabhakar Baliga MD, Department of Surgery, College of Medicine, MUSC

02:25
190 **Complement inhibition in chronic phases after traumatic brain injury reverses ongoing cognitive decline**
Khalil Mallah, Stephen Tomlinson, Christine Couch, Mohammed Alshareef, Davis Borucki, Xiaofeng Yang, Ali Alawieh, Department of Microbiology and Immunology, College of Medicine, MUSC

02:40
191 **Local Muscle Inflammation in Cancer Cachexia Derives from Multiple Cell Populations in the Muscle Microenvironment Under the Control of NF-kB**
Benjamin Pryce, Denis Guttridge, Vijay Shankar, Erin Talbert, Trudy Mackay, David J. Wang , Department of Pediatrics, College of Medicine (MD, PhD), MUSC

BREAK

03:05
192 **Different aspects of hand grip performance may be explained by connectivity of distinct sensorimotor networks in chronic stroke**
Christian Schranz, Na Jin Seo, Shradda Srivastava, Bryant A. Seamon, Barbara Marebwa, Leonardo Bonilha, Viswanathan Ramakrishnan, Janina Wilmskoetter, Truman Brown, Richard Neptune, Steve Kautz, Department of Health Sciences and Research, College of Health Professions, MUSC

03:20

193 **The splanchnic mesenchyme is the main tissue origin of fibroblasts in the pancreas during homeostasis and tumorigenesis**

Lu Han, Michael Ostrowski, Yongxia Wu, Sean Sweeney, Ulyss Roesner, Melodie Parrish, Khushbu Patel, Tony Trimboli, Julia Lefler, Cynthia D. Timmers, Xuezhong Yu, Michael Zimmermann, Angela Mathison, Raul Urrutia, Gustavo Leone, Department of Biochemistry & Molecular Biology, College of Medicine, MUSC

03:35

194 **Nutritional AGEing and RAGEing as a regulator of the tumor microenvironment**

Andrew Baldwin, David Turner, Bradley A. Krisanits, Pamela Woods, Lourdes M. Nogueira, Hong Li, Courtney Thomas, Mahtabuddin Ahmed, Gayenell S. Magwood, Marvella E. Ford, Victoria J. Findlay, and David P. Turner, Department of Pathology and Laboratory Medicine, College of Medicine, MUSC

03:50

195 **A Translational Model for Age-Related Auditory Processing Deficits**

Jeffrey A. Rumschlag, Kelly C. Harris, Hainan Lang, Carolyn M McClaskey, James W Dias, Lilyana B Kerouac, Department of Otolaryngology, Head & Neck Surgery, College of Medicine, MUSC

Session 20 Research Specialist/Technician ORAL

01:00

196 **Medicaid Patients Face Limited Access to Care for Ankle Sprains**

Caroline Hoch, Christopher Gross, Daniel Scott, Department of Orthopaedics and Physical Medicine, College of Medicine, MUSC

01:15

197 **Examining the Role of IL-4 Stimulated Memory CD8+ T-Cells in Regulating Monocyte Physiology and Activation**

Philip Broughton, Dr. Kristine Deleon-Pennell, Yusra Zaidi, Miguel Troncoso, Alexa Corker, Department of Cardiology, College of Medicine, MUSC

01:30

198 **Trends in the Utilization of Implants in Index Procedures for Early Onset Scoliosis from the Pediatric Spine Study Group**

Maxwell Marshall, Robert Murphy, Garrett Neel, William Barfield, Jason Anari, Tricia St. Hilaire, George Thompson, John Emans, Behrooz Akbarnia, John Smith, James Mooney, Department of Orthopaedics and Physical Medicine, College of Medicine, MUSC

01:45
199 **Analysis of secondary behavioral outcomes in patients undergoing tDCS and CBT for pain and opioid misuse**
Abagail Ault, Jeffrey Borckardt, Barth Kelly, Brady Kathleen, Flanagan Julianne, George Mark, Goble Layne, McCauley Jenna, Santa-Ana Elizabeth, Treiber Frank, Wilkerson Allison, Balliet Wendy, Bottonari Kathryn, Carter Lauren, Christon Arnold Lillian, Mappin Georgia, Muzzy Wendy, Wedin Sharlene, Wolf Juila, Anjinetta Yates-Johnson, Wedin Sharlene, Department of Psychiatry, College of Medicine, MUSC

BREAK

02:10
200 **Does Oral N-Acetylcysteine with taVNS-Paired Bottle Feeding Lead to Increased Feeding Volumes in Infants with Diabetic Mothers?**
Sarah Huffman, Dorothea Jenkins, Morgan Dancy, Bashar Badran, Mark S. George, Brain Stimulation Lab, College of Medicine, MUSC

02:25
201 **The IGF II-mediated fibrotic pathway proceeds through the IGF1R/IR hybrid receptor to induce SOX9, EGR1, and NEDD9 in primary human lung fibroblasts.**
Kristy Waldrep, Carol Feghali-Bostwick, Jessalyn Rodgers, Sara M. Garrett, Steven A. Rosenzweig, College of Medicine, MUSC
02:40
202 **Critical functions of a novel iron sulfur cluster transfer protein in genome replication and metabolism during cell division.**
Samuel Wood, Kyu-Ho Lee, Shasha Lin, William Harris, Kimberly K. Sutton, Wenjian Gan, C, College of Medicine, MUSC

BREAK

03:05
203 **Negative Affect and the Approach Avoidance Task: Electrocortical Evidence of Conflict Resolution**
James Lopez, Christopher Sege, Holly H. Fleischmann, Lisa M. McTeague, Department of Psychiatry, College of Medicine, MUSC

List of Abstracts

1 **Sourcing Real-World Data to Build the Determinants of Health Ontology of Mappable Elements (DHOME) to Understand Disparities**

Lauren Cuppy, Alexander Alekseyenko, Tami Crawford, College of Medicine, MUSC

Social determinants of health (SDOH) consist of an individual's natural, built, and social environment elements, which significantly affect their health outcomes. Disproportionalities in these elements generate disparities in disease prevalence and healthcare access. To help account for as many of SDOH as possible centralized repository for such elements is needed. The repository should enable a comprehensive understanding of the spatial and conceptual relationships between SDOH. We prototyped a SDOH collection from real-world data for South Carolina from public domain into a `dhomer` R-package (https://tamilyn.github.io/dhomer/). dhomer contains uniformly processed real-world data that highlight relevant attributes (e.g. health facilities, environmental contaminants, social infrastructure, etc.), compiled into a single repository to allow for geographic proximity and accessibility analyses via simple functions within the R programming language. The package integrates several datasets of factors within the natural, built, and social environment ascertained at granularities varying from point to county level. By creating a centralized repository for all SDOH data, we allow for comprehensive conceptualization of relationships between elements of an individual's environment and their effects on human health. Concurrent consideration of all data enables visualization of disparities in the natural, built, and social environment for identification of their geographical or longitudinal exacerbations. These effects are invisible when the data are considered independently. Currently, the sourced data in dhomer is enabling linkage of colorectal cancer and polyp disparities data with SDOH in a retrospective cohort study. This prototypical use case demonstrates the capabilities of the dhomer repository for spatial analyses. The long-term goal to create an ontology that links SDOH to geographic entities that define them is enabled by the data currently in dhomer and additional datasets to be added in the future.

This work was supported by SC CaDRe NIH/NCI grant U54CA210963, SC CHEC: Summer Undergraduate Research Training Program NIH/NCI grant R25CA193088

2 **An Investigation of the Relationship between Cortico- Cortical Connectivity and Upper Limb Motor Function in Stroke Survivors**

MiLana Wiltshire, Na Jin Seo, Christain Schranz PhD, College of Health Professions/ College of Graduate Studies(SURP), MUSC

Introduction: The objective was to investigate the correlation between cortico-cortical connectivity and upper extremity motor function post stroke. Due to a lesion in the brain, communications within the brain is disrupted. It is important to understand how cortico-cortical connectivity relates to motor function so that with this new knowledge specific areas and pathways of the brain can be targeted by interventions to result in a better chance of recovery. Methods: EEG during hand grip was obtained from twelve chronic stroke survivors. The average connectivity of the EEG signal between the primary motor cortex in the lesioned hemisphere and the sensorimotor network

(bilateral premotor, primary motor, and primary sensory cortices) in both the grip preparation phase and execution phase was quantified. Additionally, upper, extremity motor function was assessed using the Box and Blocks Test. For comparison, EEG connectivity for twenty healthy adults was also obtained. Result: Higher connectivity correlated with lower motor function. Conclusion: The higher connectivity may represent a compensatory reorganization in response to a disruption of the neurological pathways due to stroke.

This work was supported by NIH/NIGMS P20GM109040, NIH/NICHD 1R01HD094731

3 **Cochlear lateral wall degeneration in a mouse model of complement Factor B Deficiency**

Shabih Jafri, Hainan Lang, -Brown, Shardai -Barth, Jeremy -Atkinson, Carl, Department of Pathology and Laboratory Medicine, College of Medicine (MD, PhD), MUSC

Maintenance of endocochlear potential in the cochlea scala media is a vital component of hearing. Positive potential is maintained by marginal and intermediate cells lining the stria vascularis of the cochlear lateral wall that control Na-K transport. Recent studies of sensorineural hearing loss have shown that inflammatory responses in the cochlea are associated with strial cell degeneration and death in endocochlear potential. Furthermore, dysregulation of the complement cascade, a key pathway of the innate immune system, has been linked to neurodegenerative disorders. The aim of this study was to determine if deficiency in the alternative complement pathway affected cochlear lateral wall structure and function. Using mice deficient in complement factor B (fB-/- mice), we measured auditory brainstem response (ABR; an in vivo auditory function test) in young adult fB-/- mice. Our findings showed that fB-/- mice had significantly higher ABR thresholds compared to wildtype animals. Additionally, we examined the effect of fB deficiency on intermediate cells. Frozen sections of cochlea from fB-/- and wildtype mice were immunostained using Kir4.1 antibody, a marker of strial intermediate cells. Quantitative analysis of the results demonstrated that fB deficiency caused a significant reduction in Kir4.1 immunoreactivity in cochlea basal turns. Together, our data indicate that complement factor B plays a role in maintaining cochlea structure and function in young adult mice. Future studies will elucidate the impact of fB deficiency on other regions of the cochlea. Additionally, studies will investigate whether fB and the larger alternative complement pathway change as a function of age and whether they contribute to age-related hearing loss.

4 **Bidirectional modulation of reward seeking behavior using cell type specific optogenetic control in the nucleus accumbens**

Camille Carthy, Peter Kalivas, Reda Chalhoub, Drew Kalasky, Stephen Walterhouse, Michael Mayerink, Eric Dereschewitz, College of Medicine (MD, PhD), MUSC

Dopamine D1- and D2-receptor expressing GABAergic medium spiny neurons (D1- and D2- MSN) in the nucleus accumbens core (NAc) have been implicated in natural and drug reward processes. We aim to optogenetically manipulate D1- and D2-MSNs to identify their time-specific roles in natural reward seeking, using a mouse model of sucrose self-administration. We optogenetically manipulated D1-and D2-MSNs of the NAc in D1- and D2-cre transgenic mice with virally expressed Channelrhodopsin-2. D1- and D2-cre mice underwent 10-12 days of sucrose self-administration, during which an active nosepoke resulted in sucrose pellet delivery and a compound cue. After a 7-10 day incubation period, mice were returned to the operant chamber for post-abstinence testing, during which the cue, but not the reward, was delivered upon an active nosepoke. Optogenetically activating D1-MSNs simultaneously with cue presentation potentiated reward seeking while

activating D2-MSNs significantly reduced seeking activity. This time-locked stimulation of D1-MSNs maintained seeking activity over multiple days and reversed extinction to the context or the cue. Omitting optogenetic stimulation significantly decreased seeking activity in D1-cre mice. To test whether time-locked activation was necessary to promote seeking behavior, D1- and D2-MSNs were optogenetically stimulated randomly in an explicitly unassociated manner with the active nosepoke. This stimulation paradigm failed to restore seeking behavior in either D1- or D2-cre mice. Nonetheless, time-locked optogenetic stimulation of D1-MSNs, but not random stimulation, was sufficient to reinstate seeking behavior, in the presence or absence of the reward-associated cue. Our data indicates that time locked optogenetic stimulation of D1-MSNs in the NAc is sufficient to induce and maintain reward seeking; optogenetic activation of D2-MSNs fails to promote similar effect. We aim to further investigate the physiological D1 and D2-MSN neural activity in freely behaving animals using calcium imaging to better understand the encoding patterns of both cell types during natural reward seeking.

This work was supported by RO1 DA003906, RO1 DA012513 (PWK), NSF Grant OIA-1539034 (PWK), 5R25DA033680-09.

5 **Opacification of Sino-Nasal Imaging Correlates with SNOT22 Scores in Patients with Chronic Rhinosinusitis**

Jacob Snyder, Rodney Schlosser, Matthew Germroth, Michael Shih, Thomas Edwards, Department of Rhinology, College of Medicine, MUSC

Introduction: The incidence of chronic rhinosinusitis (CRS) is estimated to be 12.3% of the USA population, and the disease may severely impact quality of life. CTs of the sinuses may provide information on surgical targets, but correlations to symptoms remain undefined. The goal of this project was to determine the correlation between CT sinus opacification in surgical regions of interest (ROI) and SNOT-22 scores, for which higher scores indicate increased severity of sino-nasal symptoms. Methods: Thirty patients with CRS were prospectively enrolled and randomized to receive one of two intranasal corticosteroid doses or placebo (1:1:1). Coronal CT scans and SNOT22 scores at baseline and 24 weeks of therapy/placebo were acquired. ROIs and percent opacification were examined with ImageJ by two independent reviewers. Interrater agreement was assessed with intraclass correlation and kappa analysis. Change in ROI percent opacification and change in SNOT22 scores from baseline to 24 weeks were correlated. Cross-sectional ROIs and SNOT22 scores at baseline and 24-weeks were also correlated. Data were presented as (correlation coefficient, p-value). Results: Symptoms indicating more negative emotions (0.41, 0.024) or worse sleep (0.408, 0.025) improved with decreased opacification of inferior and superior ROIs, respectively. Nasal symptoms (0.539, 0.002) decreased with decreased opacification, as exemplified by nasal blockage (0.575, 0.001), need to blow nose (0.521, 0.003), sneezing (0.425, 0.019), and runny nose (0.480, 0.007). Changes in otologic and smell/taste symptoms did not correlate with changes in opacification. However, 24-week cross-sectional analysis showed that opacification of inferior ROIs correlated with improved smell/taste symptoms (-0.544, 0.002). No similar significance was observed for superior ROIs (0.291, 0.118), which examine the olfactory cleft. Conclusions: Changes in opacification of ROIs correlate with changes in specific sino nasal symptoms. Olfaction/Taste may not improve with decreased opacification of the olfactory cleft. These findings may guide rhinologists to better select impactful -

6 **Roles of Hydrogen Bond Interaction for Ca2+-Dependent Regulation of Ryanodine Receptor Calcium Release Channel**

Millar Elferdink, Naohiro Yamaguchi, Savannah Heitmann, Venkat R. Chirasani, Gerhard Meissner, Department of Regenerative Medicine and Cell Biology, College of Medicine, MUSC

Ryanodine receptors (RyRs) are the intracellular Ca2+ release channels located in the sarco/endoplasmic reticulum and play pivotal roles by releasing Ca2+ during action potentials in skeletal and cardiac muscle. Point mutations in human RYR genes are tightly associated with cardiac and skeletal myopathies; thus, defining the regulatory mechanism of RyR is important for cardiac and skeletal muscle pathophysiology. RyR channel function is activated by micromolar Ca2+, ATP, and caffeine, and is inhibited by millimolar Ca2+ and Mg2+. The aim of this study is to better understand the molecular basis of Ca2+-dependent regulation of RyR. Recent molecular and structural biology studies with skeletal isoform of RyR (RyR1) suggested that EF hand domain of RyR1 serves as a low affinity Ca2+ inhibitory site for channel function; however, the site is distal from the Ca2+ conducting channel pore site. We hypothesize that the Ca2+ binding signal to the EF hand domain is transmitted through domain interactions to close the ion channel pore. Molecular dynamics simulations showed that the EF hand domain interacts with the cytoplasmic loop between the second and the third transmembranes (S2-S3) through two hydrogen bonds. We constructed recombinant RyR1s carrying point mutations on the hydrogen bonding amino acids in the EF hand or S2-S3 loop of RyR1 and characterize the mutant RyR1 channel functions using [3H]ryanodine binding assay. Two RyR1 mutations in the EF hand domain, K4101E and K4101M, decreased affinity for Ca2+-dependent inhibition. Two mutations on the S2-S3 loop, R4736Q and R4736W, decreased Ca2+-dependent inhibition as well as Mg2+-dependent inhibition, while Ca2+-dependent activation is not modified. These results suggest that amino acids involved in hydrogen bond interaction between the EF hand and the S2-S3 loop of RyR1 play important roles in Ca2+-dependent inhibition.

This work was supported by NIH HL147054, HL153504, AR018687

7 **The effects of using a novel device for the symptomatic treatment of sinus headaches**

Matthew Germroth, Ted Meyer, Craig Salvador, BS; Shaun A. Nguyen, MD FAPCR, Department of Otolaryngology, College of Medicine, MUSC

Objective: To determine if simultaneous administration of acoustic vibration and oscillating expiratory pressure affects the severity of facial pain among patients with complaint of sinus headache. Subjects and Methods: A prospective, unblinded, single-arm pilot study was performed on subjects with sinus headache without the evidence of chronic rhinosinusitis (CRS) on exam or computed tomography at the Medical University of South Carolina. All subjects self-administered simultaneous acoustic vibrations and oscillating expiratory pressure to the nasal cavity twice daily over 4 weeks. Efficacy was assessed using 3 validated patient reported outcome measures - pain visual analog scale (VAS), brief pain inventory-short form (BPI-SF), and McGill pain questionnaire-short form (MPQ-SF). Device safety and patient satisfaction were also assessed using questionnaires. Results: Twenty-nine patients (16 females and 13 males) with the mean age of 49 (range 23-82) completed the study without any major adverse events. From baseline and at 4 week follow up, VAS improved from 59.6±15.7 to 34.6±21.7 ($p<0.001$), BPI-SF improved from 4.4±2.0 to 2.9±1.9 ($p=0.007$), and MPQ-SF improved from 12.2±6.5 to 6.5±5.2 ($p<0.001$). At study completion, approximately 70% of patients achieved a minimal clinically important difference (MCID) across all metrics. Additionally, 86% of patients would both use the device again and recommend it to others. Conclusion: Administration of simultaneous acoustic vibration and

oscillating expiratory pressure via novel device appears to be a safe treatment for sinus headaches in patients without objective evidence of chronic sinusitis. Results from this initial study are promising with regard to efficacy in treatment of sinus headaches but will require further study.

This work was supported by Healthy Humming LLC

8 **Defining the importance of proline residues in the hypervariable region of HRAS for interaction with RAF**

Megan Mazzei, John O'Bryan, Imran Khan, Department of Pharmacology, College of Graduate Studies, MUSC

RAS GTPases play a major role in the control of cell proliferation and are strongly associated with the development and progression of human cancers, making it a key target for pharmacological inhibition. The RAS family consists of 3 highly related genes, HRAS, NRAS and KRAS that encode 4 different proteins including HRAS, NRAS, KRAS4A and KRAS4B. These isoforms contain a G domain and a Hypervariable Region (HVR). The G-domains are highly similar in sequence between isoforms and are responsible for the binding and activation of RAS effectors such as the RAF Ser/Thr kinase which activates the major RAS effector pathway, RAF/MEK/ERK. However, the HVR varies greatly across the isoforms, and is the site for post-translation modifications. Given the difficulty with direct inhibition of RAS, many groups have focused on inhibiting the RAF/MEK/ERK signaling pathway. A RAS biologic inhibitor, developed in this lab, inhibits both HRAS- and KRAS-mediated ERK signaling; however, the two isoforms interact differently with RAF in the presence of this inhibitor. This difference in RAS/RAF interaction is important in understanding the biochemical differences between these RAS isoforms. We propose that the potential cause for this difference in RAF interaction with HRAS vs KRAS is the presence of proline residues at amino acids 173,174 and 179. We hypothesize that these prolines result in structural kinks that alter RAF interaction with HRAS vs KRAS. To test this hypothesis, I have mutated these proline residues to a smaller amino acid, alanine (AAA mutant). We predict that HRAS(AAA) will decrease RAS/RAF interaction compared to HRAS (G12V) in the presence of the biologic inhibitor and increase in the absence of this inhibitor. These results will help to understand the differences in RAS signaling between specific isoforms and how differences in the HVRs between RAS isoforms affect their interactions with effectors and potential inhibitors.

These studies were supported in part by an NIH R01 (CA212608) and VA MERIT Award (1I01BX002095) to J.P.O

9 **Protein Tyrosine Phosphatase Inhibition for Melanoma Therapy**

Amanda Manea, Haizhen Wang, Tiffany T. Penaloza, Xueliang Gao, Department of Cell and Molecular Pharmacology and Experimental Therapeutics, College of Medicine, MUSC

Abstract withheld from publication

10 **Novel Gal-3 Macrophage Interactions in a Murine Presbycusis Model**

Rachel Eisenhart, Cynthia Wright, Department of Pathology and Laboratory Medicine, College of Graduate Studies, MUSC

Presbycusis, also known as age-related hearing loss, is a prevalent neurodegenerative disorder that impacts roughly half of seniors over 75 in the US. The pathology of the aging cochlea involves multiple cell types and internal structures, and no definitive mechanism of presbycusis is yet understood. The stria vascularis, a critical structure in establishing the endocochlear potential, has been explored as an area of interest due to notable changes in the microenviroment and resident macrophages with age, along with demonstrated reduction of the endocochlear potential. Previous research has correlated changes in macrophage activation with a protein called Gal-3 via a type of chronic inflammation known as inflammaging, however correlation between macrophage activity and vascular degradation has yet to be expanded upon. Using immunohistochemistry and immunofluorescence microscopy, various staining protocols using Gal-3 antibodies were performed to evaluate Gal-3 positive macrophage morphology and interaction within the context of the stria microvaculature. This analysis suggests a novel hypothesis regarding a "propping" mechanic with active macrophages, which may occur due to degradation of the extracellular matrix in conjunction with inflammaging. Upon evaluation with RNA-Seq and bioinformatic techniques, significant dysregulation of genes regarding the extracellular matrix was found. This finding combined with imaging data suggests a novel perspective on the role of macrophages in the aging cochlea, opening the door to increased understanding of the pathology of aging cochlear tissue.

This work was supported by NIH (Award Number:5R25HL092611-14)

11 **Motor Activated Auricular Vagus Nerve Stimulation (MAAVNS) Facilitates Upper Extremity Functional Recovery After Stroke**

Ellen Kitchens, Bashar Badran, Brenna Baker-Vogel, Kelly Rishe, Andrew Fortune, Scott Hutchinson, Christian Finetto, Gabrielle Walker, Steve Kautz, Mark S. George, College of Medicine (MD, PhD), MUSC

Introduction: Stroke is a leading cause of disability in the US, with nearly 60% of stroke survivors reporting limitations in upper extremity function six months post-stroke. Recovery of motor control can be maximized by repetitive task-practice interventions through occupational therapy. We have developed a novel rehabilitation therapy called motor activated auricular vagus nerve stimulation (MAAVNS). MAAVNS is a closed-loop system that delivers transcutaneous auricular vagus nerve stimulation (taVNS) synchronized with movements during motor rehabilitation training to accelerate motor learning. In this randomized, double-blind trial, we are investigating whether the closed-loop MAAVNS is more effective at improving motor function than open-loop noninvasive taVNS (unpaired taVNS). Methods: Five chronic stroke survivors with unilateral motor deficits have completed this double-blinded study to date (mean age 61.2, 3 male, 2 female). Participants were randomized into treatment groups (A or B). Depending on the randomization, participants either received MAAVNS or unpaired taVNS during each of 12, 1-hour rehabilitation visits spread over 4 weeks. The Fugl-Meyer upper extremity (FMA-UE) motor assessment was collected at baseline and at completion, as well as at follow-up timepoints. Results: Both treatment groups presented with similar levels of motor impairment measured by the FMA-UE (baseline: Group X =45.3; Group Y = 44.5). After 4-weeks of treatment, Group A improved by a mean of 5.3 points, whereas group B improved by a mean of 2.5. Results are blinded to maintain integrity of the trial and updated findings will be presented in this poster. Conclusion: Although the results are still

blinded, these preliminary data are on track to test whether the timing of stimulation is important for the neuroplastic effects of VNS. This study is safe and feasible with no adverse events nor dropouts. After unblinding, we will explore the more effective intervention in a follow-up, sham-controlled trial.

This work was supported by 5P20GM109040-08 – 8346

12 **The Relationship Between LINE-1 and Inflammation in High Grade Serous Ovarian Cancer**

Savannah Stockton, Joseph Delaney, College of Graduate Studies, MUSC

Over 100,000 women die each year from ovarian cancer, which is the most fatal gynecological malignancy in the United States. Even with treatments such as chemotherapy, recurrence occurs in 70-80% of cases with poor prognosis and a high mortality rate. LINE-1 (L1) is a retrotransposon which has 2 open reading frames encoding ORF1p and ORF2P. ORF1 encodes for a chaperone protein, ORF1p, which binds to L1 mRNA to prevent degradation. ORF2 encodes for ORF2p, which has a reverse transcriptase domain which transcribes a L1 DNA strand complementary to the L1 mRNA and an endonuclease domain which cuts DNA for L1 insertion. In High Grade Serous Ovarian Cancer (HGSOC), L1 expression is upregulated through several mechanisms such as hypomethylation of the L1 promoter. This upregulation is seen early in tumor development. However, increased L1 expression is correlated with increased overall and disease-free survival. L1 inhibition leads to a decreased expression of interferon-stimulated genes. We hypothesize that the L1 DNA-RNA hybrid binds to c-GAS to activate the c-GAS-STING pathway to cause the chronic inflammatory response seen in HGSOC. To model HGSOG, OVCAR-3 cells were used and transfected with plasmids that had mutations in ORF1p and ORF2p in order to genetically modulate L1 activity. Western blots and immunofluorescence were used to detect changes in Interferon Beta production from c-GAS-STING with different types of L1 modulation.

13 **RNAi regulation of virulence in the human oral pathogen Candida albicans**

Gurbir Malhi, Andrew Jakymiw, Evan Biles, Dong Phan, Janessa Montefalco, Caroline Westwater, Department of Oral Health Sciences, College of Dental Medicine, MUSC

The human fungal pathogen Candida albicans (C. albicans) transcriptome was found to contain small RNAs bearing chemical features of RNA interference (RNAi) products prototypical of small interfering RNAs (siRNAs). Moreover, analysis of C. albicans small RNA sequencing libraries revealed that a number of sequences clustered at loci with homology to the TLO (telomere-associated) gene family. Intriguingly, TLO genes encode proteins that function in regulating a variety of virulence traits including stress resistance, morphogenesis, and biofilm formation. Consequently, to delineate the importance of these small RNAs in mediating TLO-dependent virulence in C. albicans, a bioinformatic analysis of a C. albicans GEO small RNA sequencing dataset was initially performed to identify the small RNAs that mapped to the TLO gene family, after which RT-qPCR experiments were conducted to biochemically validate their expression in C. albicans. Upon sequence screening of the small RNA dataset using the TLO3 transcript sequence as a reference, numerous small RNAs that mapped to the TLO gene family were identified, with two 22-mer small RNAs, in particular, being identified that exhibited the highest read count of all analyzed sequences. Interestingly, use of RNAfold software predicted that these two most prevalent small RNAs were found to be essentially palindromic sequences of each other, which generated a hairpin-loop structure within the TLO3 transcript. Subsequent RT-qPCR analyses also confirmed the

expression of these two small RNAs in growing cultures of C. albicans. Thus, together, these data imply that the two most prevalent small RNAs we identified bioinformatically and biochemically that map to TLO genes may be generated from a hairpin-loop structure formed within the TLO transcript, which is reminiscent of the mammalian microRNA biosynthesis pathway and could play key roles in regulating virulence in the human oral pathogen C. albicans.

This work was supported by MUSC CDM Collaborative Pilot Award, MUSC CDM SHP Research Program

14 **Inhibition of Sphingosine-1-Phosphate Receptor 2 by JTE013 Promoted Osteogenesis by Increasing Vesicle Trafficking, Wnt /Ca2+, and BMP/Smad Signaling**

Simon Lin, Hong Yu, Pandruvada Subramanya, Department of Oral Health Science, College of Dental Medicine, MUSC

Sphingosine-1-phosphate receptor 2 (S1PR2) is a G protein coupled receptor that regulates various immune responses. Herein, we determine the effect of a S1PR2 specific antagonist, JTE013, on osteogenesis by culturing murine bone marrow stromal cells (BMSCs) with osteogenic media in the presence of JTE013 (0.5 to 8 □M) or vehicle dimethylsulfoxide (DMSO). Treatment with JTE013 dose-dependently increased alkaline phosphatase and alizarin red S staining in BMSCs compared with DMSO treatment. JTE013 also enhanced alkaline phosphatase, RUNX2, osteocalcin, and osterix mRNA levels in BMSCs compared with DMSO treatment. Protein analysis revealed that JTE013 increased vesicle trafficking associated proteins, including Rac1-GTP, filamentous (F)-actin, clathrin, Early Endosome Antigen 1 (EEA1), and syntaxin 6 in BMSCs compared DMSO treatment. Treatment with JTE013 also increased RUNX2, Wnt3a, p-PLC, p-PKC, and p-CaMKII protein levels, supporting that JTE013 promoted osteogenesis via Wnt/Ca2+ pathway. Additionally, low doses of JTE013 (1 to 2□M) increased BMP2, BMP7, BMPR1A, BMPRII, and p-Smad1/5/9 protein levels. In summary, our data for the first time highlight the importance of vesicle trafficking as an important signaling pathway in regulating osteogenesis. The enhanced Wnt3/Ca2+ is associated with vesicle trafficking, which promotes the synthesis and transport of osteogenic protein and matrix vesicles, and enhances matrix mineralization.

This work was supported by R15DE027324, R21DE030865, UL1 TR001450, and MUSC CDM SHP Research Program

15 **UTILITY OF DRIVE THRU HEALTH SCREENINGS WITH THE ONSET OF COVID-19**

Kasparas Zilinskas, Anita Ramsetty, Almeera Lateef, College of Medicine, MUSC

The CARES Rural Outreach Program in St Stephen was started in 2018 to directly support the St. Stephen community through health screenings and food distribution. During the Rural Outreach Program, professional healthcare students perform health screenings that include a nutritional screen, blood pressure and blood glucose measures for participating residents of the community. Simultaneous distribution of fresh produce and shelf stable foods address concerns about food access. With the onset of the pandemic many people have avoided going to medical facilities due to apprehension regarding contracting the virus while hospitals shifted focus to acutely ill individuals being treated for COVID-19. Preventive healthcare fell among all age groups during 2020. Drive-through screenings within a community setting could continue to serve pressing needs within the community while ensuring that preventive medicine is being practiced. Drive-through

style operations for the Rural Outreach were initiated in 2020 with the most recent event in St. Stephen serving over 180 households. From the participating individuals, 79 were screened with all three recommended health screening tools. From those screened, 15 were found to have stage 1 hypertension and 10 were found to have stage 2 hypertension. Moreover, 10 people were found to have high blood sugar (defined as >160mg/dL). Moreover, based on the health screens only 29.1% of participants believed they were "about the right weight", 20.3% of participants did not exercise a single time in the past week, and 12.7% of participants had not eaten a fruit or vegetable the day before. The data from the screening event illustrated that a significant proportion of residents within this rural community have chronic conditions that were detected through this novel screening event. Drive-through screenings can deliver effective screening methods for large scale community events and possibly address gaps in healthcare delivery during the pandemic.

This work was supported by MUSC's CARES Clinic

16 **Reduced antitumor immunity in colorectal cancer tissues of African Americans compared to Caucasian Americans**

Lauren Fanning, Kristin Wallace, Silvia Guglietta, Alexander Alekseyenko, Kent Armeson, Grant Brazeal, David Lewin, Alexandria Cousart, Department of Public Health Sciences, College of Medicine, MUSC

Background: Colorectal cancer (CRC) incidence and mortality disproportionately affect African Americans (AAs) compared to Caucasian Americans (CAs). The innate the cytotoxic and adaptive immune responses in tumors are positive predictors of CRC prognosis. Yet few studies have investigated antitumor immune responses by race. Methods: From the Hollings Cancer Center (HCC) Registry, we selected a convenience sample of invasive cancer cases diagnosed between June 1st, 2000, and June 30, 2015. Immune gene expression of 579 genes was assessed for CRCs (n=30) using the NanoString nCounter platform using the immunology v2 panel. Data were analyzed using a NanoStringDiff R package, implementing negative binomial regression models of gene expression as the dependent variable and race group (AA vs. CA) as the primary predictor variable. Models were adjusted for age, sex, location within the colon, and clinical stage. Results: Several innate and adaptive cytotoxic genes were under-expressed in AAs vs. CAs. Type II (IFNG) and type III (IL28A) interferons were down-regulated ($p < 0.0001$). Genes associated with functionality of cytotoxic response (CXCL9, CXCL10, CXCL11, granzyme B, HLA.DQA1, CD9, CD70, CD86) were down-regulated ($p < 0.05$). Additionally, down-regulation of C-C motif cytokine-encoding genes (CCL16, CCL26) also support reduced cytotoxic response in AAs compared to CAs. Conclusion: Our results suggest decreased antitumor immune responses in CRCs from AAs vs. CAs. Further research on a larger number of cases is needed to confirm these results, but these results may provide clues for reducing the racial disparities in CRC outcomes.

This work was supported by R01LM012517, U54CA210963, B.Q.M.S.R., R01CA226086, MUSC COM COMETS

17 **The role of P-selectin and Complement in the Pathogenesis of Germinal Matrix Hemorrhage-Induced Secondary Injury in a Neonatal Model**

Devin Hatchell, Stephen Tomlinson, Mohammed Alshareef, Chunfang Guo, Aakash Shingala, Ramin Eskandari, Department of Microbiology and Immunology, College of Medicine, MUSC

Introduction/Rationale: Recent studies in our lab have indicated a role for complement in the initiation and propagation of neuroinflammation and hydrocephalus development post-Germinal Matrix Hemorrhage (GMH). Here we investigate a strategy to target complement inhibition specifically to sites of P-selectin expression, a relevant adhesion molecule at sites of vascular injury/inflammation, as well as investigate P-selectin's involvement in leukocyte recruitment in propagating GMH secondary injury. We prepared two fusion proteins consisting of anti-P-selectin single chain antibodies (scFv) linked to Crry, a complement inhibitor. One of the scFv targeting vehicles (2.12scFv) additionally blocked the cell adhesion site of P-selectin, whereas the other scFv (2.3) bound P-selectin without blocking its function. Methods: To complete these investigations, post-natal mice on day 4 (PND4) were subjected to collagenase induced-GMH and treated with 2.3Psel-Crry, 2.12Psel-Crry, or vehicle. Histopathological and behavioral analyses were performed at PND7,PND14,PND45. Results: After GMH injury, 2.3Psel-Crry treatment resulted in reduced mortality, infarct size, and neurological deficits, whereas 2.12Psel-Crry treatment resulted in worse outcomes. MRI analyses revealed that 2.3Psel-Crry, but not 2.12Psel-Crry, reduced post-hemorrhagic hydrocephalus (PHH) development. It was found that 2.12Psel-Crry, unlike 2.3Psel-Crry, inhibited the coagulation cascade as determined by increased coagulation time and decreased platelet aggregation. This additional activity of 2.12Psel-Crry is likely due to its blockade of P-selectin function on platelets and provides an explanation for worse outcome with 2.12Psel-Crry in this hemorrhagic condition. Conclusion: The study provided, show that GMH induces expression of P-selectin, the targeting of which with a complement inhibitor is protective. Although unexpected, the worsened outcomes with the construct that also inhibits P-selectin function were explained by its effect on interfering the coagulation cascade. Whereas the 2.3Psel-Crry construct has potential for protecting against the pathogenic sequelae of GMH, the 2.12Psel-Crry construct has potential for treatment of conditions that incorporate pathological thrombotic events, such as ischemic stroke.

This work was supported by the Neurosurgery Research and Education Foundation (NREF) through the AANS/CNS Section on Pediatric Neurological Surgery & NREF 2020-21 Research Fellowship Grant and by grants from the Department of Veterans Affairs (IK6BX005235, 1BX004256, 1RX001141), and the National Institutes of Health (NIH) (T32AI132164).

18 **Adolescent Alcohol Use is Related to Alcohol Demand**

Helen Liu, Lindsay Squeglia, Anna Kirkland, Brittney Browning, Samuel Acuff, Cori Herring, Kevin Gray, Department of Psychiatry and Behavioral Science, College of Medicine, MUSC

Introduction. Adolescent alcohol use is common and associated with long-term risk for alcohol use disorder. Understanding the relationship between motivation and alcohol consumption is important for prevention and intervention efforts. Behavioral economics suggests that alcohol use is, in part, a result of the overvaluation of alcohol. The Alcohol Purchase Task (APT) is a behavioral economic measure of motivation for alcohol. APT indices correlate with heavy drinking and negative consequences in adults, but it has not been explored in adolescents. This study aimed to understand the association between two APT demand indices and alcohol consumption within heavy drinking adolescents. Methods. Baseline data from an on-going clinical trial (K23AA025399) were analyzed. Participants (n=29; age 17-19) met criteria for heavy drinking (4-8 drinking occasions per month, ≥3 standard drinks per occasion) before completing the 17-item APT and the 90-day Timeline Follow Back. Linear regression was used to assess the association between alcohol consumption response variables (average and maximum standard drinks, per drinking occasion) and independent demand indices of intensity (total drinks at $0) and maximum alcohol expenditure

(Omax; total standard drinks*cost) from the APT. Maximum standard drinks was log transformed. Models were controlled for sex, age, and grade level. Results. Intensity (Beta=0.203 (SE=0.087), p=0.029) and Omax (Beta=0.081 (SE=0.035), p=0.028) were positively related to the response variable of average standard drinks. Similarly, intensity (Beta=0.024 (SE=0.010), p=0.026) and Omax (Beta=0.012 (SE=0.004), p=0.005) were positively related to the response variable of maximum standard drinks. Alcohol consumption decreased with increasing price points. Discussion. Our findings are consistent with earlier research in adults. Greater motivation for alcohol was related to higher real-life alcohol consumption, which means APT may be a valid marker of harmful alcohol use in adolescents. It can easily be administered in clinical settings in combination with alcohol quantification measures.

This work was supported by The National Institute on Alcohol Abuse and Alcoholism (K23 AA025399)

19 **The impact of restoring insulin receptor endocytosis on brain insulin transport and cognitive impairment.**

Alexus Williams, Catrina Robinson, Luke Watson, Crystal Smith, Stephanie Dilucia, Department of Neuroscience/Neurology, College of Graduate Studies, MUSC

Obesity, a risk factor for cognitive impairment, is associated with hyperinsulinemia-induced insulin resistance. High- fat diet mice, a mouse model of diet- induced obesity, display cognitive deficits which correlate with hyperinsulinemia and reduced brain insulin. Insulin from the periphery is thought to be transported to the brain via receptor-mediated endocytosis. Hyperinsulinemia reduces the transport of insulin to the brain; however, the mechanisms are not known. The binding of insulin to the insulin receptor leads to the tyrosine auto-phosphorylation of the receptor, which is a necessary step for the initiation of insulin receptor endocytosis. Protein tyrosine phosphatase 1B (PTP1B) dephosphorylates tyrosine on the insulin receptor. We hypothesize that hyperinsulinemia-induced increase in PTP1B inhibits insulin receptor endocytosis through tyrosine dephosphorylation, leading to reduced brain insulin levels and thereby inducing cognitive deficit. First, we sought to investigate protein expression levels of PTP1B in primary brain microvascular endothelial cells exposed to hyperinsulinemic (HI) conditions. Cells were separated into three treatment groups: 1) non-HI, 2) HI, and 3) HI + PTP1B inhibition (using a 50nM claramine treatment, a specific and selective PTP1B inhibitor). Hyperinsulinemic conditions were induced at passage 5 in cells incubated with 20nM of human recombinant insulin for 12 hours. We found that PTP1B levels are elevated in the HI cells compared to non-HI cells. PTP1B levels are decreased in the HI + claramine cells compared to the HI cells. Furthermore, we investigated whether the expected increase in PTP1B levels correlates with a reduction in insulin receptor endocytosis. To assess insulin receptor endocytosis, we isolated endosomes in endothelial cells using the same experimental conditions. We found that insulin receptor endocytosis is decreased in HI cells when compared to the non- HI cells. Insulin receptor endocytosis is slightly increased in the HI+ claramine cells when compared to the HI cells. Future studies are aimed

This work was supported by NIH NINDS (R01NS099595) NIGMS (P20 GM109040) (R25 GM072643) (R25 GM113278)

20 **Red Algae Extracts Containing Mycosporine-like Amino Acids (MAAs) may Treat Non-Healing Pathological Wounds**

Menny Benjamin, Russell Norris, Dr. Mark Hamann, Dr. Rupak Mukherjee, Dr. Amy Bradshaw, George Hanna, Department of Drug Discovery, Department of Regenerative Medicine, College of Graduate Studies, MUSC

It is estimated that 2%, or about 7 million Americans, are suffering from chronic wounds. These are refractory tissue injuries that fail to efficiently regenerate, due to degradation of the ECM and GFs from constant inflammation. In normal wound healing there are four main stages: 1) hemostasis, 2) inflammation, 3) proliferation, and 4) remodeling. But, in chronic non-healing wounds, progression into the latter stages of wound healing is stalled at the inflammation stage. There are in vitro studies suggesting that algae-derived compounds may not only stimulate the proliferation and remodeling stages, but prevent inflammatory damage. Red algae are uniquely composed of a class of compounds known as mycosporine-like amino acids (MAAs) that have been demonstrated as inhibiting collagenase, advanced glycation end products (AGEs), and free radicals like reactive oxygen species (ROSs), among other properties that are associated with non-healing wounds. As a result, various red algae species were extracted via aqueous and organic solvents to yield crude extracts containing MAAs. These extracts will be assayed for bioactivity to test the hypotheses of enhanced wound healing properties in normal human dermal fibroblasts (NHDFs). Aim 1 will test the hypothesis of induced cell proliferation and migration of skin cells treated with the crude extracts. Non-wounding and wounding cell migration assays will be used to measure gap closure rate, and proliferation markers will be detected using ICC as a qualitative assay and WB as a quantitative assay. Aim 2 will test the hypothesis of stimulated cellular fibronectin and collagen I synthesis via molecular indication of fibrous ECM deposition, which will quantify their molecular weight by WB and differentiate them of mRNA gene expression by qPCR. Aim 3 will analyze and fractionate successful extracts of their active chemical composition via HPLC and NMR spectroscopy to characterize MAAs.

21 **Predictors of abstinent smoking status at 6-months after baseline tobacco treatment in Hollings Cancer Center patients**

Alexandria Cousart, Alexandria Cousart, Benjamin Toll, Kenneth Cummings, Amanda Palmer, Department of Public Health Sciences, College of Medicine, MUSC

Nearly ⅔ of people diagnosed with cancer continue to smoke cigarettes. Continuing to smoke during this time causes cancer treatments to be less effective, can result in secondary cancers, and makes some surgeries non-viable. Therefore, cancer patients must quit smoking to improve their overall health and well-being and increase the likelihood of better treatment-related outcomes. The Tobacco Treatment Program (TTP) at MUSC contacts every Hollings Cancer Center (HCC) patient who is currently smoking and provides telehealth treatment and medication referrals. This study aims to indicate demographics factors associated with program efficacy to guide future smoking cessation initiatives. Data were obtained from follow-up calls with HCC patients 6-months after the TTP baseline treatment. A 21-question phone survey was conducted with 217 patients. The patients were then classified into former smokers (>7 days abstinent) and current smokers. Multiple logistic regression analyses were performed to determine if different smoking and demographic variables were predictive of a patient having quit smoking by follow-up. The predictors analyzed were sex, having another smoker in the household, receiving follow-up class from MUSC, talking with a healthcare professional about smoking, and using prescription medications to quit. Only prescription medications (OR 0.35: 95% 0.162,0.756) and talking with a

healthcare professional (OR 0.396: 95% CI 0.2,0.784) was shown to be significant in predicting abstinent smoking status. These findings indicate that these services have not been enough for this group of patients to help them quit. Future interventions need to focus on understanding these patients more to determine their barriers to treatment so that more effective treatment options can be made available to them.

This is a secondary analysis based on the parent study (Pro00072026) and therefore did not recieve funding.

22 **Attitudes Toward COVID-19 in South Carolina at Height of Pandemic**

Almeera Lateef, Mahsa Javid, Parker McDuffie, College of Medicine, MUSC

The COVID-19 pandemic has shaken the economic and social structure in the United States. The pandemic led to stay at home orders and accrued economic stress due to closures throughout the country. We conducted a survey for patients at a single center hospital to collect information on the patients' overall attitudes about the actions taken by the state government and how their own actions reflected the recommendations put in place. For this study, 1435 surveys were sent out to patients who previously consented to receiving a survey by email. The response rate was 27.2% (390 responses). The respondents were mostly female (68.2%), white (87.2%), and living in urban areas (72%). Statistical analyses of the responses were performed using inverse probability weighting. While most respondents stated that the actions taken by the state government were better than that of the federal government, younger adults noted that the state relaxed its precautions too early when compared to middle aged and older adults. In contrast, middle aged and older adults were more willing than young adults to get vaccinated at the time this survey was conducted. Overall, respondents perceived an existence of social disparities for the treatment options for COVID-19 and expressed a preference for a "healthcare for all" model with respect to COVID-19 testing and treatment. Moreover, the survey demonstrated that everyone would be amendable to a 4 week or 8 week lockdown if they were to be reimbursed 75% of their salary. The results of this study may provide a direction for responses from the federal and state governments as well as medical institutions to mitigate the disruption(s) to public life when facing future pandemics and/or catastrophic situations.

23 **Getting Kids Moving: Identifying the Need for Increasing Inclusive Youth Physical Activity Resources**

Allison Farrell, Amanda Giles, Department of Occupational Therapy, College of Health Professions, MUSC

Introduction: Physical activity is an important occupation, but participation looks different and has unique challenges for children with disabilities. Children with disabilities are less likely to engage in physical activity and more likely to have reduced fitness levels than their peers. Children with disabilities also have less access and opportunities to participate in inclusive physical activity. The purpose of this needs assessment is to partner with the National Center on Health, Physical Activity, and Disability (NCHPAD) to identify the barriers and limitations to creating inclusive physical activity information. Methods: A REDCap survey will be distributed by NCHPAD to parents, teachers, administrators, and community members. This survey will consist of multiple choice, Likert scale, and open ended questions to collect qualitative and quantitative data on the barriers and need for resources for inclusive physical activity. In addition, interviews will be conducted with members of NCHPAD and parents of children with disabilities to gain additional qualitative data.

Results: Data from the interviews will be transcribed and then analyzed for common themes. The quantitative data from the REDCap surveys will be analyzed to determine possible relationships and open-ended REDCap survey responses will be assessed using qualitative methods. Then all data will be brought together and summarized to determine overall findings and next steps. Conclusions: The results will be used to identify the (1) need for resources, (2) barriers to educating children with disabilities and their families on the importance of physical activity, and (3) effective strategies to implement in materials for NCHPAD.

24 **The A.B.L.E. Program: A Specially Designed Adaptive Sports Program for Youth with Moderate to Severe Disabilities**

Sarah Grace Lindsey, Sarah Grace Lindsey, Patty Coker-Bolt, PhD, OTR/L, FAOTA; Shelli Davis, MS, College of Health Professions, MUSC

Introduction/rationale: Participation in sports is an important aspect of life for children and adolescents and can provide significant physical, psychological, and social benefits (Eime et al., 2013). Youth with disabilities are also able to reap the benefits of participation in adaptive sports, but unfortunately there are a limited number of programs available for youth with significant medical conditions (Ryan et al., 2014). Therefore, the purpose of this study is to explore the need for a new, specially designed multi-sports program called "The A.B.L.E. Program (Athletes Believing Limits are Endless)" for youth with moderate to severe disabilities. Method: This prospective study required the collection of quantitative and qualitative data to determine 1) the perceptions of caregivers of children or adolescents with moderate to severe disabilities on the current state of local adaptive sport programs and desire for additional programming, 2) the perceptions of the Mount Pleasant Recreation staff as to the barriers and challenges for development of new programs, 3) the perceptions of experts in adaptive sports on how to best serve youth with more complex disabilities, and 4) current adaptive sporting opportunities available for youth with more severe disabilities. Redcap surveys, phone interviews, and in-person focus group interviews are currently being conducted. Results will be analyzed through descriptive statistics of frequencies, demographics, and preferences. Thematic analyses will determine common themes of open-ended questions with peer review of themes. Results: This study is on-going and data collection will be completed by late September. Conclusions: The results of this study will inform the development of the first adaptive multi-sports program in the Charleston area specially designed for youth with moderate to severe disabilities. The creation of the new A.B.L.E. program will assure that every child, regardless of ability, has an equal opportunity to participate in sports and recreation in their community.

25 **Preventing Pediatric Post-Intensive Care Syndrome: The New MUSC Sleep, Play, Heal Program**

Kaitlyn Schultz, Kaitlyn Schultz, Lindsay Davies, MS, OTR/L, Patty Coker-Bolt, PhD, OTR/L, FNAP, FAOTA, Occupational Therapy Doctorate, College of Health Professions, MUSC

Introduction/Rational: Previous models of care in the Pediatric Intensive Care Units (PICU) required critically ill patients to remain heavily sedated on bedrest to promote the best recovery (Herrup et al., 2017). Recent studies have shown that rest and heavy sedation may lead to long-term physical, cognitive, emotional, and/or social impairments otherwise known as Post-Intensive Care Syndrome (Woodruff & Choong, 2021). In recent years, most critically ill children are surviving significant illness and trauma leading hospitals to adopt the ICU liberation movement to reduce sedation and increase early mobility to decrease long hospital stays (Walz et al., 2020; Woodruff & Choong, 2021). The Shawn Jenkins Children Hospital at MUSC created the first ICU early mobility protocol in

the state called the Sleep, Play, Heal program. The purpose of this study is to explore (1) the attitudes and perceptions of the interprofessional team members who deliver the Sleep, Play, Heal program, (2) the outcomes of the children who have completed the program, and (3) the perceptions of families/caregivers of children who have completed the program. Methods: Prospective study with collection of quantitative and qualitative data via REDCap surveys, chart reviews, and in-person interviews with parent of children in the program and PICU staff members. Results will be analyzed using descriptive statistics, frequency of responses, and thematic analysis of open-ended questions. Results: This is an on-going study and data collection will be completed by September. It is expected that both parents and staff will have favorable opinions of this new initiative and patient outcomes will be positive. Conclusions: The results of this study will identify the benefits of the first pediatric early mobility program in the state of South Carolina for children admitted to the PICU after significant trauma and determine the early benefits and ways to improve implementation of the program.

26 **Supporting Families of Children with Cerebral Palsy: Parent Training Resources to Increase Compliance with Home Based Constraint-Induced Movement Therapy**

McRae Lawrence, McRae Lawrence, Liz Humanitzki, MS, OTR/L, C/NDT, Patty Coker Bolt PhD OTR/L FAOTA, College of Health Professions, MUSC

Background: Constraint Induced Movement Therapy (CIMT), an intervention for children with one sided hemiplegia, focuses on promoting use of the affected or weaker upper extremity (UE) in everyday activities. Modified CIMT (mCIMT) protocols are commonly used for children and involve constraint of the strong arm/hand while the weaker arm/hand is engaged in repetitive task practice. Modified CIMT is delivered over several hours a day for several weeks with an emphasis on participation in home-based daily activities. In popular mCIMT models, parents are expected to deliver a significant portion of the high dosage CIMT each week, after receiving varying degrees of training. Despite positive parent perceptions and study outcomes of home-based mCIMT models delivered by families, current parent training models are unclear and inconsistent. Therefore, there is a need to explore the types of parent training used to deliver high-quality home-based mCIMT programs. Methods: Qualitative and Quantitative data will be collected to determine 1) parent training models for mCIMT currently used at local and national pediatric clinics, 2) parent perceptions of training and adherence to home based mCIMT programs, and 3) ways to improve training and compliance for parents who are expected to deliver high quality mCIMT programs in the home, based on what exemplar mCIMT programs are doing. REDCap surveys and key informant interviews are currently being conducted and results analyzed using descriptive statistics, frequency of responses, and thematic analysis of open-ended questions. Results: This study is on-going and data collection will be completed by late September. Conclusion: The results of this study will enhance the training and resources provided to families who are expected to deliver high-quality home-based CIMT to their children. Resources could include a training manual, website with library of training videos, or an app for parent training and log of intervention delivery.

27 **Identifying the Need for Student Education on the Scope of Occupational Therapy in Addressing Sexuality and Intimacy**

Jennifer Barnett, Amanda Giles, Department of Occupational Therapy, College of Health Professions, MUSC

Introduction: Sex is a meaningful activity that falls under the scope of occupational therapy (OT) because it consists of valued roles and occupations that contribute to a client's overall health, well-being, and quality of life. Although many OT practitioners agree that exploring a client's sexuality and intimacy is integral to providing holistic, person-centered care, they feel uncomfortable addressing client concerns related to sex. The purpose of this study is to determine the need for integrating comprehensive education on sexuality and intimacy into existing Doctor of Occupational Therapy (OTD) curriculum at the Medical University of South Carolina (MUSC) to improve student confidence in initiating and facilitating discussions about sex in a rehabilitative setting. Methods: A mix of qualitative and quantitative data will be collected through an anonymous and optional REDCap survey that will be administered to students in the OTD program at MUSC to gather student feedback on addressing sexuality and intimacy within a rehabilitative setting. Results: Results will be analyzed using descriptive statistics and thematic analyses. Data collection will be finalized in early September 2021. Conclusions: The results of this study will identify (1) the need for comprehensive education on sexuality and intimacy within the MUSC OTD curriculum, (2) OT students' comfort and confidence in addressing sex and intimacy, (3) the frequency that students are facilitating discussions or witness OT practitioners facilitate discussions about client concerns related to sex, (4) social and cultural factors that make discussing sex more challenging, and (5) ways to support student learning in this area. The results of this study are vital in supporting future clinicians in providing holistic, person-centered care, which is integral to the practice of OT.

28 **Assessing the Impact of Learning Tools on Fieldwork Preparedness of Occupational Therapy Students**

Kirsten Temple, Amanda Giles, Department of Occupational Therapy, College of Health Professions, MUSC

Introduction/Rationale: The purpose of occupational therapy (OT) education is to train the next generation of therapists to be fluent in their knowledge of OT practice and competent in the translation of this knowledge into hands-on evaluation and treatment of patients. The possible benefits of using video case-based learning (CBL) for OT students are numerous and should motivate OT educators to create content that will best equip their students for future fieldwork and clinical practice. Through real-life examples, CBL aids students in connecting and applying new information by providing opportunities to critically evaluate the content and make decisions in a safe environment. Previous research shows that case studies, when done well, align with learning objectives, create empathy with the characters, stimulate student interest, and promote decision making. The purpose of this study is to assess the value of video cases as an educational tool compared to other educational content for current OT students at the Medical University of South Carolina (MUSC) prior to level-2 fieldwork. Method: A prospective study with a collection of quantitative and qualitative data to determine if the use of video CBL is appropriate and productive for OT student learning in preparation for fieldwork. A REDCap survey and interviews are being conducted to gather student feedback on learning tools including video case study. Results will be analyzed using descriptive statistics and thematic analyses. Results: This study is ongoing. Data collection will be completed in September 2021. Conclusion: The results of this study will (1) inform

the development of educational resources for OT students at MUSC (2) gather feedback from students on preparedness for fieldwork and preferred learning tools, and (3) understand which components of video case studies best aid learning.

29 **Effects of a Transfer Package on Upper-Extremity Use at Home for Stroke Patients**

Corinne Gillion, Na Jin Seo, Gabrielle Scronce, PT, PhD, Kristen Coupland, MS, OTR/L, Adam Baker, B.S., Viswanathan Ramakrishnan, PhD, Department of Rehabilitation Sciences, College of Health Professions, MUSC

Background: Approximately 795,000 people experience a stroke each year in the United States, making it a leading cause of disability. Two-thirds of stroke survivors experience an upper-extremity (UE) impairment, which decreases their participation in meaningful occupations. While stroke survivors gain UE motor skills from therapy in rehabilitation clinics, they use their affected UE less in activities of daily living at home. An intervention called Transfer package (TP) has recently been proposed. TP is a behavioral intervention that facilitates transfer of therapeutic gains from the clinic to home by encouraging patients to practice and apply new motor skills at home. Efficacy of TP has been studied using subjective assessments. Specifically, previous research shows, TP increased perceived use of affected UE in daily living. However, efficacy of TP has not been examined using objective measures such as accelerometry. Thus, the previous evidence may have been influenced by subjective biases of participants. Objective: To determine the effect of TP on paretic UE use at home through accelerometry. Methods: Secondary analysis of data from a study of UE rehabilitation and TP for stroke survivors with accelerometry measurement of UE use at home pre- and post- intervention. Our proposed study will test the hypothesis that UE use increases post-intervention. Impact: This work is expected to provide evidence to support or reject implementation of TP into therapy treatment for stroke patients. If supported, implementation of TP could allow stroke patients to improve UE use at home, leading to increased participation in meaningful activities and enhanced quality of life.

This work was supported by NIH/NIGMS P20GM109040, NIH/NICHD 1R01HD094731-01A1

30 **Social-emotional Services for Brain Injury Survivors Post Insurance Discharge**

Kelsey Reilly, Amanda Giles, Department of Occupational Therapy, College of Health Professions, MUSC

Introduction: For acquired brain injury (ABI) and traumatic brain injury (TBI) survivors, adjustment to life post hospital discharge can be overwhelming and complicated. Coping strategies and new routines that promote emotional and social well-being are needed to improve quality of life after brain injury. However, there is a gap in the availability, accessibility, and awareness of the support services provided for brain injury survivors post insurance discharge. The purpose of this needs assessment is to identify the apparent need for community integration and cognitive impairment resources for post insurance discharge ABI/TBI patients to improve their functional recovery and overall quality of life. Methods: A REDCap survey will be distributed to South Carolina occupational and physical therapists. This survey will consist of multiple choice, Likert scale, and open-ended questions to collect qualitative and quantitative data on the current discharge process and available services for brain injury survivors. In addition, interviews will be conducted with clients and staff at the Head and Spinal Cord Injury Community Outreach Center (HASCI) to gain additional qualitative data. Results: Data from the interviews will be transcribed and analyzed for common themes. The quantitative and qualitative data from the REDCap surveys will be analyzed to

determine possible relationships and themes. All data will then be brought together and summarized to determine overall findings. Conclusions: The results will be used to determine the (1) need for additional discharge resources (2) barriers to community integration after brain injury, and (3) effective materials to implement in hospital systems and at HASCI.

31 **Exploring Health Care Students' Perceptions about Race and Privilege: A Case Study of a Peer Education Program**

Chinieka Jackman, Elizabeth Brown, PhD, Madison Kimmell, Kristina Stepanova, Amy Payne, Dante Pelzer, PhD, Department of Clinical Sciences, College of Health Professions, MUSC

Introduction. Amid the racial unrest stemming from the summer of 2020, many institutions are having difficult conversations about race and the impact of racism. Educational leaders at the Medical University of South Carolina developed a Peer Education Program (PEP) for health care students to promote open dialogue about race and privilege. Methods. For four months, interdisciplinary health care students met once a month for one hour to discuss privilege, race/racism, leadership, and advocacy and their influence on health equity. Participants evaluated the program to share their perspectives on each topic. Researchers used a team-based, iterative process to code survey responses. Conventional content analysis of the participants' data captured students' experiences and revealed several themes concerning topics related to health inequities. Results. Four participants completed PEP, and three participants completed the program evaluation survey (75% response rate). Students described privilege in a positive context, using words like "freedom," "special right/advantage," and "opportunity". Race was viewed as (1) a way to discriminate, (2) a "man-made concept" used to establish racial hierarchy, and (3) insignificant due to complexity of human beings. Program strengths included topics, guest speakers, and open dialogue. Recommended changes included allotting more time for dialogue and increasing the frequency of monthly meetings. Students described their experience in PEP as "eye-opening" and "liberating". The consensus is that privilege (or lack thereof) and race/racism negatively affect health care. Participants challenged themselves to combat the health inequities imposed upon those who are minoritized and underprivileged. Conclusions. To be an influential and empathetic leader in health care, one must understand the impact that privilege and race/racism have on equitable health care. Further, effective leadership and advocacy can facilitate allyship with those whose voices are marginalized. Students in or entering health care professions can benefit from difficult peer discussions about race and privilege.

This work was supported by Scholars of Humanities and Arts Research and Education (SHARE) Grant Program

32 **Regional Socioeconomic Disadvantage is Associated with Attenuation of Amygdala Responsivity to Threat in a Community Sample of School-Aged Children**

Rachel Polcyn, Lisa McTeague, Ashley A. Huggins, Casey Calhoun, Curtisha Shacklewood, Alison Line, Laura Carpenter, Zachary Adams, Colleen Halliday-Boykins, Greg Hajcak, Jane Joseph, Carla Kmett Danielson, Department of Psychiatry & Behavioral Sciences, College of Medicine, MUSC

Adversity faced in childhood is associated with alterations in critical frontolimbic pathways involved in the pathophysiology of many psychiatric disorders. Prior studies of the impact of childhood adversity have focused primarily on individual-level socioeconomic factors, but there is emerging evidence indicating the importance of considering broader, environmental stressors that individuals living in deprived communities often encounter. The present study addresses the

impact of these community-level stressors on neurocircuitry and consequently, health outcomes. Using functional magnetic resonance imaging (fMRI), the associations between neighborhood disadvantage and neural response to predictable and unpredictable threats in a community sample of third, sixth, and ninth grade children (N=244) were assessed. Participants' home addresses were used to derive an Area Deprivation Index (ADI) score representing their neighborhood's level of disadvantage relative to state and national levels. Results indicated that greater ADI was associated with attenuation of amygdala activation in response to aversive visual stimuli, even after adjusting for individual household income. Neighborhood disadvantage may function as a unique form of chronic stress that impacts threat responsivity of the amygdala. Future longitudinal work is critical for delineating how such effects may persist across the lifespan and how health outcomes may be modifiable with community-based interventions and policies.

This work was supported by 5R01MH112209-05 Threat-Related Negative Valence Systems, Child Victimization, and Anxiety

33 **The Triad of Co-morbidity: A Characterization of the Presinillin-2 Knock Out Model**
Sophia Emetu, Federica del Monte, College of Medicine, MUSC
WITHDRAWN

34 **Cellular Viability of Partial Heart Transplant Grafts in Cold Storage**
Morgan Hill, Taufiek Rajab, Jennie H. Kwon, Brielle Jerry, Jordan Morningstar, Minoo N. Kavarana, Satish N. Nadig, Department of Surgery, College of Medicine, MUSC

Congenital heart defects are the most common types of birth defects in humans. Children with congenital heart defects frequently require heart valve replacement with an implant. Unfortunately, conventional heart valve implants do not grow. Therefore, these children are committed to serial re-operations for successively larger implant exchanges. Partial heart transplantation is a new and innovative approach to deliver growing heart valve implants. However, the transplant biology of partial heart transplant grafts remains unexplored. This is a critical barrier for clinical translation. Therefore, we investigated the cellular viability of partial heart transplants in cold storage. Histology and immunohistochemistry revealed no morphological differences in heart valves after 6, 24, or 48 h of cold storage. Moreover, immunohistochemistry showed that the marker for apoptosis activated caspase 3 and the marker for cell division Ki67 remained unchanged after 48 h of cold storage. Finally, quantification of fluorescing resorufin showed no statistically significant decrease in cellular metabolic activity in heart valves after 48 h of cold storage. We conclude that partial heart transplants remain viable after 48 h of cold storage. These findings represent the first step toward translating partial heart transplantation from the bench to the bedside because they have direct clinical implications for the procurement logistics of this new type of transplant.

This work was supported by American Association of Thoracic Surgery Surgical Investigator Program

35 **Creating an Evidence-Based High-Fidelity Simulation Crisis Scenario for the Anesthesia Provider**
Shannon McDermott, BSN, RN, Michele Ballister, DNP, APRN, CRNA, CHSE, Monica Karlen, BSN, RN,

Chloe Urig, BSN, RN, Lester Kitten, MHS, CRNA, Joey Seymour, MSN, CRNA, Lisa Rogers, DNAP, APRN, CRNA, Department of Anesthesia for Nurses, College of Health Professions, MUSC

OBJECTIVE: High-Fidelity Simulation (HFS) is an environment utilized in the instruction of anesthesia providers to develop clinical skills and manage low-incidence, high-mortality emergencies. The purpose of this quality improvement project was to create a realistic, reliable, and valid HFS crisis scenario to be utilized in the education and training of anesthesia providers. METHODS: This is a quality improvement project. A literature review was conducted to determine the best methods for constructing HFS crisis simulation scenarios for Laerdal SimMan 3G. Three scenarios were created to include Cerebral Aneurysm Rupture (CAR), Intraoperative Cardiac Arrest (ICA), and Tension Pneumothorax (TPX). Use of the Modified Delphi Technique involving experienced CRNAs ensured the HFS crisis scenarios exhibited fidelity and validity. The scenarios were vetted by third-year doctoral nurse anesthesia students in their last semester at a southeast medical center in a controlled HFS lab. Each crisis scenario was 30 minutes including pre-brief, HFS execution, debrief, and post-participation survey. RESULTS: 7 students evaluated the crisis scenarios. The mean scores for whether the scenarios provided the opportunity to meet objectives (CAR = 99.3%, ICA = 100%, TPX = 92.9% (s = 3.91%)) and for realism (CAR = 88%, ICA = 93%, TPX = 81%, (s = 6.03%)) were obtained. All participants considered each HFS crisis scenario to be 100% useful as a tool to teach and evaluate anesthesia providers. LIMITATIONS: Limitations include a limited number of participants, varying levels of fidelity, and constraints of manual operation. CONCLUSION: HFS is a useful tool in the education and training of anesthesia providers. The crisis scenarios created were realistic to the clinical setting and beneficial to anesthesia education and training.

36 **CD8+ T-cells Recruit Macrophages Following a Myocardial Infarction**

Gualberto Munoz, Kristine Deleon-Pennell, Hallie Roerden, Penny Huebsch, Department of Medicine - Cardiology, College of Medicine, MUSC

Every 39 seconds, an American will have a myocardial infarction (MI). Following MI, macrophages assist in the healing process. The initial ischemic event kills resident macrophages which are replaced by monocyte-derived macrophages. CD8+ T-cells are known regulators of inflammation and increase in the circulation and infarct post-MI. We hypothesized CD8+ T-cells regulate the recruitment and retention of monocytes post-MI. To test our hypothesis, we performed permanent occlusion on C57Bl6J mice and mice deficient in CD8+ T-cells (CD8-/-). We then collected tissue at post-MI days 0, 1, 3, 7, and 14 followed by infarct Mac3 staining to determine the macrophage timeline. Bulk RNAseq of infarct tissue was performed at post-MI days 1, 7, and 14 to establish possible genetic regulators. We clustered the data based on genetic markers of macrophage subtypes found in previous studies. Mac3 staining of WT mice showed macrophages begin to infiltrate on post-MI day 1, peaking at day 7, and trending towards baseline levels by day 14. Intriguingly, CD8-/- mice had a delay in macrophage recruitment at day 1, but by day 3, there was almost twice the amount of macrophages compared to WT. No differences were observed at day 7 post-MI, but CD8-/- mice had elevated macrophages at post-MI day 14 compared to the WT. We observed increased markers of resident-like macrophages at post-MI days 7 and 14 in infarct tissue of CD8-/- mice compared to WT. Other studies have suggested resident macrophages are cardioprotective post-MI, indicating possible benefits to CD8+ depletion post-MI. Our data indicates that CD8+ T-cells influence cardiac remodeling over the post-MI time course by playing a role in enlisting and retaining macrophages. Lastly, there is an increase in resident-like macrophages in the absence of CD8+ T-cells, which could lead to more favorable cardiac remodeling post-MI.

This work was supported by NIH R25 HL145817, U54 DA016511, AHA Innovator Project 20IPA35260039, Biomedical Laboratory Research and Development Service of the Veterans Affairs Office of Research and Development Award IK2BX003922, 2019 S&R Foundation Ryuji Ueno Award by the American Physiological Society

37 **Quality Improvement Study in Patients with Epilepsy treated with Epidiolex®: Retention Rate and Barriers to Patient Compliance**

Chanbormey Leatheng, Karla A. Mora Rodriguez, Sonal Bhatia, Leah Horstemeyer Cobb, Gustavo Carmen-Lopez, Ekrem Kutluay, Department of Neurology, College of Medicine, MUSC

Introduction: Epidiolex® is the first commercial molecular form of cannabidiol (CBD) that was approved by the FDA in 2018 for the treatment of Lennox-Gastaut (LGS) and Dravet syndromes (DS) in patients older than 2 years old. The medication has also been prescribed as adjuvant treatment for drug-resistant epilepsy and other type of seizures. Epidiolex® has aided in the improvement of patient's neuro-psychiatric diseases such depression, anxiety, conduct disorder, neurocognitive disorder, and sleep-wake disorder. Methods: At the Medical University of South Carolina (MUSC) Epilepsy Clinic, we conducted a retrospective chart review of 96 epileptic patients treated with Epidiolex® for a quality improvement study; we also surveyed 47 of those patients. Results: The results revealed seizure reduction in 69.7% of the study sample; 43.7% reported more than 50 percent reduction in seizure frequency. While the medication has shown mostly positive results, 18 of 47 surveyed patients considered discontinuing the drug, and 14 of those 18 patients stopped taking Epidiolex®. Patients discontinued the medication largely because of the side effects, which included diarrhea (n=4), medication failure (n=3), and an increase in seizures (n=3). About 16.8% (n=16) of the patients reported that they missed doses; the main reason is because they ran of medication before the next refill (n=5). These patients reported difficulties in obtaining extra medications before their assigned refill time. Other reasons for missing their doses are forgetting when to take the medication and adverse side effects. Notably, 19 of the surveyed patients were denied by insurance companies on their first request; three patients have been denied thrice before approval. Conclusion: Overall, Epidiolex® had positive results in treating these patients with epilepsy, aside from the side effects and other issues that dissuaded some patients from continuing the medication.

38 **Physiological effects of histamine 2 receptor inhibition in salt sensitive hypertension**

Samantha Perez, Daria Ilatovskaya, Mark Domondon, Callie Clarke, Ryan Schibalski, Thelma Amoah, Denisha Spires, College of Medicine, MUSC

Introduction: Histamine is an immunomodulator which plays a role in inflammation, a crucial process that disrupts kidney function. Plasma histamine levels have been shown to be elevated in kidney diseases, including salt sensitive (SS) hypertension, a disease commonly accompanied with renal inflammation. We hypothesized here that histamine receptor (HR) inhibition will affect renal function in SSH. Methods: Dahl salt-sensitive (DSS) rats fed a high salt diet (HS, 4% NaCl) were used as a model of SS hypertension. The rats received daily i.p. injections of the HR2 antagonist ranitidine (RAN, 25mg/kg) or vehicle (VEH) for 3 consecutive days while on a normal salt diet (0.4% NaCl, NS) prior to the HS diet, and for 3 consecutive days after the 21 days HS challenge. Water consumption and urine production were measured in metabolic cages. Twenty-four hours after the final injection GFR was measured and tissues were collected for examination. Trichrome and PSR staining were employed to assess renal damage, such as glomerular scores and protein cast formation. Results: In the RAN group, there was an acute decrease in urine production and water

consumption on the first day of injections while on the NS diet (p=0.02). The RAN group showed increased urine osmolality at the end of the HS diet (p=0.03). Endpoint GFR was similar for the RAN and VEH-treated animals. PSR staining analysis demonstrated similar fibrosis between the groups. Glomerular damage and protein cast formation was similar between the groups Conclusion: The Dahl SS rats treated with RAN exhibited lower water consumption, and reduced diuresis on the NS diet, and increased urine osmolality during the HS diet. Taken together, our data showed that histamine had physiological effects on fluid balance in SS hypertension; further research will be devoted to assessing the long-term effects of HR inhibition or activation in the kidney.

This work was supported by NIH R00DK105160, R01HL148115, R25

39 **Growth of the gender dysphoric transgender population in the MUSC Pediatric Endocrinology Clinic**

Thomas Agostini, Deborah Bowlby, Terry Headley, College of Medicine, MUSC

Providing endocrine gender affirming therapy to transgender youth who wish it has been linked to improved mental health outcomes [1]. Transgender youth may not seek endocrine care in South Carolina due to fear of discrimination and/or lack of affirming care [2]. In addition, legislation has been proposed to criminalize providers who provide gender affirming therapy to minors. This study aims to describe the transgender population seen in the Pediatric Endocrinology Clinic at MUSC. The population grew from 1 to 102 patients (81% Caucasian, 8% Black, 11% Other) over the past 10 years. The average age of first visit was 13.6 years (range: 4-18 years). 66.7% of patients were assigned female at birth and 33.3% of patients were assigned male at birth. 20% of patients received pubertal suppression and 50% received hormone affirming therapy and 38% patients were not on endocrine medications. Patients had comorbid psychiatric conditions, depression (53%), anxiety (37%), suicidal ideation (22%), ADHD (20%), self-harm (11%), autism spectrum disorder (4%), and death by suicide (2%). In the future, hopefully more patients and at younger ages will be referred to affirming providers so that medical options such as pubertal suppression and mental health support can be discussed with patients and families.

40 **Anesthetic Management of Post-Thoracotomy Pain Syndrome**

Courtney Williams, Angela Mund, , Department of AFN, College of Health Professions, MUSC

With the increasing prevalence of severe and chronic pain related to thoracotomy procedures, Post-Thoracotomy Pain Syndrome (PTPS), i.e., postoperative pain that persists along a thoracotomy incision for at least two months. Incidence of this syndrome has been reported in up to 80% of patients at 3 months, and 61% of patients at one year after surgery. This is attributed to the damage that can occur to muscles, nerves, and ribs during the procedure. The key to mitigating the risks of developing PTPS is prevention through rigorous and multimodal pain management techniques. Although thoracic epidural nerve blockade has been used frequently for pain management in the past, alternative methods to pain management in this population have become popular. Recent studies have evaluated the efficacy of a thoracic epidural block versus other methods of analgesia after thoracic surgery. The purpose of this review was to evaluate the evidence for using regional, neuraxial, intravenous, and other pain management methods to prevent and treat PTPS. An electronic search was performed for articles that reported the use of thoracic epidural analgesia with and without additives, patient-controlled epidural analgesia, paravertebral blocks, serratus anterior plane blocks and magnesium. Reports that examined the use of IV and oral analgesia methods were outside the scope of this review. A total of 7

prospective, blinded, randomized control trials and 1 observational study were selected for review (n=8). The synthesized results revealed the following recommendations: The serratus anterior plane block should be implemented into regular clinical practice for thoracotomy patients. Future, large-scale studies should evaluate serratus anterior plane blocks in combination with adjuncts such as dexmedetomidine or magnesium to increase patient analgesia and reduce the incidence of PTPS.

41 **Substance Use Disorder Education and its Effect on Stigma in the CRNA Population**

Michael Martz, Angela Mund, Department of Anesthesia for Nurses, College of Health Professions, MUSC

Abstract withheld from publication

42 **Concomitant Spinal Deformities in Patients with Congenital Heart Defects**

Ngozi Ogburu-Ogbonnaya, Liz L. Boyle, DR. William R. Barfield, Dr. John Costello, Dr. Robert F. Murphy, Department of Cardiology and Orthopedics, College of Medicine, MUSC

There is a known association between congenital spine anomalies/deformities and congenital heart defects. Prevalence in the literature is 20-30%. The purpose of this study was to review the local prevalence of spinal anomalies in patients with congenital heart defects. We also sought to compare outcomes in congenital heart defect patients with concomitant spinal deformity to those without spinal deformities. A comprehensive statewide pediatric congenital heart defect registry was queried for patients over a 10 year time period. Following institutional review board approval, patients were queried for concomitant congenital spinal deformities or anomalies. Univariate statistics were used to describe the two patient cohorts. Statistical comparisons were made between congenital heart defect patients with and without spinal anomaly issues. The following outcome variables were assessed: intubation and extubation, complications, mortality at birth and 30 days post-surgery were compared. An independent t-test and chi square we used as appropriate with IBM SPSS Statistics-Version 27.Over a 10 year study period, 2040 patients presented to our center with congenital cardiac defects. 19 (.93%) were diagnosed with congenital spinal anomalies with 13 (68%) males and 6 (32 %) females. The mean age was 7±standard deviation. The most frequent spinal anomalies were congenital scoliosis, myelomeningocele, and spina bifida. Comparison with 227 age and diagnosis matched controls of patients without congenital spinal anomalies was performed. There were 114 (50%) males 113 (50%) female with a mean age of 5±standard deviation. More complications existed in patients with only cardiac defects (p= .012) and the mortality rate was lower for children at discharge (p = .002). Univariate statistics demonstrated the mean for intubation to extubation in those with spinal anomalies to be 5.47±9.70 days while the patients without had a mean of 5.55±6.70 days (p= 0.171). . However, the comparable outcomes groups were statistically significant and should be investigated further.

This work was supported by NIH Grant

43 **Factors Contributing to Prolonged Ventilation in Blunt Chest Trauma and Minimal Brain Injury**

Danielle Lefebvre, Evert Eriksson, William B DeVoe MD, College of Medicine, MUSC

Modifiable factors that contribute to prolonged mechanical ventilation are of active interest, particularly in the absence of severe TBI. It is now known that surgical fixation of flail chest decreases ventilator days among other important outcomes. The effect of other fracture patterns on ICU recovery and ventilation is not well described. The objective of this study was to identify

injury and patient specific factors that independently contribute to prolonged ventilation in patients with blunt trauma and concomitant mild head injury. A retrospective review over a 2 year period was performed of patients admitted with blunt chest trauma and minimal head injury (AIS <3). Patient characteristics, number of rib fractures, character of rib fractures, and length of stay data were collected. Patient characteristics were compared to identify risk factors associated with prolonged ventilation defined as 4 days or longer. Statistics were calculated with SPSS v24 and presented as mean ± standard deviation or median (IQR). 122 patients were identified with an average age of 51 years (±19) and median ISS of 16. Seventy percent of patients were male and median number of rib fractures was 4 (3-7). On initial analysis, prolonged ventilation was significantly associated with ISS, GCS, fluid/blood product administration, laparotomy, lateral rib fractures, and sternal flail (defined as 2 rib fractures on either side of the sternum). Of these, three correlated to prolonged ventilation on linear regression analysis: admission GCS (OR=0.7 (0.6-0.9) p=0.001), units of pRBC transfused (OR=2.8 (1.6-5.0) p <0.001), and sternal flail (OR=9.4 (1.9-46.2) p=0.006). Blood transfusion, lower GCS on admission, and the presence of a sternal flail predispose to prolonged mechanical ventilation in patients who sustain concomitant blunt thoracic trauma and mild head injury. In those patients with a reassuring GCS, surgical stabilization of sternal flail may be considered to decrease ventilator days.

44 **Varying Metatarsophalangeal Arthrodesis Outcomes Between Hallux Valgus and Hallux Rigidus Cohorts**

Warren Roth, Daniel Scott, Caroline Hoch, Christopher Gross, College of Medicine, MUSC

1st metatarsophalangeal (MTP) arthrodesis is the standard operation for patients with hallux rigidus (HR) or hallux valgus (HV), but whether outcomes differ between pathologies is not well characterized. This study evaluated differences in postoperative outcomes between HR, HV, and HR+HV patients undergoing 1st MTP arthrodesis. A retrospective review was conducted on 136 patients (148 feet: HR=57, HV=47, HR+HV=44) who underwent 1st MTP arthrodesis between 2009 and 2021. Patient demographics, radiographic measurements (i.e., hallux valgus angle [HVA], intermetatarsal angle [IMA], 1st-5th metatarsal width), complication and reoperation rates, and patient-reported outcome measures (PROMs) (i.e., Visual Analogue Scale [VAS], Short Form Survey [SF-12], Patient-Reported Outcomes Measurement Information System [PROMIS], Foot/Ankle Ability Measure [FAAM], Foot/Ankle Outcome Score [FAOS]) were evaluated. Prospectively, we collected PROMs of 45 patients (50 feet) via phone interview at mean 3.04 years (range, 0.58-10.01) postoperative. Mean follow-up was 1.25 years (range, 0.25-6.14). The change in HVA (HR=-3.60, HV=-17.44, HR+HV=-15.27), IMA (-0.16, -2.80, -2.55), and 1st-5th metatarsal width (-0.98, -4.59, -4.60) were significantly different between cohorts (p<.001). There was a trend toward positive outcomes, as measured by PROMs, at the 3-year mark, although this trend was only significant for all groups with the VAS (p<.001), FAOS Quality of Life (p<.001, p=.030, p=.001), FAAM Activities of Daily Living (p<.001, p=.046, p=.002), and FAAM Total (p=.001, p=.024, p=.016) scores. The HR group significantly improved among the most PROMs at the 3-year mark (9, 5, 6). Complication and reoperation rates did not significantly differ by group, although complication (17.54%, 21.28%, 18.18%), infection (10.53%, 17.02%, 9.09%), and reoperation (15.79%, 27.66%, 18.18%) rates were highest for the HV group. The HR group had the highest nonunion rate (17.54%, 10.64%, 13.64%). This study begins to provide insight into the role that specific forefoot pathology plays in 1st MTP arthrodesis outcomes, as radiographic measures significantly differed between groups.

This work was supported by MUSC Department of Orthopedics and Physical Medicine

45 **Pediatric Firearm Injury Mortality Epidemiology**

Xzavier Killings, Annie Andrews, Elizabeth Oddo, Kelsey Gastineau, Ashley Hink, College of Medicine, MUSC

Background and Objectives: Gun violence is a leading and preventable cause of death for youth in the US. There has not been a comprehensive update on pediatric firearm injury epidemiology since 2014. The objective of this study is to examine fatal firearm injury data among youth aged 0-19. Methods: Centers for Disease Control's Web-based Injury Statistics Query and Reporting System (WISQARS) was queried for fatal injury reports from 2001-2019. Overall number of deaths due to firearm injuries was compared to deaths due to motor vehicle traffic collisions, which has been the leading cause of death for youth in the US for decades. Mortality rates (deaths/100,000 youth) were reported overall and by intent category. Proportion of firearm deaths due to homicide, suicide and unintentional shootings were reported by age group. Trends in mortality rate over time were reported by race/ethnicity and by intent. Results: In 2019, firearm injuries surpassed motor vehicle traffic collisions to become the leading cause of death for youth aged 0-19 in the US. Homicide is the most common intent across all age groups. Unintentional injuries account for 29% of the firearm deaths among 0-4 year old youth, with a decreasing proportion in other age groups. Suicide represents a significant proportion of firearm deaths in both 10-14 and 15-19 year old age groups. In 2019, Black youth had a firearm mortality rate 4.3x that of white youth and a firearm homicide rate >14x that of white youth. American Indian youth have a significantly higher firearm suicide mortality rate than all other race/ethnicity groups and the rate has increased significantly since 2001. Conclusion: Firearm injury surpassed motor vehicle traffic collisions to become the leading cause of death among youth age 0-19 in the US in 2019. There are significant racial/ethnic disparities in overall mortality rate and homicide rate.

46 **Analysis of Author Gender in the Pediatric Orthopaedic Literature from 2011-2020**

Anjali Prior, Robert Murphy, Ngozi Ogburu-Ogbonnaya BA MS, William R. Barfield PhD, James F. Mooney III MD, Sara Van Nortwick MD, College of Medicine, MUSC

Introduction: Orthopaedic surgery remains a male-dominated specialty. To date there has not been a focused analysis of gender in authorship within the pediatric orthopaedic literature. Methods: The electronic table of contents from 2011 to 2020 of 3 major pediatric orthopaedic journals [Journal of Children's Orthopedics (JCO), Journal of Pediatric Orthopedics (JPO), and Journal of Pediatric Orthopedics Part B (JPO-B)] were reviewed. Publications were reviewed for the number of articles with at least 1 female author and the number of articles with women listed as first authors. These were compared over the 10-year study period, and by individual year of publication. Statistical analysis included a general linear model with factorial one-way analysis of variance and Bonferroni post hoc testing. Results: A total of 4097 articles were reviewed. In 2020, there was a significantly higher percentage of articles with a female author when compared with 2011 (64% to 42%, P = 0.010). A female was listed as first author in significantly more publications in 2020 as compared with 2011 (23% to 10%, P = 0.031). During the 10-year study period, the highest mean proportion of articles with at least 1 female author was seen in JPO (60%), with similar findings in JCO (55%). Significantly fewer articles in JPO-B contained a female author (37%, P = 0.001). The highest percentage of publications with a female first author across 10 years was in JCO (22%), followed by JPO (20%). Significantly fewer articles with a female first author were found in JPO-B (9%, P = 0.001). Conclusion: There is an increasing proportion of publications in the pediatric

orthopaedic literature with female authors and female first authors from 2011 to 2020. In addition, there was a statistical difference in female authorship when comparing specific publications, which should be investigated further.

47 **Investigating the mechanisms underlying secondary injury following germinal matrix hemorrhage**
Aakash Shingala, Stephen Tomlinson, Mohammed Alshareef, Rosy Guo, Devin Hatchell, Ramin Eskandari, College of Medicine, MUSC

Introduction Germinal matrix hemorrhage (GMH) is a devastating neurologic condition that affects primarily premature neonates and can result in long-term sequelae, including post-hemorrhagic hydrocephalus (PHH) and periventricular leukomalacia (PVL). The mechanisms underlying these secondary injuries are not clear however, and as a result there are no effective preventative treatments. Using a murine model of GMH that recapitulates secondary injury, we investigated the role of phagocytosis in prevention of PVL. Methods Neonatal mice were injected with collagenase into the subventricular zone and were then treated with either vehicle or an activation-targeting complement inhibitor (CR2-Crry). Previous unpublished data showed that CR2-Crry treatment following collagenase injury resulted in a significant reduction in PHH at 90 days and an increase in survival compared to vehicle. Immunofluorescent staining was done for markers of white matter (MBP), phagocytosis (LAMP-1) and inflammation (GFAP). Results Animals treated with CR2-Crry had significantly less white matter destruction compared to vehicle animals as evidenced by greater corpus callosum volume at 30, 60 and 90 days post-natal. Vehicle-treated animals also had a significantly greater proportion of corpus callosum volume occupied by GFAP, a marker of astrocytes and inflammation in the brain, at 7 and 90 days. Using confocal microscopy and a three-dimensional tissue analysis, we also showed that CR2-Crry-treated animals had significantly decreased colocalization of MBP with LAMP-1 relative to animals treated with vehicle. Conclusions There are currently no treatments for preventing secondary injury following GMH, and understanding the etiology of these diseases is essential for the development of efficacious therapeutics. The data from this study shows that phagocytosis and astrocyte-mediated inflammation are critical for long-term white matter destruction and inhibition of complement activation mitigates this damage.

This work was supported by AANS/CNS Section on Pediatric Neurological Surgery & NREF 2020-21 Research Fellowship Grant, Ralph H. Johnson VA Medical Center supplemental grant: BX004256.

48 **Feasibility of resource-limited 3D imaging of the esophagus in cadaveric specimens**
Jason Erno, Steven Kubalak, Joe Carson, College of Medicine, MUSC

Imaging of the esophagus is vital for diagnosing diseases such as Barrett's esophagus, adenocarcinoma of the esophagus and squamous cell carcinoma of the esophagus. There already exist several imaging modalities such as four dimensional deflection endoscopy and CT scan to image the esophagus in various ways. However, there is a need for an inexpensive imaging modality that can be utilized in resource-limited settings and produce high fidelity 3D images which improve detection and guide treatment. In a collaboration with Pensievision, a company with proprietary machine learning algorithms for 3D imaging, we sought to use a novel inexpensive portable handheld endoscope with liquid lens as a proof of concept for visual 3D imaging of the esophageal surface. The endoscope utilizes shape-from-focus imaging, or a series of 2D images collected from a single perspective at varying focuses instead of stereoscopic imaging that requires multiple angular perspectives to generate 3D images. This approach was thought to be more

suitable for the imaging of a narrow area without much room for maneuverability like the esophagus. The computational engine is a battery powered Raspberry Pi computer that can intelligently compress data for transfer across low-bandwidth connections if needed. A principal component analysis of the 2D images was used to help extract the rough 3D structure followed by Fourier filtering, intelligent filtering, and other statistical methods to generate the final high-quality 3D image. We were able to show that 3D information is successfully captured on the device in a cadaver model with images of the heart and lower GI tract. However, the initial model was too wide to successfully image the esophagus. We developed a thinner endoscope with greater flexibility to successfully image the esophagus and are currently generating 3D models based on the esophageal data.

49 **Identification of facilitators and barriers to cochlear implant uptake in adult candidates**

Gabriel Brandner, Theodore McRackan, Cheng Ma, David Aamodt, Judy Dubno, College of Medicine, MUSC

Objectives: Despite robust literature demonstrating the benefit of cochlear implantation (CI) in adults, uptake is thought to be very low (6-10%). This study aims to identify barriers and facilitators that contribute to CI uptake and better understand patient factors associated with the decision to pursue cochlear implantation. Methods: Participants were classified into an implanted group that underwent CI or a non-implanted group that did not receive a CI despite meeting eligibility criteria. Participants completed surveys on contributing factors in their decision to undergo implantation, and completed the Cochlear Implant Quality-of-Life (CIQOL-35) profile and CIQOL-expectations instruments. Nominal data was analyzed using Chi-Square analysis or Fisher Exact test and quantitative data was analyzed by Student's t test or Mann-Whitney U test. Effect sizes were reported using Cohen's d. Results: Overall, there were minimal differences in mean pre-operative CIQOL-expectations domain scores between groups (d=0.00-0.45). The non-implanted group reported higher baseline CIQOL-35 scores for emotional (d=0.82, 0.11-1.51), entertainment (d=0.80, 0.10-1.50), and social QOL domains (d=0.58, -0.12-1.27). AzBio sentences in quiet scores were higher in the better hearing ear of the non-implanted group (d=0.80, -0.24-1.61). The most common reported barriers to pursuing cochlear implantation in the non-implanted group were fear of surgical complications and perception that hearing was not poor enough for CI surgery. Difficulty with transportation was the most common reported barrier for implanted group. All respondents within the implanted group indicated the desire for better communication abilities and listening effort burden due to hearing loss as facilitators of CI uptake. Conclusion: Higher pre-operative sentence recognition ability, CIQOL-emotional and entertainment scores appear to be potential factors that contribute to CI uptake. This study provides a better understanding of patient concerns that need to be better addressed and facilitators that can be emphasized to increase CI uptake.

This work was supported by This study was supported (in part) by the National Institutes of Health/National Institute on Deafness and Other Communication Disorders Grant T32 DC 014435.

50 **Autoantibodies Unique to Lupus Nephritis**

Ansley DeVore, Jim Oates, Rachael Werner, College of Medicine, MUSC

Systemic lupus erythematosus (SLE) is an autoimmune disease that when targets the kidneys causes lupus nephritis (LN). Among factors used to predict disease activity, anti-dsDNA antibodies have the greatest relationship to development of end-stage LN. In LN mice, autoantibodies deposited in distinct locations producing different classes. Autoantigen microarrays, including only

a small fraction of autoantibodies in SLE, showed antibodies corresponding to kidney involvement. Our aim is to use a phage display library to discover novel autoantigens that predict LN and the classification (Class III/IV proliferative vs. Class V membranous). Serum of five pure class III/IV LN and five pure class V LN patients with biopsy proven LN were compared to ten healthy individuals using phage display technology. Serum samples were included if within 100 days of kidney biopsy. Non-autoimmune controls were matched by sex, self-proclaimed race, and age within ten years of their matched LN cases. CDI Labs HuScan PHIP-Seq Antibody Profiling analyzed the samples allowing identification of antibodies against 29,371 unique human proteins and all of the NCBI v35.1 human proteome. LN will be compared to the controls and class III/IV to class V. The expected results are identification of known autoantigens for LN and detection of a variety of novel autoantigens due to the heterogenous nature of known LN autoantibody profiles. Using the Human Protein Atlas, we will determine the location of antigen expression. Antibodies binding proteins in the kidneys suggest direct binding, whereas those expressed elsewhere suggest deposition of immune complexes formed in the circulation. Negative results might suggest that three-dimensional structure is important in forming autoantigen immune complexes. Novel autoantigens discovered can be used in a validation cohort to determine performance in predicting LN class and outcomes. Discovery studies using whole human proteins (CDI Labs HuProt) could identify autoantigens that are bound in three-dimensional structures only.

This work was supported by NIH/NIDDK Institutional Training Grant, "Short-term Research Training for Health Professional Students" (T35 DK007431)

51 **The Effect of Acetaminophen on Delirium Outcomes in Cardiovascular Surgical Intensive Care Unit patients: A Retrospective Chart Review**

Kaitlyn Monahan, Department of CHP-DNAP AFN, College of Health Professions, MUSC

Delirium is a hospital-wide issue that is associated with increased hospital length of stay, increased patient morbidity, and mortality. Through a literature review on delirium outcomes, research suggests that risk factors for developing delirium are postoperative pain, increased amounts of opioids, and benzodiazepine administration. Additionally, the administration of intravenous acetaminophen can decrease the incidence and duration delirium, opioid usage, and ICU length of stay. This scholarly project aims to examine acetaminophen and its effect on delirium outcomes in cardiovascular surgical patients. This study was a retrospective chart review at the Medical University of South Carolina Cardiovascular Intensive Care Unit from January 1, 2018, to June 1, 2020. A total of 536 patient charts were obtained. Three groups were formed to compare for data analysis: The no acetaminophen (N) group, the oral (PO) group, and the intravenous and oral (IV/PO) group. Twenty-two patients did not receive acetaminophen; therefore, all twenty-two patients were utilized for data collection. The PO and the IV/PO groups were dedicated twenty-two patients to have equal sample groups. Every fifth patient was selected to randomize the PO and IV/PO groups. Data analysis for this project is currently pending on biostatistician review. Initial data shows that the age range was 18-85 with an average age of sixty-two. 54% of patients were male and 46% of patients were female. 56% of patients were designated as an ASA 4, 43% of patients were designated as an ASA 3, and 1% of patients were designated as an ASA 2. Our findings suggest that there is not a statistically significant incidence of delirium within our small sample size. Additional analysis is in progress to determine if there is an impact on secondary outcomes between the groups. Further research is needed on a larger scale to determine causative factors of delirium.

52 **Stress Among Student Registered Nurse Anesthetists and Its Impact on Wellness**
Esther Odeghe, Esther Odeghe, Dr. Ballister Michelle, Department of AFN, College of Health Professions, MUSC

Registered nurses attending doctoral programs for nurse anesthesia experience a variety of stressors throughout the course of their rigorous didactic and clinical education. Identifying these stressors could guide faculty to anticipate students' needs throughout the program. The purpose of this project is to evaluate the source and level of stress experienced by student registered nurse anesthetists (SRNA) during the three different years of the curriculum. An adapted questionnaire of the Perceived Stress Scale, Coping Behavior Inventory, and Physio-Psycho-Social Response Scale (Sheu, Lin, & Hwang, 2002) was emailed to all SRNAs in a doctor of nurse anesthesia practice program at a southeast academic medical center. 79 SRNAs received the survey, 70% (n=55) responded, and 7% (n=4) were discarded due to incomplete data. Of the 51 participants, 14% (n=7) were first-year students, 41% (n=21) were in their second year, and 51% (n=26) were in their third year. The anonymous data was collected via REDcap and analyzed using descriptive and inferential statistics. The higher the survey score the greater the stress reported. The mean stress score varied at different years of the program. The first-year students' mean score equaled 65.17. The mean score for second year students was 78.05, while the third-year students' mean score was 76.96. Transference (.369; p=0.008) and optimism (-.328; p=0.020) as coping mechanisms were statistically significant predictors of stress. The use of positive coping mechanisms increased over successive years while the use of negative coping mechanisms decreased. In conclusion, while all students' scores indicated taking care of patients as the most significate stressor, students in the second year of the curriculum reported the highest level of stress.

This work was supported by No funding required for this project

53 **Interpreting the Mini-Cog: A postoperative cognitive dysfunction screening tool**
Alyssa Farber, College of Health Professions, MUSC

Objective: To assess the need for education regarding the Mini-Cog exam and how to apply its results to an anesthetic plan to decrease the incidence of postoperative cognitive dysfunction (POCD). Methods: A needs assessment survey determined a need for education regarding the Mini-Cog exam. An education session, regarding how to interpret the results of the Mini-Cog and the recommendations for changing an anesthetic plan, was delivered to anesthesia providers with a pre- and post-test to determine if learning occurred. Results: Roughly 85% of anesthesia providers answered post-test questions correctly compared to 52% of providers answering questions correctly in the pre-test. Conclusion: After the education session, the providers felt more comfortable interpreting the Mini-Cog exam and applying it to their anesthetic practice. Further, all the providers agreed that the education was useful to their anesthesia practice.

54 **Current Adhesion Barriers in Cardiac Surgery: An Assessment of Safety and Efficacy**
William Head, Taufiek Rajab, Namrata Paladugu, Hyejin Kwon, Department of Surgery, College of Medicine, MUSC

Postoperative pericardial adhesions are an important clinical problem in cardiac surgery, contributing to increased morbidity, mortality, and economic costs from increased operating time. Adhesion barriers have been used clinically for the past four decades with research efforts focused on their use in abdominal surgery. Ultimately, limited data exists regarding barriers in cardiac

surgery. This study provides the first major systematic review of adhesion barriers in cardiac surgery. In accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analysis, a literature search was conducted using PubMed and Scopus. Adhesion barriers in each study were evaluated regarding several safety and efficacy variables, and the most frequently mentioned variables were analyzed using Excel and GraphPad Prism 5. 25 studies evaluating adhesion barriers in cardiac surgery were identified with a total of 13 barrier types and 2,919 patients. Relevant safety variables discussed were infection, bleeding events, and mortality. Relevant efficacy variables discussed were the formation of adhesions noted on re-operation and adhesion tenacity scores. The most frequently evaluated barrier was Polytetrafluoroethylene (PTFE) in 13 out of the 25 studies with an infection rate of 0.62% (n=804), a bleeding event rate of 6.44% (n=73), and an average tenacity score of 0.678 (n=143). Further assessment of safety showed that more than one barrier had infection, bleeding event, and mortality rates of 0.00%. Similarly, further assessment of efficacy showed that more than one had an adhesion formation rate of 0.00% and average tenacity score of less than 1. While PTFE has historically demonstrated efficacy in adhesion prevention, it nevertheless presents relevant safety concerns. Limited studies of other barriers have shown improvements with respect to certain variables versus others. Overall, the findings here suggest that no ideal adhesion barrier currently exists and that future ones should be developed with consideration of the unique requirements of cardiac surgery.

55 **The COVID-19 Vaccine Outreach Initiative: A Student's Response to Vaccine Hesitancy**

India Robinson, Danielle Scheurer, Alan Snyder, MD, MSCR; Lancer Scott, MD; Dirk Elston, MD; Leslie Lenert, MD, Department of Dermatology, College of Medicine, MUSC

Only 40.4% of South Carolina's population is fully vaccinated. We responded by leveraging a pre-existing partnership between student volunteers, The Medical University of South Carolina, and an artificial intelligence company (Jvion Inc.) to identify vulnerable populations and connect them to COVID-19 vaccine resources. Our aims are to improve SC vaccination rates, understand reasons underlying vaccine hesitancy, and identify barriers to vaccination. We used Jvion's Vaccine Prioritization Index to help identify SC counties at highest risk for complications associated with COVID-19. We monitored individual vaccination statuses using a novel data standard platform, VacTrac, that queries vaccination registries daily. A program to recruit volunteers was established. Census tracts were assigned to student volunteers to call patients and administer a survey, educational resources, and vaccination scheduling. Risk levels, type of intervention, response rates, survey responses, and vaccination rates are all recorded for analysis. Overall, both internal student and external volunteers were recruited. We received Full Time Equivalent funding for a volunteer/program coordinator. Seven high risk counties were identified as high-risk via Jvion's Vaccine Prioritization Index: Colleton, Georgetown, Williamsburg, Clarendon, Calhoun, Orangeburg, and Bamberg. A total of 333,000 unvaccinated MUSC patients in these high counties (>12 years old) were identified. As this is an ongoing project, we plan to analyze response rate across risk levels, compare phone vs email intervention, pre and post vaccination rates, and odds of receiving a vaccine based on risk level and type of intervention. Our team was able to leverage a pre-existing network of volunteers to develop a unique program targeting high risk communities with low vaccine rates for COVID-19. Ongoing research will quantify the impact of this intervention on vaccination rates and prevention of COVID-19 disease.

56 **Variability and Reliability of 2 Dimensional Versus 3 Dimensional Glenoid Version Measurements with 3 Dimensional Preoperative Planning Software**

Jared Reid, Richard Friedman, Bryce Kunkle, Alexander Greene, Josef Eichinger, Department of Orthopaedics, College of Medicine, MUSC

INTRODUCTION: Preoperative planning for total shoulder arthroplasty (TSA) may change based on the measured degree of glenoid version. Both two-dimensional (2D) and three-dimensional (3D) computerized tomographic (CT) scans are used to measure glenoid version with no consensus on which method is most accurate. The purpose of this study is to directly compare 2D and 3D glenoid version measurements and determine the differences between the two. METHODS: CT scans were performed on 315 shoulders undergoing anatomic or reverse TSA. 2D measurements of glenoid version were obtained manually using the Friedman method, while 3D measurements were obtained using Equinoxe 3D-reconstruction software. Two observers collected the 2D measurements two separate times, and intra- and inter-observer measurements were calculated. Groups were compared for variability using Intraclass Correlation Coefficients (ICC), and for differences in means using student t-tests. Additionally, samples were stratified by version value to understand potential sources of error between techniques. RESULTS: For 2D measurements, intra-observer variability indicated excellent reproducibility for both Observer 1 (ICC = .928, 95% CI: .911-.942) and Observer 2 (ICC = .964, 95% CI: .955-.971). Inter-observer variability measurements also indicated excellent reproducibility (ICC = .915, 95% CI: .778-.956). Overall 2D version measurement average (-4.9° ± 10.3°) was significantly less retroverted than the 3D measurement average (-8.4° ± 9.1°), ($P < .001$), with 3D measurements yielding a more retroverted value 73% of the time. When stratified on the basis of version value, there was no significant difference in the distribution of high-error samples. DISCUSSION: There was excellent reproducibility between the two observers. The 3D measurement techniques were significantly more likely to return a more retroverted measurement, and high error samples were evenly distributed, indicating no discernable trends in the degree of error observed. Shoulder surgeons should be aware that variations in different glenoid version measurement strategies could affect preoperative planning.

57 **Characterizing Retinal Dystrophy in South Carolina**

Joseph Griffith, Mae Millicent Winfrey Peterseim, Kareem Sioufi, George Magrath, Michael Lyons, College of Medicine (MD, PhD), MUSC

Purpose: To evaluate the rates and genetic characteristics of inherited retinal dystrophies (IRDs) in the state of South Carolina. Methods: A retrospective chart review was performed of patients with clinical diagnosis of retinal dystrophy. Data including presenting symptoms, visual acuity, retinal exam findings, imaging findings, and genetic results were gathered. Results: There were 332 patients with IRDs included in this study. Mean age was 37.2 (median: 34.5, range 1-81 years). The known ethnic groups included Caucasians (64%), African Americans (30%), Hispanics (3%), and Asians (2%). The most prevalent dystrophies identified were non-syndromic retinitis pigmentosa (29.2%), Stargardt's disease (8.1%), Usher's disease (8.1%), cone-rod dystrophy (7.8%), cone dystrophy (4.8%), and Leber's congenital amaurosis (4.2%). Genetic testing was performed in 101 patients (30.4%). Of those, 82 (81%) patients had known genetic mutations and 19 patients (19%) had inconclusive genetic testing. The most common gene mutations out of the patients with positive testing were USH2A in 17.0% (n=14), ABCA4 in 14.2% (n=12), CEP-90 in 7.3% (n=6), CLN3 in 7.3% (n=6), RP-1 in 4.9% (n=4), and PRRH2 in 4.9% (n=4). Conclusions: We provide initial information characterizing within the diverse population of South Carolina, which reflects global

genetic and diagnostic trends.

58 **SHP2-dependent Signaling Pathways Programming the Oral Cancer Cell Secretome**
Merrell Still, Subramanya Pandruvada, Jack Goertzen, Nico Farrar, Brad Neville, Besim Ogretmen, Department of Oral Health Sciences, College of Dental Medicine (DMD, PhD), MUSC

Head and neck squamous cell carcinomas (HNSCC) are the sixth most common cancer worldwide and account for 35,000 cancer-related deaths every year in US alone. Recent studies have implicated the presence of tumor infiltrating immune cells as independent prognostic markers in HNSCC. However, it remains unclear how cancer-cell-signaling regulates tumor immunogenicity and immune cell infiltration. Aberrant expression of Src-homology 2 domain-containing phosphatase, SHP2 has been associated with the pathogenesis of several cancers including HNSCC. We hypothesized that SHP-2/PI3K axis plays a role in dictating cancer-cell-secretome and HNSCC tumor development. Representative HNSCC cell lines were treated with lentiviral-based SHP2 shRNA (SHP2 knock down), SHP2 mutants (mutant gene over expression) or with a novel SHP2 allosteric inhibitor SHP099. And, cell viability, motility, invasion, cancer cell secretome and PI3K signaling were assayed. We show that decreased PTEN expression displayed SHP2 activation status-dependent AKT/PI3K expression. Expressing mutant SHP2-C459S (dead phosphatase) restored PTEN expression while inhibiting PI3K-AKT signaling in our PTEN-low HNSCC cell lines suggesting a link between these players. Remarkably, in comparison to SHP2-WT or SHP2-E76Q mutant (constitutively active mutation), expression of mutant SHP2-C459S besides treatment with allosteric SHP2 inhibitor, SHP099 have shown a reduced cancer cell migration and matrigel invasion with no effect on cell viability. Furthermore, cell culture-conditioned media obtained from SHP2-modulated HNSCC cell lines presented a distinct and selective immune cell chemoattraction in vitro with increased CD8+T cells while limiting macrophage migration suggesting altered secretome composition following SHP2 inhibition and a probable anti-tumor response. Cell culture-conditioned media analysis conducted using antibody arrays and mass spectrometry further confirmed the altered secretome in SHP2WT cell lines. Furthermore, we observed decreased tumorigenesis in HNSCC humanized mouse model following SHP2 knockdown endorsing altered tumor cell landscape following SHP2 inhibition. Our findings support that SHP-2/PI3K axis inhibition strategies may have therapeutic potential.

This work was supported by Supported in part by American Cancer Society Institutional Research Grant awarded to Hollings Cancer Center, MUSC and Faculty Start-up research funds from JBE College of Dental Medicine.

59 **Treating Congenital Cutaneous Candidiasis in a Preterm Infant**
Chelsea Shope, Lara Wine Lee, Samantha Karlin, Alexandra Ritter, Colleen Cotton, College of Medicine, MUSC

Congenital cutaneous candidiasis is a common condition in premature and very low birth weight (VLBW) infants that begins as mild scaling in flexural sites and most commonly progresses to erythematous skin lesions with diffuse scale that tends to desquamate or erode. Early treatment with intravenous (IV) fluconazole prevents worsening systemic illness and deterioration. Dermatology was consulted on a 13-day old neonate born at 23 weeks 5 days, admitted to the NICU, for dry, scaly skin for two days. At eight days, he clinically decompensated and met sepsis criteria and was treated with antibiotics and fluconazole. Blood cultures were negative, and these medications were discontinued. Examination showed diffuse pink scaly skin over the back and

extremities, with lesser amounts over the face, neck, chest and abdomen. Numerous spores and pseudohyphae were seen on potassium hydroxide (KOH) prep. IV fluconazole was restarted along with topical Mepitel for eroded areas. At day seven, his skin and clinical status was improving, but due to persistent active skin involvement, another week of treatment was recommended. At day 10, he was transitioned to PO fluconazole due to losing IV access and returned to IV formulation three days later. After 21 days of treatment, the patient's back and neck remained pink and scaly with evidence of active infection on repeat KOH prep. Ultimately the lesions resolved with the addition of a 7-day course of IV micafungin. Congenital cutaneous candidiasis is common in premature neonates but is often overlooked until the patient's condition deteriorates. Dermatologists should be consulted early to prevent the harmful sequelae of severe infection. The use of IV fluconazole is paramount to expeditious resolution of the disease. Although the bioavailability of fluconazole is similar in the oral and IV preparations, it is possible that in a premature neonate, oral fluconazole could have less systemic absorption.

60 **Acute Onset Esotropia with Increased Screen Time: a case series**

Jared Tallo, Edward Cheeseman, Anastasia Alex, MD, Mae Millicent Peterseim, MD, James Bowsher, MD, College of Medicine, MUSC

Background: Near-work requires convergence of the eyes in addition to accommodation. The purpose of this study was to describe a series of cases of acute onset esotropia in pediatric patients in the setting of increased screen time with no other identifiable causes. Case presentations: Nine patients, ranging from 11-22 years of age, presented to the pediatric ophthalmology clinic with complaints of eye crossing and diplopia in the setting of increased near-work and screen time during the COVID-19 pandemic. Physical exam confirmed the presence of concomitant esotropia in all cases. Neuroimaging was obtained and ruled out structural disease as a cause of acute onset esotropia. History was negative for head trauma or medication changes. Most patients presented with a large angle esotropia (>30 prism diopters) at both near and distance. All required strabismus surgery to correct. Post-operatively, alignment improved to near orthotropia with some increase in ability to achieve fusion. Conclusions: An increase in near-work and screen time during the COVID-19 pandemic may have triggered the acute onset of concomitant esotropia or decompensation of previously controlled intermittent esotropia. Fortunately, the esotropia was correctable by surgical intervention.

61 **Evaluating the Role of IFNLR1 Receptor Dynamics and Plasticity in Regulating Cellular Response to Interferons**

John Evans, Eric Meissner, Laura Novotny, College of Medicine (MD, PhD), MUSC

Abstract withheld from publication

62 **Identifying Quality Improvement Opportunities in Efforts to Reduce Racial and Ethnic Disparities that Persist Among the Management of Anemia in Pregnancy**

Latyra Gibbs, College of Medicine, MUSC

Iron deficiency is the most common cause of anemia due and most commonly can be attributed to chronic blood loss, inadequate intake, inadequate gut absorption, or increased demand for the mineral. During pregnancy, the demand for iron increases in efforts to supply oxygen to the growing fetus. Due to this physiologic change, many pregnant people commonly develop this anemia with the national prevalence being 21.55 per 1,000 women. Anemia in pregnancy

disproportionately affects non-Hispanic Black women, with the prevalence being at least two times higher than that of non-Hispanic White women. With this knowledge, retrospective chart review of all deliveries completed at MUSC between January 2020 and June 2020 was conducted. With the intent to identify opportunities for improving the management and diagnosis of IDA in pregnancy and the presence of racial and ethnic disparities among maternal anemia, patient demographics (race and ethnicity), hemoglobin on presentation to the Labor and Delivery ward and the administration of red blood cell transfusions within the peripartum and postpartum periods were assessed. Upon the review of 1,436 cases, 48.68% of the birthers identified as White, 33.98% as Black, and 11.42% Hispanic. Of the birthers who presented for delivery with Hgb < 10 g/dL, more than half were Black (55.89%) while 30.26% were White and 10.26% Hispanic. Of the birthers who presented for delivery with Hgb < 10 g/dL and received at least one red blood cell transfusion, nearly half were Black or African American (46.51%) while 32.56% were White and 18.6% Hispanic. From the results, IDA was found to be more prevalent among non-Hispanic Black women. In efforts to address this disparity, areas for improvement include more aggressive screening of IDA in the antepartum period, enhanced patient education and the utilization of intravenous iron infusions.

63 **Validation of a Highly Accelerated Flow Technique for the Simultaneous Evaluation of Flow in the True and False Lumens in Thoracic Aortic Dissection**

Gabrielle Young, Akos Varga-Szemes, Tilman Emrich, MD U. Joseph Schoepf, MD Fei Xiong Akos Varga-Szemes, MD PhD, College of Medicine, MUSC

Aim: to validate a prototype highly accelerated magnetic resonance pulse sequence for the flow characterization of the false and true lumens in models of type B aortic dissection. Methods: Silicone aorta models with different dissection flap anatomy were connected to a flow loop pressurized to match human blood pressure. Pressure was confirmed and monitored by pressure transducers. A state-of-the-art 3T scanner was used for MRI with ECG gating generated from pressure curves. Initially, reference thru-plane flow acquisitions were performed using a conventional flow technique. The acquisition was then repeated with different velocity encoding (VENC) sensitivities to capture fast (true lumen) and potential slow (false lumen) flow. Next, the prototype flow technique was used at the same aortic locations which is able to capture the flow in the true and false lumen simultaneously, regardless the difference in flow speed between the two compartments. Flow evaluation was performed using a dedicated software application by semi-automated segmentation of the aortic true and false lumens across the cardiac cycle and processed to report time-averaged mean velocity and mean/peak flow volumes. Results: We successfully performed MRI scans of three different silicone TBAD phantoms under controlled flow (100cm/s) and pressure conditions (160mmHg) in the flow loop. The conventional flow technique with VENC 100cm/s reliably measured flow in the true lumen; however, the technique captured mostly noise in the false lumen. Conversely, the low VENC technique (60cm/s) was able to detect slow flow in the false lumen; however, it showed aliasing in the true lumen. In comparison, the prototype flow technique with combined VENC 100-80-60cm/s reliably detected flow in both the true and the false lumens in a simultaneous fashion. Quantitative assessment of flow rate demonstrated excellent agreement between the conventional 100cm/s and the prototype in the true lumen, and conventional 60m/s and prototype in the false.

This work was supported by Dr. Paul McDermott, REPMMS Program, NIH R25 grant

64 **Chronic Kidney Disease and in-hospital outcomes among patients treated with thrombolysis for acute ischemic stroke**

Henry Best, Erin Weeda, Shayma Al Zaidi, College of Pharmacy, MUSC

Data on the efficacy and safety of thrombolysis in individuals with chronic kidney disease presenting with ischemic stroke is sparse. We assessed the association between chronic kidney disease and in-hospital outcomes in acute ischemic stroke encounters receiving thrombolysis. Using administrative data from the 2013 and 2014 United States National Inpatient Sample, adult acute ischemic stroke encounters treated with thrombolysis were identified. Patients with chronic kidney disease were identified via diagnostic coding. We used multivariable regression to evaluate the relationship between chronic kidney disease and intracerebral hemorrhage (ICH), in-hospital mortality and length of stay (LOS) after adjusting for age and comorbidities. Of 13,993 encounters receiving thrombolysis for acute ischemic stroke, 12.4% (n= 1,739) had chronic kidney disease. ICH occurred in 7.6% of patients, 7.0% experienced in hospital mortality and mean LOS was 7.5 days. Chronic kidney disease did not increase the odds of ICH (odds ratio [OR]= 1.00; 95% confidence interval [CI]= 0.83-1.20) or in-hospital mortality (OR= 1.19; 95% CI= 0.99-1.42). LOS was slightly longer (mean difference=0.39 days 95%; CI= 0.15-0.62) among those with chronic kidney disease. Among encounters treated with thrombolysis for acute ischemic stroke, chronic kidney disease was not associated with a higher adjusted odds of ICH or in-hospital mortality and LOS was only slightly longer among these individuals.

65 **Sex divergent effects of lofexidine on heroin seeking in male and female rodents**

Jordan Carter, Carmela Reichel, Angela Kearns, Michael Kong, Department of Neuroscience, College of Graduate Studies (MSTP), MUSC

Introduction: Epidemiologic studies have repeatedly confirmed the strong comorbid relationship between post-traumatic stress disorder (PTSD) and opioid use disorder (OUD). Stress plays a dual role in OUD as a precursor to drug intake and a relapse precipitant. This duality has led researchers to posit that stress reduction may be a viable option to treat OUD, especially with comorbid PTSD. Lofexidine, an alpha-2-adrenergic receptor agonist, is the first FDA approved non-opioid treatment for opioid withdrawal syndrome, presumably due to its ability to alleviate withdrawal-induced stress. Yet, despite this approval, no studies have directly evaluated the impact of lofexidine on stress-related heroin seeking or comorbid OUD-PTSD. Methods: We combined acute restraint stress and contingent heroin self-administration (HSA) in male and female rodents to study the impacts of lofexidine on HSA. Rats were restrained for 2h in the presence of an odor cue (stress-CS) to condition an association between them. The effects of lofexidine were tested during maintenance of HSA. Reinstatement of heroin seeking was evaluated in the presence of the stress-CS and heroin associated cues with varying doses and schedules of lofexidine or vehicle administration. Results: All lofexidine doses (100, 150, 200µg/kg) decreased active nose pokes (ANPs) and intake during HSA in males and females. During reinstatement, lofexidine (100 and 200µg/kg) decreased ANPs in response to the stress-CS and heroin cues. These effects, along with depressed locomotor activity, occurred in sham and stress males and sham females. Stress females were impervious to lofexidine's effects. An ongoing study is evaluating effects of lofexidine given for ≥6 days at 40µg/kg, better approximating clinical use. Discussion: Although locomotor suppression accompanied lofexidine's reduction in stress and heroin cued reinstatement, stress females were not impacted. This sex difference is important as it implicates lofexidine may be a less effective treatment for comorbid OUD and PTSD in females.

This work was supported by NIDA P50-DA016511, NIDA U54-DA016511, NCATS TL1-TR001451, NCATS UL1-TR001450

66 **Heat Shock Protein 27 is an Important Early Regulator and Platform Molecule in P. gingivalis-Driven Selective Autophagy**

Bridgette Wellslager, Özlem Yilmaz, Nityananda Chowdhury, Department of Oral Health Sciences, College of Graduate Studies, MUSC

Abstract withheld from publication

67 **The importance of hand function for stroke survivors' quality of life**

Corey Morrow, Kit Simpson, Michelle Woodbury, Department of Health Sciences and Research, College of Health Professions, MUSC

There are 7.8 million stroke survivors in the US and 77% experience chronic hand impairment. However, it is unknown how much hand function impacts adult patients' overall quality of life compared to other deficits like strength and Activities of Daily Living (ADLs). It is difficult to compare the weighted importance of each sub-scale of function because they have very distinct outcome measures. Converting these measures into utility weights to calculate quality of life allow for the comparison of interventions in rehabilitation and across medical disciplines. A commonly used measure of patient centered outcomes is a quality-adjusted life year (QALY). QALYs are calculated from utility weights measured on a scale of 0 to 1.0. For example, a utility weigh of 0.8 represents 80% of a healthy year of life. A recent meta-analysis calculated utility weights for the Stroke Impact Scale (SIS) and Modified Rankin Scale (mRS) for a group of stroke survivors. These established mean utility weights for all subscales of the SIS in relation to the 6 levels of the mRS. This study showed hand function has greater impact on patients' quality of life than physical strength and Activities of Daily Living (ADLs) across all levels of the mRS. For example, patients with mRS 4 reported 0.08 utility weight for hand function and a 0.29 utility weight for ADLs with an overall utility weight of 0.31. This shows general utility weights applied to stroke outcome measures such as the mRS may underestimate the absolute importance of hand function to patients. Thus, it is important to examine utility and quality of life research for upper extremity assessments to provide specific utility weights for different levels of hand function. We will report on the general population's value of different levels of hand function.

This work was supported by TL1 TR001451, UL1 TR001450

68 **Cadherin complexes recruit PIWIL2 to suppress transposons and pro-tumorigenic transformation**

Alyssa Risner, Antonis Kourtidis, Joyce Nair-Menon, Colin McDowell, Vamsi Gangaraju, Department of Regenerative Medicine and Cell Biology, College of Graduate Studies, MUSC

Introduction. Recent studies have shown that in addition to genomic instability and oncogene expression, more than 50% of tumors also have increased transposon activity. Transposons are mobile DNA elements that are widespread in the human genome; however the reasons for their increased activity in somatic tumors are currently unknown. We have evidence of a novel interaction linking epithelial adherens junctions with transposon regulation. More specifically, our data have revealed an interaction of E-cadherin and p120 catenin, core components of adherens junctions, with PIWIL2 (Piwi-like RNA-Mediated Gene Silencing 2). PIWIL2 is a member of the Argonaute family of proteins and is a key component of the PIWI-piRNA processing pathway that is

responsible for transposon silencing. Hypothesis. We hypothesize that the adherens junctions recruit PIWIL2 and suppress transposon activity in differentiated cells to maintain genomic integrity and the normal epithelial phenotype. Methods and Results. Through immunofluorescence staining, confocal microscopy, and co-immunoprecipitation studies, we found co-localization and association of PIWIL2 with E-cadherin and p120 catenin at adherens junctions of well-differentiated breast and colon epithelial cells, whereas this association is lost in cancer cells. Furthermore, our data show that E-cadherin depletion results in mis-localization of PIWIL2, as well as of TDRD1, another member of the PIWI complex. Interestingly, E-cadherin depletion also results in upregulation of the LINE1 transposon and γ-H2AX, an indicator of DNA double-stranded breaks. Conclusions. We will further elucidate PIWIL2 recruitment to mature adherens junctions of well differentiated epithelial cells and examine its biological role as a novel tumor suppressor. We will accomplish this by using human breast and colon cell lines for shRNA knockdown assays, piRNA transposon RNA-seq, and obtain patient samples for immunohistochemistry. Since both loss of junctional integrity and increased transposon activity are universal events in cancer, this study has the potential to deepen our understanding of tumorigenesis.

This work was supported by TL1 TR001451 & UL1 TR001450, NIH/NCI R21 CA246233-01A1, NIH/NIGMS P20 GM103499 (SC INBRE)

69 **Kv3 channel positive modulation decreases ethanol binge drinking**

Kathy Lindquist, Patrick Mulholland, Reginald Cannady, Jennifer A. Rinker, Department of Neuroscience, College of Graduate Studies, MUSC

According to the 2019 National Survey on Drug Use and Health, about 14.5 million people have been diagnosed with alcohol use disorder (AUD). Although many factors contribute to the development of AUD, the NIAAA estimates that genes account for almost 50% of the risk. Using bioinformatic analyses, our lab identified a negative correlation between medial prefrontal cortex (mPFC) Kcnc genes, which encode Kv3 channels, and ethanol intake. The mPFC is a brain region essential for executive function, sensitive to ethanol, and houses neuronal subpopulations such as pyramidal neurons (PN) and parvalbumin interneurons (PVI). Kv3 channels are highly expressed in PVIs, which play a role in neural excitation/inhibition balance and higher cognitive processes impacted in AUD. Given the relationship between Kv3 channels and alcohol consumption, we sought to determine the role of Kv3 channels with regards to alcohol drinking using the Kv3 positive modulator AUT3 and AUTpro while monitoring PVI activity surrounding drinking bouts. In vivo fiber photometry was used to record GCaMP activity of either PVIs or PNs in the prelimbic mPFC during drinking of either ethanol or sucrose in a modified drinking in the dark paradigm. Administration of AUT3 or AUTpro decreased ethanol intake without impacting sucrose intake or locomotor activity. This decrease in drinking accompanied an increase in GCaMP signal of PVI surrounding ethanol drinking bouts. Additionally, we compare baseline activity to that of PNs in prelimbic mPFC, where we show that PN GCaMP activity was higher than untreated PVIs surrounding a drinking bout, but lower than PVIs when AUT3 is administered. The calcium signal during sucrose drinking also differed between PVIs and PNs, showing distinction between PVI and PN activity. This preliminary data characterizes PN and PVI activity surrounding ethanol drinking bouts, and that Kv3 positive modulators could be a potential therapeutic option for heavy alcohol drinking.

70 **Exploring the Impact of Advanced Glycation End Products on Macrophages Polarization in the Mouse Mammary Gland**

Kendell Peterson, Victoria Findlay, Bradley A Krisanits, Lourdes M Nogueira, David P Turner, Department of Molecular and Cellular Biology and Pathobiology Program, College of Graduate Studies, MUSC

Advanced glycation end-products (AGEs) are endogenous metabolites formed as by-products of sugar metabolism and oxidative stress. They are a ligand for the receptor for AGE, or RAGE. High exogenous AGE increases RAGE activation promoting chronic inflammation, a well observed inducer of genomic instability, a hallmark of cancer progression. This correlation makes it compelling to observe the impact of AGEs on normal mammary gland development, specifically during pubertal growth, a known window of susceptibility, as these aspects haven't been extensively investigated. Previous studies in the lab have shown that a high AGE diet leads to mammary dysregulation with abnormal stromal cell recruitment and/or expansion around TEBs and AGE-mediated pre-neoplastic lesions. The prevalent cell types within the abnormal stroma were fibroblasts and macrophages. Macrophages exhibit incredible plasticity in normal and cancer tissues and their function is also largely dictated by their surrounding microenvironment. Through NFkB signaling, AGE: RAGE activation is believed to induce macrophage polarization to a pro-inflammatory M1 phenotype. However, in the tumor microenvironment, macrophages typically acquire the pro-tumorigenic M2 phenotype. Therefore, we hypothesize that AGEs induce pro-tumorigenic M2 polarization within the mammary gland, thereby increasing breast cancer risk, and that this polarization is RAGE-dependent. We will isolate mammary glands from wild-type, RAGE heterozygous and RAGE homozygous null mice utilizing a dietary AGE model where mice are fed either a high AGE or control diet from weaning and throughout pubertal growth. We will assess AGE-mediated macrophage polarization and whether this is RAGE-dependent. Macrophage polarization will be assessed by flow cytometry utilizing selective pan M1 and M2 surface markers. Marker expression will be confirmed by quantitative PCR. The results of this study will provide insight into the role of AGEs in early progression and may provide insight into early intervention strategies that target macrophages.

This work was supported by SREB-STATE DOCTORAL SCHOLARS PROGRAm

71 **Proteasome-mediated protein catabolism fuels antitumor immunity**

Megan Tennant, Jessica Thaxton, Katie Hurst, Brian Riesenberg, Alex Andrews, Lee Leddy, David Neskey, Guillermo Rangel Rivera, Chrystal Paulos, Elizabeth Hill, Peng Gao, Lauren Ball, Department of Microbiology and Immunology, College of Graduate Studies, MUSC

Metabolic rewiring is a strategy to enhance antitumor potency of T cells through promotion of cell-intrinsic energy resources that sustain antitumor function. However, the interaction between metabolic remodeling and the capability of T cells to maintain protein synthesis in tumors is not understood. Here, we show that antitumor metabolism is dependent on proteasome-mediated catabolism; thereby sustaining protein synthesis in the nutrient stress of solid tumors. Inhibition of the proteasome abolished antitumor translation and efficacy in T cells infused into tumor-bearing mice. Protein catabolism was required for ATP generation in T cells under tumor stress, indicating a role for the proteasome as a master regulator of antitumor bioenergetics. Furthermore, we show that proteosome activity is negatively regulated by both glycolysis and the mammalian target of rapamycin complex 1 by dampening protein translation and inflammatory cytokine synthesis in

vivo. In the present study we demonstrate the previously unknown role for the proteasome to fuel antitumor immunity in the context of adoptive T cell therapy and checkpoint inhibition.

This work was supported by T32 DE01755, 1RO1CA348359-010, T32 5T32AI132164-04, T32 CA 193201

72 **GABA Concentrations in the Anterior Cingulate Cortex are Associated with Impulsivity Scores in Adolescent Heavy Drinkers: A 1H-magnetic Resonance Spectroscopy Study**

Brittney Browning, Lindsay Squeglia, Anna Kirkland, Helen Liu, Cori Herring, Department of Neuroscience, College of Graduate Studies, MUSC

Adolescence is a phase of neurodevelopment that is strongly associated with increased reward seeking and impulsivity, which is thought to be an underlying reason for alcohol initiation and later transition into problematic alcohol use. Despite this, the neurobiology of impulsivity in heavy drinking adolescents is poorly understood. Therefore, this study aimed to investigate the relationship between the inhibitory neurotransmitter γ-aminobutyric acid (GABA) with measures of impulsivity and drinking. Data from 22 heavy drinking adolescents enrolled in an ongoing clinical trial (K23AA025399) were analyzed. Participants completed the Barratt Impulsiveness Scale (BIS-11) and 1H-magnetic resonance spectroscopy (MRS) to quantify GABA within the anterior cingulate cortex. In addition to overall BIS score, BIS subcategories of attention, cognitive instability, motor, perseverance, self-control, and cognitive complexity were analyzed. Simple linear regression was used to explore the associations between 1) BIS scores and GABA levels, 2) drinking measures and GABA levels, and 3) BIS scores and drinking measures. GABA concentrations were positively associated with total BIS scores (β= 17.402, SE=6.597, p=0.016), as well as two sub-factors: perseverance (β= 3.716, SE= 1.447, p=0.018) and self-control (β= 5.375, SE= 2.240, p=0.026). Perseverance was negatively associated with total standard drinks (β=-15.875, SE= 7.516, p=0.47). No other significant models were found for BIS, GABA, or drinking measures. These findings suggest a positive relationship between GABA levels in the ACC, a region of brain associated with emotion and impulse control, and impulsivity measures within heavy drinking adolescents. Future studies should explore if alcohol use could be moderating the relationship between GABA and impulsivity as this may help inform more targeted prevention and treatments efforts for alcohol use disorder. Additionally, longitudinal studies could determine if the relationship between GABA and impulsivity predates/influences alcohol initiation, which may explain the lack of associations between drinking measures in our cross-sectional study.

73 **Gene and Environmental Interaction for the Pathogenesis of Cardiac Alzheimer's**

Helen Butler, Federica del Monte, Marice McCrorey, Stephanie Dilucia, Gianlorenzo Daniele, Amy Mackos, Loren Wold, Department of Cardiology (MCBP), College of Medicine and College of Graduate Studies, MUSC

Introduction: Alzheimer's Disease (AD) and Heart Failure (HF) are age-dependent diseases linked by pathological protein aggregates. Over common genetic traits, environmental modifiers may predispose individuals to developing heart and brain dysfunction through an accelerated misfolding process. Environmental air pollution (AP) exposure is associated with poorer cardiovascular and cognitive function independently. However, AP exposure has not been evaluated concurrently on cardiac and cognitive function and the mechanism by which AP alters organ function is unknown. We propose AP accelerates the pathological accumulation of protein aggregates via changes to lung microbiome, ROS production and oxidative stress. We aim to characterize the function of both

organs and explore the mechanisms by which AP may accelerate aggregate pathology. Methods: Three-month-old wildtype and AD-prone mice (APPswe/PS1□E9) were subjected to three months of exposure (6 h/day, 5 days/week) to either air particulate matter (<2.5 µm diameter, PM2.5) or filtered air (FA) using the Ohio air pollution exposure system (OASIS-1). Following exposure, mice underwent behavioral and echocardiographic assessment. Blood, bronchoalveolar lavage fluid (BALF) and organs were collected for analysis. Results: Our results indicate that PM2.5 exposed mice display a disinhibited behavioral phenotype, dysfunction in spatial learning and memory, and a precipitated diastolic dysfunction, all of which are common features of AD patients. The BALF microbial communities and ROS indicators are under analysis. Conclusions: Our results indicate PM2.5 exposure worsens cognitive and cardiac function in both WT and AD prone mice. Statistical analysis will determine if there is a synergistic effect in our model, wherein PM2.5 exposure accelerates disease onset in genetically predisposed individuals. Results of such analysis could indicate the use of HEPA filters to protect susceptible individuals (i.e. nursing homes). Ongoing studies will investigate the mechanisms by which exposure to PM2.5 impairs cardiac and cognitive function (i.e. accelerating aggregate pathology).

This work was supported by 5R01-AG057046 8C873, T32: T32GM132055

74 **Determining the Role of Skeletal Muscle Ceramides in the Pathology of Cancer Cachexia**

Victoria Spadafora, Denis Guttridge, Erin Talbert, Besim Ogretmen, Natalia Oleinik, Department of Biochemistry, College of Graduate Studies (MSTP), MUSC

Abstract withheld from publication

75 **Role of Porphyromonas gingivalis in mediating ceramide-dependent mitophagy in oral squamous cell carcinoma**

Megan Sheridan, Besim Ogretmen, Nityananda Chowdhury, Han Lee, Zdzislaw Szulc, Mohamed Kassir, Subramanya Pandruvada, Özlem Yilmaz, Department of Biochemistry and Molecular Biology, College of Graduate Studies, MUSC

Abstract withheld from publication

76 **Inhibition of ferroptosis using UAMC-3203 in the post stroke period does not impact cognitive outcomes in diabetic rats**

Mia Edgerton, Adviye Ergul, Ashley Phoenix, Raghavendar Chandran, Victoria Wolf, Yasir Abdul, Sarah Jamil, Weiguo Li, and Adviye Ergul, Department of Pathology and Laboratory Medicine, College of Graduate Studies, MUSC

Introduction: Post-stroke cognitive impairment (PCSI) contributes to significant long-term disability in stroke victims. 30% of ischemic stroke victims in the United States also have diabetes, which increases the risk of hemorrhagic transformation as well as PCSI. Ferroptosis, an iron-induced cell death can instigate increased oxidative stress and contribute to impaired neurovascular repair leading to PSCI in diabetes. This study was designed to test the hypothesis that inhibiting ferroptosis in the post-stroke period will improve cognitive recovery in diabetic animals. Methods: 8 weeks after diabetes onset, male rats underwent 60 min middle cerebral artery occlusion (MCAO). On Day 3, after stroke injury was confirmed by MRI, animals were randomized to UAMC-3 (2mg/kg) or vehicle treatment for 2 weeks. Sensorimotor and cognitive behavioral tests were

performed after 8 weeks of MCAO. Results (Table 1): 60 min occlusion caused significant acute neurological deficits. There were no differences in indices measured by novel object recognition (NOR), Y-maze and sucrose preference tests. Interestingly, step through latency in passive avoidance test (PAT) was lower in the UAMC-3203 group. Conclusion: Treatment with a ferroptosis inhibitor for 2 weeks after stroke did not impact recognition and working memory but worsened aversive learning in diabetic male rats. Further evaluation of tissue markers of neurovascular degeneration, inflammation and ferroptosis are required to better understand whether ferroptosis contributes to poor stroke recovery in diabetes.

This work was supported by IMSD, VA, NIH

77 **Understanding the role of the insulin receptor during transport and signaling in post stroke cognitive impairment.**

Crystal Smith, Catrina Robinson, , Department of Neurology, College of Graduate Studies, MUSC

Hyperinsulinemia, characterized as elevated levels of insulin circulating in the blood, is a risk factor for cognitive decline; however, the mechanisms are poorly understood. Hyperinsulinemia leads to a deficiency in brain insulin levels. A deficiency in brain insulin levels is associated with impaired insulin signaling, which is important for neuroplasticity, synaptogenesis, and cognition. Our previous studies demonstrated that impaired insulin signaling correlated with cognitive impairment in high-fat diet mice, a model of hyperinsulinemia. We hypothesize that inhibiting brain insulin signaling through the use of intranasal insulin affibody, which binds to the insulin and reduces downstream insulin signaling, will lead to impaired cognition. This reduction is evident by a decrease in the ratio of phosphorylated protein kinase B (pAkt) to protein kinase B (Akt), which is activated by insulin. To explore our current hypothesis, 16 week old C57BL6J male and female mice on a standard diet were administered the intranasal affibody for 5 days. Cognition was assessed through the novel object location (NOL) and novel tactile (NTR) recognition behavioral tests. The animals participated in NOL and NTR, 8 weeks before receiving the intranasal treatment to establish baseline and 3 days after receiving 5 g of the intranasal insulin affibody treatment or saline. Preliminary results indicate animals receiving 5 L of the insulin affibody perform worse on the NOR and NTR behavioral test, as well as having decreased pAkt/Akt expression observed through western immunoblotting. Our preliminary studies reveal that brain insulin is important for normal cognitive function.

This work was supported by NINDS R01NS099595, IMSD NIGMS R25GM072643

78 **Identifying aMCI network models of cognitive domains via functional connectomics**

Duncan Nowling, Jane Joseph, Graham Warner, Nicholas Bustos, Katherine Barlis, Department of Neuroscience, College of Graduate Studies, MUSC

Many studies apply resting functional MRI (rs-fMRI) connectomics to understand neurocognitive risk profiles for Alzheimer's Disease in amnestic Mild Cognitive Impairment (aMCI), Alzheimer's prodromal stage. However, most studies focus on only a few cognitive domains at a time. This study used Graph Theory (GT)-based connectome mapping to create predictive models of 7 cognitive domains, generating more complete network profiles of aMCI. We expect that each cognitive domain will have a unique network profile in both its GT values and important predictive regions. 90 rs-fMRI scans from the Alzheimer's Disease Neuroimaging Initiative, were used to isolate connectome features that predicted: Mini-Mental State Examination (MMSE), Logical

immediate (LIMM) and delayed (LDEL), Trails A (TRAA) and B (TRAB), Multilingual Naming Test (MINT), and Rey Auditory Verbal Learning Test (RAVLT) immediate scores. GT measures of strength* (STR), eigenvector centrality (EVC), and clustering coefficient (CC) were calculated from connectivity matrices based on time series from 276 a priori brain regions. Models were built using SPSS Automatic Linear Modeling tool. Best model per cognitive score was defined as that which yielded at least 50% significant models across 20 cross-validations. Network profile results: LIMM was predicted by auditory and post central gyrus nodes based on CC, RAVLT was predicted by postcentral sensory and posterior cingulate cortex nodes based on CC, TRAA was predicted by precuneus, middle frontal, fusiform, and paracingulate gyrus nodes based on EVC, and TRAB was predicted by posterior cingulate, entorhinal, superior parietal, frontal pole, and temporooccipital cortex nodes based on EVC. This indicates aMCI cognitive domains have different important functional connectome profiles, indicating different aspects of functional organization and communication affect different cognitive domains. This warrants further work in identifying interactions and differences in the network dynamics of cognitive processes disrupted during prodromal AD, to develop clinically meaningful phenotypes.

This work was supported by Dr. Jane Joseph's NIA grant, 5R01AG55132 "Using connectomics to characterize risks for Alzheimer's Disease"

79 **Severe Post-Stroke Gait Impairments: Rancho Los Amigos Observational Gait Analysis vs. Quantitative Analyses**

Jasmine Cash, Mark Bowden, John Kindred, Department of Health Sciences and Research, College of Health Professions, MUSC

Rancho Los Amigos Observational Gait Analysis (RLA) is a standardized method of clinical gait assessment consisting of eight phases: initial contact, loading response, mid-stance, terminal stance, pre-swing, initial swing, mid-swing, and terminal swing. The use of RLA post-stroke has not been validated. Post-stroke gait analysis can prove challenging because in those with severe hemiparesis not all RLA-defined phases are identifiable. The purpose of this report was to compare the eight RLA phases with a simplified 6-bin approach based on recorded ground reaction forces, demonstrated to be impervious to impairment severity. The 6-bins are defined by: 1) first double-limb support, 2-3) first and second 50% of single-leg stance (mid-stance), 4) second double-limb support, 5-6) first and second 50% of swing. Anterior-posterior ground reaction force (AP-GRF) and peak sagittal hip and knee angles from one participant (F, 63) with severe hemiparesis were analyzed and compared to a healthy control. In the healthy participant initial contact and the loading response corresponded with bin 1, mid- and terminal swing corresponded with bin 6, and the middle 4 events were identical between methods. In the subject with hemiparesis, the RLA-defined phases were undetectable (terminal stance), indistinguishable (mid/terminal swing), or prolonged (loading response and mid-stance). Ipsilateral peak knee flexion (46.66o), typically the beginning of mid-swing, occurred without full contralateral bodyweight alignment. Peak hip extension (20.76o), usually the end of single limb support (terminal stance), occurred simultaneous to body weight alignment (end of mid-stance). However, the bin method allowed for event detection of all phases using only AP-GRF in both participants. While RLA is a standard of observational gait analysis, those with severe post-stroke hemiparesis may benefit from a quantitative analysis with more simply-defined phases, and can be utilized regardless of diagnosis or severity of disability.

80 **Drinking Frequency Modulates Functional Brain Activity in Chronic Alcohol Abusers During 2-Back Spatial Working-Memory Task**

Graham Warner, Jane Joseph, Flanagan J, Benitez A, Barlis K, Richardson J, Stomberg-Firestein, Bustos N, Lawson A, College of Graduate Studies, MUSC

Chronic alcohol abuse is a serious public health issue that has recently been exacerbated as Americans sought refuge from the stress and isolation of the COVID-19 pandemic in the bottom of a glass of wine, beer, or liquor. Problematic drinking has been linked to a myriad of health issues and premature death. Neurobiologically, excessive drinking has been linked to widespread reductions in gray matter volume, aberrant functional activity, and consequently, impairments in a variety of cognitive domains. Spatial working-memory is one such domain with numerous studies reporting deficits in heavy drinking populations. To elucidate the relationship between spatial working-memory and chronic alcohol abuse 18 participants with Alcohol Use Disorder (AUD) and two non-AUD chronic heavy drinkers performed a spatial 2-back task during an fMRI scan. Individual-subject general linear modeling analysis was conducted to determine which voxels showed greater BOLD activity during correctly identified 2-back events (hits) compared to successful memory storage events (the trials two prior to a hit). A group level analysis was then conducted to determine which of the identified voxels correlated with drinking frequency (percentage of days where subjects drank as established by the Timeline Follow Back). This analysis revealed a cluster of 171 voxels primarily located in the right postcentral gyrus and edging into the right precentral gyrus which displayed a significant positive correlation ($r=0.715$, $p<0.001$) with drinking frequency. These results suggest that more frequent drinkers show higher BOLD activation in the right postcentral gyrus and right precentral gyrus more during successful memory storage than hits compared less frequent drinkers. This may indicate that frequent drinkers recruit these regions more heavily than infrequent drinkers in order in order to compensate for functional deficits resulting from frequent drinking.

This work was supported by MUSC Center on Aging

81 **Regulatable complement inhibition of the alternative pathway mitigates age-related macular degeneration pathology in a mouse model**

Nathaniel Parsons, Bärbel Rohrer, , Department of Ophthalmology, College of Graduate Studies, MUSC

Background: Age-related macular degeneration (AMD) occurs after age 65. AMD has two forms, dry (atrophic) and wet (angiogenic). AMD is a multifactorial disease; risk factors include aging, smoking, and complement dysregulation. The amplification loop of the complement alternative pathway (AP) is responsible for the majority of complement activation on cell surfaces and extracellular membranes in animal models of this disease. The AP is inhibited naturally by circulating complement protein factor H (fH). Complement component C3 (C3) protein increases and decreases respective to complement activation. In wet AMD, complement effector molecules increase angiogenesis, activate microglia and recruit immune cells, amplifying the complement-microglia inflammatory feedback loop, leading to tissue damage. Methods: The C3 promoter (−1005 to +251), pC3, was cloned into a pTR backbone and plasmids (pC3-mCherry/CR2-fH) were synthesized and utilized to generate adeno-associated virus serotype 5 (AAV5) vectors. pC3 activation was determined in transiently transfected ARPE19 cells stimulated with H_2O_2 and normal human serum (+/- TT30 or NAC). Laser-induced choroidal neovascularization (CNV) was analyzed in subretinally injected mice treated with AAV5-pC3-mCherry/CR2-fH, using imaging

(optical coherence tomography, OCT), functional (electroretinography, ERG) and molecular (western blotting, complement activation) readouts. Results: Proof of concept was provided that pC3 is modulated in a complement and oxidative stress-dependent manner in human ARPE19 cells, examining mCherry fluorescence. Safe concentrations of AAV5-pC3-CR2-fH were identified using ERG and OCT (1010 - 1011 vg/mL). The expression of CR2-fH significantly reduced CNV in a dose dependent manner when compared to mCherry-treated animals. CR2-fH expression reduced CNV-associated ocular C3 complement activation. Conclusions: Here we add to our body of work on complement inhibition for AMD-like pathology driven by AAV vector delivery to the RPE. Specifically, we demonstrated that regulating AP inhibition in a complement-dependent manner can ameliorate pathology.

This work was supported by NIH-NINDS Award 1F99NS124188-01A1 SREB-State Doctoral Program Award NEI: EY030072 Department of Veterans Affairs Award RX000444

82 **The effects of COVID-19 on the Medical University of South Carolina's Presidential Scholars Program**

Parker Rhoden, Parker Rhoden, Dustin Mueller, Grant Brazeal, Kristin Wallace, Jillian B. Harvey, Department of Healthcare Leadership and Management, College of Health Professions, MUSC

The Presidential Scholars Program (PSP) is an interprofessional student development program at the Medical University of South Carolina (MUSC). Engaging students from the six colleges at MUSC and the Charleston School of Law, the PSP is traditionally organized as a one-year, in-person program where students develop short-term projects with community stakeholders to address complex medical issues affecting Charleston. Due to the COVID-19 pandemic, however, the in-person and direct community engagement program objectives were modified. A remote learning approach was adopted for the 2020-2021 scholars cohort and centered on the production of master classes with expert panels from the community. This case study aims to describe the delivery and outcomes of the altered PSP format for 2020-2021 cohort. At the end of the term, PSP scholars were administered a REDCap survey with 16 questions assessing student perceptions of aspects of the PSP experience. Students were asked to respond to quantitative questions using a five-point Likert scale of agreeableness (1=strongly disagree and 5=strongly agree) and qualitative open response questions. Descriptive statistics were used to summarize student responses. A total of 20 out of 41 total students within the cohort responded (48.7% response rate). 85% of respondents agreed or strongly agreed that the PSP helped them better understand other healthcare professions. 70% agreed or strongly agreed with the statement, "My leadership skills have increased due to my participation in the program." All respondents indicated a preference for some in-person meetings if COVID-19 were not a factor. Additionally, 35% of respondents indicated that interdisciplinary projects involving service to their community would be most beneficial for their career goals for interprofessional learning. Many of the PSP students felt better prepared for interprofessional teamwork, and that their leadership skills increased. Online learning proved to be productive, and some elements were retained in the 2021-2022 program curriculum.

83 **Considerations in the Use of the Presenilin-2 Haploinsufficient Murine Model**
Stephanie DiLucia, Federica del Monte, Sophia Emetu, Kennedy Simmons, Catrina Sims-Robinson, Department of Medicine: Cardiology, College of Graduate Studies (MSTP), MUSC

Introduction/Rationale: Heart failure (HF), Alzheimer's disease (AD), and diabetes are, individually, leading causes of morbidity and mortality amongst older adults. Beyond overlapping epidemiologic profiles, all three share a common pathophysiology that rests in proteotoxicity and altered calcium dynamics. The presenilin genes, mutations in which were first associated with the onset and progression of familial AD and, later, familial and sporadic cases of idiopathic HF, encode a protein family involved in Ca2+ homeostasis and protein processing. Specifically, presenilin-2 (PS2) is expressed in the brain, heart, and pancreas. While known that proper Ca2+ trafficking is vital to these organs, the distinct role of PS2 and its relation to cognitive, cardiovascular, and metabolic disease remains largely unknown. Here, we propose that loss of PS2 may link these pathologies and aim to characterize the PS2 haploinsufficient (PS2+/-) murine model. Methods: Cardiac, cognitive, and metabolic function in PCR-confirmed PS2+/- and C57Bl/6J mice were characterized at 3- and 7/8-months of age via echocardiography, behavioral assessment, and glucose/insulin measurements, respectively. Organs were procured for morphometrics and molecular analysis. Results: Surprisingly, cardiac and pancreatic PS2 protein abundance increased by 36% (n=3, p=0.1) and 38% (n=3, p=0.06), respectively. Thus, contrary to genotyping, these mice were preliminarily described as PS2 over-expressors (PS2OE). PS2OE display early behavioral disinhibition and trend towards memory impairment. Aged mice develop significant memory deficits and pulmonary congestion; no significant metabolic phenotype emerged at either age. Conclusion: We hypothesize that the inconsistencies between genotypes and protein abundance are the likely result of cassette instability or genetic shift following long-term breeding. Future studies will include whole genome analysis of the existing colony to better interpret the observed phenotype and reexamination of a true PS2+/- colony. These findings will provide considerations for use and breeding of PS2+/- mice and novel insight into the potential ramifications of PS2 over-expression.

This work was supported by MUSC discretionary funds, 5TL1TR001451-07, 5R25HL096316-10

84 **Catalytic Modulation of Receptor Protein Tyrosine Phosphatases by the Inactive D2 Domain**
Colin Welsh, Lalima Ahuja, Preeti Pandey, Department of Pharmacology, College of Graduate Studies, MUSC

Protein tyrosine phosphatases (PTPs) are a crucial class of post-translational modification enzymes responsible for removing a phosphoryl group from a substrate tyrosine. PTPs can be both membrane bound or cytosolic; among the membrane-bound receptor PTPs are enzymes that contain dual intracellular phosphatase domains. In every occurrence of these tandem phosphatase domains, the first domain (D1) is catalytically active, while the second domain (D2) is catalytically inactive, referred to as a pseudophosphatase. The question remains as to why nature has preserved this inactive domain despite the inherent cost of doing so. Previous research has indicated a modulatory role of the D2 impacting the catalytic activity of the D1 domain. Despite some literature regarding the D1-D2 relationship, there is a significant gap in knowledge of the specific allosteric network that enables such modulation. We utilize molecular dynamics simulations employing modern force fields in order to investigate the minute details of the D1-D2 relationship and corroborate theoretical results with experimental biochemical assays of purified protein. Through the use of such contemporary techniques, we aim to elucidate key elements contributing to the specific molecular communication network that must govern the modulatory

role played by the D2 pseudophosphatase on the D1 catalytic domain.

85 **Effect of Self-Directed Home Therapy Adherence combined with TheraBracelet on Post-Stroke Hand Recovery**

Gabrielle Scronce, Na Jin Seo, Viswanathan Ramakrishnan, Amanda Vatinno, Corey Morrow, Allison Pennington, Department of Health Sciences and Research, College of Health Professions, MUSC

Hand impairment is a common consequence of stroke that results in long-term disability and reduced quality of life. Complete hand recovery is seldom obtained even with standard-of-care rehabilitation treatment. Recovery can be augmented through prescription of self-directed therapy activity at home, and also by use of rehabilitation devices such as a peripheral sensory stimulation device. However, the clinical effects of a combination of self-directed therapy paired with a stimulation device at home, along with adherence to such a regimen, are unknown. The objective of this study was to determine the effect of adherence to self-directed therapy combined with an investigational stimulation device, TheraBracelet, on hand function for stroke survivors. In a double-blind, randomized controlled trial, 12 chronic stroke survivors were assigned to a treatment or control group (n=6/group). All participants were instructed to perform 200 repetitions of therapeutic hand tasks 5 days/week while wearing TheraBracelet 8 hours/day everyday, for 4 weeks. The treatment group received subsensory vibration from the TheraBracelet device, while the control group received no vibration. At a weekly visit, participants submitted repetition/wear adherence logs, completed hand function assessment (Stroke Impact Scale Hand domain), and received new therapy tasks for the following week. Wear adherence was >100% for both groups. Repetition adherence was comparable between groups but varied greatly among participants. A linear mixed model analysis was used to examine how group and total repetitions adhered affect change in hand function at each week from the baseline. In the model fitted to the data, there was a significant interaction between repetitions and group ($p=.01$), with greater adherence resulting in greater hand function change for the treatment group ($R^2=0.88$), but not for the control group. This study demonstrates that adherence to self-directed therapy at home combined with subsensory stimulation may affect recovery outcomes in stroke survivors.

This work was supported by NIH/NIGMS P20GM109040, NIH/NICHD 1R01HD094731-01A1

86 **The Impact of Intranasal Administration of BDNF on Functional Recovery in a Neonatal Mouse Model of Hypoxic Ischemia**

Serena-Kaye Sims, Catrina Robinson, Taylor Lowry, Lilly McGonegal, Madelynne Saddow, Department of Neurology, College of Medicine, MUSC

A neonatal stroke is a medical condition that occurs when an infant's blood supply is disturbed within the first 28 days of life. One of the causes of neonatal stroke is hypoxia, an event when oxygen deprivation causes the brain to panic. Neonatal ischemic treatment is limited to more supportive care such as hyperthermia and hyperbaric oxygen therapy. Previous studies in adult stroke have reported that administering brain derived neurotrophic factor (BDNF) in the acute post-ischemic period reduces cell death and infarct volume. Hence, while BDNF may be a useful therapeutic target for adult ischemic strokes, BDNF as a potential therapy following neonatal stroke has not been explored. Our overall hypothesis is that intranasal BDNF will improve functional recovery including overall brain health and development following neonatal stroke For our model of hypoxic ischemic, a ligation of the right carotid artery was induced which is followed by a two-hour exposure to an 8% oxygen/ 92% nitrogen in an enclosed chamber in postnatal day 7 mice.

Pups were subjected to a 2 h hypothermia in a temperature-controlled chamber as a standard of care. Mice received BDNF intranasal infusions while awake. A solution of recombinant human BDNF (Harlan Laboratories .1uM in saline) was administered with a Gilson pipette, 3uL at the same time each day for 7 days into each nasal cavity. The objective of these studies is to address these gaps in knowledge and evaluate the role and therapeutic potential of BDNF in neonatal stroke recovery. Preliminary results suggest a differential impact of intranasal BDNF on pro and mature BDNF in cortical and hippocampal brain regions, which correlate with cognitive and motor outcomes. Our results suggest that higher levels of mature BDNF are predictive of better improvements at day 28 on cognitive and motor assessments.

This work was supported by Cobre in Stroke Recovery Pilot Project Program- Medical University of SC, NIH Blueprint D-SPAN K00 Award

87 **ISMN and Cilostazol Treatment Prevents Temporal Changes in the Brain Microstructure of Diabetic Rats following Microemboli Injection: Relevance to Vascular Cognitive Impairment and Dementia (VCID)**

Raghavendar Chandran, Adviye Ergul, Weiguo Li, Xingju Nie, Joshua Voltin, Lianying He, Sarah Jamil, Maria Fatima Falangola, Department of Pathology and Laboratory Medicine, College of Medicine, MUSC

Diabetes doubles the risk of VCID, but underlying reasons for this are not understood and preventive therapeutic strategies are lacking. We showed that diabetic but not control rats develop progressive cognitive decline in a microemboli (ME) model of VCID. Given that cerebrovascular dysfunction is a common pathology between diabetes and VCID, we hypothesized that improvement of endothelial function in diabetes prevents ME-mediated white matter injury. Our treatment paradigm was based on the ongoing LACI-2 trial which assesses the efficacy of isosorbide mononitrate (ISMN) and cilostazol (CZL) in the prevention of small vessel disease (SVD) progression. Seven-eight weeks after diabetes onset, control and diabetic rats were treated with ISMN/CZL for 4 weeks, then injected with cholesterol ME and monitored longitudinally using three different MRI parameters - diffusion tensor imaging (DTI), diffusional kurtosis imaging (DKI) and cerebral blood flow (CBF). We previously reported decreased fractional anisotropy and increased diffusivity at 12 weeks after ME injection in diabetic rats, indicating possible loss of tissue integrity in the cortex and hippocampus. In the current study, we detected a time effect in the DTI and DKI metrics for both groups measured in cortex, hippocampus as well as in corpus callosum, internal and external capsule but in most of them there was no disease/group-effect. Also, CBF was higher in diabetic rats at all time points. This suggests that drug treatment with ISMN/CZL before ME injection prevented the possible deleterious effects of the latter in the diabetic rats by improving the endothelial integrity and it is a viable preventive and possibly therapeutic strategy for VCID.
This work was supported by Adviye Ergul: VA Merit Award (BX000347), VA SRCS Award, NIH awards (R01NS083559, PO1HL134604, and NS104573), Weiguo Li: NIDDK DiaComp Pilot and Feasibility Grant (17AU3831 supported by DK076169 and DK115255) and Raghavendar Chandran: AHA Postdoctoral Fellowship (831316)

88 **Linking Structural and Functional Connectivity for Upper Extremity Motor Recovery after Stroke**
Adam Baker, Na Jin Seo, Christian Schranz, Ph.D., Janina Wilmskoetter, Ph.D., Jens Jensen, Ph.D., Department of Health Sciences and Research, College of Health Professions, MUSC

Background: Stroke is one of the leading causes of disability in the world, commonly inducing functional sensorimotor impairments. Often, these deficits present in the upper extremities (UE), restricting the capability to complete activities of daily living. While stroke causes focal lesions in the brain, studies have shown that stroke also causes white matter disconnection distant from the lesion itself, an important consideration for functional connectivity and recovery. Diffusion Kurtosis Imaging (DKI) and electroencephalography (EEG) are tools allowing the assessment of structural and functional connectivity, respectively. We believe that functional connectivity relies on structure, and these neurological biomarkers together may explain UE motor recovery after stroke. Objective: To examine if baseline structural connectivity explains the change in functional connectivity in response to UE rehabilitation therapy and associated UE motor recovery outcome among stroke survivors. Methods: In a parent study, 76 stroke survivors will receive UE rehabilitation therapy for 6 weeks. EEG will be collected at baseline, therapy completion, and 1-month follow-up. UE motor recovery will be assessed as change in the standardized clinical functional score from the baseline. Specific to this proposed study, we will additionally obtain DKI at baseline. We will examine if subgroups of stroke survivors can be identified using methods such as cluster analysis, to explain UE motor recovery and functional connectivity change based on structural connectivity. We will consider covariates such as age, time since stroke, stroke location, presence of motor evoked potential, and baseline clinical assessment score. Impact: This research is expected to elucidate mechanisms of post-stroke recovery and response to rehabilitation treatment. This research may also have valuable implications for individualizing post-stroke rehabilitation treatments based on these neurological biomarkers to maximize recovery outcomes after stroke.

This work was supported by NIH/NIGMS P20GM109040, NIH/NICHD 1R01HD094731

89 **Can Transcutaneous Auricular Vagus Nerve Stimulation (taVNS) Attenuate Increases in Heart Rate Associated with the Cold Pressor Test?**
Christopher Austelle, Mark George, Christopher T. Sege, Danielle L. Taylor, Lisa M. McTeague, E. Baron Short, Bashar W. Badran, Department of Psychiatry, College of Medicine (MD, PhD), MUSC

Introduction: Transcutaneous auricular vagus nerve stimulation (taVNS) may be able to treat disorders characterized by sympathetic hyperactivity via the vagus nerve's parasympathetic functions. Previous studies have demonstrated that acute taVNS decreases heart rate in healthy individuals (mediated parasympathetically), but little is known regarding the effects of taVNS on an induced stress response. The cold pressor test (CPT) is a validated stress induction technique that can reliably elicit a sympathetic stress response with marked increases in heart rate, anxiety, stress, and pain. The CPT offers a unique opportunity to evaluate the effects of taVNS on a stereotypical stress response. Methods: This pilot trial will recruit up to 20 neurotypical participants to complete a 1-visit randomized, crossover study investigating the effects of taVNS on the stress response elicited by the CPT. Subjects will receive active taVNS concurrent with a CPT followed by sham taVNS concurrent with a second CPT. Order of stimulation condition (active versus sham) will be randomized. Physiologic data will be collected throughout the visit, as well as subjective ratings of anxiety, stress, and pain. Results: The primary outcome will be heart rate, measured continuously - before, during, and after each round of taVNS/CPT. Other autonomic measures will be collected as

well. Subjective ratings of anxiety, stress, and pain will be assessed as secondary outcomes. Recruitment has not yet begun; however, up-to-date results will be included in the final presentation. Conclusion: We hypothesize that the parasympathetic effect of taVNS will attenuate the typical sympathetic response elicited by the CPT. Thus, the characteristic increase in heart rate response to the CPT will be decreased in the active compared to sham taVNS condition. If taVNS is able to attenuate a sympathetic stress response, it should be investigated further as a potential treatment for anxiety and other disorders characterized by sympathetic hyperactivity.

This work was supported by R25 DA020537

90 **3D Mandibular Kinematic Analysis of the Temporomandibular Joint**

Cherice Hill, Hai Yao, Feng Wei, Shuchun Sun, Nadine Almpani, Marshall Wilson, Brooke Damon, Michael Lecholop, Martin Steed, Janice Lee, Clemson-MUSC Bioengineering Program, Department of Oral Health Sciences, College of Dental Medicine, MUSC

Evaluation of human temporomandibular joint (TMJ) kinematics is essential in determining TMJ function, assessing temporomandibular disorder (TMD) risk, and examining intervention options. The objective of this study was to evaluate 3D mandibular kinematics during a mandibular open-close movement in individuals with and without disc derangement using optical tracking. 37 healthy subjects (19 males [29.5 (11.1 years)], 18 females [31.0 (9.3 years)] and 16 females [33.4 (13.3 years)] with disc derangement or chronic pain were recruited (IRB approval at University at Buffalo and University of Missouri-Kansas City). CBCT and MRI imaging was used to categorize subjects and reconstruct 3D models for co-registration of kinematic data. Flexion-extension, abduction-adduction, and axial rotation were recorded for the left and right TMJs separately during 10 mandibular open-close cycles using a custom-designed JAWS-3D optoelectronic jaw tracking system. Maximum rotation and translation in each plane of motion (3D) and rotation and translation magnitudes of the lateral condylar pole relative to the fossa bone were computed. Independent t-tests evaluated effects of sex and pathology (SPSS V23, alpha=0.05). No asymmetry between left and right TMJ motion or differences between healthy male and healthy females TMJ motion were observed. Maximum rotation in the frontal ($p=0.04$) and sagittal ($p=0.05$) planes, rotation magnitude ($p=0.05$) , maximum superior-inferior translation ($p=0.01$), and translation magnitude ($p=0.04$) were significantly larger in females with disc derangement or chronic pain compared to healthy controls. Greater rotation and translation of the mandibular condyle during a habitual open-close task may place greater demand and strain on TMJ tissues, which may contribute to increased risk of TMD development. Continuing functional assessments of frequent oral behaviors are necessary to inform risk assessment and determination of necessary orthognathic and orthodontal surgical interventions. Future investigations should include continuous kinematic analyses throughout habitual and maximum oral movements as a supplement to discrete analyses.

This work was supported by R01DE021134, P20GM121342, T32DE017551

91 **Immune response modulation in post myocardial infarction**

TOOLIKA SINGH, DONALD MENICK, Tajinder Dhammu, Miller W. Shealy, Rajendran JC Bose, Jason R. McCarthy, College of Medicine, MUSC

Abstract withheld from publication

92 **Central Amygdala Dynorphinergic Neuron Activity in a Mouse Model of Voluntary Alcohol Drinking**

Christina Lebonville, Patrick Mulholland, Harold Haun, William Griffin, Jennifer Rinker, Howard Becker, Department of Psychiatry and Neuroscience, College of Medicine, MUSC

The central amygdala (CeA), as well as dynorphin/kappa opioid receptor signaling within this region, has been implicated in responses to both stress and ethanol. Adaptations in CeA dynorphin/kappa opioid receptor signaling may underlie aberrant behaviors that result from the interaction of stress and prolonged alcohol drinking. In this study, we probed the engagement of CeA dynorphin-expressing neurons during voluntary consumption of ethanol using fiber photometry. To accomplish this, a virus allowing expression of a Cre-dependent calcium sensor, GCaMP7f, was infused into the CeA of dynorphin-Cre transgenic mice. Simultaneously, a fiber optic ferrule was implanted into the CeA to allow for recording calcium-dependent neuronal activity from dynorphin-expressing neurons in the CeA during alcohol drinking. Mice were given access to 20% ethanol in their home cages for 2-hours/day, 5-days/week for three consecutive weeks. During these sessions, lickometer circuitry in the home cage allowed for time-locked recorded GCaMP7 activity in CeA dynorphin neurons to bouts of licking on the ethanol bottle. Preliminary analysis of GCaMP7 activity from this CeA neuronal population indicates an increase in calcium transients during bouts of licking for ethanol, but not during bouts of drinking water or sucrose, indicating these neurons are uniquely engaged during ethanol consumption. These data relate cellular activity of dynorphinergic neurons in the CeA to active ethanol drinking and inform cell population level mechanisms that may drive the complex interactions between stress and alcohol in AUD. We want to thank the Ralph H. Johnson VA Medical Center for resources used to conduct this research.

This work was supported by Supported by NIAAA grants (P50 AA010761, R01 AA02653, U01 AA014095, U01 AA020929, U01 AA020930, F31 AA027420, F32 AA029026, K01 AA025110) and VA Medical Research (BX000813)

93 **Novel P-selectin targeted complement inhibitors reduce limb injury following ischemia/reperfusion and vascularized composite graft transplantation**

Chaowen Zheng, Stephen Tomlminson, Jerec Ricci, Qinqin Zhang, Satish Nadig, Pablo Engel, Junfei-Jin, Carl Atkinson, Department of Microbiology and Immunology, College of Medicine, MUSC

The complement pathway has long been recognized as a potential druggable target for a variety of inflammatory conditions. Very few complement inhibitors have been approved for clinical use, but a great number are in clinical development, nearly all of which systemically inhibit complement. There are benefits of targeting complement inhibition to sites of activation/disease in terms of efficacy and safety, and here we describe P-selectin targeted complement inhibitors, with and without a dual function of directly blocking P-selectin-mediated cell-adhesion. The constructs are characterized in vitro and in murine models of hindlimb ischemia/reperfusion injury and hindlimb transplantation. Both constructs specifically targeted to reperfused hindlimb and provided protection in the hindlimb ischemia/reperfusion injury model. The P-selectin blocking construct was the more efficacious, which correlated with less myeloid cell infiltration, but with similarly reduced levels of complement deposition. The blocking construct also improved tissue perfusion and, unlike the nonblocking construct, inhibited coagulation, raising the possibility of differential application of each construct, such as in thrombotic vs. hemorrhagic conditions. Similar outcomes were obtained with the blocking construct in the transplantation model, and treatment also

significantly increased allograft survival. Both constructs bound mouse and human P-selectin which may facilitate potential translation. This study was supported by the NIH, VA, DoD, and Ralph H. Johnson VAMC.

This work was supported by NIH (U01AI32894 and R56AI56383 to ST and CA), the Dept. Veteran's Affairs (BX005235 to ST), the Dept. of Defense (RT190030 to ST).

94 **Impact of IFNLR1 expression and engagement with lambda interferons on hepatitis B infection**

Laura Novotny, Eric Meissner, Gray Evans, Sarah Stephenson, Department of Infectious Diseases, College of Medicine, MUSC

Hepatitis B virus (HBV) is a human pathogen that causes chronic liver infection that can result in liver cirrhosis or hepatocellular carcinoma. Worldwide, 250 million individuals are infected with HBV and the chronic nature of this infection is due to the ability of the virus to deposit a stable, covalently closed circular DNA (cccDNA) form of its genome within the nucleus of hepatocytes. Current therapeutic regimens include Interferon-alpha or nucleos(t)ide analogues, however these approaches only suppress viral replication, do not clear the virus and moreover, can have undesirable side effects. Lambda interferons (IFNLs) are cytokines that bind to a heterodimeric receptor comprised of IFNLR1 and IL10RB and induce anti-viral responses. Uniquely, IFNLR1 has restricted expression on hepatocytes, mucosal cells and select immune cells. Clinically, IFNLR1 expression is elevated in some HBV patients. We hypothesized that modulation of IFNLR1 expression on hepatocytes or immune cells and engagement of the receptor with IFNLs will promote resolution of HBV infection. To address this premise, we utilized human hepatoblastoma cell lines: wild type HepG2 and variants engineered to express the NTCP receptor engaged by HBV (HepG2-NTCP) or in which HBV is stably expressed (HepG2.2.15). We generated inducible, FLAG-tagged IFNLR1 constructs for each of the three receptor isoforms and verified expression by qRT-PCR, fluorescent microscopy and flow cytometry. The constructs permitted titratable expression of IFNLR1 as revealed by western blot. We further show that treatment of HepG2.2.15 cells with IFNL3 reduced the quantity of HBV DNA detected in both culture supernatants and within cell lysates compared to mock, thus clearance of HBV was induced. Further, use of human induced pluripotent stem cells differentiated to iHeps permitted a biologically-relevant extension to our work. The ability to modulate a key host receptor and/or deliver a potent therapeutic has potential to mitigate the burden of chronic HBV infections.

This work was supported by COBRE 1-P20GM130457-01A1

95 **All the Risk, None of the Reward: An Analysis of the Reward Response in Depressed Youth**

Robert James, Carla Danielson, Christopher Sege, Greg Hajcak, Lisa McTeague, Department of Psychiatry and Behavioral Sciences, College of Medicine, MUSC

Increasing rates of suicide in the United States have lead to a renewed focus on the importance of mental health (National Survey on Drug Use Health, 2017). Depression among children has received special attention, and a better understanding of the unique neuropsychological changes that occur in this population can help decrease the risk of depression and suicide. One such neuropsychological area of interest is the alteration in reward processing that occurs in depression. Previous studies among adults have suggested a strong negative association between depression and an appropriate reward response (Keren et. Al., 2018); however, data focusing on such changes in children remains limited, specifically when addressing children with a history of trauma. The

current study seeks to add to this body of knowledge by assessing the neuroelectrical indicators of reward processing in children and adolescents with depression and a history traumatic exposure. The sample is composed of participants ranging from the 3rd to 10th grade (n=288) who were enrolled in the NIMH R01-funded CHARM study (1R01MH112209; PI: Danielson). Participants were administered the Children's Depression Inventory (CDI), the Children's Depressive Experiences Questionnaire (CDEQ), and the UCLA PTSD Index at the time of enrollment. They were then asked to participate in a gambling task (as a measure of reward processing) in which they pressed a button to choose between two doors. One door would lead to a monetary prize, while the other would lead to a monetary loss. During this process, electroencephalography (EEG) was measured to quantify the differences in event-related potential (ERP) between monetary loss and monetary gain among subjects. Results suggest a decrease in ERP among depressed participants receiving a reward when compared to non-depressed controls. Detailed statistical analysis and findings, clinical implications, and recommendations for future child psychiatry research will be discussed in the poster presentation.

This work supported by NIMH R01

96 **Examining the association between pre-adolescent mental health and caffeine consumption in the Adolescent Brain and Cognitive Development (ABCD) Study**

Dominque Black, Squeglia Lindsay, John Redhead, B.S., & Alexis Garcia, Ph.D, Department of Addiction Sciences, College of Medicine (MD, PhD), MUSC

Introduction: With the increasing attention on child mental health and the initiation of substance use, we sought to investigate the association between caffeine consumption and social-emotional functioning in 10-year-old children. The increasing prevalence of caffeinated beverages targeted towards adolescents and children demonstrates the need to examine how these substances may be related to their emotional well-being. Methods: Adolescent Brain and Cognitive Development (ABCD, Data release 3.0) baseline data for 10,548 youth and their parents were examined (Mage= 9.91 years, SD = .62, Male = 52%, White = 66%, Hispanic = 19%). Youth reported on their average weekly caffeine intake (i.e., soda, energy drink, coffee, tea) over a 6-month period. Parents completed a broadband questionnaire (CBCL) to assess their child's emotional and behavioral functioning. T-scores for the internalizing and externalizing scales were examined. Generalized additive mixed modeling (GAMMA4) regressions were used to examine the association between these psychological predictors and caffeine consumption. Results: All analyses controlled for age, sex, race/ethnicity, parent marital status, education, and family income. After controlling for demographic variables, children with higher levels of externalizing problems reported greater caffeine consumption, beta = .03, $p < .001$. There was a null finding for internalizing problems. Post-hoc analyses explored the extent to which the externalizing syndromes (rule breaking and aggression) were associated with caffeine consumption. After accounting for internalizing problems, rule breaking was significantly associated with caffeine, beta = .02, $p < .05$. Children with higher levels of rule breaking behavior reported greater caffeine consumption. Conclusion: Children with higher levels of rule breaking report greater caffeine consumption. This finding elucidates which children are at-risk for surpassing the recommended dose (no caffeine before age 12, AAP) of daily caffeine use. Caregivers and health providers should monitor 1) rule breaking and 2) caffeine consumption in pre-adolescent children.

97 **Oral bacteria Porphyromonas gingivalis spreads intercellularly through gingival epithelium using ER autophagic vesicles**

Ayana Paul, Ozlem Yilmaz, Bridgette Wellslager, Department of Oral Health Sciences, College of Graduate Studies, MUSC

Abstract withheld from publication

98 **Molecular Choreography of Vaccinia Virus Genome Encapsidation**

Esteban Castro, Paula Traktman, Matthew Greseth, Paula Traktman, Department of Biochemistry and Molecular Biology, College of Graduate Studies, MUSC

Vaccinia virus (VV) is a large DNA virus and the prototype of the Poxviridae family. The VV life cycle is unique in that it occurs entirely within host cell cytoplasm. The virus encodes ~200 proteins that mediate the complex steps of infection and culminate in the production of new viral progeny. We are particularly interested in the viral genome, which undergoes robust replication followed by encapsidation into nascent virions. Encapsidation of viral DNA (vDNA) is a complex, poorly understood process. Previous work from our laboratory and others has shown that the essential viral proteins A13, A32, and I6 are crucial for vDNA encapsidation; however, further research is required to understand how these proteins contribute to efficient and specific encapsidation of vDNA. In the absence of either A13, A32 or I6, vDNA encapsidation is abrogated and results in the accumulation of cytoplasmic DNA crystalloids, structures of high electron density, that can be seen in electron micrographs. Without DNA encapsidation, the yield of infectious mature virions is severely compromised. Our goal is to further understand the molecular choreography of these three proteins in accomplishing genome encapsidation. Our model posits that A13, which resides in the viral membrane, may interact with and position A32, allowing the ATPase activity of A32 to pump vDNA into the forming virion. Recognition of the vDNA may be accomplished by interactions between A32 and I6, which binds specifically to telomeres of the vDNA molecule. To support this working model, key motifs within the three proteins will be disrupted to observe effects on protein interactions and vDNA encapsidation. By elucidating the vDNA encapsidation mechanism, these disruptions will determine if the three proteins act as a trimeric protein complex. Further definition of target protein interactions using inducible recombinants and temperature-sensitive mutants will test facets of our model of VV encapsidation.

This work was supported by RO1 GM131412, Startup Funds from MUSC, 2 R25 GM113278-06A1

99 **Subcellular Targeting of Induced CYP2E1 in the Brain During Alcohol Use**

Hyland Gonzalez, Jessica Hartman, Baylee Westbury, Patrick Mulholland, College of Graduate Studies, MUSC

Alcohol is a commonly abused substance that contributes to numerous health problems including liver damage and neurological deficits. It is thought that the ethanol metabolite acetaldehyde mainly drives toxicity from ethanol use. One way this metabolite is created is cytochrome P450 2E1 (CYP2E1), which is expressed within cells in the endoplasmic reticulum and mitochondria. Previous research has demonstrated that alcohol induces CYP2E1 in the brain, but how much of the enzyme is targeted to the mitochondria is unknown. We hypothesize that chronic alcohol consumption will (1) lead to increased CYP2E1 expression in brain mitochondria in specific brain regions, and (2) that increased mitochondrial CYP2E1 will result in increased production of acetaldehyde and mitochondrial dysfunction. We will test this hypothesis using two complementary systems: testing

brain region-specific expression of CYP2E1 in mice after acute or chronic ethanol drinking through immunofluorescent staining, and using the model organism Caenorhabditis elegans that has been modified to express the CYP2E1 gene genetically targeted to mitochondria or ER and treated with acute or chronic ethanol exposure. We are currently optimizing immunofluorescent staining procedures for the mouse brain tissue. Our anticipated results are that CYP2E1 subcellular induction will be brain region-specific. In the worm model, preliminary results have shown that worms expressing mitochondrial-targeted CYP2E1 were more susceptible to ethanol-induced locomotor effects compared to the wildtype strain and the ER-targeted CYP2E1 strain. This may be due to mitochondrial dysfunction in the muscle cells, neurons, or both. In ongoing experiments, we will test mitochondrial function in the whole worm and in the specific muscle and neuronal cells to determine the mechanism of ethanol toxicity. The findings of this project will lead to deeper understanding of how the brain adapts to alcohol consumption and potential targets for prevention of alcohol-induced neural damage and for treatment of alcohol use disorder.

This work was supported by MUSC PREP 2R25GM113278-06A1, Charleston ARC P50 AA010761

100 **In Vivo Two-Photon Imaging of Prelimbic Cortex during Alcohol Seeking in Mice**

Kion Winston, Jim Otis, Jen Rinker, Department of Neuroscience, College of Graduate Studies, MUSC

Alcohol use disorder is characterized by the development of uncontrolled use of alcohol despite negative consequences. This excessive use co-develops with persistent changes in prelimbic prefrontal cortical (PL-PFC) activity that is associated with increased vulnerability for relapse and cortically driven inflexible behavior. However, little is known about the precise PFC activity which develop with alcohol use. Here, we use multiphoton (MP) microscopy to monitor PL-PFC activity changes with single-cell resolution during alcohol-seeking across the development of dependence. To do so, we developed a novel procedure wherein mice can self-administer alcohol (15% v/v) while head-restrained under a MP microscope. Mice received intra-PL-PFC microinjections of AAV8-CaMKIIa-GCaMP7f and implantation of a gradient refractive index lens to allow visualization of calcium activity dynamics. PL-PFC neuronal calcium activity was recorded to establish activity dynamics in the alcohol naïve state. Animals were allowed to drink alcohol in their home cage for 2 weeks to establish a stable preference for alcohol and were then trained to self-administer alcohol in the head-fixed operant set-up. Mice underwent head-restrained alcohol self-administration in this manner until stable responding was established, and baseline PL-PFC neuronal activity was recorded during operant responding, prior to the development of dependence. Mice were then exposed to chronic intermittent ethanol (CIE) vapor every other week to induce dependence. Following each week of CIE, animals were head-restrained under a MP microscope and allowed to self-administer alcohol to examine changes in PL-PFC signaling. Initial results indicate that, consistent with previous research, the PL-PFC shows a gradual decrease in excitatory activity following the development of alcohol dependence. Additional analyses examine whether these changes are restricted to discrete neuronal ensembles and longitudinally track activity changes in single neurons from the pre- to post-dependent state. The results from these studies could reveal the precise PL-PFC activity dynamics which develop with excessive alcohol

This work was supported by MUSC Post-Baccalaureate Research Education Program, 2R25GM113278-06A1

101 **Accelerated rTMS for Cognitive Rehabilitation in Chronic Stroke: A Safety and Feasibility Study**

Bridgette Holland, Lisa McTeague, Holly H. Fleischmann, James W. Lopez, Kevin A. Caulfield, Stephanie Fountain-Zeragoza, Michael U. Antonucci, Andreana Benitez, Mark S. George, Department of Psychiatry & Behavioral Sciences, College of Medicine, MUSC

Nearly 70% of patients with chronic stroke demonstrate impairment in at least one cognitive domain. Effective cognitive rehabilitation approaches have been established for focal cortical deficits such as neglect and aphasia, but treatments for more prevalent and diffusely represented cognitive impairment remain elusive. Repetitive transcranial magnetic stimulation is a promising intervention for targeting the multiple demand network that undergirds domain general cognitive processing. Furthermore, a delivery schedule readily paired with other rehabilitation interventions could be especially powerful. We examined the safety of accelerated rTMS as well as its feasibility in a delivery schedule interleaved with computerized cognitive training in individuals with chronic stroke and cognitive impairment. Fourteen chronic stroke patients with intact left prefrontal cortex who met DSM-5 criteria for mild neurocognitive disorder completed open-label high-dose rTMS (intermittent theta burst) to left dlPFC (600 pulses, eight sessions/day for three days), interleaved every 15 minutes between cognitive training sessions. Participants completed at pre- and post-treatment: 1) neuroradiological lesion characterization and safety assessment with flair, diffusion, susceptibility, angiography, perfusion gradient and volumetric scans, 2) neuropsychological and psychosocial assessment as well as assessment of neglect and aphasia, and 3) ratings of treatment acceptability and credibility. No study-related adverse events occurred as indexed in neuroradiological, neuropsychological or subjective quantitative or qualitative report of side effects. Accelerated rTMS was rated as acceptable and credible with no more than minor discomfort in line with conventional once daily delivery schedules. Retention was feasible as all participants who began treatment completed. This is the first comprehensive neuroradiological and neuropsychological examination of the safety of accelerated rTMS in chronic stroke, or any condition. Across objective and subjective indices, up to 24 sessions of accelerated intermittent theta burst rTMS was safe, acceptable, and tolerable, even in a neurologically vulnerable condition such as chronic stroke.

This work was supported by 5P2C HD086844 Kautz (PI) NICHD National Center for Neuromodulation for Rehabilitation (NC NM4R) Pilot Project #17: Neuromodulation & Plasticity in Cognitive Control Neurocircuitry in Chronic Stroke

102 **Low nutrient availability drives increased macropinocytosis and MEK inhibitor resistance in KRASG12R-mutant Pancreatic Ductal Adenocarcinoma**

Amanda Linke, Aaron Hobbs, Rachel Burge, Department of Pharmacology, College of Graduate Studies, MUSC

Pancreatic ductal adenocarcinoma (PDAC) is the third most deadly human cancer with a dismal five-year survival rate of 10%. KRAS is mutated in over 95% of PDAC tumors and is a key driver of PDAC tumorigenesis. Mutant KRAS is constitutively active and drives proliferation through the upregulation of numerous signaling and metabolic pathways to support tumor proliferation. Despite the promise of targeted inhibitors of the RAF-MEK-ERK MAPK signaling pathway, arguably the most critical RAS-mediated proliferative signaling pathway, clinical trials targeting oncogenic MEK/ERK signaling as a single-agent therapy have been unsuccessful. The PDAC tumor microenvironment has been shown to be deplete of glucose and free amino acids, suggesting that PDAC relies heavily on nontraditional metabolic processes for proliferation such as

macropinocytosis, the nonselective uptake of proteins and molecules from extracellular spaces, and autophagy, a mode of cellular recycling. Macropinocytosis has been shown to be elevated in PDAC cell lines and human tumors. Despite recent findings describing the limited nutrient availability in the tumor microenvironment, cell culture studies supporting the use of MEK/ERK inhibitors are predominately preformed in a high glucose medium. By utilizing a minimal glucose medium supplemented with bovine serum albumin, a large protein that is absorbed via macropinocytosis, we show that this growth medium drives resistance to MEK MAPK inhibition. To evaluate whether PDAC cells proliferating in a low glucose medium can be sensitized to MEK inhibition, we have performed a CRISPR/Cas9 loss-of-function screen targeting the druggable genome to determine effective therapeutic combinations under these conditions. To follow up on our in vitro screen, we will evaluate the therapeutic efficacy of our findings in 2D and 3D proliferation assays. These studies will describe novel treatment strategies for PDAC patients with elevated macropinocytosis.

This work was supported by PREP

103 **Understanding the Role of microRNA-204 in Driving Neuroendocrine Differentiation During Prostate Cancer Progression**

Deavian Harvin, Victoria Findlay, , Department of Pathology and Laboratory Medicine, College of Graduate Studies, MUSC

Neuroendocrine Prostate Cancer (NEPC) is a very aggressive form of prostate cancer with no effective treatments and short life expectancy. Studies to identify novel treatments for, and early biomarkers of, progression to this devastating disease is an active area of research. MicroRNAs (miRNA) are noncoding RNAs that negatively regulate gene expression and affect cancer widely because of their ability to function as oncogenes or tumor suppressors. We and others have shown that a specific miRNA, miR-204, plays a role in prostate cancer (PrCa) and we have evidence that it may be an early biomarker of progression to NEPC. This is particularly relevant as once clinically diagnosed life expectancy is 7-10 months. Our hypothesis is that miR-204 overexpression will increase PrCa progression and neuroendocrine differentiation (NED) in mouse models of prostate cancer. We address the hypothesis with the following specific aims: (1) to determine whether miR-204 expression increases prostate cancer progression in a spontaneous prostate cancer mouse model; and (2) to determine whether miR-204 promotes NED in a spontaneous PrCa mouse model. We developed a novel dox-inducible miR-204 transgenic mouse and crossed it with a prostate specific driver and the C3-TAg mouse to generate a trigenic mouse for our studies. At 20 weeks we extracted the prostate and performed immunohistochemistry and H&E staining to examine the ventral lobes of the prostate. We have successfully extracted prostates from 32 mice, including 9 experimental mice. They have been sliced and stained for H&E assessment. Histological grading is currently ongoing. We predict that we will find higher grade lesions in the miR-204 trigenic mice and ongoing studies will determine whether these lesions contain markers of neuroendocrine differentiation.

104 **Midfoot Charcot Deformity Correction is Well Maintained with Beam Fixation**
Alexander Guareschi, Christopher Gross, Andrew Moore, Caroline Hoch, J. Brett Goodloe, Daniel Scott, College of Medicine, MUSC

Beaming arthrodesis has been shown to restore plantigrade position and balanced load distribution across the midfoot, correcting the Meary angle and reducing the incidence of plantar ulceration. This study evaluates the outcomes of beaming arthrodesis in a series of patients with midfoot Charcot arthropathy. We retrospectively identified 13 patients with midfoot Charcot who underwent medial column beaming arthrodesis between 2013 and 2020 by a fellowship-trained foot and ankle surgeon at an academic medical center. Data collected from patient charts included demographics, medical history, Brodsky classification, concomitant procedures, union status, postoperative complications, and reoperation rate. Additionally, Meary angle was measured on lateral radiograph for each patient prior to operation and at three months, six months, one year, and two years postoperatively. Mean follow-up time was 1.40 years (range, 0.28-3.34 years). The incidence of diabetes was 76.92% (n=10), while the average hemoglobin A1c was 6.63%. Preoperative ulcers were found in seven (53.85%) patients. There was a 53.85% postoperative fusion rate with a mean time to fusion of 49.86 days. The Meary angle was recorded preoperatively (16.07±5.50 degrees) and postoperatively at three months for ten patients (5.75±6.28 degrees), at six months for eight patients (6.84±7.77 degrees), at one year for six patients (5.73±9.01 degrees), and at two years for four patients (4.60±5.81 degrees). Two patients showed an increase in this angle, despite operative treatment. A greater preoperative Meary angle was significantly associated with shorter time to reoperation (r=-0.908, p=.033). Five (38.46%) patients developed an infection, of which four (80.00%) required reoperation (i.e., incision and drainage=2, hardware removal=1, amputation=1). Our results suggest that beaming is effective in restoring medial column anatomy and improving foot collapse in Charcot. Healthy soft tissue pre-procedure may also decrease the risk of postoperative infection. Additional research should also be conducted to compare the outcomes of beaming arthrodesis with those of other midfoot reconstruction techniques.

105 **Risks of Preoperative Opioid Therapy on Forefoot and Hindfoot Surgery Success**
Kevin Shrake, Christopher Gross, William Newton, BS; Caroline Hoch, BS; Daniel Scott, MD, MBA, College of Medicine, MUSC

Past studies in total joint arthroplasty and orthopaedic trauma have found that preoperative opioid therapy correlates with increased postoperative opioid use and lesser surgical outcomes. We hypothesized that patients undergoing forefoot or hindfoot foot and ankle surgery with preoperative chronic opioid use would have increased likelihood of postoperative opioid use, complications, and re-operation. Thus, a retrospective review was conducted of forefoot, midfoot, and hindfoot surgeries between 2015 and 2020 by a single surgeon at an academic center. Opioid and benzodiazepine use, comorbidities, demographics, patient-reported outcome measures (PROMs) (i.e., Foot and Ankle Outcome Score [FAOS], Foot and Ankle Ability Measure [FAAM]), and postoperative outcomes were reviewed. A total of 326 patients with a mean follow-up up of 2.12 years (range, 1.00-4.98) were included. Records of preoperative analgesic use were limited to 69 patients, 90-day postoperative use to 90, and 180-day postoperative use to 116. Overall, 17 patients used opioids and 16 used benzodiazepines preoperatively. Statistical analysis included correlation, multivariate regression, Student t-test, and Chi-squared test. Our results demonstrated preoperative opioid use was significantly associated with continued postoperative use at 90 and 180 days postoperatively. Likewise, preoperative benzodiazepine use was significantly associated

with continued postoperative use at 90 and 180 days postoperatively. Also, both preoperative opioid (user=29.41%, non-user=9.62%) and benzodiazepine (user=31.25%, non-user=9.43%) use were significantly associated with increased complication rates. Only postoperative opioid use at 90 days significantly differed by whether the patient had a history of trauma (trauma=18.46 MME, no trauma=52.77). Furthermore, opioid use at 90 days postoperatively was predictable by concomitant psychiatric disease and high BMI, while only BMI predicted opioid use at 180 days postoperatively. Psychiatric disease was the only significant predictor of benzodiazepine use at 180 days postoperatively. In conclusion, physicians should consider this data when prescribing analgesics to help appropriately council patients on postoperative expectations.

106 **Predicting Vitamin D Status: Post-hoc Analysis of Traditional Biochemical Safety Measurements in Infants Less than Seven Months**

Grace Pouch, Carol Wagner, Authors: Myla Ebeling (2), Judy R. Shary (2), Bruce W. Hollis PhD (2), Cynthia R. Howard MD (3) Affiliations: (2) Division of Neonatology, Department of Pediatrics, Shawn Jenkins Children's Hospital, Charleston, SC 29425 (3) Department of Pediatrics, University of Rochester, Rochester, NY 14620

Background: To ensure the safety of higher dose vitamin D supplementation in pregnant and lactating mothers urinary calcium/creatinine ratios (UCa/Cr), serum calcium, and serum 25(OH)D concentrations are closely monitored. To achieve optimal maternal and infant vitamin D status, while avoiding hypercalcemia, safety measures assessing vitD supplementation must be reliable; this is not the case in infants prior to 7 months of age. Objective: Analyze the association between UCa/Cr ratio, serum calcium, iPTH, 25(OH)D, and 25(OH)D/iPTH ratio in infants in order to determine whether evidence supports the use of these parameters as valuable measures of hypervitaminosis D or toxicity in infants. Methods: ¬A series of analyses were performed on the cohort of infants who participated in the National Institute of Child Health and Human Development lactation vitD supplementation trial to determine the association between UCa/Cr ratio, serum calcium, iPTH, 25(OH)D, and 25(OH)D/iPTH ratio. Results: Upon multivariate analysis, serum calcium significantly associated with 25(OH)D (p=0.0441), iPTH (p=0.0017) and 25(OH)D/iPTH ratio (p=0.0001). Infant UCa/Cr did not associate with 25(OH)D but did associate with iPTH (p=0.0008) and 25(OH)D/iPTH ratio (p=0.0001). The correlation between UCa/Cr and 25(OH)D/iPTH ratios was significantly stronger than the association between UCa/Cr ratio and iPTH. Serum calcium more strongly correlated with 25(OH)D/iPTH ratio versus 25(OH)D and iPTH. Conclusion: In this healthy cohort of infants 1 to 7 months old, UCa/Cr and serum calcium are more valid indicators of 25(OH)D/iPTH ratio than either 25(OH)D or iPTH alone. Moreover, serum calcium (and not UCa/Cr) is a valid indicator of infant total circulating 25(OH)D.

This work was supported by Funded in part by NIH 5R01HD043921, NIH RR01070, MUSC Department of Pediatrics, and by the South Carolina Clinical & Translational Research (SCTR) Institute, with an academic home at the Medical University of South Carolina, NIH/NCAT Grant number UL1 TR000062

107 **A novel Thioredoxin protein of Porphyromonas gingivalis is important for intracellular survival in human gingival epithelial cells**

Danielle Vines, Özlem Yilmaz, Kayla Anderson, Casey Derieux, Bridgette Wellslager, Nityananda Chowdhury, Department of Oral Health Sciences, College of Dental Medicine, MUSC

Background: Porphyromonas gingivalis is an opportunistic Gram (-) anaerobe strongly involved in chronic periodontitis. P. gingivalis can survive in gingival epithelial cells (GECs) using thioredoxin-like protein (PGN_1181) to withstand the GEC oxidative stress. Objective: To better understand the role that PGN_1181 plays in the intracellular survival of P. gingivalis, by comparing the intracellular levels of a PGN_1181-deleted isogenic mutant strain (ΔPGN_1181) against its wild-type strain ATCC 33277. Methods: Human primary GECs were incubated with wild-type or isogenic PGN_1181-deficient mutant strain, respectively. Infected GECs were fixed, stained with a rabbit polyclonal antibody against P. gingivalis 33277 followed by Alexa-Fluor-488 conjugated secondary antibody. Actin was labeled using Phalloidin red, and DAPI was used to stain nuclei. The samples were visualized under super-resolution confocal microscopy and fluorescence intensities for each strain were quantified by NIH-Imaging software. At each time point, intracellular bacteria were also quantified by in situ antibiotic protection assay using P. gingivalis-specific 16S-rRNA primers by qPCR. The strains were grown in P. gingivalis selective growth media at 37°C, and turbidity of culture was measured at 600 nm over 78 h. Results: Quantitative analysis of confocal imaging showed that the intracellular level of ΔPGN_1181 strain was significantly decreased compared to the wild-type ATCC 33277 over 24 h ($p < 0.05$). Similarly, the quantitative antibiotic protection assay results showed significant decrease in intracellular survival for ΔPGN_1181 strain in GECs ($p < 0.05$). The bacterial growth assay in bacterial culture media showed that the mutant strain ΔPGN_1181 grew similarly to the wild-type strain ($p > 0.05$). Conclusions: Mutant strain ΔPGN_1181 appears to be survival deficient in GECs over time in contrast to the wild-type strain. The observed differences among the two isogenic strains suggest that this putative thioredoxin protein of P. gingivalis may provide important protection against host-induced oxidative stress for intracellular pathogen elimination.

This work was supported by CDM SHP program, NIH grant R01DE030313 (Ö.Y), NIH grant R01/R56DE016593 (Ö.Y)

108 **The Role of Complement C3a/C3aR in Commensal Gut Microbiota Actions on Osteoclastogenesis**

Hayden VandenBerg, Chad Novince, Megan B. Kuhn, Amy J. Warner, Matthew D. Carson, Jessica D. Hathaway-Schrader, Chad M. Novince, College of Dental Medicine, MUSC

Abstract withheld from publication

109 **Optimizing Glioblastoma Mouse Models to Provide an Accurate Framework for Differentiating Tumor Recurrence, Acute Radiation Necrosis, and Chronic Radiation Necrosis with Diffusion Kurtosis Imaging**

Connor Stephenson, Arabinda Das, Scott M. Lindhorst M.D Arunprasad Gunasekaran M.D. Milad Yazdani M.D Daniel G. McDonald MS Libby Kosnik Infinger MD, MPH Abhay K. Varma M.D. William A. Vandergrift III M.D. Sunil J. Patel M.D. Pierre Giglio, M.D. David Cachia M.D., College of Medicine, MUSC

Radiation induced damage in glioblastoma (GB) patients typically presents as neural necrosis, either acutely or chronically. Additionally, the treatment might fail, and tumor recurrence (TR)

might be observed. The issue beings with the presentation of these conditions on follow-up imaging studies. Chronic radiation necrosis (RN) presents with anatomic imaging characteristics nearly identical to TR. The inability to differentiate between these conditions can lead to additional surgeries or deviation from effective treatments. Developing a model to better predict this can better guide patient treatment protocols. We transplanted GL261 mouse GB cells into C57BL/6 mice. Tumor grafting was confirmed with MRI 2 weeks post-transplant. Fractional doses of 12Gy and 60Gy were administered to the tumor on an alternating-day schedule to ensure consistent induction of RN. One tumor section received 100% of a dose fraction to induce RN; the tumor edge received 50% of a dose fraction to promote TR. DKI images were acquired with two-shot spin echo-echo planar imaging methods. Biomarkers was compared by liquid biopsy, H&E staining. And Immunohistochemistry analysis of sacrificed mice. Axial T2-weighted MRI and DKI sequence at 2 weeks post implantation demonstrated edema indicative of TR. One week later, the T2-weighted imaging sequences demonstrated continued tumor progression. In a separate mouse with high dose (60 Gy) radiation treatment, T2 and DKI demonstrated both areas of tumor and suspected central RN. This result demonstrated that our proposed model for radiation induction was effective at achieving its goal of creating some areas of tumor necrosis and other areas of TR. All cases of GB and RN decreased in neuronal numbers at 4 weeks and a sustained increase in TNF-a, iNOS, and other inflammatory cytokines. H&E staining results showed typical pathological features of GB and RN, and TR in each case, indicating a successful outcome for our stated goal.

110 **Subdural Evacuation Port System and Middle Meningeal Artery Embolization for the Treatment of Chronic Subdural Hematoma: A Single Center Experience**

Craig Salvador, Alejandro Spiotta, Brian Saway, Warren Roth, Guilherme Porto, College of Medicine, MUSC

Introduction: Middle meningeal artery (MMA) embolization has become a minimally invasive treatment for chronic SDH (cSDH). In combination with surgical techniques such as Subdural Evacuation Port System (SEPS), these procedures present a potentially safer management strategy to a challenging and recurring pathology. We present a review of a single center's patients undergoing both procedures and their clinical and radiographic outcomes. Methods: A retrospective review was performed of patients who underwent a SEPS placement as well as an MMA embolization for cSDH between January 2018 and 2021 at a single institution. Variables reviewed included demographics, peri-operative imaging including post-operative non-contrased CT of the head 2-4 weeks post intervention, and functional outcome scores. Results: 25 patients (30 cSDHs; 10 right, 10 left, 5 bilateral) with a mean age of 65.52 years ? 15.96, underwent evacuation with a SEPS and an MMA embolization. 5 of these patients had undergone a previous SEPS for cSDH and returned for SEPS and MMA embolization for a re-accumulation of the cSDH. In the entire cohort, following SEPS placement and MMA embolization, 3 patients (n=3, 12%) required retreatment, 2 of these patients with repeat SEPS (n=2, 8%) and one with craniotomy (n=1, 4.0%). Following MMA embolization, Complications include: 1 facial nerve palsy and 1 patient with left-sided hemiplegia secondary to thromboemboli. Mean cSDH width (mm) changed from 17.13 pretreatment to 9.87 post treatment and to 5.84 at outpatient head CT. Mean MLS (mm) changed from 7.2 pretreatment to 3.5 post-treatment and to 2.5 at outpatient head CT. Mean mRS improved from 1.72 a t admission to 1.32 at follow-up. Conclusion: Here we demonstrate the largest case series to date of patients undergoing both a SEPS placement as well as an MMA embolization for cSDH. We show that the rate of patients requiring operative craniotomy for evacuation is comparable

111 **Addressing Racial Disparities in Hypertension Control through Implementation of a Telephone-Based Outreach Intervention at a Federally Qualified Health Center**

Rohith Raman, Bradi Granger, Holly Biola, Melanie Bakovic, Tiffany Hayes, Colette Whitney, Dominique Bulgin, Yunah Kang, Cameron Eck, L'Tanya Gilchrist, Awanya Caesar, Joan Chaplin, College of Medicine, MUSC

Background: The high prevalence of uncontrolled hypertension (systolic blood pressure (SBP) ≥140 mmHg or diastolic BP (DBP) ≥90 mmHg) among Black patients represents a significant racial health disparity in the US. This study evaluated the effectiveness of a telephone-based strategy for inviting Black male patients with severe hypertension to weekly self-management education classes, and assessed how the outreach intervention itself correlated with relevant quality improvement outcomes, including improved BP and primary care follow-up among our clinic population of Black men with severe hypertension. Methods: A cohort of 265 Black men with BP≥160/100 mmHg at the most recent clinic visit were identified using an EpicTM report. Telephone outreach was used to invite the cohort to attend weekly in-person classes, where patients received a free BP cuff for home use, learned self-monitoring skills, and learned how to implement healthy lifestyle changes. Logistic regression analysis was performed to determine the associations between being reached by phone with (1) class attendance and (2) follow-up appointment attendance. Results: A majority were single (57.4%, n=152), 49.1% had history of alcohol or substance use (n=130), and 35.8% (n=95) were uninsured. After controlling for sociodemographic factors, being reached by phone was significantly associated with increased likelihood of patient attendance at future follow-up appointments (OR=1.91; p=0.038) but not with class attendance (OR=2.45; p=0.155). Patients who attended a follow-up appointment experienced significant reductions in both SBP and DBP during the intervention period (p<0.01). Conclusions: Successful telephone contact was associated with increased likelihood of attending a follow-up visit at the clinic and with a reduction in BP, which also highlights the importance of confirming a working telephone number for patients at every visit. Our findings suggest that telephone-based outreach is efficient to implement and can be undertaken by clinicians to address the challenges posed by racial disparities in hypertension control.

This work was supported by Project was supported by grants from the CDC (NU38OT000289), AAPM, and AHA.

112 **Hyperemesis Gravidarum induced Wernicke's Encephalopathy: An Unusual Presentation of Altered Mental Status**

Caroline Brailsford, Caroline Brailsford, Dr. Jordan M. Spencer DO, Sophia S. Urban, MD, MPH, George Book, MD, College of Medicine, MUSC

Wernicke's encephalopathy (WE) is a reversible but life-threatening acute neurological disorder resulting from vitamin B1 deficiency. WE is most commonly associated with heavy alcohol consumption. However, in pregnancy, hyperemesis gravidarum can rapidly deplete thiamine due to poor intake, fetal sequestration and increased metabolic demand. When treated early, neurologic outcomes are good. However, permanent impairments and pregnancy loss are common in WE, therefore rapid diagnosis and treatment with thiamine supplementation is essential. We report a rare cause of altered mental status in the setting of WE due to hyperemesis gravidarum in a 28 year old woman at 14 weeks gestation. The patient presented to our hospital with intractable nausea and vomiting, altered mental status and nystagmus. A diagnosis of WE was established based on clinical presentation, MRI findings and detection of low Vitamin B1. Following administration of

high dose thiamine, the patient's mental status greatly improved. As altered mental status remains one of the most common features of the disorder, we emphasize the importance of early thiamine supplementation and consideration of WE in the differential diagnosis of pregnant patients with hyperemesis gravidarum presenting with AMS.

113 WITHDRAWN

114 **Collagen Hydroxyproline Analysis of Colon Cancer Polyps in Patients within the Appalachian Mountain Region.**

Alexander Sougiannis, Peggi Angel, College of Medicine, MUSC

Abstract withheld from publication

115 **Helping Infants with Congenital Heart Defects: Enhancing Parent and Therapist Engagement Through Infant Massage**

Catherine Flynn, Catherine Flynn, Courtney Jarrard, OTR/L, C/NDT, Patty Coker-Bolt, PhD, OTR/L, FAOTA, Department of Occupational Therapy, College of Health Professions, MUSC

Introduction: Infants born with congenital heart defects (CHD) may experience post-operative growth challenges, such as failure to thrive, difficulties with feeding and weight management, and neurodevelopmental impairments (Lambert et al., 2017). Several recent studies have explored the use of touch-based therapies, such as infant massage, to improve developmental outcomes of these fragile infants (Lambert et. al., 2017; Harrison, 2020) but no studies have explored how to promote successful parent engagement in this intervention. The purpose of this study is to determine training and education models to promote successful parent engagement in infant massage. Methods: Qualitative and Quantitative data is being collected using interviews, chart reviews, observation, and REDCap surveys to further understanding 1) the perception of healthcare providers (OT/PT/SLP, Nursing, MD) on the use of touch-based interventions (i.e., massage) for infants with CHD and 2) the perceptions of parents/caregivers of infants with CHD including the potential benefits and challenges for family participation in touch-based interventions. Results will be analyzed through thematic analysis and descriptive statistics of frequency of responses. Results: The study is on-going and data collection will be completed by late September. Conclusions: The results of this study will inform the development of parent education resources to engage families in therapeutic infant massage in the cardiac unit at MUSC Children's Hospital. Resources could include an app for parents with information about infant massage and how to maximize use of this therapeutic intervention. An immersive learning workshop will also be developed to educate families and staff about infant massage and tools for families to promote parent participation.

116 **How to Address Challenges with Early Intervention for Infants of Underrepresented Families: Helping the Babies at MUSC High Risk Clinic**

Daijah Washington, Daijah Washington, Amy Ruddy-Humphries CNP, Dr.Patricia Coker-Bolt PhD, OTR/L, FNAP, FAOTA, Department of Occupational Therapy, College of Health Professions, MUSC

Introduction/Rationale: Technology and evidence-based practices in neonatal care have improved the survival rates of fragile infants. Unfortunately, a large percentage of at-risk infants demonstrate developmental delays by school age (Doyle et al., 2021). This disproportionally impacts families of lower socioeconomic status who have more difficulty accessing services for at-risk infants and tend to be less satisfied when services (Little et al., 2015). Well-designed early intervention (EI) programs

have the potential to ameliorate long-term developmental deficits for at-risk infants. Although several recent studies have highlighted exemplar family-centered EI models, there are few, if any, currently being used in SC (Little et. al, 2015). There is a need to improve participation of underrepresented families in home-based EI services. This study will explore 1) the current EI models used in SC, 2) the perceptions of underrepresented families who receive EI services, and 3) the perceptions of therapists and early interventionist staff who deliver EI services in the home-environment. Method: A prospective study with collection of both quantitative and qualitative data to determine: 1) the types of EI resources provided to families of at-risk infants after discharge from the neonatal unit, 2) the knowledge of families regarding additional supports and resources once receiving EI services, and 3) the perceptions of EI therapists and staff on current barriers to providing EI services in SC. Data will be collected via REDCap surveys, in-person interviews and observations of care at the MUSC High Risk Clinic. Results will be analyzed using descriptive statistics, frequency of responses, and thematic analysis of open-ended questions. Results: This study is on-going and data collection will be completed by late September. Conclusion: The results of this study will support the development of new resources and programming offered by the MUSC High-Risk Clinic to enhance EI services for underrepresented families and at-risk infants.

117 **Coming Home: Improving Post-Adoption Adjustment for Families at the MUSC International Adoption Clinic**

Brittany Randall, Patty Coker-Bolt PhD, OTR/L, FNAP, FAOTA, Angela LaRosa M.D. MSCR, Shannon Hemberger MOT, OTR/L, CSRS, College of Health Professions, MUSC

Children adopted internationally from Eastern European or Asian countries often experience adverse conditions prior to their adoption to the United States and are more likely to have special needs. The adoptive families are often unaware of the extent of their child's disabilities until after the adoption is complete. As a more complete picture of their child emerges, the months following adoption can be a stressful adjustment period. It is evident that caregiver access to post-adoption resources could make the difference in keeping a family together. The purpose of this study is to explore the strategies and resources which are provided at international adoption clinics to improve the adoption experience for children and families. A prospective study with collection of quantitative and qualitative data to determine 1) the types of resources provided at well-known international adoption clinics at children's hospitals in the US, 2) the perceptions of families and caregivers whose child has received services at the MUSC clinic, and 3) the perceptions of staff and providers including their opinions on current barriers and challenges to providing family resources. REDCap surveys, phone interviews, and in-person interviews are currently being conducted. Results will be analyzed using descriptive statistics, frequency of responses, and thematic analysis of open-ended questions. This study is on-going and data collection will be completed by late September. The results of this study will inform the development of the parent resources to enhance the services provided at the MUSC International Adoption Clinic. Resources could include connections to support groups, emailed resources, book recommendations, videos, brochures, social media groups, and developmental charts.

118 **Effects of Dry Needling on Spinal Reciprocal Inhibition**

Anna Zuloaga, Gretchen Seif, Alan Phipps, Anna Zuloaga, Rachel (Abby) McLaughlin, Blair Dellenbach, and Aiko Thompson, Department of Physical Therapy, College of Health Professions, MUSC

Objective: Spinal reciprocal inhibition is an important spinal mechanism of motor control. It is often impaired in persons after stroke, negatively impacting locomotion; at the same time, it changes in response to therapeutic interventions (e.g., FES). An increasing number of physical therapists worldwide have been administering trigger point deep dry needling (DDN) to treat post-stroke spasticity. Yet, currently, effects of DDN on spinal somatosensory processing are not well understood. Thus, to understand neurophysiological mechanisms of DDN, we are investigating the effects of DDN on spinal pathways in persons with and without stroke. Design: Before and 0, 90 minutes, and 72 hours after DDN of the medial gastrocnemius (MG) at myofascial trigger points, reciprocal inhibition of the soleus, MG and lateral gastrocnemius (LG) was examined while the participant stood and maintained his/her standing posture and triceps muscle activity. Passive ankle range of motion (ROM) was also measured before and after DDN. Setting: University Participants: 13 adults of 22-57 years old (median 37.5) without known neurological conditions. Intervention: Trigger point dry needling to the medial gastrocnemius Main Outcome Measure(s): Reciprocal inhibition of ongoing muscle activity elicited by common peroneal nerve (CPN) stimulation. ROM. Results In the MG and LG, there was no systematic changes in the amount of inhibition across participants or measurement times. Soleus inhibition elicited by suprathreshold CPN stimulation was increased significantly at 0 minute and 72 hours post DDN ($p>0.05$). Ankle dorsiflexion ROM was increased by 4 deg at 0 minutes and 72 hours post DDN. Conclusion DDN alters soleus inhibition, which may partially explain increased ankle ROM post DDN. In order to understand how DDN affects reciprocal inhibition in the stroke-impaired CNS, studies of individuals after stroke are currently underway.

119 **Clinical and Radiographic Outcomes Following Reverse Total Shoulder Arthroplasty in Patients 60 Years of Age and Younger**

Garrett Neel, Richard Friedman, Marissa Boettcher, Josef Eichinger, College of Medicine, MUSC

Introduction: While initially indicated for use in older patients, reverse total shoulder arthroplasty (rTSA) is being increasingly used in younger patients. The purpose of this study is to utilize larger population numbers to compare the clinical and radiographic outcomes of patients under the age of 60 to those aged 60-79 following primary rTSA. Methods: 154 patients under 60 years old and 1,764 patients aged 60-79 were identified from an international multi-institutional WIRB approved registry with a minimum 2-years follow-up. All patients were evaluated and scored preoperatively and at latest follow-up using 5 outcome scoring metrics and 4 active range of motion (ROM) measurements. Results: Mean follow-up was 47 months. Patients under 60 were more often male ($p = 0.023$), had a higher BMI ($p = 0.0002$), higher rates of previous surgery (57% vs 27%, $p <0.0001$), higher rates of post-traumatic arthritis (11% vs 5%, $p = 0.003$) and inflammatory arthropathy (13% vs 4%, $p <0.001$), and lower rates of rotator cuff tear arthropathy (25% vs 38%, $p = 0.001$). There were no statistical differences in ROM between the groups but patients under 60 had statistically significant lower function scores, lower outcome metric scores, and higher pain scores at latest follow-up. Complication rates were similar, but young patients were more likely to require revision (5.2% vs 1.8%, $p=0.004$). Younger patients also had lower satisfaction scores (86% vs 92%, $p = 0.006$). Conclusion: At a mean follow-up of 47 months, primary rTSA patients under age 60 years had worse clinical outcomes compared to those aged 60-79 years, with lower outcome

scores, increased pain, lower function scores and less patient satisfaction. While complications were similar, younger patients had a threefold increased risk of revision.

120 **Quality of Care in US Critical Access Hospitals: A Systematic Review**
Olivia Reszczynski, Paula Chatterjee, College of Medicine, MUSC

Critical Access Hospitals (CAH) are rural safety-net hospitals that are specially designated to ensure access to healthcare in rural areas. Given the importance of providing high-quality care for rural communities, many CAHs have begun to participate in federal quality improvement initiatives, such as value-based payment programs and public reporting of performance on quality measures. However, little is known about how well CAHs perform on quality measures broadly. To fill this gap, we performed a narrative systematic review on evidence of CAH performance on quality measures compared to non-CAHs over the last twenty years. We identified peer-reviewed articles on CAH quality published between 2000-2020 after searching PubMed, CINAHL, and Scopus databases. Because many studies reported performance on multiple quality measures, we investigated each measure individually to determine if CAHs performed better or similar to, or worse than non-CAHs. Among 31 articles, CAHs performed better or similar to non-CAHs on quality measures established by the Centers for Medicare & Medicaid Services (CMS) or the Agency for Healthcare Research and Quality (AHRQ). On measures of mortality, CAH hospitals performed worse on acute myocardial infarction (AMI), but better or similar on congestive heart failure (CHF) and pneumonia mortality. Patient experience measures showed CAH performing as well or better than non-CAHs. Performance on patient experience measures and certain condition-specific mortality measures are similar between CAHs and non-CAHs. These findings may provide reassurance to policymakers interested in improving patient outcomes for rural communities and bolstering rural health care systems.

121 **Electrical Stimulation of the Trigeminal Nerve Improves Olfactory Sensitivity in Healthy Individuals: A Randomized, Sham-Controlled Trial**
Elise Gruber, Bashar Badran, Georgia O'Leary, Chris W. Austelle, Sarah Huffman, Alex Kahn, Lisa McTeague, Thomas Uhde, and Bernadette Cortese, Department of Psychiatry, College of Medicine, MUSC

Background: The olfactory and intranasal trigeminal nerves comprise two distinct sensory pathways which are responsible for human smell function. Environmental odorants bind to and activate pathway-specific odorant receptors which transmit smell signals to the central nervous system (CNS). Damage to these pathways, as seen with aging, inflammation, or CNS injury, causes decreased odorant perception which can lead to comorbidities such as malnutrition, depression, cognitive dysfunction, and impaired memory retention. Currently, there are limited interventions available to treat smell loss, which effects most individuals over the age of 60 and is a persistent complication of viral illnesses, such as COVID-19. In this pilot trial, we aim to understand whether electrical stimulation of the trigeminal nerve via trigeminal nerve stimulation (TNS) or transcranial direct current stimulation (tDCS) modulates odor sensitivity in healthy adults. Methods: 20 healthy adults (12 female, mean age = 27) were recruited for a three-visit, randomized, double-blind, sham-controlled trial. Participants were randomized to receive one of three stimulation modalities (TNS, tDCS, or sham) at each visit. Odor detection thresholds were obtained at baseline, immediately post-intervention, and 30-minutes post-intervention. Participants also completed a sustained attention task and mood assessments at each time point. Results: Our findings demonstrate a significant stimulation x odor x time interaction ($F[2,76]=3.56$, $p=.024$). Detection of the trigeminal-

dominant odorant, guaiacol (GUA) was significantly enhanced by active TNS (+16% and +9% from baseline at the 1st and 2nd follow-up time points, respectively) and by tDCS (+12% and +14%, respectively). No significant changes in detection of the olfactory-dominant odorant, phenyl ethyl alcohol (PEA), were noted at either time point following active TNS or tDCS. Conclusion: TNS is a safe, accessible, noninvasive method for boosting olfaction. Future studies should determine the full effects and durability of TNS on smell function across different stimulation parameters, odorants, and patient populations.

This work was supported by MUSC Psychiatry Chairman's Fund (Badran)

122 **An Exploration of Curricular Needs for Entry Level Occupational Therapy Doctoral Students to Increase Cultural Responsiveness and Communication with Clients from Diverse and Underserved Communities**

Nikki Kardouni, Cristina Smith Reyes, Department of Occupational Therapy, College of Graduate Studies, MUSC

Background and Significance The need for education in cultural awareness, cultural competence, and cultural responsiveness for occupational therapy students and/or clinicians dates back as far as 2006. At this time there is no formal curriculum to address the educational needs of diversity in occupational therapy. Standardizing educational tools for educators will help to develop cultural responsiveness in curricula and promote culturally effective service delivery. This needs assessment study will inform the development of standardized curriculum tools to promote transformative learning for entry-level doctoral occupational therapy students. The purpose of this long-term doctoral capstone project is to provide standardized academic curricular tools to promote increased cultural competence and cultural responsiveness for students through enhanced understanding and communication skills to ultimately improve therapeutic interventions and outcomes for clients. Methods This presentation will discuss completion of a RedCap Survey for students regarding their knowledge of how diversity and communication affect occupational therapy evaluation and treatment outcomes. A RedCap survey for Educators will also be discussed regarding teaching materials with explicit instruction in diversity and communication. Results Data collection and analysis from the RedCap surveys will be discussed with regard to creating standardized educational tools for entry level occupational therapy doctoral students to develop cultural responsiveness and promote culturally effective service delivery. Conclusion The findings from this needs assessment will be utilized to develop standardized tools for promoting cultural responsiveness in occupational therapy and provide a model for other health professions. These tools will address the educational standards for ACOTE Standard B.1.2, Sociocultural, Socioeconomic, Diversity Factors, and Lifestyle Choices.

123 **Carbohydrate-Binding Protein Galectin-3 and its Role in Age-Related Hearing Loss**

Blake Howard, Hainan Lang, College of Medicine, MUSC

Age-related hearing loss (presbyacusis) is progressive bilateral hearing loss that affects approximately 4 out of 5 adults over the age of 85 in the United States. Presbyacusis is a multifactorial condition with many pathways and factors other than noise exposure alone. The exact mechanisms by which it occurs, however, remains a mystery. One prevalent theory is that inflammation in the cochlea due to immune-metabolic causes contributes to presbyacusis. Using mouse models of presbyacusis and RNA-seq analysis, preliminary data has shown a significant

increase in Galectin-3 (Gal-3) in the lateral wall of the aging mouse cochlea in presbyacusis. Gal-3 is a carbohydrate-binding protein that has emerged as a key regulator and marker of inflammation in many diseases. Gal-3 is a known activator of macrophages and microglia, which is thought to be its mechanism of disease onset and progression. There is limited research on the roles of Gal-3 in hearing loss, however. Our hypothesis is that dysregulation of Gal-3 in the lateral wall with aging has a negative impact on cochlear structure and function that contributes to presbyacusis. Slides of cochlear tissue of young (2-3 month) and old (24-28 month) CBA/CaJ mice were double stained with Gal-3 and Iba-1, a known macrophage marker, and the lateral walls were examined under fluorescence microscopy. The shapes of the cells were almost exclusively ramified macrophages in the young mice, while unknown large round cells in addition to amoeboid and ramified macrophages were seen in the old mice. The number of cells in general was also increased in the old mice. Finally, there was a greater number of cells that stained with exclusively Gal-3 or Iba-1 in the old mice. These findings suggest that increased Gal-3 has a significant correlation, and possibly causation, with changes to the structure and function of the cochlea in presbyacusis.

124 **Adverse outcomes comprehensively worse among children and transition-aged youth with comorbid Autism Spectrum Disorder (ASD) and Disruptive Behavior Disorders (DBD) across lifespan**

Nicole Vonada, Andrea Boan, Catherine C Bradley, PhD; Rosmary Ros-Demarize PhD, Laura A Carpenter, PhD, College of Medicine, MUSC

Research considering long-term outcomes of children with ASD has established that externalizing behaviors are associated with worse outcomes. Yet, few studies have examined how DBD diagnosis impacts outcomes of children with ASD. This study investigates long-term outcomes of children with comorbid ASD and DBD, measured as lifetime prevalence of ED visits, psychiatric hospitalizations, psychotropic medication usage, criminal justice system involvement, and maltreatment. Data for this study come from an epidemiological autism dataset (SC ADDM Network), which was linked with datasets from state agencies: SCRFA, DMH, DJJ, DSS, and Medicaid, as part of the Carolina Autism Transition Study (CATS) comparing individuals with ASD (n=394) and ASD+DBD (n=212). The ASD+DBD group (75.0%) was more likely to be treated in the ED than the ASD group (56.9%) [Adjusted OR (95%CI) = 2.28 (1.5, 3.4)]. Those with ASD+DBD (41.1%) were more likely to receive DMH services vs. ASD (13.2%) [aOR: 4.6 (3.0, 7.1)]. The ASD+DBD group was more likely to receive 1) psychotropic medications (93.6%) vs. ASD group (63.1%) [aOR: 8.53 (4.6, 15.8)]; 2) antidepressants (62.4%) vs. ASD (26.2%) [aOR: 4.67 (3.1, 7.0)]; 3) antipsychotics (69.6%) vs. ASD (17.0%) [aOR: 11.14 (7.1, 17.4)]; and 4) stimulants (71.4%) vs. ASD (33.4%) [aOR: 4.99 (3.3, 7.5)]. Those with ASD+DBD were more likely to be criminally charged as a juvenile (6.4%) than those with ASD (0.2%) [aOR: 38.9 (4.8, 316.8)]. The ASD+DBD group was more likely to experience maltreatment than the ASD group. Participants with comorbid ASD+DBD experienced comprehensively worse long-term outcomes than participants with ASD alone in terms of health service utilization, psychotropic medication use, and negative life experiences of criminal justice involvement and maltreatment across the lifespan. Further investigation is needed to determine if targeted therapy should be individualized to meet the needs of this comorbid population.

125 **Impact of gestational age on glucose tolerance test and risk of fetal overgrowth**

Haley Hopkinson, Matthew Finneran, Ralitza Peneva, Ryan Cuff, Department of OB/GYN, College of Medicine, MUSC

Current guidelines for diagnosis of gestational diabetes mellitus (GDM) recommend a 1-hour glucose tolerance test (GTT) between 24-28 weeks' gestation. Since insulin resistance gradually increases throughout pregnancy, it is possible that earlier screening may miss women at risk for hyperglycemia and fetal overgrowth. The aim of this study was to compare different GTT screening time frames and the rate of large for gestational age (LGA) birth weight. This was a retrospective cohort study of women with singleton gestations and GTT values collected at 24-32 weeks' gestation. Patients were stratified into cohorts in two-week intervals based on timing of GTT. The primary outcome was rate of LGA (birthweight >90th percentile for age) with a normal GTT (< 135 mg/dL). Secondary outcomes were the rate of elevated GTT and subsequent elevated 3 hour GTT between cohorts. Logistic regression was used to generate adjusted odds ratios (aOR) and confidence intervals (CI) for the primary outcome adjusting for confounders. 10,915 women met inclusion criteria for the study, and 810 (7.9%) delivered an LGA neonate. Median GTT results increased with advancing gestation (range 107-113 mg/dL, p< .001) and the likelihood of an elevated 1-hour GTT increased with advancing gestation (range 20.3%-27.2%, p< .002; Table 1). These results were significant after adjustment with the greatest odds of elevated GTT at 30-31 weeks (aOR 1.7, CI 1.4-2.0, Table 2). However, no association was found for LGA in women with a normal GTT at any time frame. Further, timing of GTT did not affect result of the 3-hour GTT (p=.200). Median GTT values and the likelihood of an elevated 1-hour GTT result both increased with advancing gestational age. However, women with a normal GTT did not have increased rates of LGA regardless of GTT timing nor were results of the 3-hour GTT affected if 1-hour GTT was elevated.

126 **Verbal Autopsy: A systematic literature review for data acquisition methods to determine under-5-mortality and causes of death in low resource settings**

Stiles Harper, Tram Jones, Dr. Nancy Hagood, MD, Department of Global Health, College of Medicine, MUSC

The majority of countries with high under 5 mortality rates (U5MR) do not possess the vital registration systems that collect the data necessary to calculate the morality rate and determine cause of death (COD). The verbal autopsy (VA) instrument is an imperfect tool developed out of necessity to acquire this basic medical data to help guide population-based medical policy and therapy in these countries. Preliminary data from Bouzi, Haiti shows an U5MR of 18% (double the Haitian national average) and COD proportions in line with the World Health Organization. The credibility of this data, combined with this shockingly high U5MR demands a more precise, standardized study ascertaining the true U5MR and COD contributions within Bouzi. We performed a targeted systematic review of the literature utilizing specified keyword filters in four search engines for published and unpublished data. We screened 16,158 articles, reviewed 448 abstracts, and excluded 442 papers. From the selected studies: we determined that a VA questionnaire was indicated to accomplish our study purpose; we selected a 2-phase protocol structure composed of a preliminary civil vital registration (CVR) interview followed by a VA interview in qualified families; and we decided the structure and content of the questionnaire itself. The well-documented benefits of VA instrument utility in countries that lack vital registries, combined with our need for population data to initiate and guide population-based care for the children of Bouzi, confirmed our need for this study. The data generated from this study will help

accurately diagnose the largest contributors of U5M in Bouzi and allow us to focus our therapies accordingly.

This work was supported by MEDICAL UNIVERSITY OF SOUTH CAROLINA, CENTER FOR GLOBAL HEALTH

127 **Diversity in the Pediatric Heart Transplant Surgeon Workforce Between 2000 and 2020**

Olivia Walkowiak, Taufiek Rajab, William Hardy, Lauren V. Huckaby, Morgan Hill, Suyog Mokashi M.D., Minoo N. Kavarana M.D., Department of Surgery, College of Medicine, MUSC

Introduction: Diversity in the cardiothoracic surgery workforce is essential to addressing sexual and racial disparities within the field. We analyzed the demographic changes in the population of pediatric surgeons performing heart transplants (HTx) between the years 2000 and 2020. Methods: Surgeons from the UNOS database were classified by sex into male or female, while race was separated into non-Hispanic White (White), non-Hispanic Black (Black), Hispanic and non-Hispanic Asian (Asian) through images from institutional websites. These classifications were used to determine the composition of the workforce of surgeons performing HTx each year between 2000-2020 on patients <18 years old. Results: As shown in Figure 1, pediatric cardiothoracic surgeons performing HTx in 2000 were 97.6% male and 2.4% female. By 2020, it changed to 96.8% male and 3.2% female. With regards to race, in 2000 there were 89.3% White surgeons, 0.0% Black, 2.4% Hispanic and 8.3% Asian. In 2020, it shifted to 71.6% White, 4.2% Black, 3.2% Hispanic and 21.1% Asian. Conclusions: Over the last twenty years there has been an increase in diversity in the cardiothoracic surgery workforce, yet the overwhelming majority of pediatric heart transplant surgeons are still White and male. When compared to the general United States population, female, Black and Hispanic surgeons are severely underrepresented, while Asian surgeons are overrepresented. These results demonstrate the need for more effective efforts in increasing the diversity of the cardiothoracic surgical workforce.

This work was supported by FLEX Funds for Research/Scholarly Projects through the Medical University of South Carolina College of Medicine

128 **The Role of Prostaglandin E2 in PD-1 Expression on THP-1-derived Macrophages and Mouse CD8+ T-cells**

David Wilson, Raymond DuBois, Dingzhi Wang, Jie Wei, and Bo Cen, College of Medicine, MUSC

Introduction: Colorectal adenomas are precursors of colorectal cancer (CRC). Pro-inflammatory states associated with colorectal adenomas significantly predispose for colorectal tumorigenesis via upregulation of cyclooxygenase-2 (COX-2) and prostaglandin E2 (PGE2) synthesis. The PGE2/COX-2 axis allows cancer cells to progress and evade attack from immune cells via increasing immunosuppressive cell activity, disrupting antigen-presenting and T-cell functions, and interrupting innate leukocyte responses. The purpose of this study was to demonstrate that PGE2 can upregulate expression of PD-1, an immunosuppressive signaling receptor, in THP-1-derived macrophages and mouse CD8+ T-cells. Methods: THP-1 cells were differentiated into macrophages via phorbol 12-myristate-13-acetate administration. Following incubation with PGE2, the cells were analyzed with western blot and qRT-PCR. CD8+ T-cells were isolated from mice spleens, incubated with PGE2, and analyzed utilizing flow cytometry and qRT-PCR. Results: Western blot analysis of THP-1-derived macrophages incubated in 0.1μM, 0.3μM, and 1.0μM PGE2 demonstrated increased PD-1 expression. qRT-PCR analysis of THP-1-derived macrophages incubated in 0.1μM, 0.3μM, and

1.0µM PGE2 demonstrated 3.030-fold, 5.712-fold, and 2.683-fold increased PD-1 mRNA expression, respectively. qRT-PCR of mouse CD8+ T-cells incubated in 0.1µM and 0.3µM PGE2 demonstrated 1.874-fold and 9.594-fold increased PD-1 mRNA expression, respectively. Flow cytometry demonstrated that 9.14% and 9.35% of mouse CD8+ T-cells incubated in 0.1µM and 0.3µM PGE2 expressed PD-1, respectively, while 4.65% of control cells expressed PD-1. Conclusion: Our in vitro data shows PGE2 inducing PD-1 expression in THP-1-derived macrophages and mouse CD8+ T-cells. Greater PD-1 expression would allow cancer cells to progress safe from the host immune system. These data demonstrate that PGE2 produced in the colorectal tumor microenvironment promotes immune evasion by suppressing tumor-infiltrating CD8+ T-cell cytotoxicity and macrophage phagocytosis via induction of PD-1. Because of PGE2's immunosuppressive effects, NSAIDs and COXIBs are effective at preventing and treating CRC by inhibiting PGE2 synthesis via COX-2 blockade.

129 **Single incision latissimus dorsi surgical technique: a three button repair**

John Pike, Josef Eichinger, Brett Goodloe, Kirsi Oldenburg, College of Medicine, MUSC

Introduction: Due to the infrequent occurrence of latissimus dorsi insertional avulsions or tendon ruptures, there is no clear evidence on the optimal surgical fixation strategy. A three suture unicortical button repair technique through a single incision offers an anatomic reconstruction of the broad insertional footprint with adequate exposure. This fixation strategy is the preferred technique by the senior author. Methods: This surgical technique was demonstrated by recording a video of it being performed. A patient with physical exam and MRI findings consistent with a latissimus dorsi tear was prepped for surgery. The patient was positioned in the lateral decubitus position with the arm was flexed, adducted, and internally rotated to allow for full visualization of the posterior axillary fold. To repair the tear, a three suture unicortical button repair technique through a single incision was done. Postoperative rehabilitation and clinical assessments were done to recover from the surgery and asses its outcome. Results: The patient's clinical examination at 8 months postsurgery revealed restoration of the anatomy of the posterior axillary fold and symmetric muscular appearance. At the one year postsurgery follow-up, a subjective shoulder value of 100% with no pain and restoration of all functional activities without limitations was reported. Conclusion: The three suture buttons provide the greatest anatomical fixation and help distribute force. Unicortical button fixation eliminates the risk of iatrogenic injury via bicortical button fixation and provides similar, if not better biomechanical properties to interference screw fixation in regards to subpectoral biceps tenodesis. Additionally, the senior author believes that a three button repair provides enough solid fixation to allow for earlier range of motion activity of the shoulder joint to prevent stiffness, although, as with other described rehabilitation programs, return to strengthening and sport participation does not begin prior to 3 months.

130 **Provider Perception of Risk as a Barrier to Implementation of a High-Sensitivity Troponin Accelerated Diagnostic Protocol**

John Hall, Andrew Matuskowitz, MD, Mathew Gregoski, PhD, Steven Saef, MD, College of Medicine, MUSC

Background: The extent to which perception of patient risk by emergency department (ED) clinicians affects adherence to high-sensitivity troponin accelerated diagnostic protocols (HST-ADP) is unknown. We sought to quantify ED clinician comfort levels with discharging patients identified as increased risk by traditional risk stratification modalities for acute coronary syndrome (ACS) but low-risk by a validated HST-ADP. Methods: This was a cross-sectional descriptive survey study

distributed to all ED clinicians at an urban academic medical center. Four clinical vignettes classified hypothetical patients as low-risk for 30-day ACS according to the 0/1-hour HST-ADP. Vignettes additionally identified patients with HEART scores of 4 or 6 (2 cases each). One patient in each subset had pre-existing coronary artery disease (CAD). ED clinicians self-reported comfort levels with patient discharge from the ED on a 10-point Likert scale. Results: Of the 66 eligible participants, 36 (55%) participated in the survey. ED clinicians reported a mean comfort level of 6.07 (95% CI 5.34-6.80) with regard to discharging the vignetted patients. They reported higher mean comfort levels for discharging patients with HEART scores of 4 compared to those with HEART scores of 6 (mean difference 3.61, 95% CI 2.19-5.03). There were no differences in clinician comfort levels regarding presence or absence of CAD or between clinician types (attending, resident, advanced practice provider). Conclusions: ED clinicians accustomed to the HEART Pathway demonstrated limited comfort discharging patients identified as moderate risk by the HEART score, despite simultaneous classification as low-risk by the 0/1-hour HST-ADPs. Reported comfort levels were greater with lower HEART scores. Comfort levels of ED clinicians were not affected by the presence or absence of CAD and did not vary between clinician types. Further study of ED clinician decision-making for patients with chest pain based on use of the HST-ADP in actual practice is justified.

This work was supported by National Center for Advancing Translational Sciences of the National Institutes of Health under Grant Number UL1 TR001450

131 **Cost Analysis of Procedure Delays in the MUSC Vascular/Interventional Radiology Department among Floor and ICU Patients for December 2020**

Nathan Leaphart, Marcelo Guimaraes, Kirkpatrick Gillen, Matthew Bridges, Anand Mulji, Kelsey Duckett, Department of Vascular/Interventional Radiology, College of Medicine, MUSC

Purpose: To analyze the lengths and associated costs of procedure delays in the MUSC Vascular/Interventional Radiology (VIR) Department among Floor and ICU patients for December 2020. Methods: All inpatient procedures performed by VIR in December 2020 were analyzed. Of the 190 inpatient VIR procedures performed in this month, 175 were included and 15 were excluded due to difficulty obtaining Hospital Account Records (HARs). Using EPIC, each procedure's consult order and exam dates were obtained as well as the patient's location within the hospital. Using the hospital location, procedures were grouped into those for "Floor" and those for "ICU" patients. Delays were defined as differences in consult order and exam dates. Consult orders placed after 5 p.m. were considered as the next business day, weekend days were not counted into delays for nonemergent procedures, and delays were not calculated for multiple, subsequent procedures that stemmed from one consult order. The HARs for the patients with delayed procedures were obtained. For the total cost of a procedure delay, daily costs were summed from the date of the consult order to the day prior to the procedure. The total cost was then divided by the number of delay days to calculate the average daily cost. Results: Out of 175 procedures, 61 delays were counted with 58 being with Floor patients and 3 being with ICU patients. The average length of a delay was 1.3 days with a range of 1 - 6 days. The average total cost of a delay was $3,654.63 with a range of $348.62 - $15,449.23. The mean average daily cost was $2,928.13 with a range of $211.99 - $11,286.65. The mean average daily cost was $2,787.54 for Floor patients and $5,646.22 for ICU patients. For December 2020, the grand sum of the total delay costs was $222,932.40.

132 **Is There a Psychiatric Diagnosis in Chronic Ankle Instability Patients?**

John Allen, Christopher Gross, Caroline Hoch, Daniel Scott, Christopher Gross, Department of Orthopedics, College of Medicine, MUSC

Ankle instability is a common clinical entity that sometimes develops into chronic ankle instability (CAI), leading to continued pain and disfunction. However, there is very limited data to date on what impact common psychiatric pathology may have on patients' experience with CAI. This study aimed to investigate the association between psychiatric diagnosis and CAI, and whether having a diagnosed psychiatric illness impacts the outcome of CAI. We hypothesized that a concomitant diagnosis of psychiatric pathology with CAI would be significantly associated with lower postoperative patient-reported outcome measures (PROMs). We conducted a retrospective chart review on 429 patients (435 ankles) who were treated at an academic medical center between 2012 and 2021. Psychiatric diagnoses included anxiety (n=186), depression (n=171), insomnia (n=96), post-traumatic stress disorder (PTSD) (n=34), bipolar disorder (n=13), and obsessive-compulsive disorder (OCD) (n=11). In total, 211 patients eventually underwent surgery by a fellowship-trained orthopaedic foot and ankle surgeon. Statistical analysis was performed using Student t-test and Chi-squared test. The results showed a significant association between surgical treatment of CAI and a diagnosis of anxiety (p=.037), depression (p=.048), PTSD (p=.049), and bipolar disorder (p=.008). Patients with and without a PTSD diagnosis significantly differed in postoperative FAOS pain (p=.033), FAOS daily living (p=.015), FAOS quality of life (p=.027), and FAAM activities of daily-living (p=.005) scores. Additionally, patients with and without an OCD diagnosis significantly differed in postoperative FAOS symptoms+stiffness (p<.001), FAOS daily living (p<.001), FAOS quality of life (p<.001), FAAM activities of daily-living (p=.035), and FAAM total (p=.003) scores. No postoperative PROMs differed by anxiety, depression, insomnia, or bipolar disorder. Neither reoperation rate or a post-traumatic CAI diagnosis differed by any psychiatric illness. In conclusion, CAI patients with concomitant anxiety, depression, PTSD, or bipolar disorder were significantly more likely to receive surgical intervention than those without a diagnosis.

133 **Factors associated with caregiver adherence to mobile health interstage home monitoring in infants with single ventricle heart disease**

Sydney Reed, Sinai Zyblewski, Shahryar Chowdhury, Frances Woodard, College of Medicine, MUSC

Mobile health (mHealth) technology is an emerging tool in interstage home monitoring for infants with single ventricle heart disease. This study sought to describe adherence to mHealth monitoring, to identify factors and outcomes associated with adherence to mHealth monitoring, and to compare outcomes of traditional paper log vs mHealth monitoring. This was a retrospective, single-institution study of infants with single ventricle anatomy or biventricular shunt-dependent defects who were followed between November 2011 to October 2020. Subjects were grouped into paper vs. mHealth era and by frequency of mHealth (0% vs. <50% vs. >50%). The analysis included 214 infants. 109 (50.9%) infants were in the paper group and 105 (49.1%) were in the mHealth group. There were no differences in interstage mortality between groups. Within the mHealth group, 16 (15.2%) had 0% adherence, 25 (23.8%) had <50% adherence, and 64 (61.0%) had > 50% adherence. The adherent groups had a higher percentage of infants who were male (p=0.02), white race (p<0.01) and non-Hispanic or non-Latino ethnicity (p<0.01), mothers whose primary language was English (p<0.01), mothers who were married (p<0.01), and prenatal diagnosis of fetal cardiac disease (p=0.03). Adherent groups had a higher percentage of infants who had non-Medicaid primary insurance (p<0.01) and lived in a neighborhood with a higher median household income (p<0.04). Adherence was not associated with interstage mortality, unplanned cardiac

reinterventions, or hospital readmissions. Use of multilanguage, low literacy, affordable mHealth options for interstage home monitoring warrants further investigation.

This work was supported by NIH/NIDDK Institutional Training Grant "Short-term Research Training for Health Professional Students" (T35 DK007431)

134 **COVID-19 Modifications of Offseason and Preseason Training for NFL Athletes Are Associated with Increased Risk of Regular Season Injuries**

Evan Bailey, Harris Slone, J. Brett Goodloe, Rachel McNeely, Sophia Traven, Shane Woolf, College of Medicine, MUSC

Objectives: COVID-19 altered National Football League (NFL) player and team training during the 2020 offseason. All preseason games were cancelled resulting in absence of game play before the first week of the regular season. Thus concerns exist regarding injury susceptibility of players during regular season games. The purpose of this study was to evaluate and compare injury rates during the 2020 NFL season versus injury rates from the unaffected 2017-2019 seasons. We hypothesized there would be an increased injury rate and an increased rate of season ending injuries during the modified 2020 season. Methods: The NFL's public injury database was queried to identify players placed on the injury lists throughout the 2017-2020 seasons. All players listed as "out" and on the injured reserve due to physical injury were included in the data set. For further stratification, injury incidence was separated based on position. Time missed due to COVID-19 illness was not included. Injury rates were expressed as injuries per 1000 athlete exposures (AE).

Results: Overall, 893 individual players missed games due to injury during the 2020 NFL regular season compared to an average of 743 over the 2017-2019 seasons. Defensive players at all positions had a statistically significant increase in injury incidence from an average of 7.54 to 10.20 injuries per 1000 AE. Defensive backs were most affected with a 46% increase in players injured. There was no statistically significant difference in season ending injuries for any position.

Conclusions: The COVID-19 stricken 2020 NFL regular season saw an increased rate and incidence of injuries. Specifically, defensive players had a higher incidence of injury overall with defensive backs experiencing the greatest increase in injury rates.

135 **Effects of body positioning on laryngeal penetration and aspiration in children with unilateral vocal cord paralysis.**

Neil Monaghan, Clarice Clemmens, Heather McGhee, Erick Yuen, Shaun Nguyen, College of Medicine, MUSC

Objectives: To evaluate laryngeal penetration and aspiration in upright and sidelying positions in children with unilateral vocal cord paralysis (VCP) that underwent modified barium swallow study (MBSS). Methods: A retrospective chart review of pediatric patients with a diagnosis of unilateral vocal cord paralysis (VCP) who underwent modified barium swallow study (MBSS) was performed. Patients were identified using diagnostic code for VCP and based on diagnosis via flexible laryngoscopy. Once identified, MBSS notes were reviewed for data regarding laryngeal penetration, tracheal aspiration, and body position (upright and/or sidelying) during the exam. Information was also collected on the various consistencies tested including thin, nectar thick, and honey thick liquids. The order of positioning was recorded in patients that underwent both positions during the study. Data was analyzed using chi square analysis. Results: 811 patients that underwent MBSS between 2011 and 2014 were screened, and 90 patients were isolated with unilateral vocal cord

paralysis. Of those 90 patients, 23 underwent MBSS in both sidelying and upright positions. When all 90 patients were evaluated, there were no significant increases in penetration or aspiration in the upright position with thin liquids. Importantly, among these 23 patients that underwent the study in both positions, we found no significant difference in penetration or aspiration between body position with any consistency. Conclusions: Penetration and aspiration were not associated with body position in patients that underwent MBSS at our institution. However, due to an incomplete data set and small sample size of those that underwent MBSS in both positions, these results should be explored further prospectively.

This work was supported by MUSC Department of Otolaryngology-Head and Neck Surgery NIH/NIDCD Institutional Training Grant (T32 DC014435)

136 **The Impact of Changes in Renal Function During Waitlist Time on Outcomes after Heart Transplantation**

Paul Brocklebank, Arman Kilic, Jennie H. Kwon, MD, Z. A. Hashmi, MD, Chakradhari Inampudi, MBBS, Brian A. Houston, MD, Lucas J. Witer, MD, Ryan J. Tedford, MD, College of Medicine, MUSC

Background and Aim This study evaluated the impact of changes in renal function during the waitlist period on post-transplant outcomes of orthotopic heart transplantation (OHT). Methods The United Network for Organ Sharing registry was used to identify adult patients undergoing isolated OHT from 2010-2020. Patients were stratified by whether their National Kidney Foundation chronic kidney disease (CKD) stage improved, worsened, or remained unchanged between listing and transplantation. Univariate analysis and multivariable Cox regression were conducted to determine whether change in estimated glomerular filtration rate (eGFR) or change in CKD stage predicted 1-year mortality after OHT. Results Of 22,746 patients, the majority of patients remained in the same CKD stage (59.6%), and the frequencies of patients progressing to improved (19.3%) and worsened (21.1%) CKD stages were similar. Temporary mechanical circulatory support (MCS) was associated with improved CKD stage and durable MCS with worsened CKD stage ($p<0.001$). Post-OHT dialysis was most common in patients with worsened CKD stage (13.2%) and least common in the improved cohort (9.4%) ($p<0.001$). Kaplan-Meier unadjusted 1-year survival rates after OHT were similar between CKD change groups (log-rank $p=0.197$). Multivariable analysis demonstrated no risk-adjusted effect of change in eGFR ($p=0.113$) or change in CKD stage ($p=0.076$) on 1-year mortality after OHT. Conclusions Approximately 20% of patients improve CKD stage and 20% worsen CKD stage between listing and OHT, with the remaining 60% having unchanged CKD stage. Worsening CKD stage predicts increased likelihood of post-OHT dialysis, but CKD stage change does not predict 1-year survival following OHT.

This work was supported by NIH/NIDDK Institutional Training Grant, "Short Term Research Training for Health Professional Students" (T35 DK007431)

137 **Fall Prevention Deserves Your Attention: Analysis of MUSC In-Patient Fall Events in 2020 with Emphasis on Drug Interventions**

Bethany Burnette, Nicole Pilch, Michael Duong, Shelby Kolo, College of Pharmacy, MUSC

Introduction: In-patient fall events are a source of morbidity and mortality and lead to an increase in hospital related costs. Literature shows that high-risk medications are inappropriately given and contributes to falls. Historically, our centers focused on nursing/physical therapy interventions, but have not engaged the pharmacist to help mitigate fall risk. A common cause analysis of falls would

aid in understanding the variables associated. We sought to determine if fall events occurred more frequently in patients who were given high-risk medications and what the most common modifiable variables were. Methods: Retrospective, cross-sectional analysis of adult inpatient fall events reported during calendar year 2020 occurring at 2 different hospital buildings in Charleston, SC: Ashley River Tower (ART) and Main Hospital (MH). Investigation of electronic medical records (EMR) was performed using a standardized approach. Variables included: hospital location, time, gender, age, ethnicity, renal/hepatic impairment, high-risk medications, hypotension, restroom, ambulation, and altered mental status. Variables were cross analyzed by location, time, and age. A post-hoc analysis of restroom-related falls were analyzed. Results: 292 falls were analyzed. Baseline characteristics: 63% received >3 high-risk medications, 42% restroom-related, 22% ambulation-related. Of the restroom falls, 11% received diuretics prior. Patients <75 y.o. with 3 high-risk medications had more falls compared to patients >75 (66% vs 34%). Of patients <75 y.o., 50% fell during night shift, 66% received>3 high-risk medications, 42% were restroom-related. Conclusion: Patients given >3 high-risk medications fall more often. However, falls associated with more medications didn't occur in patients >75 years old. Falls were commonly restroom-related, of which diuretics were a common cause. Data suggests that pharmacists should play a role in medication timing, preventing duplicate therapies, ensuring home medications are restarted as reported, and educating nurses. In addition, reviewing medications pre and post fall could help mitigate fall related morbidity and mortality.

138 WITHDRAWN

139 **Effects of Dry Needling on Spinal Reflexes**

Rachel McLaughlin, Gretchen Seif, Alan Phipps, Anna Zuloaga, Blair Dellenbach, and Aiko Thompson, College of Health Professions, MUSC

Research Objective: Spasticity can lead to changes in spinal and supraspinal pathways which can lead to decreased function and quality of life in persons with stroke. Physical therapists worldwide have been administering trigger point deep dry needling (DDN) to treat post-stroke spasticity. Yet, currently, effects of DDN on spinal somatosensory processing are not well understood. To understand the neurophysiological mechanisms of DDN, we are currently investigating the effects of DDN on spinal somatosensory pathways in persons with and without stroke. Design: Before, 0 minutes, 90 minutes, and 72 hours after DDN of the medial gastrocnemius (MG) the H-reflex and M-wave recruitment curves are measured in the soleus, MG and lateral gastrocnemius (LG). Passive ankle range of motion (ROM) before and after DDN. Setting: University Participants: 13 adults (median 37 years old; mean 36.3 +/- 12.4) without known neurological conditions. Interventions: DDN Main Outcome Measure(s): H-Reflex and ROM Results: MG H-reflex latency was prolonged by 1-3 ms at 0- and 90-minutes post (in 10/13 individuals) and in 6/13 in the soleus and 2/13 in the LG. In the MG, H-reflex amplitude was significantly decreased at 72 hours post (p=0.004 by paired t-test) by ?13%. Dorsiflexion ROM was increased by ?4 deg at 0 minutes and 72 hours post. Conclusion: DDN produces acute short-term effects (shown in the H-reflex latency shift at 0- and 90-minutes post) and significant long-term effects (shown in the reduced H-reflex at 72 hours post) in spinal pathways of the treated MG. To understand whether DDN affects the intact CNS and stroke-impaired CNS similarly or differently, studies of individuals after stroke are currently underway.

140 **Post-hemorrhagic Hydrocephalus and Ventricular Tapping: Weaning Protocols and Factors Affecting Success**

Christopher Litts, Ramin Eskandari, Thomas Larrew, MD, Pearce Jackson, Tyler Vasas, Mohammed Alshareef, MD, Libby Infinger, MD, MPH, Ramin Eskandari, MD, MS, College of Medicine, MUSC

Background: Despite advances in neonatal care, post-hemorrhagic hydrocephalus (PHH) remains the largest subtype of hydrocephalus in North America and accounts for a significant amount of morbidity and mortality in preterm infants. Protocols for temporizing treatment and the need for definitive cerebrospinal fluid (CSF) diversion vary dramatically. In this report, we describe findings using early ventricular access device (VAD) placement with prolonged VAD weaning instead of early shunting and the implications for permanent CSF diversion. Methods: Preterm infants with PHH with VADs between 2017-2021 were included. Weight-based VAD tapping protocol until 38 weeks gestational age (GA) was followed by weaning through decreasing VAD tap frequency. Wean success was ultrasound based using biventricular diameter (BVD) and third ventricle measurements. Definitive CSF diversion followed two unsuccessful wean attempts. Demographics, ventricle size, and outcomes were analyzed. Results: 33 patients were included, 11 (33.3%) were weaned from VAD tapping, not requiring permanent CSF diversion. Successfully weaned patients trended towards older GA at birth (30.7 weeks vs 27.8 weeks) and at VAD placement (p=0.08 and 0.06 respectively). Although not statistically significant, patients not requiring definitive CSF diversion demonstrated smaller BVD at VAD placement and at 38 weeks GA and a greater decrease in BVD from tapping initiation to 38 weeks. Conclusions: Patients historically who were shunted at a certain weight were able to be successfully weaned using prolonged weaning protocol. Non-modifiable factors (GA at birth) and modifiable (ventricular size and amount of decrease in ventricular size) may be predictive of successful weaning. This study demonstrates promising results yet more patients will improve our predictive ability

141 **Step 1 is Pass/Fail, Now What? Can clinical clerkship grades be used as a reliable metric to screen General Surgery residency applicants?**

Laura Campbell, Christian Streck, Kristen Quinn, Laura Campbell, Andrea Abbott, College of Medicine, MUSC

For decades, the 3-digit Step 1 score has been used to competitively evaluate and compare candidates during the residency application process; however, in 2022 all scores will be converted to pass/fail. Another quantitative measure will likely gain importance in its stead, one such being clerkship performance grades. This study aims to determine the consistency and reliability of clerkship grades for general surgery applicants. Candidates' Medical Student Performance Evaluation (MSPE) letters from 146 unique US medical schools were reviewed for number of grading tiers used and honors criteria from the 2019 application cycle. The median number of grading tiers for each core clerkship was four. Over a third of medical schools (35.5%) do not provide an overall medical student performance rank. Schools in the Central US region more often rank their students in five tiers compared to the South ($p<0.005$). Variable percentages of students achieve the highest honor tier across the core clerkships; an average of 35% of students meet the highest honors criteria in Surgery. More students at US News and World Report Top 20 medical schools achieve the highest honors tier, and this was found to be statistically significant across every clerkship and overall class rank ($p<0.05$). Medical schools grading variability may challenge residency programs' ability to stratify desirable applicants. In conclusion, further transparency and standardization may be required to compare students objectively and fairly from medical schools

across the country.

142 **Resilience culture in healthcare teams during COVID-19**

John Ambrose, John Ambrose, Diana M. Layne, Ken Catchpole, Heather Evans, and Lynne S. Nemeth, College of Nursing, MUSC

Introduction: Resilience allows teams to function at their optimal capacity and skill level. The SARS-CoV-2 (COVID-19) pandemic created a perfect opportunity to study resilience culture during a time of limited healthcare team experience, unestablished protocols, and the concern for personal protective equipment (PPE). Rationale: Little is known about healthcare team resilience as a phenomenon. The existing definitions and empirical referents may not capture the nature of healthcare team resilience, as the traditional focus has been placed on individual resilience. This qualitative research examines this phenomenon in teams and builds a bridge between resilience engineering and individual resilience. Methods: A purposive snowball sample initiated in-depth semi-structured interviews guided by 3 preliminary interviews. Immersion Crystallization was used to guide the analysis and its interpretation. An adapted model of the healthcare team was employed to frame the data. It combined the Advanced Team Decision-Making (ADM) model and The Systems Engineering for Patient Safety (SEIPS) framework version 1.0. Results: Twenty-six interprofessionals from across the United States were interviewed in this ongoing research. Three clusters of themes were identified, each with 5 or more sub-themes. Resilience culture: themes include: "living in Covid land versus 'just visiting'", "the wild west", "reverence versus disregard", "quicksand wisdom". Resilience barriers: themes included "communicating vs paying attention", "the cost versus the investment"," lost and unknown" "becoming a monster", and "dead time". Resilience facilitators: themes included "ohana & hānai", "team alchemy", "experience matters" and "true leadership". Conclusions: The adapted model is useful to understand the system and processes in which healthcare teams worked during COVID-19. The data suggests an established team identity may improve the team's cognition and function, team member experience has a greater impact on team function than the number of team members, team mental health practices, and both physical and emotional, connection appear to perpetuate healthcare team resilience.

143 **Effect of Preexisting Hypertension on Pregnancy Outcomes among Women with Systemic Lupus Erythematosus (SLE)**

Azalfa Lateef, Diane Kamen, Dulaney Wilson, Jim Oates, Gary Gilkeson, College of Medicine, MUSC

Introduction: Advances in medicine for women with SLE have led to improved pregnancy outcomes, but pregnancies are still considered high-risk and disparities remain. Hypertension (HTN) rates are higher among women with SLE compared to non-SLE controls. The goal of our study is to examine the effect HTN has on pregnancy outcomes in women with SLE. Methods: Women with SLE and at least one pregnancy enrolled in a single center longitudinal prospective registry were included. Self-reported pregnancy outcomes included live births, spontaneous abortion, pre-term birth, low birth weight, and pre-eclampsia. Pregnancies were classified as either 1) before SLE diagnosis or 2) during/after SLE diagnosis and as either 1) with preexisting HTN or 2) without preexisting HTN (including those with HTN diagnosed after delivery). Differences by groups were evaluated with chi-square test of homogeneity or Fishers exact test. The association of pregnancy outcomes with HTN was evaluated with logistic regression; SLE diagnosis and race were evaluated as potential confounders. Results: The analytic cohort consisted of 919 pregnancies (n=437 women) of which 714 (77.7%) were live births. Pregnancies in women with an existing SLE diagnosis showed lower frequencies of live births ($p<0.001$) and higher frequencies of pre-eclampsia, low-

birth weight, spontaneous abortions and preterm labor (all p<0.001). Prior HTN was significantly associated with pre-eclampsia (p=0.03), low-birth weight (p=0.04), higher frequency of spontaneous abortions (p=0.003) and lower frequency of live births (p=0.04). 719 (78.2%) of the pregnancies were among Black mothers, however race when adjusted for SLE diagnosis was not associated with significant differences in adverse pregnancy outcomes. Conclusion: Preexisting HTN in women with SLE negatively impacted their pregnancy outcomes, though complicated by race and the timing of SLE diagnosis. Knowing the effects of potentially modifiable risk factors like HTN can help inform strategies to improve pregnancy outcomes in this population.

This work was supported by National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) of the National Institutes of Health under Award Numbers K24 AR068406 (DLK), P30 AR072582 (DAW, GSG, JCO, DLK) and supported by the South Carolina Clinical & Translational Research (SCTR) Institute at the Medical University of South Carolina, NIH/NCRR Grant number UL1 TR001450.

144 **Complement peptide C3a interacts with Candida cell wall components to mediate antifungal activity**

Janessa Montefalco, Caroline Westwater, Silvia Vaena, Jessica Dinh, Department of Oral Health Sciences, College of Dental Medicine, MUSC

Abstract withheld from publication

145 **Tranexamic Acid Associated with Less Wound Complications in Hindfoot Surgery**

Andrew Moore, Daniel Scott, Ryan O'Leary, Benjamin Smith, Caroline Hoch, Christopher Gross, Department of Orthopaedics, College of Medicine, MUSC

Background: Tranexamic acid (TXA) is an increasingly popular antifibrinolytic therapy used to decrease bleeding during orthopaedic surgery and postoperative swelling. We sought to review of the effect of TXA on outcomes of total ankle arthroplasty (TAA), hindfoot fusions, and other related hindfoot surgeries. Methods: We conducted a retrospective review of 252 patients undergoing hindfoot fusions and/or TAA between 2015 and 2020 by a single fellowship trained foot and ankle surgeon. There were 221 eligible procedures (216 patients) (TAA=72, subtalar fusion=47, ankle fusion=36, double arthrodesis=33, tibiotalocalcaneal fusion=20, triple arthrodesis=8, total talus=4, and pantalar fusion=1). Wound complications, union status (for fusions), readmissions and reoperations were recorded and compared between TXA (n=101) and non-TXA (n=120) cohorts. Subgroup analysis was performed for TAAs and hindfoot fusions. Mean follow-up was 453 days (range, 90-1,707). Independent sample t-tests, chi-square tests, and Fisher's exact tests were utilized. Results: There were no significant differences in demographics, comorbidities, preoperative diagnoses, or smoking status between cohorts. The TXA group exhibited significantly less postoperative infections requiring oral antibiotics (5.9% vs. 15.0%, p=.031). These included superficial (p=.161) and deep infections requiring reoperation (p=.129). Subgroup analysis of hindfoot fusions (n=145) revealed significantly shorter time to fusion between TXA and non-TXA groups (146 vs. 202 days, p=.049), fewer reoperations (8.6% vs. 21.8%, p=.036), shorter follow-up (349 vs. 473 days, p=.030), fewer active smokers (5.2% vs. 16.1%, p=.045), and more patients with Charcot neuroarthropathy (20.7% vs. 5.7%, p=.006). Subgroup analysis of TAAs showed fewer cases of superficial infections (2.3% vs. 27.6%, p=.002) and delayed wound healing (25.6% vs. 48.3%,

p=.047) in the TXA cohort. Conclusion: We found TXA use in hindfoot surgery associated with a statistically significant overall reduction in wound infections requiring antibiotics, quicker time to union in hindfoot fusions, and fewer infections requiring antibiotics and lower rates of delayed wound healing in TAA.

146 **Preventing central venous catheter (CVC) associated venous thromboemboli (VTE) among pediatric patients**

Ingrid Bonilla, Elizabeth Mack, Stephanie Santana, Riley Dunnam, Corinne Corrigan, Department of Pediatrics, College of Medicine (MD, PhD), MUSC

Background: CVC VTE have a mean attributable cost of $27,686 and length of stay of 8.1 days in children compared to controls. In 2018 we had 25 VTEs, and 24 of these were CVC VTEs thus we sought to implement prevention strategies. We aim to capture and improve compliance with the CVC VTE prevention factors for all CVC insertions and educate inserters on the bundle so as to reduce CVC VTE. Methods: Prevention factors include CVC line size (catheter-vessel diameter ratio of 1 to 2), number of insertion attempts (2 or less), and tip location (superior vena cava or superior vena cava right atrial junction if above the diaphragm, inferior vena cava if below the diaphragm). Factors were accessed through procedure notes. A REDCap survey was deployed to the inserter for factors not identified in the procedure note. To improve situational awareness, we shared provider-specific dashboards which included overall compliance, compliance with each factor, and number of lines inserted associated with CVC VTEs. Radiology and incident report data was used to capture outcomes data. Results: There was a reduction from 2018 to 2020 in both CVC VTE and total VTE (24 to 18 or 25% less CVC VTE, 25 to 21 or 16% less total VTE) despite a 15% increase in CVC. In 2019, we began capturing bundle compliance and in 2020 overall bundle compliance remains low at 10% (63% CVC tip location, 17% line size, 84% for insertion attempts). Lack of response to survey was noted as noncompliant for the missing elements. Conclusion: Our data enhances understanding of the specific factors contributing to VTE and provides awareness to inserters about their individual compliance and outcomes data related to CVCs inserted. In the future, we aim to incorporate bundle elements into a standardized note template and address barriers to compliance.

147 **Host-adaptive Porphyromonas gingivalis targets pro-inflammatory Interleukin-6 trans-signaling in epithelial cells**

Jaden Lee, Ozlem Yilmaz, Nityananda Chowdhury, College of Dental Medicine (DMD, PhD), MUSC

Abstract withheld from publication

148 **CD26 defines responsiveness to neoadjuvant checkpoint blockade**

Hannah Knochelmann, David Neskey, Amalia Rivera-Reyes, Joshua Horton, Michael Bobian, Megan Wyatt, Carsten Krieg, Kent Armeson, Mark Rubinstein, Chrystal Paulos, Department of Microbiology & Immunology, College of Medicine (MD, PhD), MUSC

Abstract withheld from publication

149 **Association between nailfold capillaroscopy abnormalities and autoimmune disease in pediatric populations**

Andraia Li, Lara Wine Lee, Connor Burke, Colby Purvis, Department of Dermatology & Dermatological Surgery, College of Medicine, MUSC

Objective: Time to diagnosis of autoimmune disease in pediatric populations can take years but nailfold capillaroscopy (NFC) may identify early signs of autoimmune disease. The aim of this study is to assess the association between nailfold capillary abnormalities and autoimmune disease in children. Methods: A systematic search of PubMed, EMBASE and Scopus was performed to identify all studies published before March 17, 2021. Observational studies reporting NFC outcomes in children with autoimmune disease and healthy controls (HCs) were eligible for inclusion. Odds ratios (OR) and 95% confidence intervals (CI) were pooled using a random-effects meta-analytical model. Results: Nine of 3665 studies reporting on 620 patients (377 subjects, 243 controls) were included. Pediatric patients with autoimmune disease were 9.88 (95% CI 3.16 to 30.87, I2= 80.1%) times more likely to have abnormal nailfold capillaries than HC. Of the capillaroscopic features, dilated capillaries (OR 27.90, 95% CI 2.17 to 349.05, I2= 59.9%) were most likely abnormalities observed on NFC. This was followed by the likelihood of reduced capillary density (<7 capillaries/mm) (OR 19.91, 95% CI 3.79 to 105.52, I2= 0%), giant capillaries (OR 12.87, 95% CI 2.38 to 69.45, I2= 0%), hemorrhages (OR 13.89, 95% CI 5.34 to 36.16, I2= 0%) and %), and avascularity (OR 10.38, 95% CI 2.20 to 49.04, I2= 0%). Conclusions: Children with autoimmune disease are significantly more likely to have nailfold capillary abnormalities. NFC may be useful in identifying early signs of underlying rheumatic disease and potentially decrease the time to diagnosis for this patient population.

150 **Enhancing the efficacy and safety of a human complement inhibitor for treating post-transplant cardiac ischemia reperfusion injury by targeting to a graft-specific neoepitope**

Mohamad Mahdi Sleiman, Stephen Tomlinson, Chaowen Zheng, Xiaofeng Yang, Songqing He, Carl Atkinson, Department of Microbiology and Immunology, College of Medicine (MD, PhD), MUSC

Background: Post-transplant ischemia reperfusion injury (IRI) is a recognized risk factor for subsequent organ dysfunction, alloresponsiveness, and rejection. The complement system is known to play a role in IRI and represents a therapeutic target. Complement is activated in transplanted grafts when circulating IgM antibodies bind to exposed ischemia-induced neoepitopes upon reperfusion, and we investigated the targeting of a human complement inhibitor, CR1, to a post-transplant ischemia-induced neoepitope. Methods: A fragment of human CR1 was linked to a single chain antibody construct (C2 scFv) recognizing an injury-specific neoepitope to yield C2-CR1. This construct, along with a soluble untargeted counterpart, was characterized in a cardiac allograft transplantation model of IRI in terms of efficacy and safety. Results: CR1 was similarly effective against mouse and human complement. C2-CR1 provided effective protection against cardiac IRI at a lower dose than untargeted CR1. The increased efficacy of C2-CR1 relative to CR1 correlated with decreased C3 deposition, and C2-CR1, but not CR1, targeted to cardiac allografts. At a dose necessary to reduce IRI, C2-CR1 had minimal impact on serum complement activity, in contrast to CR1 which resulted in a high level of systemic inhibition. The circulatory half-life of CR1 was markedly longer than that of C2-CR1, and whereas a minimum therapeutic dose of CR1 severely impaired host susceptibility to infection, C2-CR1 had no impact. Conclusion: We show the translational potential of a human complement inhibitor targeted to a universal ischemia-induced graft-specific epitope, and demonstrate advantages compared to an untargeted counterpart in terms of efficacy and safety.

This work was supported by NIH (U01AI32894 and R56AI56383 to ST and CA), the VA (BX005235 to ST), DoD (RT190030 to ST), an award from Enduring Hearts and the AHA (18PRE34070023 to MS) and 111 Project from Ministry of Education and State Administration of Foreign Experts Affairs of the People's Republic of China (D17011 to ST, CA and SH).

151 **The Role of Complement in Propagating Neuroinflammation in Chronic Traumatic Brain Injury - A Transcriptomic Analysis**

Amer Toutonji, Stephen Tomlinson, Mamatha Mandava, Silvia Guglietta, College of Medicine (MD, PhD), MUSC

Activation of the complement system propagates neuroinflammation and brain damage early and chronically after traumatic brain injury (TBI). The complement system is complex and comprises more than 50 components, many of which remain to be characterized in the normal and injured brain. Moreover, complement therapeutic studies have focused on a limited number of histopathological outcomes, which while informative, do not assess the effect of complement inhibition on neuroprotection and inflammation in a comprehensive manner. Using high throughput gene expression technology (NanoString), we simultaneously analyzed complement gene expression profiles with other neuroinflammatory pathway genes at different time points after TBI. We additionally assessed the effects of complement inhibition on neuropathological processes. Analyses of neuroinflammatory genes were performed at days 3, 7, and 28 post injury in male C57BL/6 mice following a controlled cortical impact injury. We also characterized the expression of 59 complement genes at similar time points, and also at 1- and 2-years post injury. Overall, TBI upregulated the expression of markers of astrogliosis, immune cell activation, and cellular stress, and downregulated the expression of neuronal and synaptic markers from day 3 through 28 post injury. Moreover, TBI upregulated gene expression across most complement activation and effector pathways, with an early emphasis on classical pathway genes and with continued upregulation of C2, C3 and C4 expression 2 years post injury. Treatment using the targeted complement inhibitor, CR2-Crry, significantly ameliorated TBI-induced transcriptomic changes at all time points. Nevertheless, some immune and synaptic genes remained dysregulated with CR2-Crry treatment, suggesting adjuvant anti-inflammatory and neurotropic therapy may confer additional neuroprotection. In addition to characterizing complement gene expression in the normal and aging brain, our results demonstrate broad and chronic dysregulation of the complement system after TBI, and strengthen the view that the complement system is an attractive target for TBI therapy. (VA funded)

This work was supported by Department of Veterans Affairs (1BX004256, 1RX001141 and IK6BX005235)

152 **ADAMTS5 is Required for Subchondral Bone Formation in the Mandibular Condyle**

Alexandra Rogers-DeCotes, Christine Kern, Sarah E. Porto, College of Dental Medicine (DMD, PhD), MUSC

Abstract withheld from publication

153 **Rib Construct for Early-onset Spinal Deformity (EOSD)**
Daniel Bonthius, Hai Yao, Richard Gross, MCBP, College of Graduate Studies (MSTP), MUSC

Early-onset spinal deformity (EOSD) is deformity that begins before 10 years of age. Current intra-spinal based treatments for early onset spinal deformity, such as growing rods with pedicle screw fixation, have high complications rates and limited effectiveness. The rib construct is an alternative extra-spinal technique that uses rib-based fixation for correcting early onset spinal deformity. This represents a paradigm shift from seeking spinal correction to emphasizing correction of malalignment of the thorax with extra-spinal rib fixation. Rib fixation with the rib construct can be achieved with either: 1) off-label laminar hooks, which are already commercially available for spinal fixation to the lamina but can also be used on the ribs, or 2) rib hooks as part of our novel patented R-FIX (Rib-FIXation System). The present study consists of two parts. First, the biomechanics, mechanism, and clinical outcomes of this technique were investigated using rib fixation with off-label laminar hooks. Second, a rib hook instrumentation system was created with rib hooks specifically designed for the unique anatomy of the ribs. This system was validated in cadavers and biomechanical testing was performed in preparation for FDA clearance. The results suggest that the rib construct is a highly safe and effective technique for correcting EOSD. Off-label laminar are acceptable to use for rib fixation. Clinical results indicated that the rib fixation with laminar hooks provides superior spinal deformity sagittal plane correction and similar coronal plane correction with lower complication rates, compared to other techniques previously studied. R-FIX rib hooks designed specifically for rib fixation were produced and validated, with favorable features that may further reduce the risk of complications with this technique.

This work was supported by TL1 TR001451, UL1 TR001450, and 1F31AR076917-01A1

154 **Risk Prediction By Quantitative Analysis Of Pre-Procedural CTA Provides Superior Prediction Of Mortality Compared To Conventional Risk Scores In Transcatheter Aortic Valve Replacement**
Franco Godoy, Uwe Schoepf, Tilman Emrich, Gilberto Aquino, Josua Decker, Moritz Halfmann, Landin Carson, Akos Varga-Szemes, Department of Radiology and Radiological Science, College of Medicine, MUSC

Purpose: To assess the predictive value of pre-procedural, comprehensive cardiac CT-based risk score for mortality in patients undergoing transcatheter aortic valve replacement (TAVR). Methods and Materials: One hundred and sixty-eight patients with severe aortic stenosis who had previously undergone TAVR were retrospectively evaluated in this 24-months follow up study. Mortality was the primary endpoint. Pre-TAVR CTAs with 10-100% phases were analyzed to calculate several cardiac parameters. ROC curve analysis were performed to acquire the optimal cutoff for all parameters, and based on the cut-offs a binary score was created for each parameter. This score was then summed up into a dedicated CT score reaching from 0 to 6 points. Groups were built for patients with 0 (Gr 0), 1-3 (Gr 1) and >3 (Gr 2). Survival analysis was done by Kaplan-Meier Analysis and hazard ratios (HR). CT Score was adjusted for clinical parameters and the Society of Thoracic Surgeons (STS) score for mortality currently used to risk stratify TAVR patients. Results: Median follow-up was 21 months. There were 38 deaths (22%). Mortality significantly differed between the CT risk score groups: Two-year survival was 100% in Gr 0, 81% in Gr 1 and 44% in Gr 2 (Figure). CT risk score (HR 4.6; 95% CI 2.2-9.4; $p<0.001$) was independently associated with mortality after adjustment for variables predictive on univariable analysis and clinical parameters. When adjusted for the STS risk score, CT Score (HR 4.3; 2.2-8.4; $p<0.001$) remained significantly predictive. Adding CT score to the STS score significantly improved its c-index from 0.637 to 0.765

for prediction of mortality. Conclusions: Pre-TAVR, a comprehensive CT score independently predict post-TAVR mortality beyond clinical parameter and improves the current clinical risk-stratifying tool. CTA-based functional assessment has the potential to improve risk stratification and post-treatment surveillance in patients undergoing TAVR.

155 **RIDD is required for the prevention of chronic GVHD by targeting IRE-1α/XBP-1s signaling**

Hee-Jin Choi, Xue-Zhong Yu, Chih-Hang Anthony Tang, Linlu Tian, Yongxia Wu, M. Hanief Sofi, Taylor Ticer, Steven D. Schutt, Chih-Chi Andrew Hu, Department of Microbiology and Immunology, College of Medicine (MD, PhD), MUSC

The benefit of allogeneic hematopoietic stem cell transplantation (allo-HCT) is limited by a major complication, chronic graft-versus-host disease (cGVHD). The ER stress response is of great importance to secretory cells including B cells. By using conditional knock-out (KO) mice model, we demonstrated that the IRE-1α/XBP-1s pathway, one of the major ER stress response mediators, plays a critical role in B cell pathogenicity on the induction of cGVHD. Endoribonuclease activity of IRE-1α not only activates XBP-1s transcription factor but also cleaves other ER-associated mRNAs through regulated IRE-1α-dependent decay (RIDD). Besides, it is known that ablation of XBP-1s production leads to unleashed activation of RIDD. Therefore, we hypothesized that RIDD plays an important role in B cells during cGVHD development. In this study, we found that B cells deficient for XBP-1s reduced ability to induce cGVHD, which however was reversed by inactivation of IRE-1α, highlighting the role of RIDD in controlling cGVHD. Activation of RIDD targets IgM mRNA, a contributor to organ damage and fibrosis in cGVHD, which correlated with dysregulated expression of MHC II and costimulatory molecules in B cells. We also demonstrated that alloreactivity of T cells, especially CD4 T cells, can be recovered by suppressing RIDD in XBP-1s-deficient B cells. Since IRE-1α carrying a S729A mutation shows ablated RIDD activity without effect on XBP-1s, we investigated the contribution of B cells from S729A knock-in mice to confirm the role of RIDD in B cells. We found that B cells from S729A mice increased GVHD severity. S729A B cells showed significant increases in IgM secretion, GC cell differentiation, and the expression levels of MHCII and co-stimulatory factors. In conclusion, these results provide a novel insight on how ER stress response regulates B cell activity after allo-HCT and suggest RIDD is an important mediator for reducing cGVHD pathogenesis.

This work was supported by R01 HL 140953

156 **Antibiotic Disruption of the Gut-Liver-Bile Acid Axis Impairs Late Skeletal Maturation through Suppressed Osteoblastogenesis**

Matthew Carson, Chad Novince, Amy Warner, Jessica Hathaway-Schrader, Brooks Swanson, Joy Kirkpatrick, Dmitry Kondrikov, William Hill, John Lemasters, Alexander Alekseyenko, Yongren Wu, Hai Yao, Jose Aguirre, Caroline Westwater, Department of Oral Health Sciences, College of Graduate Studies, MUSC

Abstract withheld from publication

157 **Sex differences in CD8+ T-cells in Response to Male DAMPs.**

Alexa Corker, Kristine Deleon-Pennell, Philip Broughton, Kimberly Oviedo, Department of Cardiology, College of Graduate Studies, MUSC

Men have a higher risk of having a myocardial infarction (MI) compared to age-matched pre-menopausal women however, after menopause risk of MI increases similarly in women compared to men. Damage associated molecular patterns (DAMPs) are released after an MI to initiate inflammatory activation and recruitment. We hypothesized that estrogen may be dampening the immune cell response to cardiac DAMPs. Splenic CD8+ T-cells were isolated from healthy males and females (n=3/sex) using magnetic bead separation. DAMPs were collected by exposing male hearts to 3 cycles of liquid nitrogen for 5 minutes followed by 28°C for 30 minutes. Isolated CD8+ T-cells were cultured in RPMI media (0.1% antibiotics) supplemented with 1) 10% fetal bovine serum (FBS), 2) 0.1% FBS, 3) DAMPs, 4) estrogen, 5) DAMPS+ estrogen (D+E), or 6) DAMPS+ estrogen+ estrogen blocker (EB) for 24 hours. After stimulation, cells were stained with live/dead marker (1:1000), CD44 (1:50), and cell trace (1:400) and measured by flow cytometry. While no differences were observed after DAMPs, male CD8+ T-cells treated with estrogen had a significant increase in viability compared to the 0.1% FBS group. Female CD8+ T-cells but not males had increased CD44 demonstrating an increase in activation after exposure to DAMPS, estrogen, and D+E compared to the 0.1% FBS group. Only female CD8+ T-cells demonstrated a significant increase in proliferation when exposed to DAMPs compared to the 0.1% FBS group. This increase in proliferation also resulted in a decrease within the non-proliferative cells in female CD8+ T-cells when exposed to DAMPs, estrogen, D+E, and EB. Female CD8+ T-cells had a more robust response compared to males after DAMP stimulation. This may lead to prolonged inflammation and adverse wound healing post MI. Our data suggests estrogen inhibits DAMP-induced cellular proliferation thus protecting from inflammation.

This work was supported by NIH T32GM132055 and HL145817, the AHA Innovator Project 20IPA35260039, and the Biomedical Laboratory Research and Development Service of the Veterans Affairs Office of Research and Development Award IK2BX003922. This work was also financially supported, in part, by the 2019 S&R Foundation Ryuji Ueno Award that was bestowed upon KYD-P by the APS.

158 **Essential role for the neurodevelopmental disorder-linked gene, MEF2C, in inhibitory neuron function and neurotypical behaviors**

Yongjoo Cho, Christopher Cowan, Ahlem Assali, Evgeny Tsvetkov, Department of Neuroscience, College of Graduate Studies (MSTP), MUSC

The MEF2 (Myocyte Enhancer Factor 2) family of transcription factors regulate gene expression controlling cell differentiation and synapse development. Loss-of-function mutations or deletions of the MEF2C gene cause a neurodevelopmental disorder, termed MEF2C Haploinsufficiency Syndrome (MCHS), that includes symptoms of autism spectrum disorder (ASD), intellectual disability, seizures, and motor and sensory abnormalities. MEF2C is highly expressed in excitatory forebrain neurons and GABAergic inhibitory neurons, but its role in GABAergic neurons, and the relevance to MCHS-like phenotypes in mice, is unknown. To study the role of MEF2C in GABAergic populations during mouse development, we bred Vgat (vesicular GABA transporter)-Cre mice, which express cre recombinase broadly in early developing GABAergic neurons, with a floxed Mef2c loss-of-function mouse to create offspring that are GABAergic cell-specific Mef2c heterozygous mutants (Mef2c cHetVgat-cre). We then subjected these mutants and littermate

controls to a battery of tests measuring MCHS-relevant phenotypes, including spatial working memory, anxiety-like behavior, social preference, sensory sensitivity, and Pavlovian learning and memory. Mef2c cHetVgat-cre mice showed significant deficits in spatial working memory and social preference, both of which are prefrontal cortex (PFC)-dependent. Interestingly, we noted that conditional Mef2c knockout mice (Mef2c cKOVgat-cre) showed embryonic and early postnatal lethality, probable seizures, and severe motor coordination problems, highlighting the importance of MEF2C function in GABAergic populations. We hypothesize that MEF2C plays a cell-autonomous role in GABAergic interneurons to control the balance of excitatory and inhibitory synaptic transmission in the developing and mature brain, which in the Mef2c cHet mice might be critical for PFC-dependent learning and memory and sociability. Future directions include further characterization of deficits through a learning and memory-specific behavioral battery and single nuclei sequencing and bioinformatics approaches to evaluate both the relative abundance of GABAergic neuron cell types in the prefrontal cortex and to functionally characterize differential gene expression using gene ontology.

This work was supported by TL1 (JYC), NIH/NIMH R01MH111464 (CWC)

159 **Vascular Cognitive Impairment: Novel Endothelial Mechanisms and the Impact of Mediterranean Diet**

Jensen Tomberlin, Adviye Ergul, Onder Albayram, John Kurtz, Department of Neuroscience, College of Graduate Studies, MUSC

Vascular contributions to cognitive impairment and dementia (VCID), a range of disorders with complex etiology, is the second leading cause of dementia behind Alzheimer's Disease (AD). One subset of VCID, vascular dementia, is characterized by hypoperfusion and white matter degeneration due to arteriosclerotic small vessel disease (SVD). Despite the prevalence of this disease, our understanding of the endothelial mechanisms involved in hypoxic injury from SVD is limited, lowering our ability to develop targeted therapeutics and optimize preventative lifestyle modifications like the Mediterranean Diet (MD). Preliminary data in our lab indicates that hypoxic injury leads to endothelial-specific alterations in tau hyperphosphorylation, mitochondrial dysfunction, and mature brain-derived neurotrophic factor (mBDNF) levels. Therefore, our hypothesis is that hypoxia-mediated endothelial P-tau pathology and mitochondrial dysfunction promotes vasotrophic uncoupling of the brain vasculature, leading to VCID. In conjunction, We believe that MD intervention prevents uncoupling and subsequently prevents/delays neurovascular dysfunction and cognitive decline in male and female mice. To test this, male and female mice will be administered a control or novel MD intervention 1 month prior to hypoxic injury using the bilateral carotid artery stenosis (BCAS) model. Mice will continue their diet regimen and be assessed for cerebral blood flow (CBF), cognitive dysfunction, and motor dysfunction at 1- & 3-month timepoints. Following euthanasia, tissue samples from deep cortical regions will be examined for endothelial-specific aberrant tau formation, mitochondrial dysfunction, and reduced mBDNF. Funding provided through the following: TL1Training Fellowship []; MUSC SCORE [U54DA016511]; VA IK6 [BX004471], [BX000347]; & NIH [RF1NS083559], [RO1NS104573].

This work was supported by TL1, MUSC SCORE [U54DA016511], VA IK6 [BX004471,BX000347], NIH RF1 [NS083559], NIH RO1 [NS104573]

160 **The Role of Extracellular Vesicles in the Propagation of Scleroderma-Associated Lung Fibrosis.**
Joe Mouawad, Carol Feghali-Bostwick, College of Medicine (MD, PhD), MUSC

Fibrosis is characterized by the excessive accumulation of connective tissue components which form the extracellular matrix (ECM). Pulmonary involvement in fibrotic diseases, like Systemic Sclerosis (SSc), results in high morbidity and mortality. In its severe form, SSc-related lung fibrosis is progressive, resulting in loss of function. As such, lung fibrosis remains the leading cause of death in SSc. While most research on SSc has been focused on treating the pathology of lung fibrosis, the question on what drives the progression of fibrosis throughout the lungs, and other visceral organs, remains unanswered. Lung fibroblasts have long been implicated in the progression of pulmonary fibrosis through their activation to myofibroblasts and secretion of excessive ECM. However, characterization of extracellular vesicles (EVs), which are intercellular communication tools, during myofibroblast activation in lung fibrosis remains unexplored. Using two models of lung fibrosis: a) in-vitro assays, with primary human lung fibroblasts (pLFs), and b) ex-vivo assays using human lung tissues in organ culture, we showed that fibrotic pLFs and lung tissues release EVs that induce myofibroblast activation and promote the development of fibrosis in normal pLFs. Our findings provide new insights on how EV communication is a platform implicated in the incessantly progressive nature of SSc-related lung fibrosis. In summary, our results will lead to the identification of potential new EV-mediated targets for the development of anti-fibrotic therapies.

This work was supported by Scleroderma Foundation predoctoral award.

161 **STAT3 in cancer-associated fibroblasts promotes an immunosuppressive tumor microenvironment**
Julia Lefler, Michael Ostrowski, Katie MarElia-Bennett, Department of Biochemistry and Molecular Biology, College of Graduate Studies, MUSC

One of the defining characteristics of pancreatic ductal adenocarcinoma (PDAC) is the formation of a dense stroma comprised of cancer associated fibroblasts (CAFs) and immune cell populations. This stroma is immunosuppressive and can act as a physical barrier against common therapeutic treatments. Attempts to therapeutically target the PDAC stroma have yielded contradictory results, suggesting both tumor promoting and tumor limiting roles for CAFs. These studies emphasize the need to understand important transsignaling pathways between CAFs, tumor cells, and the immune microenvironment. IL-6 is a pleiotropic cytokine involved in several physiological functions and its increased expression is strongly associated with poor survival rates in PDAC patients. STAT3 is a major downstream target of IL-6, and its aberrant activation has been implicated in PDAC tumor progression and immune evasion. IL-6 expression and the IL-6/STAT3 signaling axis in PDAC has been characterized in epithelial tumor cells, however its stromal-specific function on PDAC has yet to be elucidated. We hypothesized that the STAT3 signaling axis in pancreatic CAFs contributes to the immunosuppressive and fibrotic phenotype seen with disease progression. Employing CreLoxP technology, the fibroblast specific protein-1 (Fsp-Cre) transgene was used to conditionally delete STAT3 in fibroblasts in the PdxFlp; KrasG12D; p53 frt/frt (KPF) PDAC mouse model developed by our lab. Deletion of STAT3 in fibroblasts significantly increased the survival in a cohort of KPF mice compared to those with intact STAT3. In preliminary investigations, we found an increase in CD8+ T cell infiltration but a decrease in regulatory T cells in the STAT3-deleted cohort. We also observed a decrease in immunosuppressive M2 macrophage populations and an increase in M1 macrophages in the STAT3-deleted cohort. These preliminary results demonstrate a previously unexplored role of IL-6/STAT3 signaling in fibroblasts during PDAC progression.

This work was supported by Hollings Cancer Center Fellowship

162 **Using hepatocytes derived from PNPLA3 I148M iPSCs to model Nonalcoholic Fatty Liver Disease (NAFLD)**

Caren Doueiry, Stephen Duncan, Department of Regenerative Medicine, College of Graduate Studies (MSTP), MUSC

Background: The incidence of Nonalcoholic Fatty Liver Disease (NAFLD) is dramatically increasing in adults and children, while an effective pharmacologic treatment remains unavailable. NAFLD can progress from lipid accumulation in the liver to more severe inflammation, cirrhosis, and cancer. It is the most common cause of chronic liver disease and is projected to be the leading cause of hepatocellular carcinoma (HCC) and end-stage liver disease in the next decade. Decompensated cirrhosis, a consequence of NAFLD, is the fourteenth most common cause of death in adults. HCC, another consequence, is the third most common cause of cancer mortality. Many etiologies contribute to NAFLD. A polymorphism in the Patatin-like Phospholipase Domain Containing Protein (PNPLA3 I148M) has the most significant association with the disease and all stages of its progression. A roadblock to identifying potential treatments for PNPLA3-induced NAFLD is the scarcity of a cellular platform that recapitulates PNPLA3 I148M-mediated onset of steatosis in human hepatocytes. We used hepatocytes generated from our PNPLA3 (I148M) iPSCs to model the effect of the polymorphism on lipid content and lipid droplet accumulation, providing a platform to identify small molecules with potential therapeutic value using an established high-throughput screening platform. Methods: The C to G substitution found in the PNPLA3 gene was introduced into iPSCs by using CRISPR-Cas9. The homozygous integration of the mutation in our iPSCs was verified using polymerase chain reactions as well as DNA sequencing. Using established protocols, we differentiated the resulting cells into hepatocytes and measured the efficiency of differentiation. Results: Our PNPLA3 I148 iPSC-induced hepatocytes showed hepatic marker expression as well as an increase in lipid content compared to wildtype iPSC-induced hepatocytes. Conclusion: We conclude that human iPSC-derived hepatocytes can be used to effectively model the onset of NAFLD in the presence of the PNPLA3 I148M variant.

163 **Proteomic analysis for potential therapeutics in treating osteoarthritis**

Jen Xu, Patrick Woster, Leticia Reyes, Department of Drug Discovery, College of Medicine (MD, PhD), MUSC

Osteoarthritis is a debilitating disease without a cure that affects 32.5 million US adults, with the majority of people affected being over 60 years old. Usually by the time osteoarthritis starts manifesting symptoms, the disease has become severe. The medications that are currently administered to patients are for symptom control and have systemic side effects. Several drugs that target matrix and subchondral bone showed potential but have failed clinical trials mainly because of musculoskeletal toxicity. In order to understand more about the proteins involved in this disease, we used a human chondrocyte cell model for osteoarthritis where we stimulated primary human chondrocytes with interlekin-1beta (IL-1beta). We then performed mass spectrometry analysis of the supernatant of the IL-1beta stimulated chondrocytes compared to a control. The results showed that several proteins are secreted by the IL-1 beta stimulated chondrocytes, including certain complement factors. The change in the completement factors was further confirmed with western blots. The mechanism of the complement system and cascade in osteoarthritis has not been widely explored. Further study could lead to a targeted therapy for osteoarthritis.

This work was supported by T32 GM 008716-23

164 **Optimized Transcranial Direct Current Stimulation (tDCS) For Higher and More Focal Cortical Electric Fields**

Kevin Caulfield, Mark George, Department of Neuroscience, College of Graduate Studies, MUSC

Background: Transcranial direct current stimulation (tDCS) is a noninvasive method of stimulating the brain to treat over 20 neurological and psychiatric diagnoses. Typically, tDCS passes electrical current through 35cm2 rectangular electrodes placed on the scalp and directly above the cortical target. However, emerging data suggest that placing the electrodes surrounding the target could produce higher intensities at the cortical level. Here we used electric field (E-field) modeling to test the effects of different electrode placements, sizes, and locations on E-field intensity and focality at the cortical target. Methods: We randomly selected 200 human connectome project (HCP) participants (100 women) with anatomical MRI scans from the HCP open source database. Using each MRI scan, we computed 15 E-field models per person (3000 total) with 2mA stimulation targeting the left motor cortex in common montages (bilateral motor and motor-supraorbital) and also using a new strategy (anterior posterior pad surround (APPS)-tDCS) to surround the motor cortical target. Results: APPS-tDCS produced higher and more focal E-fields than bilateral motor and motor-supraorbital placements ($p < 0.0001$). Using smaller than typical electrodes (1cm2) and placed 5cm apart surrounding the motor target, APPS-tDCS could produce E-fields with 102% higher magnitude and 83% more focality than bilateral motor and motor-supraorbital electrode placements with the same 2mA stimulation intensity (all $p < 0.0001$). Conclusions: APPS-tDCS is an efficient tDCS method that enables higher and more focal E-fields in every prospective application of tDCS. Whereas some researchers have tested the effects of 4mA stimulation, APPS-tDCS can deliver the same cortical E-field with just 2mA, and with fewer off-target effects. Future directions include testing the prospective efficacy of APPS-tDCS for multiple neurological and psychiatric diagnoses, including post-stroke rehabilitation and depression. By delivering higher E-fields, it may be possible to increase response rates to tDCS transdiagnostically.

This work was supported by COBRE for Stroke Recovery, NC NM4R

165 **Priming Upper Extremity Motor Practice with Aerobic Exercise (PUMP-Ex) - A Preliminary Report on Feasibility and Efficacy**

Emerson Hart, Ryan Ross, Michelle Woodbury, Chris Gregory, Department of Health Sciences and Research, College of Health Professions, MUSC

Introduction Stroke often leaves survivors with lasting motor impairments. An overwhelming majority of stroke survivors exhibit upper extremity (UE) hemiparesis and only a small portion fully recover UE function. Although a multitude of factors contribute to post-stroke recovery, receiving individualized and progressive rehabilitation and neuroplasticity (i.e. the ability of the brain to adapt) are cornerstones of recovery. Duck Duck Punch (DDP) is an interactive video game designed to enhance UE movement quality via individualized, progressive movement practice. Aerobic exercise (AEx) training has been shown to enhance global cognition, executive function, and processing speed indicating its ability to enhance brain function. Emerging evidence indicates that AEx acutely enhances neuroplasticity; thus using AEx as a "primer" for UE rehabilitation (i.e. DDP) may provide an optimal environment in the brain for motor recovery. Methods Five chronic stroke survivors completed a 6-week intervention (3 sessions weekly). Each session consisted of 15 minutes of AEx on a recumbent bike performed at an intensity of 70% heart rate reserve followed

by 200 repetitions of upper extremity movements during DDP. During exercise, rating of perceived exertion and heart rate data were collected. During DDP, data describing total minutes played, targets hit, heart rate, rating of perceived exertion, and pain were collected. Assessments of UE motor impairment and function and aerobic capacity testing were completed before and after the intervention. Results A 6-week intervention combining AEx and DDP appears feasible. Patients completed all sessions, and preliminary efficacy data suggests an improvement in UE function and aerobic capacity. Conclusions This preliminary report suggests that combining AEx and DDP is feasible and may elicit improvements in UE function and aerobic capacity in chronic stroke survivors. This novel approach to stroke rehabilitation may promote a perpetual cycle of enhanced functional recovery, reduced disability, and improved overall health.

This work was supported by VA CDA-2 1IK2RX003540-01A1, IDeA NIGMS NIH P20-GM109040, T32 DC0014435

166 **Investigating the redox regulation of histone deacetylase 5 in drug-seeking behavior**

Daniel Wood, Christopher Cowan, Ethan Anderson, Makoto Taniguchi, Department of Neuroscience, College of Graduate Studies (MSTP), MUSC

Substance Use Disorder is a chronic, relapsing behavioral disorder characterized by compulsive drug seeking and use despite adverse consequences to the individual. During the course of drug use, there are persistent neuroadaptations that occur in the nucleus accumbens (NAc), a brain region associated with reward and motivation. These neuroadaptations entrench maladaptive drug seeking behavior in response to drug-associated stimuli. In abstinent drug users, relapse can be triggered by drug-associated environmental cues long after drug-cessation. Although the molecular mechanisms underlying relapse triggers are not fully understood, research has pointed to the epigenetic regulation of gene expression as an important process involved in the lasting association between reinforced behavior and drug-associated stimuli. Our lab has previously shown that the epigenetic enzyme, histone deacetylase 5 (HDAC5), functions in the NAc as a critical negative regulator of addiction-related behavior in rodents. HDAC5 is a signal-responsive enzyme that shuttles between the cytoplasm and the nucleus, where it functions to repress associated gene transcription. Prior research including our own indicates that HDAC5 may be regulated by drugs of abuse through the oxidation of two conserved cysteines within HDAC5's c-terminal region, which form a disulfide bond following exposure to oxidative conditions. Mutation of these cysteines appears to disrupt HDAC5's anti-relapse function through a non-canonical mechanism, as this mutant retains specific repressor function and exhibits unaltered subcellular localization. Our data point toward a critical role of these conserved cysteines in HDAC5 anti-relapse action and suggest that they may be regulated by drug-induced redox signaling. Future studies will investigate the role of these cysteines in intrinsic HDAC5 enzymatic function and in binding of essential co-repressors, as well as the in vivo regulation of these cysteines by cocaine exposure.

167 **Synthesis and evaluation of novel, small molecule inhibitors of spermine oxidase as neuroprotective agents**

Amelia Furbish, Patrick Woster, Seth Ruimveld, Department of Drug Discovery and Biomedical Sciences, College of Pharmacy, MUSC

Production of reactive chemical species and the associated secondary injuries have been implicated across multiple forms of clinically challenging neurotoxic disease states and are considered one of the key processes linked with neurodegeneration and neuronal cell death. A variety of studies have

demonstrated that dysregulation of polyamine metabolism represents a key pathway associated with this form of neuronal injury. During periods of oxidative stress, the polyamine catabolizing enzyme spermine oxidase (SMOX) is highly upregulated, increasing the conversion of spermine to spermidine. Depletion of spermine, a known free-radical scavenger, results in increased intracellular concentrations of reactive oxygen species (ROS). In addition, catabolism of spermine by SMOX results in the production of toxic byproducts, including H2O2 and 3-aminopropanal (3-AP). 3-AP undergoes spontaneous conversion to ammonia and acrolein, a toxic aldehyde with the ability to conjugate with DNA and inactivate vital cellular proteins. It follows that reduction of SMOX activity using a specific small molecule inhibitor would reduce ROS and acrolein content in neuronal tissue and prevent the resulting neurotoxicity. Currently available SMOX inhibitors lack potency and exhibit poor selectivity for SMOX, limiting their utility as probe compounds for studying this pathway. We conducted virtual and physical high-throughput screening assays of our in-house proprietary compound library to identify a series of hit compounds with inhibitory activity against SMOX. A synthetic route for derivatization of selected hit compounds was developed for the generation of a small compound library, and additional derivatives were identified through similarity searching. Development and characterization of potent and selective SMOX inhibitors will serve to further elucidate the impact of polyamine catabolism on mechanisms of neuronal injury. In addition, inhibition of SMOX may represent a novel therapeutic target for the prevention of neuronal injury. In this presentation, the synthesis and preliminary biological evaluation of novel SMOX inhibitors will be discussed.

This work was supported by TL1 TR001451 & UL1 TR001450, NIH 1R01CA204345 (PMW)

168 **Mechanisms Controlling Regression of Cardiac Fibrosis by Removal of Pressure Overload**

Lily Neff, Amy Bradshaw, An O. Van Laer, Catalin F. Baicu, Michael R. Zile, Department of Medicine, College of Graduate Studies, MUSC

Background: Aortic stenosis can progress into left ventricular pressure overload (LVPO) that can contribute to the development of heart failure. One treatment for aortic stenosis is surgical aortic valve replacement which normalizes hemodynamic load in patients, but myocardial interstitial fibrosis does not fully regress. Treatments that target cardiac interstitial fibrosis remain an unmet need. Objective: Determine cellular mechanisms that contribute to remodeling of extracellular matrix (ECM) before and after LVPO. Methods: Transverse aortic constriction (TAC) induced LVPO, and after 4wks TAC, suture removal (unTAC) relieved LVPO, normalizing hemodynamic load. Protein production was measured by histology, immunoblot, and addressable laser bead immunoassay. Five time points were studied: control, 2wk TAC, 4wk TAC, 4wk TAC + 2wk unTAC, and 4wk TAC + 4wk unTAC. Results: Collagen volume fraction (CVF) increased by 64% at 2wk TAC and 204% at 4wk TAC, versus baseline. Collagen crosslinking enzymes, Lysyl oxidase (LOX) and LOXL2, were increased in TAC. CVF did not decrease at 2wk unTAC, but degradation of fibrillar collagen, measured by collagen hybridizing peptide (CHP) reactivity, was significantly increased. Cathepsin K, matrix metalloproteinase 3 (MMP3), and pro-MMP2 were significantly increased at 2wk unTAC. CVF decreased by 38% in 4wk unTAC versus 4wk TAC, but CHP reactivity was significantly decreased versus 2wk unTAC. Moreover, the macrophage marker IBA1 was significantly increased at both 2wk TAC and 2wk unTAC. Pro-inflammatory cytokines, IFN-gamma and IL1-beta were elevated in unTAC, but not in TAC, suggesting phenotypic differences in macrophage population in unTAC versus TAC myocardium. Conclusions: In response to TAC, collagen deposition and ECM proteins implicated in fibrotic progression were increased. After unloading of the myocardium, fibrosis and ECM deposition proteins decreased, while collagen

degradation activity increased demonstrating active remodeling. CHP reactivity, cytokine levels, and colocalization support the role of pro-degradation macrophages in active remodeling of the unTAC myocardium.

This work was supported by V.A. Merit Award I01 CX001608, T32GM132055

169 **Modulating anti-tumor reactive T cells with hydrogen sulfide**

Nathaniel Oberholtzer, Shikhar MEhrotra, , Department of Surgery, College of Graduate Studies (MSTP), MUSC

Abstract withheld from publication

170 **Kinematic Motion Analysis of Healthy and Osteoarthritic Human Thumb Basal Joints**

Mary Walker, Yongren Wu, Shuchun Sun, Daniel Gordon, Nicholas Bain, Alex Chiaramonti, Elizabeth Nadeau, Dane Daley, Thierry Bacro, Hai Yao, Department of Bioengineering, College of Graduate Studies, MUSC

The trapeziometacarpal (TMC) joint (thumb basal joint) is the most common site of disabling osteoarthritis (OA) in the upper limb. The TMC joint is a complex saddle shaped joint with limited bony constraint that provides the thumb with a unique range of mobility. Previous pathophysiologic studies demonstrated palmar articular cartilage degeneration, volar beak ligament deterioration, and shift of joint contact (palmar to dorsal) during OA progression. To our knowledge, the pathological kinematic patterns in osteoarthritic TMC joints under functional motions remain unclear. Our hypothesis is that the metacarpal rotation and translation on trapezium vary between healthy and osteoarthritic TMC joints under functional motions. By integrating an optical motion tracking approach and computed tomography (CT) anatomic imaging, this study aims to quantify the relative rotational angles and translational displacements of the metacarpal on the trapezium in healthy and osteoarthritic TMCs under different thumb motions. Our results showed that a significant decrease in displacement along a helical axis was observed in mid/late stage osteoarthritic specimens (n=2) when compared to healthy/early-stage osteoarthritic specimens (n=3) in flexion, extension, abduction, adduction, and functional key pinch ($p < 0.05$). Similarly, a significant decrease in rotational angle along a helical axis was observed in mid/late-stage osteoarthritic specimens in flexion, extension, and adduction when compared to healthy/early-stage joints ($p < 0.05$). In healthy/early-stage osteoarthritic specimens, the superior range of motion could be explained by delicate joint congruency or the beginning of beak ligament deterioration, while in mid/late-stage osteoarthritic specimens with a fully deteriorated beak ligament, a limited range of motion is seen - possibly due to development of palmar osteophytes and change of articulating surface curvature that help to stabilize the joint. This study provided new information to help understand TMC pathomechanics and represented our primary step toward the long-term goals regarding TMC OA early diagnosis and treatment.

This work was supported by SC TRIMH

171 **Advancing peptide siRNA-carrier designs through stereochemistry and D-amino acid modifications to enhance gene silencing**

Charles Holjencin, Andrew Jakymiw, Colton Feinberg, Travis Hedrick, Gregory Halsey, Robert Williams, Priya Patel, Evan Biles, James Cummings, Chance Wagner, Naren Vyavahare, Department of Oral Health Sciences, College of Dental Medicine (DMD, PhD), MUSC

The 599 peptide has been previously shown to effectively deliver siRNAs to cancer cells, inducing targeted-oncogene silencing, with a consequent inhibition of tumor growth. Although effective, this study was undertaken to advance the 599 peptide siRNA-carrier design through stereochemistry and D- amino acid modifications. Consequently, 599 was modified to generate eight different peptide variants, incorporating either different stereochemical patterns of L/D-amino acids or a specific D-amino acid substitution. Upon analysis of the variants, it was observed that these modifications, could in some instances, increase/decrease the binding, nuclease/serum stability, and complex release of siRNAs, as well as influence the gene silencing efficiencies of the complex. Modifications to 599 also affected cellular uptake and intracellular localization patterns of siRNA cargo, with one particular variant, comprising a specific D-amino acid substitution, capable of mediating a more ordered binding of siRNAs to specific cellular projections, identified as filopodia. Interestingly, this particular variant also exhibited the most enhanced delivery of siRNAs into cells and gene silencing, thus, implying that this specific change to the 599 peptide design could be responsible for directing a more efficient mode of siRNA drug delivery, resulting in the enhancement of gene silencing. Moreover, measurements of the physicochemical properties of the 599 peptide variants in complex with siRNAs, including particle size, zeta potential, and polydispersity index, did not reveal any distinguishable characteristics between the complexes that could account for the observed differences in siRNA cellular uptake patterns or that would imply that these differences were a consequence of variances in particle aggregation properties. Thus, taken together, these data demonstrate the utility of peptide stereochemistry, as well as the importance of a key D-amino acid modification, in advancing the 599 carrier design for the enhancement of gene silencing in cancer cells.

This work was supported by NIDCR T32DE017551, NIDCR R21DE027231, MUSC Summer Health Professions Research Program - College of Dental Medicine, MUSC Summer Undergraduate Research program - College of Graduate Studies, US Government Federal Work-Study Program

172 **A Novel Regional Target for studying a mouse model of PTSD: The Dorsal Peduncular Cortex**

Krysten O'Hara, Patrick Mulholland, Dr. Jen Rinker, Heyam Saleh, Christina Lebonville, Dr. Howard Becker, Department of Neuroscience, College of Graduate Studies, MUSC

Over 8 million adults in the US suffer from Post-Traumatic Stress Disorder (PTSD). Loss of executive control, emotional dysregulation, social withdrawal, and altered decision making are all symptoms of PTSD associated with changes in the medial prefrontal cortex (mPFC). Functional and structural imaging in individuals with PTSD, and post-mortem analyses have shown alterations in protein expression, regional volume loss, and differential connectivity between the mPFC and regions regulating fear, anxiety, and stress. Preclinically, the mouse single prolonged stress (mSPS), a complex single-day series of stressors (physical restraint, group forced swim, predator odor exposure and isoflurane until unconscious), reliably induces behavioral, physiological, and molecular phenotypes similar to individuals with PTSD. The dorsal peduncular cortex (DP), an understudied region of the rodent mPFC, regulates aspects of behavioral, neural, and physiological sympathetic nervous system activation, like heart rate and blood pressure, as well as social

avoidance. However, the role of the DP in regulating PTSD-like phenotypes in mice is unknown. In the present experiments, RNA-seq analysis of the DP following mSPS incubation (7 days post-SPS) revealed significant down-regulation of 619 genes and significant up-regulation of 506. Further pathway analysis demonstrated mSPS alterations in neuronal structure, G-Protein coupled receptor pathways, and synaptic signaling. Additionally, exposure to mSPS altered choice behavior on the cost-benefit-conflict (CBC) task, a complex choice behavioral paradigm pitting the risk/cost of aversive bright light against a highly rewarding solution. Specifically, mice exposed to mSPS shift their preference on the CBC task to the low-risk/low-reward choice. Together, our data indicate that the DP is a promising target for studying molecular, genetic, and behavioral changes that occur after mSPS. Future work will examine cell-type and circuit specific changes as potential targets to reverse behavioral and physiologic changes resulting from mSPS.

Acknowledgements: Ralph H. Johnson VA Medical Center & Charleston Alcohol Research Center

173 **Neuronal Signature of Cocaine Seeking Behavior in the Nucleus Accumbens Core**

Reda Chalhoub, Peter Kalivas, Camille Carthy, Drew Kalasky, Stephen Walterhouse, Constanza Garcia-Keller, Department of Neuroscience, College of Graduate Studies (MSTP), MUSC

Abstract withheld from publication

174 **The osteogenic and antimicrobial effects of strontium and chloride-containing bioactive glasses**

Dustin Mueller, Hai Yao, Daniel Bonthius, Xiaojing Chen, Department of Oral Health Sciences and Clemson-MUSC Bioengineering Program, College of Dental Medicine (DMD, PhD), MUSC

INTRODUCTION: Bioactive glasses have been shown to have potent osteogenic inductive properties. These properties along with their antimicrobial potential has led to increasing interest in research. Enhancing these properties with the inclusion of different ions has been the next logical step in the development of these bioactive glasses. This project aims to elucidate the bioactivity, cytotoxicity, and antimicrobial properties of novel strontium chloride and chloride-based bioactive glasses. METHODS: New bioactive glass formulations were designed and synthesized for this study. The cytotoxicity of the glasses was evaluated using an alamarBlue assay. The differentiation ability of the glasses was evaluated using an ALP assay and qPCR. Various osteogenic differentiation markers were used in the qPCR against the HPRT housekeeping gene. Data was analyzed using the deltadeltaCT method. RESULTS: The addition of chloride and strontium to the glass showed no significant increase in cytotoxicity in MC3T3-E1 cells. These formulations also showed an increase in differentiation as determined through increases in RunX2, OCN, and other markers when compared to a negative control and bioactive glass without chloride or strontium content. Strontium chloride showed higher rates of differentiation markers when compared to chloride alone. The strontium chloride and chloride glasses showed strong antimicrobial ability using a broth dilution MIC determination. DISCUSSION: The data suggests that these chloride-based glasses provide better antimicrobial and differentiation properties, without increasing the cytotoxicity. These improvements have led to a potentially new bone grafting therapy.

This work was supported by T32DE017551-13

175 **TLR9 activation bolsters B cell - T cell interactions and expands potent antitumor CD8+ T cells**

Aubrey Smith, Chrystal Paulos, Hannah M. Knochelmann, Megan M. Wyatt, Amalia M. Rivera-Reyes, Guillermo O. Rangel Rivera, Michael B. Ware, Anna C. Cole, Connor J. Dwyer, David M. Neskey, Mark P. Rubinstein, Bei Liu, Jessica E. Thaxton, Eric Bartee, Department of Microbiology and Immunology, College of Graduate Studies, MUSC

Immune-based therapies have reshaped the landscape of cancer patient care, especially in patients with late-stage disease. Despite advancements, many patients fail to respond to immunotherapies such as adoptive T cell transfer (ACT) or relapse. Therefore, potent immunotherapies are needed which benefit these difficult to treat populations. Our team has demonstrated that ACT can be bolstered against a highly aggressive mouse model of melanoma by co-administering a Toll-like receptor (TLR) agonist, CpG. CpG broadly activates proinflammatory pathways in vivo, however, co-administration of TLR agonists with cell therapy induced toxic side effects. We hypothesized that in vitro application of TLR agonists could support the expansion of a potent T cell product while circumventing toxicities associated with in vivo administration. To test our hypothesis, we employed a mouse model of ACT, Pmel-1, in which CD8+ T cells express a transgenic TCR that recognizes a melanoma antigen. We implanted mice with subcutaneous B16F10 melanoma and treated them with Pmel-1 T cell therapy expanded under traditional conditions or with the TLR9 agonist, CpG. T cells expanded from a CpG-treated culture were more effective at controlling tumor outgrowth and extending survival than traditionally expanded T cells. Instead of acting directly on T cells to impart enhanced antitumor properties, CpG acted indirectly on T cells via activating B cells in culture. Finally, by blocking an array of inflammatory cytokines or costimulatory pairs in culture, we found that the CpG-bolstered B cell/T cell axis is dependent on direct B-T cell interactions via costimulatory molecules. Collectively, these findings build on our understanding of how B cells license T cells with potent antitumor immunity and can be readily translated to meaningful improvements to T cell-based therapies for patients with cancer.

This work was supported by NCI F31 CA232646-01A1 and Hollings Cancer Center Graduate Fellowship (A.S.S.), Hollings Cancer Center Proteomics Pilot Award (A.S.S. and C.M.P.), NCI R01 CA175061, R01 CA208514 (C.M.P.)

176 **Immunostimulatory effects of a novel small molecule CD38 inhibitor and application for treatment of neuroblastoma**

Catherine Mills, Patrick Woster, Thomas Benton, Megan Francis, Dalan Soloman, Ivett Pina Gomez, Yuri Peterson, Department of Drug Discovery and Biomedical Science, College of Graduate Studies, MUSC

High-risk (HR) neuroblastoma (NB) accounts for 15% of all pediatric cancer deaths. While the advent of immunotherapy for HR patients has modestly improved five-year event-free survival (EFS) to just under 50%, there remains an unmet medical need for the development of new, more efficacious therapeutics. Refractory disease for HR NB patients can often be attributed to chemotherapy resistance and immunotherapy failure. The ectoenzyme CD38 is an immunomodulating protein that is expressed constitutively on natural killer (NK) cells and other immune cells in the tumor microenvironment (TME). Furthermore, CD38 is complicit in the production of immunosuppressive and pro-angiogenic adenosine (ADO) via its hydrolytic conversion of NAD+ to critical intermediates in the ADO pathway. Higher ADO levels and increased CD38 expression in the bone marrow of HR NB patients have been correlated with poor prognosis. We have designed and synthesized a novel small molecule which inhibits CD38-hydrolase activity.

We have demonstrated that this inhibitor produces immunostimulatory effects in NK cells via enhanced cell proliferation and interferon gamma (IFN-γ) production in vitro. Additionally, we have shown that NK cells treated with our CD38 inhibitor exhibit enhanced cytotoxicity towards NB cells following combination treatment with the immunocytokine ch14.18-IL2. Our studies have designed and synthesized the first small molecule inhibitors of CD38-hydrolase activity specifically for use in HR NB immunotherapy.

This work was supported by South Carolina SmartState Endowment Fund (PMW)

177 **The effect of non-invasive transcutaneous auricular vagus nerve stimulation (taVNS) on hypoxic-ischemic injury in newborn rats**

Melanie Wiley, Mark George, Catrina Sims-Robinson PhD, Heather A. Boger PhD, Dorothea D. Jenkins MD, Department of Neurosciences, College of Medicine (MD, PhD), MUSC

Introduction. Neonatal hypoxic-ischemic encephalopathy (HIE) is an acute neurologic syndrome where decreased blood flow and oxygen to the brain causes acute and chronic brain dysfunction. The only proven neuroprotective intervention for HIE is hypothermia treatment started within 6 hours of birth. Even with hypothermia treatment, HIE results in long-term deficits in 50% of survivors. Pre-clinical adult stroke studies demonstrate that vagus nerve stimulation (VNS) has anti-inflammatory effects and attenuates brain damage. Transcutaneous auricular VNS (taVNS) is safe and feasible in infants and may improve the motor skill of bottle feeding. Could taVNS administered shortly after HIE birth have neuroprotective effects? We hypothesize that a combined hypothermia-taVNS treatment will improve motor function, attenuate infarct volume, and decrease inflammation compared to hypothermia alone. Methods. The HIE model includes ligation of the right common carotid artery in postnatal day 7 (P7) rats followed by 90min hypoxia (8% oxygen) and 2hr hypothermia. taVNS or sham taVNS was administered using a bipolar electrode placed on the auricular concha region for 30min, [30sec trains, 0.5msec duration, 20Hz frequency, followed by 4.5min breaks]. Experimental groups include +HIE/+taVNS, +HIE/-taVNS, and -HIE/-taVNS. To assess motor function, grasping reflex and forelimb grip strength tasks were assessed prior to surgery through P10. Infarct volume was assessed at 72h after injury by staining coronal sections with cresyl-violet. Results. Thirty-four rat pups underwent surgery with an 8.82% mortality rate. taVNS was well tolerated by the P7 rats when delivered below perceptual threshold (0.4-1.1mA). There was no difference in elementary motor function or infarct volume between any group. Conclusion. Future studies will include unilateral external carotid artery ligation and 1.5hr hypoxia for a more severe brain injury. These initial pre-clinical studies in neonates are important in determining whether taVNS may translate as a treatment to improve outcomes after neonatal HIE.

This work was supported by Tiny Blue Dot Foundation, South Carolina Clinical and Translational Research Institute (SCTR) Training Program in Translational and Team Sciences (TL1) NIH grant# 5TL1TR001451-07

178 **The Role of MyoD as a Promoter of Cell Survival in Rhabdomyosarcoma**

Alexander Oles, Denis Guttridge, Peter Yu, Sudarshana Sharma, Priya Londhe, Eric Hill, Ryan D. Roberts, David J. Wang, Department of Pediatrics, College of Graduate Studies (MSTP), MUSC

Abstract withheld from publication

179 **Interaction Between Fam3c And Lifr Regulates Self-Renewal In Mammary Epithelial Cells**

William Streitfeld, Philip Howe, Annamarie Dalton, Breege Howley, Department of Biochemistry and Molecular Biology, College of Graduate Studies, MUSC

Our lab has characterized a mechanism of TGF-beta-mediated epithelial-to-mesenchymal transition (EMT) in normal murine mammary gland (NMuMG) cells through heterogenous nuclear ribonucleoprotein E1 (hnRNP E1, hereafter "E1"). Knockdown of E1 (E1KD) in NMuMG cells (1) induces EMT, tumorigenesis, and metastasis, (2) increases translation of mRNA encoded by the Fam3c gene, and (3) increases transcription/translation of the leukemia inhibitory factor receptor (Lifr) gene. Fam3c and Lifr have been shown to interact by coimmunoprecipitation/radiography, and there is a correlation between Fam3c expression and phosphorylation of the Lifr effector STAT3. In immunocompromised mice, orthotopic grafts of NMuMG cells with E1KD (E1KD cells) with additional knockdown of either Fam3c or Lifr display a decrease in tumor initiation, growth, and metastasis relative to control cells. E1KD cells also demonstrate attenuation of migratory capacity following knockout (KO) of Fam3c, and attenuation of self-renewal capacity following KO of Fam3c or Lifr. These data suggest that mammary carcinoma progression following loss of E1 expression involves regulation of Fam3c and Lifr, and further suggest that loss of E1 expression results in a Fam3c/Lifr-promoted breast cancer stem-cell (BCSC) phenotype. The mechanisms involved in Fam3c-mediated EMT and Fam3c/Lifr-mediated BCSC induction are unknown. Characterization of BCSCs will advance our understanding of drug resistant/dormant cancer and identify targets for chemotherapeutic interventions. To interrogate the mechanism(s) involved in Fam3c/Lifr-dependent BCSC phenotype, transcriptomic analysis was performed. Analysis of our RNA-seq data revealed changes in gene expression patterns associated with EMT and BCSC phenotypes in Fam3c and Lifr KO cells. Additionally, cells with Fam3c KO demonstrated downregulation of the Lifr gene. This data allows us to conclude that Fam3c participates in the regulation of Lifr expression and identifies a potential mechanism of Fam3c/Lifr-induced maintenance of self-renewal. Continued investigation will reveal the pathways and mechanisms involved in Fam3c/Lifr-mediated disease progression in vivo.

This work was supported by NIH grant #1F31CA257145-01, NIH grant #R088904

180 **Epithelial adherens junctions regulate ECM remodeling via miRNAs**

Amanda Daulagala, Antonis Kourtidis, Catherine Bridges, Joyce Nair-Menon, Department of Regenerative Medicine and Cell Biology, College of Graduate Studies, MUSC

Colon cancer is the third most common and second deadliest type of cancer. Colon cancer is broadly characterized by compromised epithelial integrity and aberrant extracellular matrix (ECM) remodeling. However, a possible connection between epithelial integrity and ECM remodeling that contributes to the disease progression, has not been explored. The Adherens Junction (AJ) is a cell-cell adhesion complex, composed of E-cadherin and the catenin family of proteins, essential for maintenance of epithelial tissue integrity. We have shown that the p120 catenin partner PLEKHA7 is critical for epithelial integrity. In addition, we have found that PLEKHA7 recruits core components of the RNAi machinery at mature apical AJs, to regulate miRNA levels and activity. Loss of PLEKHA7 results in disruption of junctional localization of the RNAi machinery, miRNA dysregulation, oncogene upregulation, and pro-tumorigenic colon cell behavior, in vitro and in vivo. Interestingly, RNA sequencing in colon epithelial Caco2 cells revealed that a set of mRNAs of ECM remodeling markers namely, MEP1A, MMP1, LOX, and CTGF, was among the top increased upon PLEKHA7 depletion. We confirmed increased protein expression of these mRNAs upon PLEKHA7 depletion by

western blot analysis. Bioinformatics analysis identified five PLEKHA7-regulated miRNAs, namely miR-203a, miR-24, miR-30b, miR-30c and let-7g to potentially target these ECM-related mRNAs. We are currently verifying targeting of the ECM-related mRNAs by these miRNAs, using miRNA mimics. Furthermore, enzymatic activity assays showed that MMP1 and LOX have indeed increased activities upon PLEKHA7 depletion. Preliminary examination of colon tissues from a PLEKHA7 knockout mouse model using second-harmonic generation shows collagen reorganization in the submucosa, which is in agreement with the roles of MMP1 and LOX in ECM remodeling. Our data reveal a novel mechanism, through which epithelial adherens junctions regulate ECM remodeling through miRNA activity.

This work was supported by R01 DK124553-01A1 R21 CA246233-01A1 Abney Graduate Fellowship Award, Hollings Cancer Center, MUSC

181 **Regionally specific losses in gray and white matter in Alcohol Use Disorder: Implications for non-invasive brain stimulation**

Daniel McCalley, Colleen Hanlon, , Department of Neuroscience, College of Graduate Studies, MUSC

Background: Transcranial Magnetic Stimulation (TMS) is a neural-circuit specific tool to decrease drinking among individuals with Alcohol Use Disorder (AUD). The ability of TMS to modulate brain circuitry relevant to AUD is dependent upon 3 factors which may be compromised in heavy drinkers: 1) gray matter volume (GMV) at the stimulation site, 2) scalp-to-cortex distance and 3) white matter volume (WMV) between the stimulation site and downstream targets. This study tested the hypotheses that these aspects of neural architecture are compromised in AUD patients, and that, accordingly patients may need a higher TMS dose to modulate the cortex and afferent targets. Methods: Magnetic resonance images were acquired from 44 individuals with AUD and 44 age-matched healthy controls (n=88). Whole brain voxel-based morphometry was conducted. Subsequent region-of-interest analysis was performed at three EEG 10-20 sites commonly used in TMS for AUD: FP1 (left frontal pole), F3 (left DLPFC) and C3 (left motor cortex), and within three relevant white matter tracts: FP1-ventral striatum, F3-dorsal striatum, and the corticospinal tract. Scalp-to-cortex distance and TMS electric fields were assessed at these EEG sites. Results: Individuals with AUD had significantly lower GMV within all three TMS target locations ($F_{1,264}=14.12$, $p=0.0002$) as well as within all three white matter tracts ($F_{1,264}=12.08$, $p=0.001$). There was no difference in scalp-to-cortex distance between the AUD and the healthy control group at any tested cortical location ($F_{3,252}=1.906$, $p=0.129$). Conclusions: Individuals with AUD had significantly lower GMV and WMV in multiple areas of interest for TMS treatment, however these volumetric reductions did not impact scalp-to-cortex distance. Given previous studies which have shown that TMS-evoked changes in cortical and subcortical activity are dependent on gray and white matter, these data suggest that individuals with AUD may need a higher dose of TMS in order to sufficiently modulate neural circuits of interest.

This work was supported by F31AA028426, R01AA027705, R21DA044503, R01DA044471, P20GM109040

182 **Conditioning hPSC-Derived Cardiac Fibroblasts for Isogenic Cardiac Organoid Development**
Charles Kerr, Ying Mei, Department of Regenerative Medicine, College of Graduate Studies, MUSC

Annually, there are ~790,000 cases of myocardial infarction (MI) in the United States. Typically, MI progresses into heart failure where patients have a high risk of mortality within 5 years after diagnosis. While animal models provide a valuable model system of MI, interspecies' differences lead to inaccurate recapitulation of human myocardium. To address this, we developed 3D human cardiac organoids through self-assembly of human pluripotent stem cell (hPSC)-derived cardiomyocytes, adult cardiac fibroblasts, endothelial cells, and stromal cells. To capture patient specific responses to MI within cardiac organoids, we've investigated incorporating hPSC-derived cardiac fibroblasts (hPSC-CF) for replicating adult cardiac fibroblast hallmarks of fibrosis within cardiac organoids for applications in disease modeling. However, hPSC-CFs exhibit an immature and fibrotic phenotype limiting their biomimicry of quiescent and stress-responsive adult cardiac fibroblasts. To improve the recapitulation of adult cardiac fibroblast phenotypes, we've examined prolonging culture of hPSC-CF on decellularized extracellular matrix (DECM) coated tissue culture substrates to mimic the natural environment of myocardium to facilitate cardiac fibroblast maturation. Our results suggest that neither prolonging culture nor DECM coated tissue culture substrates improved hPSC-CF organization and fibrosis within cardiac organoids. Additionally, fibrosis within hPSC-CF cardiac organoids was enhanced through our MI protocol. Yet, DECM coated substrates reduced hPSC-CF fibrotic gene expression while prolonging culture exacerbated fibrotic genes. Further, pharmacological inhibition of TGFb signaling reduced hPSC-CF fibrosis within cardiac organoids demonstrating that TGFb inhibition could enhanced hPSC-CF functionality. In conclusion, this study demonstrates that hPSC-CFs can be conditioned towards an adult cardiac fibroblast phenotype through TGFb modulation and cell culture substrate manipulations.

This work was supported by 1F31HL154665-01 T32 HL007260 1R01HL133308 P30 GM103342

183 **Treatment with a site-targeted complement inhibitor reduces visual deficits following traumatic brain injury**
Davis Borucki, Stephen Tomlinson, Wenxue Wang, Shahid Husain, Baerbel Rohrer, Department of Neuroscience, College of Graduate Studies (MSTP), MUSC

Introduction: There is a clinical need for a better understanding of the mechanisms driving chronic dysfunction after traumatic brain injury (TBI) and therapeutic approaches to alleviate them. It is estimated that more than 5 million Americans are living with a chronic TBI-related disability, including a significant population of veterans. These chronic disabilities include motor, cognitive and visual dysfunction. The development of visual deficits following TBI is significantly delayed, suggesting that ongoing neuroinflammatory changes rather than the initial injury contribute to their development. The complement system is a key contributor to neuroinflammation. Complement is activated acutely following injury, and through a self-amplification loop contributes to chronic inflammation and neuronal loss. We hypothesized that complement activation within the visual system contributes to ongoing visual decline, and that treatment with the site-targeted complement inhibitor CR2-factor H would prevent visual system decline. Methods: We subjected mice to an open-skull controlled cortical impact and treated them with 16 mg/kg of a targeted complement inhibitor or saline intravenously one hour after injury. Changes in motor dysfunction were assessed using Noldus CatwalkXT and open field ambulation. Changes in cognition were assessed using the Barnes Maze. Testing was conducted at the Ralph H. Johnson VA Medical Center. Changes in visual acuity were assessed using the optokinetic response. Microgliosis and

astrogliosis in the visual system were assessed by immunohistochemistry for Iba-1 and GFAP, respectively. Results: Treated mice showed improvements in motor function and performance in the Barnes maze. One week after injury, treated mice showed an improvement in visual acuity. Inhibition of the complement system resulted in reduced inflammation in the visual system. This suggests that the complement system plays a mechanistic role in the development of visual deficits after TBI, and that early inhibition of complement activation after TBI has therapeutic potential for ameliorating visual and other deficits.

This work was supported by W81XWH-20-1-0939, 2T32GM008716-21

184 **PI3K inhibition promotes levels of stemness in a dose dependent manner and enhances their mitochondrial fitness**

Guillermo Rangel Rivera, Chrystal Paulos, Dwyer Connor Jude, Knochelmann Hannah Marie, Smith Aubrey, Ware Brandon Michael, Cole Anna Camille, Wyatt Megan, Department of Microbiology and Immunology, College of Graduate Studies (MSTP), MUSC

Adoptive T cell therapy (ACT) is a novel therapeutic approach for cancer patients who have become refractory to chemotherapy and immunotherapy. Patients treated with this cellular therapy have exhibited durable responses against solid tumors. However, a sizeable proportion of patients remain unresponsive to this last effort approach. Current ACT protocols expand T cell to high numbers at the cost of T cell persistence diminishing therapeutic efficacy, in part by activating PI3K signaling. The PI3K signaling pathway plays a central role in the activation, metabolic engagement and differentiation of T cells. We hypothesized that by inhibiting the PI3K delta subunit, which is uniquely expressed in lymphocytes, we would enrich both stemness features and the bioenergetic competence of tumor specific T cells. To test this we inhibited the PI3K delta pathway with the FDA approved inhibitor Idelalisib using a log10 titration and examined the transcriptional, phenotype and metabolic function of the expanded cells after a week of in vitro culture. PI3K delta inhibition in vitro enhanced tumor immunity and survival in a dose dependent manner. High doses of Idelalisib enriched T cells with features of stemness that were sustained even after chronic antigen exposure. We found that Idelalisib increased mitochondrial mass and membrane potential, while reducing mitochondrial reactive oxygen species. Intriguingly, at the transcriptional level we found that fatty acid oxidation was not enhanced, suggesting an alternative pathway involved in the enhanced spare respiratory capacity of PI3K delta inhibited T cells. These findings indicate that blocking PI3K delta in T cells is sufficient to mediate lasting tumor immunity of adoptively transferred T cells by preserving stemness features and improving mitochondrial fitness. Our data suggest that addition of Idelalisib to ACT expansion protocols could greatly improve T cell therapies for solid tumors by rewiring T cell stemness and promoting mitochondrial fitness.

185 **Combined primary and secondary ocular blast injury model for translational research**

R. Glenn Hepfer, Hai Yao, Peng Chen, Jie Fan, Craig Crosson, Department of Oral Health Sciences, College of Dental Medicine (DMD, PhD), MUSC

Ocular blast injuries result from a variety of damage mechanisms. Primary blast waves cause damage with local increases in pressure. Secondary injuries from projectiles cause penetrating and blunt trauma. Current models separate these mechanisms. The goal of this study is to produce and test a repeatable and controllable combined injury model in ex vivo porcine eyes and in in vivo rabbits. A custom device was fabricated that produces a primary blast wave, secondary penetrating injury, and blunt trauma. The physical effects of pressure, blade length, and blunt

force were measured or calculated with a pressure transducer, microscopy, and projectile velocity, respectively. Immediate pathological effects were measured on fresh, intact porcine eyes. The blast pressure, penetration depth, and blunt force were varied. Porcine corneas were analyzed with cornea strip extensiometry and histology. Wound healing was observed in New Zealand white rabbits with ophthalmic exams at regular intervals and with histology at days 3 and 14 following injury. The injury model produced consistent and controllable peak pressure, blade length, and blunt force. In porcine eyes, corneal strip extensiometry showed a decrease in elastic modulus ($p<0.01$, ANOVA) and ultimate stress ($p<0.01$, ANOVA) with increased blade length. Histology showed that the wound depth correlated with blade length. In the in vivo study, the injury was consistently observed with fluorescein staining in ophthalmic exams and collagen imaging in histological analysis. By day 3, epithelial cells migrated and proliferated in the wound, and by day 14, scar tissue was observed through alpha-smooth muscle actin staining. Our results demonstrate a novel model that combines damage mechanisms underlying blast injury. The model produces measurable damage in ex vivo porcine eyes and in in vivo rabbits. The model could be used to assess any compounding effects of blast injury mechanisms and to test multipronged therapies for these injuries.

186 **lncRNA Neat1/hemoglobin subunit beta axis regulates neuronal dysfunction in sepsis-associated encephalopathy**

Yan Wu, Hongkuan Fan, Department of Pathology and Laboratory Medicine Research, College of Medicine, MUSC

Although sepsis incidence has steadily increased in recent years, sepsis morality rates have declined leading to an expanding population of sepsis survivors. This population frequently suffers from sepsis-associated encephalopathy (SAE) which has been associated with long-term functional sequelae including cognitive impairment and anxiety. The pathogenesis of sepsis-induced cognitive impairment is poorly understood although growing evidence indicates that neuroinflammation and related excitotoxicity may play a role. We established a mouse model of SAE using a cecal ligation and puncture (CLP) model. Anxiety-like behavior and long-term memory deficits were assessed post sepsis. We demonstrated that septic mice exhibit anxiety-like behavior, memory impairment and decreased dendritic spine density ($P<0.05$). lncRNA Nuclear Enriched Abundant Transcript 1 (Neat1) level was significantly increased ($P<0.05$) in neuronal cells in septic mice. We performed RNA - protein pull-down assays in lysed neuronal cells followed by LC-MS/MS analysis and identified Neat1 directly interacted with hemoglobin β subunit (Hbb), preventing its degradation. Furthermore, we demonstrated that the Neat1/Hbb axis inhibited PSD-95 expression levels ($P<0.05$) and decreased dendritic spine density ($P<0.05$). Neat1 knockout mice exhibited decreased Hbb levels, increased PSD-95 and dendritic spine density in neurons and decreased anxiety and memory impairment ($P<0.05$). Intriguingly, Neat1 silencing via a novel GapmeR antisense oligonucleotide ameliorated sepsis-related dendritic spine loss and reduced cognitive dysfunction ($P<0.05$). In conclusion, we demonstrated a potential novel role for the Neat1/Hbb axis in SAE and uncovered a previously unknown mechanism for the neuronal dysfunction after sepsis, which may lead to a novel treatment strategy.

187 **Comparison of chemotherapy agents for delivery by thermosensitive liposomes in a computational model**

Krishna Ramajayam, Dieter Haemmerich, Department of Pediatrics, CRI, College of Medicine, MUSC

Introduction: Thermosensitive liposomes are hyperthermia-activated drug delivery systems that enable localized delivery of chemotherapy agents. Various chemotherapeutic agents have been encapsulated in TSL, but few studies examined the impact of drug properties on delivery efficacy when combined with TSL. Objectives: In this study, we have developed computational models to compare four chemotherapy agents encapsulated in thermosensitive liposomes (TSL): doxorubicin (Dox), idarubicin (Ida), pirarubicin (Pir) and cisplatin (Cis). Methods: The computational model was based on the commonly used Krogh cylinder model, where a representative capillary and surrounding tissue are simulated. TSL-encapsulated drug entered the capillary assuming instant and complete drug release (i.e. assuming ideal TSL). For TSL-Dox, we also simulated an actual TSL formulation (LTSL-Dox) where experimentally determined drug release kinetics at 43˚C was fed into the computer model. All drugs were administered at the maximum tolerated dose (MTD) for humans. Transcapillary transport, cell uptake and cell survival were calculated based on parameters extracted from earlier published data for the four drugs. Results: Bioavailable tumor drug concentrations were (mean[range] in µg/ml): 88.1[82.8-94.7] (TSL-Dox), 157.1[69.8-366.5] (TSL-Ida), 190.3[81-424.2] (TSL-Pir), 39.2[38.7-39.8] (TSL-Cis) and 59.9[51.5-65.6] (LTSL-Dox). TSL-Ida and TSL-Pir resulted in higher tumor drug accumulation than TSL-Dox and LTSL-Dox. Estimated cell survival fraction (mean[range] in %) was 5.1[4.7-5.4] (TSL-Dox), 0.4[0.0092- 1.7] (TSL-Ida), 2.7[0.7-5.6] (TSL-Pir), 11.6[11.5-11.8] (TSL-Cis) and 7.1 [6.5-8.1](LTSL-Dox). Conclusions: The drugs with fastest extraction (i.e. high vascular permeability) and fastest cell uptake (Pir, Ida) resulted in considerably enhanced tumor uptake compared to the other drugs, with idarubicin being the most effective in tumor cell killing. However, fast cell uptake also resulted in reduced drug delivery to cells distant from the vessel for TSL-Pir. Mathematical models may thus help in evaluating various drugs for optimal delivery with thermosensitive liposomes.

This work was supported by NIH under Grant RO1CA181664, NSF under Grant NSF/EPSCoR GEAR A20-0236-001, National Institutes of Health under Grants C06 RR015455 and C06 RR018823, flow cytometry shared resource at the Hollings Cancer Center, Medical University of South Carolina under Grant P30 624CA138313.

188 **FRONTAL LOBE NEUROMETABOLITE ALTERATIONS ASSOCIATED WITH HEAVY ALCHOL USE: A META-ANALYSIS OF PROTON MAGNETIC RESONANCE SPECTROSCOPY STUDIES**

Anna Kirkland, Lindsay Squeglia, Brittney Browning, Lorenzo Leggio, Dieter Meyerhoff, Department of Psychiatry and Behavioral Sciences, College of Medicine, MUSC

Heavy alcohol use is associated with alterations in brain metabolite concentrations. Measuring the chronic effects of alcohol on brain metabolite levels with proton magnetic resonance spectroscopy (MRS) is important for understanding the neurobiological mechanisms underlying alcohol use disorder (AUD) and the development of neuroscience-based treatments. The purpose of this meta-analysis was to summarize neurometabolite level alterations related to heavy alcohol use relative to controls. Following PRISMA guidelines, PubMed, PsycINFO, and Scopus were searched using the terms "magnetic resonance spectroscopy" or "MRS" with "alcohol use disorder", "alcoholism", "alcohol dependence", and "alcohol abuse" (N=796). Each study had to report at least one voxel-of-interest (VOI) in the frontal lobe and absolute or relative levels of N-acetylaspartate (NAA), choline-containing metabolites, and/or creatine-containing metabolites. Heavy alcohol use was defined by

DSM criteria for AUD or by frequency/quantity. Effect sizes were measured with Hedge's g and random-effects modeling was used. Twenty-one studies were identified with VOIs located in the anterior cingulate cortex (ACC, n=14), frontal gray matter (GM) (n=14), and frontal white matter (WM) (n=15). Compared to controls, heavy alcohol use was related to less NAA in the ACC (g= -0.71, 95% CI: -1.32 to -0.09, p=0.03), frontal GM (g= -0.48, 95% CI: -0.76 to -0.20, p=0.001), and frontal WM (g= -0.54, 95% CI: -0.77 to -0.31, p<0.001). Lower levels of choline metabolites were also found in frontal GM (g= -0.26, 95% CI: -0.46 to -0.05, p=0.02) and frontal WM (g= -0.33, 95% CI: -0.56 to -0.10, p=0.01). Lower levels of NAA and choline-containing metabolites may indicate a decrease in neuronal or axonal viability and decreased cerebral cell synthesis and membrane turnover, respectively. MRS can help identify the location and types of brain metabolite deficits in heavy alcohol use, as well as specific pharmacological treatments that might effectively target these neurometabolic disturbances.

This work was supported by T32 DA007288-29

189 **The perioperative patient experience during COVID-19**

Kristen Quinn, Andrea Abbott, Andrew Dippre, Melinda Ryan, Rupak Mukherjee PhD, Prabhakar Baliga MD, Department of Surgery, College of Medicine, MUSC

Access to elective surgical procedures has been impacted by the COVID-19 pandemic. We sought to understand the patient experience by developing and distributing an anonymous online survey to those who underwent non-emergency surgery at a large academic tertiary medical center between March and October 2020. The survey was completed by 184 patients; the majority were Caucasian (84%), female (74.6%), and ranged from 18 to 88 years old. Patients were likely unaware of case delay as only 23.6% reported a delay, 82% of which agreed with that decision. Conversely, 44% felt that the delay negatively impacted their quality of life. Overall, 82.7% of patients indicated high satisfaction with their care. African American patients more often indicated a 'neutral' versus 'satisfactory' hospital experience ($p<0.05$) and considered postponing their surgery ($p<0.01$). Interestingly, younger patients (<60) were more likely than older (≥60) patients to note anxiety associated with having surgery during the pandemic ($p<0.01$), feeling unprepared for discharge ($p<0.02$), not being allowed visitors ($p<0.02$), and learning about the spread of COVID-19 from healthcare providers ($p<0.02$. These results suggest that patients are resilient and accepting of changes to healthcare delivery during the current pandemic; however, certain patient populations may have higher levels of anxiety which could be addressed by their care provider. These findings can help inform and guide ongoing and future healthcare delivery adaptations in response to care disruptions.

190 **Complement inhibition in chronic phases after traumatic brain injury reverses ongoing cognitive decline**

Khalil Mallah, Stephen Tomlinson, Christine Couch, Mohammed Alshareef, Davis Borucki, Xiaofeng Yang, Ali Alawieh, Department of Microbiology and Immunology, College of Medicine, MUSC

Introduction/Rationale: Traumatic Brain Injury (TBI) is a risk factor for dementia and cognitive decline in chronic phases after injury. The underlying pathological mechanisms that link TBI to cognitive decline are not well understood. We previously demonstrated a role for complement in mediating ongoing secondary injury and cognitive deficits up to 1 month after murine TBI. In this work, we investigated the role of complement in neuroinflammation and cognitive decline for up to 6 months after murine TBI. Methods: We used a murine controlled cortical impact (CCI) TBI

model. Starting at 2 months after injury, groups were treated with PBS or with CR2-Crry in an acute or continuous treatment paradigm. Motor and cognitive function was analyzed by a battery of tests conducted at the Ralph H. Johnson VA Medical Center. Histopathological and immunological analyses were carried out on brain sections collected at 6 months post-TBI. Results: In vehicle treated animals, there was ongoing cognitive decline over 6 months post-TBI, which was accompanied by complement deposition in the perilesional area, as well as microgliosis and astrogliosis. Complement inhibition in the chronic phase after TBI did not improve motor function measured at 6 months, but ongoing cognitive decline was reversed by continuous treatment with CR2-Crry. Complement (C3) deposition was reduced in the continuous CR2-Crry treatment group, which correlated with a decrease in microglia/macrophage and astrocyte activation. Furthermore, cognitive decline was linked to a reduction in synaptic density, that was in turn linked to microglial phagocytosis of C3 opsonized synapses, and which was reversed with CR2-Crry treatment. Conclusions: There is an ongoing complement mediated expansion of lesion and neuroinflammatory response at 6 months after murine TBI, which is associated with cognitive deficits. Complement inhibition interrupted this degenerative neuroinflammatory response and reversed cognitive decline, even when therapy was delayed until 2 months after TBI.

This work was supported by Department of Veterans Affairs (VA) (1BX004256, 1RX001141 and IK6BX005235) National Institute of Health (NIH) (T32AI132164)

191 **Local Muscle Inflammation in Cancer Cachexia Derives from Multiple Cell Populations in the Muscle Microenvironment Under the Control of NF-kB**

Benjamin Pryce, Denis Guttridge, Vijay Shankar, Erin Talbert, Trudy Mackay, David J. Wang, Department of Pediatrics, College of Medicine (MD, PhD), MUSC

Over the past decades, the role of systemic inflammation in cancer cachexia has garnered much attention, characterized by increases in circulating inflammatory cytokines as a contributing factor in muscle wasting. However, studies from our own laboratory and others have found it challenging to recapitulate the same levels of circulating cytokines found in mouse models of cancer cachexia to those measured in plasma from cachectic cancer patients. Given that we had previously shown that skeletal muscle undergoes damage and initiates a regenerative program during cancer cachexia, we speculated that muscle wasting might also be associated with a more local muscle inflammatory condition. Using a variety of assays in multiple mouse models and samples from pancreatic cancer patients undergoing cachexia, we found that cachectic muscles overall exhibit an inflammatory profile. This local muscle inflammation is characterized by the accumulation of immune cells, predominantly represented by macrophages. Consistently, these cells were elevated in muscle biopsies from cachectic pancreatic cancer patients compared to weight stable cancer patients and control patients without cancer. Since the NF-kB signaling pathway plays a prominent role in tissue inflammation and was shown to impair a regenerative response in muscle progenitor cells (MPCs) leading to muscle wasting in cancer, we hypothesized that NF-kB was involved in regulating local muscle inflammation in cancer cachexia. Indeed, genetic ablation of NF-kB canonical signaling in MPCs, as well as myofibers, led to the decrease in macrophages and inflammatory cytokines. To expand the characterization of macrophages in cachectic muscle we purified CD45+ immune cells from hindlimb muscles of C-26 tumor bearing mice and performed single cell RNA sequencing. Results revealed the identification of multiple populations with immune properties that interestingly are marked by NF-kB activity to potentially contribute to the recruitment of macrophages. Based on our findings, we propose that NF-kB canonical signaling

serves as

192 **Different aspects of hand grip performance may be explained by connectivity of distinct sensorimotor networks in chronic stroke**

Christian Schranz, Na Jin Seo, Shradda Srivastava, Bryant A. Seamon, Barbara Marebwa, Leonardo Bonilha, Viswanathan Ramakrishnan, Janina Wilmskoetter, Truman Brown, Richard Neptune, Steve Kautz, Department of Health Sciences and Research, College of Health Professions, MUSC

Introduction: Stroke survivors often suffer from upper extremity impairment, which impacts the ability of an individual to perform activities of daily living. There is substantial heterogeneity in presentation of upper extremity impairment as well as response to rehabilitation therapy among individual following a stroke This heterogeneity poses a significant hurdle in clinical decision making for rehabilitation treatments. Therefore, it is of paramount importance to improve our understanding of the origin of heterogeneous presentation of upper limb impairment, so that rehabilitation therapies can be personalized for maximal effectiveness. Specifically, we hypothesize that distinct brain networks are responsible for different aspects of hand grip performance. Methods: 22 chronic stroke survivors (>6 months post stroke) were assessed for biomechanical grip performances. Specifically, reaction time, relaxation time, maximum force, force directional control, and force level estimation performances were obtained. These 5 grip performances represent the individual's abilities to contract/relax muscles timely, ability to apply grip force with an adequate direction and amount for a given task, and strength, respectively. In addition, each participant's brain connectome was reconstructed from structural diffusion weighted MRI. To identify brain networks related to grip performance, we performed two-step factor analysis with 10 regions of interests (ROIs) within a connectome that are involved in sensorimotor control. We examined if connectivity between certain ROIs distinctly correlated with the 5 grip performances. Results: Factor analysis identified 7 sensorimotor networks. Of these, 5 distinct networks' connectivity correlated best with each of the 5 biomechanical grip performances. Discussion: These results suggest that connectivity of different networks may be responsible for different biomechanical grip performances which leads to different clinical presentations of upper extremity impairment. Understanding distinct brain networks associated with different grip performance behaviors may facilitate development of personalized rehabilitation interventions to directly target the responsible brain network for individual patients.

This work was supported by VA Office of Research and Development (ORD), with additional support from the VA/ORD Rehabilitation R&D Service (1I01RX001935), Senior Research Career Scientist award 1IK6RX003075, National Institutes of Health (NIHP20GM109040) with help from the Ralph H. Johnson VA Medical Center.

193 **The splanchnic mesenchyme is the main tissue origin of fibroblasts in the pancreas during homeostasis and tumorigenesis**

Lu Han, Michael Ostrowski, Yongxia Wu, Sean Sweeney, Ulyss Roesner, Melodie Parrish, Khushbu Patel, Tony Trimboli, Julia Lefler, Cynthia D. Timmers, Xuezhong Yu, Michael Zimmermann, Angela Mathison, Raul Urrutia, Gustavo Leone, Department of Biochemistry & Molecular Biology, College of Medicine, MUSC

The normal pancreas is mainly comprised of three epithelial cell subtypes and sparsely interspersed resident fibroblasts. In contrast, pancreatic cancer is characterized by desmoplasia, an abundant stroma with cancer associated fibroblasts (CAFs) being the major cellular component. Despite the

abundance and critical roles of CAFs modulating cancer progression, their tissue(s) of origin remains controversial. Here we performed comprehensive lineage tracing studies to examine the potential tissue sources of pancreatic CAFs. The pancreatic epithelium (through epithelium-to-mesenchyme transition), bone marrow (through circulation) and pancreatic resident fibroblasts (through their proliferation) are possible sources from which CAFs arise in pancreatic cancer. We found that the fetal splanchnic mesenchyme, the cell layer surrounding the endoderm from which the pancreatic epithelium originates, gives rise to the majority of normal resident fibroblasts in the pancreas. In a genetic mouse model of pancreatic cancer, these resident fibroblasts expand and constitute the bulk of CAFs observed in tumors. Meanwhile, the bone marrow and pancreatic epithelium only contribute to a minor portion of resident fibroblasts and CAFs. Furthermore, single cell RNA sequencing identified gene expression profiles in resident fibroblasts and CAFs that are similar to those in splanchnic mesenchyme, suggesting persistent gene signatures within this mesenchymal lineage. Together, this study identifies the splanchnic mesenchyme as the fetal origin of pancreatic resident fibroblasts and CAFs.

This work was supported by ACS postdoctoral fellowship (PI, PF-20-114-01-DDC), NCI F32 fellowship (PI, F32CA254238), NCI T32 training grant (trainee, T32CA193201)

194 **Nutritional AGEing and RAGEing as a regulator of the tumor microenvironment**

Andrew Baldwin, David Turner, Bradley A. Krisanits, Pamela Woods, Lourdes M. Nogueira, Hong Li, Courtney Thomas, Mahtabuddin Ahmed, Gayenell S. Magwood, Marvella E. Ford, Victoria J. Findlay, and David P. Turner, Department of Pathology and Laboratory Medicine, College of Medicine, MUSC

Purpose: Advanced glycation end products (AGEs) are reactive metabolites, formed endogenously by oxidative stresses or absorbed from diet, that accumulate in the body over time. Red meat, dairy, and processed sugar-laden foods are especially high in AGEs and can lead to obesity and increased cancer risk. Despite increasing epidemiological evidence for oncogenic potential, cause and effect relationships are lacking. The objective was to confirm that increased exposure to AGEs resulting from nutritional intake creates a pro-tumorigenic microenvironment that encourages prostate cancer growth. Methods: We used the heat driven formation of glyoxidative, oxidative and lipoxidative stresses in mouse chow to reproduce the AGEs found in vivo. Syngeneic xenograft and spontaneous prostate and breast cancer mouse models were fed AGE specific diets and the effects of chronic AGE consumption on tumor growth assessed. To gain mechanistic insight, human and mouse two compartment co-culture models using primary fibroblasts and matched tumor epithelial cells were then used to assess the effects of AGEs on extracellular crosstalk in the TME. Results: Consumption of dietary AGEs promotes prostate tumor growth, aggression and metastasis. Dietary-AGEs promoted neoplastic growth by functioning as ligand to the transmembrane receptor for AGE (RAGE) expressed in the prostate tumor stroma. RAGE activation triggered development of 'activated fibroblasts', which express cancer associated fibroblast markers, NFkB, MYC and pro-tumorigenic paracrine secretion. Fibroblast activation was accompanied by decreased expression of androgen receptor and increased expression of neuroendocrine differentiation markers in tumor epithelial cells. AGE exposed primary fibroblasts isolated from patient tissue conferred tumor promoting abilities when cultured with patient matched tumor epithelial cells. Conclusions: The data demonstrates a direct cause and effect relationship between dietary-AGEs and neoplastic growth. This work lays the foundation for strategies aimed at reducing AGE exposure in the diet to improve health and reduce cancer incidence.

This work was supported by NIH R01 research grant, NIH T32 ITOS post doctoral fellow

195 **A Translational Model for Age-Related Auditory Processing Deficits**

Jeffrey A. Rumschlag, Kelly C. Harris, Hainan Lang, Carolyn M McClaskey, James W Dias, Lilyana B Kerouac, Department of Otolaryngology-Head & Neck Surgery, College of Medicine, MUSC

Auditory nerve (AN) function degrades with age, leading to decreased afferent input, poorer neural synchrony, and auditory processing deficits. Acute damage to the inner ear can also lead to AN loss, resulting in decreased response amplitudes and a loss of neural synchrony. The auditory midbrain compensates for this loss of peripheral AN activity via amplification (central gain). However, even though amplitudes are increased, neural synchrony remains disrupted. It is unknown whether the same process occurs with age. We hypothesized that the aging auditory system compensates for decreased input from the ear by amplifying the signal in the midbrain, but that the amplification does not improve neural synchrony. AN and midbrain function were assessed via electrophysiologic responses. Measurements of amplitude and neural synchrony were compared across age groups for mice and humans. In both mice and humans, results were consistent with central gain, with larger age-related amplitude reduction observed at the level of the AN than at the midbrain. In contrast, measures of neural synchrony were significantly lower in the auditory nerves and midbrains of older mice and humans than those in younger groups. These translational findings demonstrated that age-related neural degeneration contributes to central gain, largely preserving midbrain potentials, but is unable to recover losses in neural synchrony. Persistent deficits in neural synchrony may contribute to auditory processing deficits observed in both older mice and humans. Furthermore, we can use this translational model to further investigate the underlying pathologic changes that contribute to functional deficits in the aging auditory system.

This work was supported by NIH, NIDCD

196 **Medicaid Patients Face Limited Access to Care for Ankle Sprains**

Caroline Hoch, Christopher Gross, Daniel Scott, Department of Orthopaedics and Physical Medicine, College of Medicine, MUSC

Background: Prior research has found Medicaid patients face difficulty scheduling appointments with orthopaedic surgeons compared to those with other insurance. Recently, a number of states have expanded Medicaid coverage as part of the Affordable Care Act. Our goal was to determine whether individual state Medicaid expansion status, as well as patient insurance status, affected access to care for patients with ankle sprains. Methods: Four pairs of Medicaid expanded (Kentucky, Louisiana, Iowa, Arizona) and unexpanded (North Carolina, Alabama, Wisconsin, Texas) states were chosen. Twelve practices from each state (N=96) were randomly selected from the American Orthopaedic Foot and Ankle Society directory. Each clinic was called twice to request an appointment for a fictitious 16-year-old with a first-time ankle sprain with either in-state Medicaid insurance or Blue Cross Blue Shield (BCBS) private insurance. Results: An appointment was obtained at 63 (65.6%) clinics when calling with BCBS and at 44 (45.8%) clinics when calling with Medicaid (p=.006). There was a statistically significant difference in successful appointment scheduling based on insurance status in Medicaid unexpanded states (p=.007). However, there was no difference in Medicaid expanded states. In all states except Iowa, a Medicaid expanded state, there were more appointments scheduled using BCBS than with Medicaid. The three main reasons for appointment denial were inability to provide an insurance identification number (47.1%), insurance status (23.5%), and whether the patient was referred (17.6%). The waiting period for an

appointment was not different depending on insurance status or Medicaid expansion status. Conclusion: For patients with first-time ankle sprains, access to care is more difficult using Medicaid insurance rather than private insurance, especially in Medicaid unexpanded states. Healthcare policy makers and orthopaedic surgeons should be aware of this disparity, and work to improve orthopaedic foot and ankle access for Medicaid patients.

197 **Examining the Role of IL-4 Stimulated Memory CD8+ T-Cells in Regulating Monocyte Physiology and Activation**

Philip Broughton, Dr. Kristine Deleon-Pennell, Yusra Zaidi, Miguel Troncoso, Alexa Corker, Department of Cardiology, College of Medicine, MUSC

Interleukin (IL)-4 has been linked to improved cardiac wound healing via alterations in macrophage and T-cell populations. The goal of this study was to determine if proteins secreted by IL-4 stimulated CD8+ T-cells would regulate monocyte physiology, ultimately improving cardiac wound healing after an MI. Isolated splenic naïve CD8+ T-cells from day 0 (no MI) mice (n=5/sex/stimulation) were cultured in RPMI with either 0.1% FBS (unstimulated), 10% FBS (positive control) or 0.1% FBS+ IL-4. After 24 hours of stimulation, cells and media were collected and separated by centrifugation. The cell pellet was stained and analyzed for markers of activation (CD44) and memory (CD27) by flow cytometry. Conditioned media (secretome) was collected for stimulation of bone marrow monocytes (n=4; females only). After 4 hours of stimulation with either the secretome or RPMI supplemented with 0.1% FBS (negative control) or 10% FBS (positive control), monocytes were analyzed for viability, phagocytosis, and macrophage phenotype by flow cytometry. Monocyte migration after stimulation was measured using electric cell-substrate impedance sensing. After IL-4 stimulation, CD8+ T-cells displayed a shift from effector (CD44+ CD27-) to the memory phenotype (CD44+ CD27+; $p<0.05$ vs unstimulated cells). Interestingly, bone marrow monocyte viability was decreased by 15% when stimulated with the secretome of IL-4 treated CD8+ T-cells compared to unstimulated CD8+ T-cells. Phagocytosis was slightly elevated though not significant ($p=0.07$) in monocytes that were stimulated with the secretome from the IL-4 group compared to the unstimulated CD8+ T-cells. No differences were found in expression of F4/80 ($p=0.532$) or M1 marker CD86 ($p=0.471$). The secretome of IL-4 stimulated T-cells increased monocyte migration after wounding similar to levels of the positive control. In summary, IL-4 stimulation activated memory-like CD8+ T-cells which in turn initiated monocyte migration but decreased monocyte viability indicating a regulatory role in macrophage biology post-MI.

This work was supported by The NIH HL145817 and T32GM132055, the AHA Innovator Project IPA35260039, the Biomedical Laboratory Research and Development Service of the VA Office of Research and Development Award IK2BX003922

198 **Trends in the Utilization of Implants in Index Procedures for Early Onset Scoliosis from the Pediatric Spine Study Group**

Maxwell Marshall, Robert Murphy, Garrett Neel, William Barfield, Jason Anari, Tricia St. Hilaire, George Thompson, John Emans, Behrooz Akbarnia, John Smith, James Mooney, Department of Orthopaedics and Physical Medicine, College of Medicine, MUSC

Introduction: Due to the rarity and complexity of Early Onset Scoliosis (EOS) cases, patient registries were developed to combine clinical information from multiple institutions to maximize patient care and outcomes. This study examines the history and trends regarding the use of index growth friendly devices for EOS from the Pediatric Spine Study Group (PSSG). Methods: All index

growth-friendly implants were queried from registry inception until October 2020. Scoliosis etiology, device/implant type, and geographic area/institution at which the procedure took place were recorded. Results: From 1994 to 2020, 2786 patients underwent index growth friendly surgery at a mean age of 6.2±2.9 years. EOS etiology was heterogeneous (513 idiopathic, 718 congenital, 621 syndromic, 915 neuromuscular). There were 908 Traditional Growing Rods (TGR) (32.3%), 922 Vertical Expandable Prosthetic Titanium Rib devices (VEPTR) (33.1%), 5 hybrid VEPTR/TGR (0.18%) and 951 Magnetically Controlled Growing Rods (MCGR) (34.2%) implanted across 56 different institutions during that time period. Comparing 1994 (3 TGR implants) to 2020 (80 total implants, 12 TGR, 6 VEPTR, 66 MCGR), there was a 2566% increase in index implant insertions annually ($p = .0001$). In 2009 the initial MCGR was added to the registry as a growth friendly implant, and implantation has increased 6500% to the number entered in 2020 (1 in 2009, and 66 in 2020, $p = .0001$). MCGR has now surpassed both TGR and VEPTR as the most common growth friendly implant (127 index TGR and VEPTR procedures combined in 2008 compared with a total of 14 TGR and VEPTR combined in 2020 (89% decrease, $p = 0.0001$). Discussion: The number of growth friendly implants reported in the registry as part of the initial surgical management of EOS has increased tremendously over the past 20 years. The MCGR is currently the predominant type of device utilized for index surgical procedures by group members, surpassing the use of VEPTR and TGR in 2014.

199 **Analysis of secondary behavioral outcomes in patients undergoing tDCS and CBT for pain and opioid misuse**

Abagail Ault, Jeffrey Borckardt, Barth Kelly, Brady Kathleen, Flanagan Julianne, George Mark, Goble Layne, McCauley Jenna, Santa-Ana Elizabeth, Treiber Frank, Wilkerson Allison, Balliet Wendy, Bottonari Kathryn, Carter Lauren, Christon Arnold Lillian, Mappin Georgia, Muzzy Wendy, Wedin Sharlene, Wolf Juila, Anjinetta Yates-Johnson, Wedin Sharlene, Department of Psychiatry, College of Medicine, MUSC

One of the limitations of tDCS is the difficulty in localizing currents and subsequent difficulty of predicting behavioral outcomes of a particular electrode placement. This project attempts to address this limitation by analyzing behavioral outcomes on a study population undergoing tDCS over the dorsolateral prefrontal cortex (DLPFC) by analyzing longitudinal change in four other behavioral outcomes associated with the target brain region. A series of repeated measures factorial ANOVAs were run on data taken from 73 participants who were randomized to receive either real (N=44) or sham (N=29) tDCS paired with Cognitive Behavioral Therapy (CBT) weekly for 11 weeks. All analyses were conducted with group assignment as a between subjects factor and time as a within subjects factor, and yielded that the main effect of time was significant for anxiety ($F=6.122$, $p=.016$), depression ($F=6.762$, $p=.011$), pain catastrophizing ($F=30.782$, $p<0.000$), and sleep ($F=17.820$, $p<0.000$). However, no significant interaction was found between time and group assignment, suggesting that while the CBT treatment showed significant improvements in these non-target behavioral outcomes, those improvements were not significantly aided by the addition of tDCS. This is despite previous analyses of these data yielding significant improvement of the target variable in the group that received real tDCS over the group that received sham tDCS.

This work was supported by NIH NIDA

200 **Does Oral N-Acetylcysteine with taVNS-Paired Bottle Feeding Lead to Increased Feeding Volumes in Infants with Diabetic Mothers?**

Sarah Huffman, Dorothea Jenkins, Morgan Dancy, Bashar Badran, Mark S. George, Department of Brain Stimulation Lab, College of Medicine, MUSC

Preterm infants and infants with hypoxic ischemic encephalopathy (HIE) are at high risk for motor dysfunction due to brain injury and have difficulty learning the complex motor sequence of feeding. In the parent study of transcutaneous auricular VNS (taVNS)-paired with bottle feeding in neonates failing oral feeds, we found that none of the 8 infants of diabetic mothers (IDM) exposed to poor glucose control during pregnancy attained full oral feeds. Hyperglycemia-induced CNS oxidative stress was present in these infants by MR spectroscopy and predicted the ability to learn to feed with taVNS treatment. N-acetylcysteine (NAC) is an FDA-approved antioxidant that is safe in neonates, boosts CNS glutathione, and may facilitate taVNS-induced plasticity and motor learning by normalizing intracellular redox state. We administered NAC by nasogastric tube to achieve steady state for 4 days before starting NAC with taVNS-paired feeding for 10 days. Outcome measures are 1) increase in daily oral feeding volumes over 10d, before and during NAC+taVNS; 2) NAC plasma PK 3) MRS glutathione before and after treatment. We enrolled 2 IDM exposed to poor glucose control at 40.7 weeks gestational age. Baby A's mother was on insulin at birth (33 weeks) and had active COVID pneumonia. Baby B's mother (34 weeks) had Hgb A1c of 10.4% at birth. Both infants achieved full oral feeds within 7-10 days. Baby A increased from mean 45ml/kg/d over 10d before treatment to 93ml/kg/d during NAC+taVNS. Baby B increased from mean 71ml/kg/d over 7 days before treatment to 99ml/kg/d during treatment. This early data suggests that NAC with taVNS-paired bottle-feeding may increase oral daily feeding volumes in IDM infants.

This work was supported by NC NM4R NICHD NIH P2CHD086844; COBRE P20 GM109040

201 **The IGF II-mediated fibrotic pathway proceeds through the IGF1R/IR hybrid receptor to induce SOX9, EGR1, and NEDD9 in primary human lung fibroblasts.**

Kristy Waldrep, Carol Feghali-Bostwick, Jessalyn Rodgers, Sara M. Garrett, Steven A. Rosenzweig, College of Medicine, MUSC

Systemic sclerosis (SSc)-associated pulmonary fibrosis is characterized by excessive production of the extracellular matrix (ECM). SSc results in high morbidity and mortality with lung disease being the primary cause of death. Type 2 insulin-like growth factor (IGF-II) is overexpressed in tissues and fibroblasts derived from SSc lungs. We previously reported that IGF-II mediates pulmonary fibrosis by activating fibroblasts into myofibroblasts, altering the TIMP:MMP ratio, and inducing transforming growth factor beta (TGFb). Our goal was to characterize the mechanism by which IGF-II promotes a fibrotic phenotype. We stimulated primary human lung fibroblasts from normal donors (NLs) with recombinant IGF-II and investigated the receptors and downstream factors that mediate its response. We show that IGF-II signals via the IGF1R/IR hybrid receptor to promote fibrosis. Furthermore, IGF-II significantly increases gene and protein expression of transcription factors sex-determining region Y box 9 protein (Sox9) and early growth response 1 (Egr1). Accordingly, we report significant induction of Sox9 protein in the cytoplasm and nucleus of NLs after IGF-II treatment. Similarly, protein levels of full-size Egr1 and its splicing isoform increase in the cytoplasmic and chromatin-bound fractions of NLs. In tumor cells, Sox9 regulates NEDD9/HEF1/Cas-L, a scaffolding protein that modulates protein-protein interactions in cell signaling pathways. IGF-II increased NEDD9 protein levels with subcellular localization unique to

the different isoforms. Increases in NEDD9 total levels were paralleled by increased phosphorylation. Furthermore, IGF-II increased fibronectin 1 (FN1), collagen 1, and collagen 3, and decreased matrix metalloproteinase-1, a collagenase that degrades the ECM, thus promoting a pro-fibrotic environment. In summary, our findings suggest that IGF-II induction of fibrosis is mediated through the IGF1R/IR hybrid receptor, and is characterized by increased Sox9, Egr1, and NEDD9 as well as increased ECM components and decreased ECM degradation, thus tipping the balance in favor of fibrosis.

This work was supported by This work was supported by R01 HL153195 from NIH/NHLBI.

202 **Critical functions of a novel iron sulfur cluster transfer protein in genome replication and metabolism during cell division.**

Samuel Wood, Kyu-Ho Lee, Shasha Lin, William Harris, Kimberly K. Sutton, Wenjian Gan, College of Medicine, MUSC

Iron-sulfur clusters perform an important role as redox-reactive prosthetic groups for enzymes regulating both metabolism and DNA replication. Mature iron-sulfur clusters are transferred to extramitochondrial client proteins via the cytoplasmic iron-sulfur assembly (CIA) targeting complex, consisting of MMS19, CIA2B, and CIA01. We recently identified the, Coiled-coil Domain Containing protein 117 (CCDC117) as an additional member of this complex: co-immunoprecipitation and western blot analysis demonstrated that CCDC117 directly interacted with CIA2B via the C- and N-termini of CCDC117. Functionally, cellular depletion of CCDC117 resulted in an increase in DNA damage, decreased rates of DNA synthesis, and apparent cell cycle delay at the G1/S checkpoint, supporting the hypothesized role of CCDC117 as a mediator of iron-sulfur cluster delivery to CIA targets regulating genome replication and repair. Iron-sulfur clusters also regulate bioenergetic metabolism by facilitating redox reactions in the electron transport chain. These clusters are delivered to mitochondrial cytochrome proteins via the ostensibly independent and mitochondrial-specific iron sulfur cluster (ISC) pathway. Interestingly, Agilent Seahorse assays confirmed not only preserved mitochondrial respiration in cells depleted of CCDC117 protein relative to controls, but an significant increase in both oxygen consumption and ATP production, indicating elevated levels of oxidative phosphorylation. This was not apparently due to wholesale shifts in cellular uptake or mitochondrial compartmentalization of iron. Instead, a transcriptional upregulation of key genes involved in fatty acid synthesis was observed, coupled with an increase in cellular fat accumulation as measured by Oil Red O lipid staining. These studies implicate CCDC117 as a multi-faceted regulator of cell proliferation and oxidative metabolism via its role in the targeted delivery of iron sulfur clusters.

This work was supported by Saving Tiny Hearts Society, South Carolina COBRE in Oxidants, Redox Balance and Stress Signaling (P20GM103542)

203 **Negative Affect and the Approach Avoidance Task: Electrocortical Evidence of Conflict Resolution**

James Lopez, Christopher Sege, Holly H. Fleischmann, Lisa M. McTeague, Department of Psychiatry, College of Medicine, MUSC

Electrocortical correlates of approach/avoidance processing have been examined in healthy and psychiatric samples with an Approach-Avoidance Task (AAT) in which participants use a joystick. While AAT event-related potential (ERP) work has putatively tested effects of emotion on N200 (conflict resolution) and LPP (picture processing) components (e.g. Ernst et al., 2013), it, to date, typically has used only disorder-relevant (as opposed to generally emotional) images in psychiatric samples and/or has not included neutral stimuli. Here, then, we tested how emotional arousal impacts AAT ERPs in healthy and clinically anxious individuals using generally unpleasant, pleasant, and neutral pictures. 17 anxious treatment-seekers and 18 controls completed an AAT in which each trial presented an unpleasant, pleasant, or neutral scene with a blue or green border that signaled whether participants should rapidly push or pull a joystick to decrease or increase image size. Using 32 active sensors, a frontal N200 component was found to have decreased amplitude during emotional compared to neutral push trials and increased amplitude during emotional compared to neutral pull trials, Valence X Response $F(2,32)=15.9$, $p<.001$. For a parietal LPP, amplitude was enhanced for unpleasant compared to neutral images regardless of response condition, Valence $F(2,32)=7.7$, $p=.004$. For both components, clinical status did not moderate any effect. Together, then, effects suggest general emotional arousal effects on approach/avoidance response processing (N200) that are not impacted by clinical anxiety.

This work was supported by MUSC Department of Psychiatry Chair's Research Development Fund (CRDF