Perry V Halushka
55th Annual Research Day 2020

MUSC
MEDICAL UNIVERSITY OF SOUTH CAROLINA

Poster and Oral Presentation Program

POSTER PRESENTATIONS

9:00 am - 10:30 am		Abstracts	Webex link
Session 1:	Undergraduate	01-04	Session 1 link
Session 2:	Clinical / Professional / Masters – I	05-09	Session 2 link
Session 3:	Clinical / Professional / Masters – II	10-15	Session 3 link
Session 4:	Clinical / Professional / Masters – III	16-21	Session 4 link
Session 5:	PhD – I	22-27	Session 5 link
Session 6:	PhD – II	28-33	Session 6 link
Session 7:	PhD – III	34-39	Session 7 link
Session 8:	Postdoc / Resident / Fellow / Staff Scientist	40-45	Session 8 link
Session 9:	Research Specialist / Technician	46-51	Session 9 link

ORAL PRESENTATIONS

1:00 pm - 2:30 pm		Abstracts	Webex link
Session 10:	Clinical / Professional / Masters – I	052-057	Session 10 link
Session 11:	Clinical / Professional / Masters – II	058-063	Session 11 link
Session 12:	PhD - I	064-069	Session 12 link
Session 13:	PhD – II/III	070-075	Session 13 link
Session 14:	PhD – IV/V	076-081	Session 14 link
Session 15:	Postdoc / Resident / Fellow / Staff Scientist	082-087	Session 15 link
Session 16:	Research Specialist / Technician	088-093	Session 16 link

SPECIAL AWARD SESSIONS

11:00 am - 12:30 pm		Webex link
Sigma Xi:	Poster & Oral	Sigma Xi link
Interprofessional:	Poster	Interprofessional - poster
Interprofessional:	Oral	Interprofessional - oral
Ralph H Johnson VA Medical Center:	Poster	VA - poster
Ralph H Johnson VA Medical Center:	Oral	VA - oral
John Vournakis Innovation:	Poster & Oral	Innovation link
Health Humanities:	Poster & Oral	Health Humanities link
Center on Aging:	Poster	Aging - poster
Center on Aging:	Oral	Aging - oral

Session 1	Undergraduate	POSTER

9:00 – 9:08 AM

1 High-fat diet impairs tactile discrimination memory and leads to problem solving deficits

Tyler Stone, Luke Watson, Alexus Williams, Catrina Robinson, College of Graduate Studies, Department of Neurology, MUSC.

9:10 – 9:18 AM

2 Changes in Adolescent HIV Knowledge Following a Prevention Intervention

Declan Sykes, Nada M. Goodrum, Angela D. Moreland, April Borkman, Alyssa Rheingold, Carla Kmett Danielson, College of Medicine, Department of Department of Psychiatry and Behavioral Sciences, MUSC.

9:20 – 9:28 AM

3 Does Medication Reduce Alcohol Experimentation in Preadolescents with Attention-Deficit/Hyperactivity Disorder?

Briana Hunt, Alexis M. Garcia, Ph.D., Brittany N. McKenzie, B.S., Rachel L. Tomko, Ph.D., Brittany E. Bryant, D.S.W, Lindsay Squeglia, College of Medicine, Department of Psychiatry and Behavioral Sciences, MUSC.

9:30 – 9:38 AM

4 Severity of Cannabis Use Disorder and Perceived Problems Due to Use in Adolescents with and without Depression or Anxiety

Jenny Nankoua, Jade Tuttle, Erin McClure, Lindsay Squeglia, Kevin Gray, Rachel Tomko, College of Medicine, Department of Psychiatry and Behavioral Sciences, MUSC.

Session 2	Clinical / Professional / Masters I	POSTER

9:00 – 9:08 AM

5 AGE:RAGE Signaling Pathway as a Target in Neuroendocrine Prostate Cancer

DeMarcus Woolfork, Bradley A Krisanits, Arabia Satterwhite, Lourdes M Nogueira, Ashley Evans-Knowell, David P Turner and Victoria J Findlay, Victoria Findlay, College of Graduate Studies, Department of Pathology and Laboratory Medicine, MUSC.

9:10 – 9:18 AM

6 Functional importance of renal histamine receptors and their signaling in the collecting ducts

Mikhail Fomin, Anastasia Sudarikova, Ying Zhao, Morgan Spicer, Regina Sultanova, Mark Domondon, Daria Ilatovskaya, College of Graduate Studies, Department of Department of Medicine/Nephrology, MUSC.

9:20 – 9:28 AM

7 Cause and Effect Relationships Between Glycation and the Ancestry Specific Tumor Stroma

Courtney Lloyd, Bradley A. Krisanits, Pamela Woods, Dion Foster, Lourdes M. Nogueira, Bria Sanders, Laura Spruill, Marvella E. Ford, Mahtabbudin Ahmed, Victoria J. Findlayand David P. Turner, David Turner, College of Graduate Studies, Department of Pathology, MUSC.

9:30 – 9:38 AM

8 Combining Transcutaneous Auricular Vagus Nerve Stimulation (taVNS) with Transcranial Magnetic Stimulation (TMS) to Enhance Cortical Excitability

Alex Kahn, Sean Thompson, Bashar Badran, College of Graduate Studies, Department of Institute of Psychiatry, MUSC.

9:40 – 9:48 AM

9 Unna Boots and Dermatologic Disease: A retrospective review

Gabriella Santa Lucia, Alan Synder, John Plante, Alexandra Ritter, Dr. Dirk Elston, College of Graduate Studies, Department of dermatology, MUSC.

Session 3	Clinical / Professional / Masters II	POSTER

9:00 – 9:08 AM

10 Neural reactivity in response to alcohol and trauma cues with depression severity as a moderator in patients with comorbid alcohol use disorder and posttraumatic stress disorder

Zahraa Atoui, Jane E. Joseph, Laura Lohnes, Kevin Gray, Elizabeth Santa Ana, Sudie E. Back, Amber Jarnecke, College of Medicine (MD, PhD), Department of Department of Psychiatry and Behavioural Sciences, MUSC.

9:10 – 9:18 AM

11 Interleukin-6 is necessary but not sufficient for abdominal aortic aneurysm development

Raj Patel Patel, SarahRose Hall, Nicholas Ward, Hayes Lanford, Tyler Grespin, Rupak Mukherjee, Jeffrey Jones, Jean Marie Ruddy, Jean Ruddy, College of Medicine, Department of Vascular Surgery, MUSC.

9:20 – 9:28 AM

12 Neuroanatomical networks associated with associative and taxonomic semantic errors during speech production in individuals with post-stroke aphasia.

Jesse Varkey, , Leonardo Bonilha, College of Medicine, Department of Neurology, MUSC.

9:30 – 9:38 AM

13 Impact of Maternal and Child Vitamin D Supplementation during Lactation on Acute Infection: a Randomized Controlled Trial

Kari VanEvery, MPH, RD, John E. Baatz, Judith Shary, Myla D. Ebling, Carol Wagner, College of Medicine, Department of Neonatology, MUSC.

9:40 – 9:48 AM

14 A Novel Perfusate to Preserve Vascular Mechanical Capacity

Devin Mahon, Raj Patel, SarahRose Hall, Rupak Mukherjee, Demetri Spyropoulos, Jean Ruddy, College of Medicine, Department of Surgery, MUSC.

9:50 – 9:58 AM

15 Differences in Bone Mineral Content and Bone Mineral Density of Infants Receiving Direct vs. Indirect Vitamin D Supplementation: A Randomized Controlled Lactation Study

Laura Andrews, Kristen Phlegar, Judith Shary, Myla Ebeling, John Baatz, Carol Wagner, College of Medicine, Department of Department of Neonatology, MUSC.

Session 4	Clinical / Professional / Masters III	POSTER

9:00 – 9:08 AM

16 Nursing swallow screens for cervical spine surgery patients: A systematic review

Janet Horn, Teri Lynn Herbert, Heather Bonilha, College of Health Professions, Department of Health Sciences and Research, MUSC.

9:10 – 9:18 AM

17 Creating an Efficient Training Program for a New Post-Stroke Rehabilitation Device

Laura Judy, Corey Morrow, MOT, OTR/L, Amanda Vatinno, MS, OTR/L, Amanda Giles, OTD, OTR/L, Jillian Harvey, PhD, and Emily Johnson, PhD, Na Jin Seo, College of Health Professions, Department of Department of Health Professions, MUSC.

9:20 – 9:28 AM

18 Examining Racial Differences in Privilege and Social Class: Use of a Modified Privilege Walk to Promote Discussions on Racial Inequities

Aramis Gregory, Trevaris Morris, Elizabeth Brown, College of Health Professions, Department of Health Professions, MUSC.

9:30 – 9:38 AM

19 Maladaptive Reward Seeking Behavior Influenced by Changes in PVT to NAc Neurons After Heroin Use

Preston Siegler, Kelsey Vollmer, James Otis, College of Graduate Studies, Department of Neuroscience, MUSC.

9:40 – 9:48 AM

20 Non-invasive brain stimulation as a tool to decrease chronic pain in current opiate users: a parametric evaluation of two promising cortical targets

Julia Imperatore, Daniel M. McCalley, Jeffery J. Borckhardt, Kathleen T. Brady, Colleen Hanlon, College of Graduate Studies, Department of Psychiatry and Behavioral Sciences; Neurosciences, MUSC.

9:50 – 9:58 AM

21 Factor Analysis of a MUSC Telemedicine Provider Satisfaction Survey

Parker Rhoden, Jillian B. Harvey, MPH, PhD; James T. McElligott, MD, MSCR; Kit Simpson, DrPH;, Jillian Harvey, College of Health Professions, Department of Department of Healthcare Leadership and Management, MUSC.

Session 5	PhD I	POSTER

9:00 – 9:08 AM

22 Role of Porphyromonas gingivalis in Mediating Ceramide-dependent Mitophagy in Oral Squamous Cell Carcinoma

Megan Sheridan, Dr. Özlem Yilmaz, Dr. Nityananda Chowdhury, Besim Ogretmen, College of Graduate Studies, Department of Biochemistry and Molecular Biology, MUSC.

9:10 – 9:18 AM

23 Design, synthesis, and validation of CD38 inhibitors as immuno-therapeutics against cancer

Thomas Benton, Catherine Mills Pieter Burger Yuri Peterson Patrick Woster, Patrick Woster, College of Graduate Studies, Department of Drug Discovery, MUSC.

9:20 – 9:28 AM

24 Role of IFNLR1 Receptor Dynamics and Plasticity in Regulating Cellular Response to Type-III Interferons

John Evans, Christiana S. Kappler, Ray Liu, Juliana D. Carten, Cody M. Orr, Sarah Stephenson, Paula Traktman, Stephen A. Duncan, Eric G. Meissner, Eric Meissner, College of Medicine (MD, PhD), Department of Medicine, MUSC.

9:30 – 9:38 AM

25 CD26 defines responsiveness to neoadjuvant checkpoint blockade

Hannah Knochelmann, Amalia Rivera-Reyes, Joshua Horton, Michael Bobian, Megan Wyatt, Carsten Krieg, Kent Armeson, Mark Rubinstein, Dongjun Chung, Chrystal Paulos, David Neskey, College of Graduate Studies (MSTP), Department of Otolaryngology -- Head and Neck Surgery, MUSC.

9:40 – 9:48 AM

26 Cell Type-specific Expression of Npas4 is Required for Cocaine-reinforced Learning and Memory

Brandon Hughes, Makoto Taniguchi, Christopher Cowan, College of Graduate Studies, Department of Neuroscience, MUSC.

9:50 – 9:58 AM

27 Targeting Mitochondria as an Adjuvant Therapy for Cisplatin-Resistant Ovarian Cancer

Zachary Hough, Gyda Beeson, Robin Muise-Helmericks, College of Graduate Studies, Department of Department of Regenerative Medicine, MUSC.

Session 6	PhD II	POSTER

9:00 – 9:08 AM

28 Cardiomyocyte death and fibrotic scarring in the infarcted neonatal mouse heart

Mary Mohr, Shuang Li, Patrick Roddy, Ge Tao, College of Graduate Studies, Department of Regenerative Medicine, MUSC.

9:10 – 9:18 AM

29 Transcriptomic analysis of engineered, multicellular cardiac organoids reveals similarities to human myocardium

Charles Kerr, Dylan Richards, Ying Mei, Ying Mei, College of Graduate Studies, Department of Department of Regenerative Medicine and Cell Biology, MUSC.

9:20 – 9:28 AM

30 Tau-spiracy: A Developing Mechanism for Cardiac Dysfunction

Stephanie DiLucia, Rakez Kayed, Anna Ellsworth, Federica del Monte, College of Medicine (MD, PhD), Department of Department of Medicine, Division of Cardiology, MUSC.

9:30 – 9:38 AM

31 Evaluating the Influence of Individual Cerebral Architecture and Alcohol Cue-Reactivity Patterns on AUD Treatment Outcome

Daniel McCalley, Julia P. Imperatore, Ingrid E. Contreras, Colleen Hanlon, College of Graduate Studies, Department of Psychiatry and Behavioral Sciences; Neurosciences, MUSC.

9:40 – 9:48 AM

32 Temporal Encoding of Cocaine Seeking and Refraining from Seeking in Different Neuronal Populations of the Nucleus Accumbens Core

Reda Chalhoub, Constanza Garcia-Keller, Rusty Nall, Jasper Heinsbroek, Ana-Clara Bobadilla, Peter Kalivas, College of Graduate Studies (MSTP), Department of Neuroscience, MUSC.

9:50 – 9:58 AM

33 Elucidating the Mechanism of PCBP1 Regulated Transcription at Cancer Gene Promoters

Joseph Karam, Bidyut Mohanty, Philip Howe, College of Graduate Studies, Department of Biochemistry and Molecular Biology, MUSC.

Session 7	PhD III	POSTER

9:00 – 9:08 AM

34 Metabolic requisites for T cell protein translation in tumors

Megan Tennant, Katie E. Hurst, Alex M. Andrews, Lee R. Leddy, David M. Neskey,, Lauren E. Ball, and Jessica E. Thaxton, Jessica Thaxton, College of Graduate Studies, Department of Orthopedics and Physical Medicine, Microbiology and Immunology, Hollings Cancer Center, MUSC.

9:10 – 9:18 AM

35 SPARC by Bone Marrow-Derived Cells Contributes to Myocardial Fibrosis in Pressure-Overload

Lily Neff, Hannah Riley, Ryan Kelly, An Van Laer, Shaoni Dasgupta, Catalin Baicu, Lindsay McDonald, Amanda LaRue, Michael Zile, Amy Bradshaw, College of Graduate Studies, Department of Cardiology, Division of (Dept. of Medicine), MUSC.

9:20 – 9:28 AM

36 ANP affects mitochondrial function in the renal cortex during salt-sensitive hypertension

Morgan Spicer, Regina Sultanova, Mark Domondon, Ryan Schibalski, Krisztian Stadler, Daria Ilatovskaya, Daria Ilatovskaya, College of Graduate Studies (MSTP), Department of Department of Medicine, Nephrology, MUSC.

9:30 – 9:38 AM

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

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

9:40 – 9:48 AM

38 Cell-targeted collagen imaging proteomics in breast cancer

Denys Rujchanarong, Michael C Ostrowski Ph.D., Peggi Angel, College of Graduate Studies, Department of Department of Pharmacology, MUSC.

9:50 – 9:58 AM

39 Triazole-based reversible inhibitors of spermine oxidase and implications for amelioration of neuronal injury

Amelia Furbish, Houston, Aubree, Patrick Woster, College of Graduate Studies, Department of Drug Discovery and Biomedical Sciences, MUSC.

Session 8	Postdoc / Resident / Fellow / Staff Scientist	POSTER

9:00 – 9:08 AM

40 Sex Differences in Cognitive and Psychological Outcomes of Stroke: Impact of Diabetes

Victoria Wolf, Aunay Miller, Raghavendar Chandran, Weiguo Li, Adviye Ergul, College of Graduate Studies, Department of Pathology & Laboratory Medicine, MUSC.

9:10 – 9:18 AM

41 Characterization of Human Temporomandibular Lateral Capsule-Ligament Complex Ultrastructure, Biochemistry and Biomechanics

Cherice Hill, Matthew Coombs, Daniel Bonthius, Sarah Cisewski, Marshall Wilson, Hai Yao, College of Dental Medicine, Department of Clemson-MUSC Bioengineering Program, Department of Oral Health Sciences, MUSC.

9:20 – 9:28 AM

42 Pain and Pain Catastrophizing as Predictors of Depression, Anxiety, and Opiate Misuse in Veterans and Veteran Family Members with Chronic Pain

Abagail Ault, Lester Shayla, Mappin Georgia, Santa Ana Elizabeth, Christon Lilian, Wedin Sharlene, Bottonari Kathryn, Balliet Wendy, Carter Lauren, Muzzy Wendy, McCauley Jenna, Imperatore Julia, George Mark, Jeffrey Borckardt, College of Medicine, Department of Psychiatry and Behavioral Sciences, MUSC.

9:30 – 9:38 AM

43 RAS inhibition limits neuroblastoma tumorigenesis and promotes Retinoic acid induced differentiation in a subset of NBL tumors

Vinodh Rajagopalan, , John O'Bryan, College of Graduate Studies, Department of Pharmacology, MUSC.

9:40 – 9:48 AM

44 Stabilization of Gap and Tight Junctions Ameliorates Ischemia-Reperfusion Injury in a Porcine Model of Renal Transplantation

Leah Plumblee, Jane Kilkenny, MD; Kunal Patel, MD PhD; Patterson Allen; Herman Connor; Logan Langerude BS; Domonique Rivers; Satish Nadig, MD PhD, Carl Atkinson, College of Graduate Studies, Department of Microbiology and Immunology, MUSC.

9:50 – 9:58 AM

45 Analytical methods for characterization of collagenous soft tissue

Glenn Hepfer, Peng Chen, Matthew Coombs, Hai Yao, College of Dental Medicine, Department of Oral Health Sciences, MUSC.

Session 9	Research Specialist / Technician	POSTER

9:00 – 9:08 AM

46 Serum and Glucocorticoid Inducible Kinase-1 Drives Aortic Macrophage Accumulation in Hypertension and Abdominal Aortic Aneurysms

SarahRose Hall, Tyler Grespin MS, Rupak Mukherjee PhD, Jeffrey A. Jones PhD, Jean Marie Ruddy, College of Medicine (MD, PhD), Department of Surgery, MUSC.

9:10 – 9:18 AM

47 The Role of ER-alpha in the Transcription of Pro-Fibrotic Mediators

Alisa Savchenko, Carol Feghali-Bostwick, DeAnna Baker Frost, College of Medicine, Department of Department Of Medicine, Division of Rheumatology, MUSC.

9:20 – 9:28 AM

48 Compensatory Gain at The Brainstem Represents Increased Neural Recruitment in the Face of Age-Related Declines in Neural Synchrony

Lilyana Kerouac, Brendan J. Balken, James W. Dias, Carolyn M. McClaskey, Kelly Harris, College of Medicine, Department of Otolaryngology - Head and Neck Surgery, MUSC.

9:30 – 9:38 AM

49 Sex differences in renal mitochondrial function of young healthy rats

Ryan Schibalski, Regina Sultanova, Mark Domondon, Allison McCrimmon, Krisztian Stadler, Daria Ilatovskaya, College of Medicine, Department of Medicine/Nephrology, MUSC.

9:40 – 9:48 AM

50 The Effects of Zero Gravity Parabolic Flight on Transcranial Magnetic Stimulation (TMS) Motor Threshold

Claire Cox, James W. Lopez, Holly H. Fleischmann, Kevin A. Caulfield, Jeffrey J. Borckardt, William H. DeVries, Philipp Summers, Suzanne Kerns, Colleen A. Hanlon, Lisa M. McTeague, Mark S. George, Bashar W. Badran, Donna Roberts, College of Medicine, Department of Radiology, MUSC.

9:50 – 9:58 AM

51 Effects of atrial natriuretic peptide on mitochondrial bioenergetics in cortical collecting duct cells

Thelma Amoah, Yuliia Kashyrina, Mark Domondon, Ryan Schibalski, Mikhail Fomin, Regina Sultanova, Daria Ilatovskaya, College of Graduate Studies, Department of Nephrology, Division of (Dept of Medicine), MUSC.

Session 10	Clinical / Professional / Masters I	ORAL

1:00 – 1:08 PM

52 Role of CTA Surveillance in Managment of Endovascular Repair of Aortic Dissection

Brandon Sloan, Anna Lena Emrich, M.D., Marc Katz, M.D., U. Joseph Schoepf, M.D., Tilman Emrich, M.D.,, Sanford Zeigler, College of Medicine, Department of Department of Surgery, MUSC.

1:10 – 1:18 PM

53 Sociodemographic Factors Affecting Perceived Stress During Pregnancy and the Impact on Immune-Mediator Concentrations

Caroline McLeod, Myla D. Ebeling RA, John E. Baatz PhD, Judy R. Shary MS, Jennifer R. Mulligan, PhD, Carol Wagner, College of Medicine, Department of Neonatology, MUSC.

1:20 – 1:28 PM

54 Plasma Sphingolipid Profiles Associated with Atherosclerosis in Systemic Lupus Erythematosus

Olivia Harden, Waleed Twal, Jim Oates, Samar Hammad, College of Medicine, Department of Regenerative Medicine and Cell Biology, MUSC.

1:30 – 1:38 PM

55 Commensal Gut Microbiota: A Novel Regulator of Craniofacial Skeletal Development

Joy Kirkpatrick, Naoto Ohkura, Nan Hatch, Chad Novince, College of Dental Medicine (DMD, PhD), Department of Oral Health Sciences, MUSC.

1:40 – 1:48 PM

56 Effectiveness and Safety of Maternal Vitamin D Supplementation on Fetal Bone Mineral Density and Content

Kristen Phlegar, Laura Andrews, Myla Ebling, John Baatz, Judith Shary, Carol Wagner, College of Medicine, Department of Neonatology, MUSC.

1:50 – 1:58 PM

57 Carbohydrate Binding Protein Galectin-3 and It's Role in Macrophage Activation and Chronic Cochlear Inflammation in Age Related Hearing Loss

Phillip Elvis, Junying Tan, Kenyaria Noble, Jeremy Barth, Hainan Lang, College of Medicine, Department of Pathology and Laboratory Medicine, MUSC.

Session 11	Clinical / Professional / Masters I	ORAL

1:00 – 1:08 PM

58 The Effect of Demographic, Stroke, and Clinical Characteristics on Neglect Severity Scores

Emerson Hart, Michelle Woodbury, Annie Simpson, Emily Grattan, College of Health Professions, Department of CHP OT & HRS, MUSC.

1:10 – 1:18 PM

59 Determining the Effects of TheraBracelet on Upper Extremity Deficits: Reaching vs Grasping

Allison Pennington, Amanda Vatinno, MS, OTR/L, Corey Morrow, MOT, OTR/L, Na Jin Seo, College of Health Professions, Department of Occupational Therapy, MUSC.

1:20 – 1:28 PM

60 Predicting Individual Post-Stroke Upper Extremity Motor Recovery Using EEG

Amanda Vatinno, Christian Schranz, PhD, Viswanathan Ramakrishnan, PhD, Leonardo Bonilha, MD, PhD, Na Jin Seo, College of Health Professions, Department of Occupational Therapy, MUSC.

1:30 – 1:38 PM

61 The Effect of Sensory Impairment Severity on TheraBracelet Efficacy

Jenna Blaschke, Amanda Vatinno, MS, OTR/L, Corey Morrow, MS, OTR/L, Na Jin Seo, College of Health Professions, Department of Occupational Therapy Department, MUSC.

1:40 – 1:48 PM

62 Can Noninvasive Brain Stimulation Improve Working Memory in Healthy Aging Adults? Insights from Electric Field Modeling

Kevin Caulfield, Aprinda Indahlastari, Nicole R. Nissim, James W. Lopez, Holly H. Fleischmann, Adam J. Woods, Mark George, College of Graduate Studies, Department of Psychiatry, MUSC.

1:50 – 1:58 PM

63 Heart Failure Symptom Clusters: An Integrative Review

Alexandra Ruppe, Gayenell Magwood, Sarah Miller, Alexandra Ruppe, College of Nursing, Department of College of Nursing, MUSC.

Session 12	PhD I	ORAL

1:00 – 1:08 PM

64 NF-κB mediates resistance to cell stressors in epithelial and hematological cancers but not rhabdomyosarcoma (RMS)

Alexander Oles, , Denis Guttridge, College of Graduate Studies (MSTP), Department of Pediatrics, MUSC.

1:10 – 1:18 PM

65 In Situ Intraepithelial Localizations of Opportunistic Pathogens, Porphyromonas gingivalis and Filifactor alocis, in Human Gingiva

Jaden Lee, Ralee Spooner, Nityananda Chowdhury, Bridgette Wellslager, Zachary Evans, Ozlem Yilmaz, College of Dental Medicine (DMD, PhD), Department of Department of Oral Health Sciences, MUSC.

1:20 – 1:28 PM

66 Targeting Mek/Erk Signaling in the Treatment of Mitral Valve Prolapse

Tyler Beck, , Russell Norris, College of Graduate Studies (MSTP), Department of Regenerative Medicine and Cell Biology, MUSC.

1:30 – 1:38 PM

67 PLEKHA7 is an intrinsically disordered protein that phase separates and binds RNAs at the adherens junctions of epithelial cells

Mary Bridges, Alyssa Risner, Valentina Ortega, Jensen Tomberlin, Kathleen Garrabrant, Joyce Nair-Menon, Antonis Kourtidis, College of Graduate Studies, Department of Regenerative Medicine and Cell Biology, MUSC.

1:40 – 1:48 PM

68 Let's Hang Out!: A Live Online Group Play Intervention Addressing Clinical Socialization Gaps for Adolescents with Autism Spectrum Disorder during the COVID-19 Pandemic

Melanie G. Wiley, Danielle W. Lowe, Erin M. Hopper, James S. Truelove, Jennifer A. Warthen, McLeod F. Gwynette, College of Medicine (MD, PhD), Department of Department of Psychiatry and Behavioral Sciences, MUSC.

1:50 – 1:58 PM

69 The Effect of Complement Inhibition on Neuroinflammmation after Traumatic Brain Injury - A High Throughput Analysis

Amer Toutonji, Silvia Guglietta, Mamatha Mandava, Carsten Krieg, Stephen Tomlinson, College of Medicine (MD, PhD), Department of Microbiology and Immunology, MUSC.

Session 13	PhD II / III	ORAL

1:00 – 1:08 PM

70 Mechanoregulation of the Adherens Junction - associated RNAi machinery through cross-talk with the Extracellular Matrix

Amanda Daulagala, John Yost, Amirreza Yeganegi, Catherine Bridges, Joyce Nair-Menon, William J. Richardson, Michael Yost., Antonis Kourtidis, College of Graduate Studies, Department of Regenerative Medicine and Cell Biology, MUSC.

1:10 – 1:18 PM

71 Physical Activity Negates the Oncogenic Effects of Lifestyle-associated Advanced Glycation End-Products

Bradley Krisanits, Pamela M. Woods, Lourdes M. Nogueira, Laura Spruill, Marvella E. Ford, Victoria J. Findlay, David Turner, College of Graduate Studies, Department of Pathology and Laboratory Medicine, MUSC.

1:20 – 1:28 PM

72 Brain microvascular insulin receptor dysfunction may underly increased risk for early onset dementia during obesity

Luke Watson, Guadalupe Sanchez, Alexus S. Williams, Taylor Lowry, Catrina Sims-Robinson, College of Graduate Studies, Department of Neurology, MUSC.

1:30 – 1:38 PM

73 STAT3 in Cancer-Associated Fibroblasts Promotes an Immunosuppressive Tumor Microenvironment in PDAC

Julia Lefler, Katie MarElia, Blake E. Hildreth III, Katie A. Thies, Maria C. Cuitino, Michael Ostrowski, College of Graduate Studies, Department of Biochemistry and Molecular Biology, MUSC.

1:40 – 1:48 PM

74 Identification of a novel potential therapeutic target for liver fibrosis

Nour Hijazi, Zengdun Shi, Don Rockey, College of Graduate Studies (MSTP), Department of Medicine, MUSC.

1:50 – 1:58 PM

75 Delayed treatment with a site-targeted complement inhibitor reduces cognitive deficits following traumatic brain injury

Davis Borucki, Khalil Mallah, Christine Couch, Wenxue Wang, Shahid Husain, Baerbel Rohrer, Stephen Tomlinson, College of Graduate Studies (MSTP), Department of Microbiology & Immunology, MUSC.

Session 14	PhD IV / V	ORAL

1:00 – 1:08 PM

76 Induction of fibrosis in lung tissues and fibroblasts results in decreased free anti-fibrotic proteins with a corresponding increased packaging in extracellular vesicles.

Joe Mouawad, , Carol Feghali-Bostwick, College of Medicine (MD, PhD), Department of Professor, MUSC.

1:10 – 1:18 PM

77 The design and synthesis of immunomodulatory CD38-PROTAC molecules for the treatment of neuroblastoma

Catherine Mills, Thomas Benton, Pieter Burger, Yuri Peterson, Patrick Woster, College of Graduate Studies, Department of Drug Discovery and Biomedical Sciences/Pharmacy, MUSC.

1:20 – 1:28 PM

78 Reactive oxygen species regulate HDAC5 function: implications for drug addiction

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

1:30 – 1:38 PM

79 Minocycline-Induced Dysbiosis of Gut Microbiota Disrupts Metabolism and Post-Pubertal Skeletal Development

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

1:40 – 1:48 PM

80 Myocardial Fibrosis in Mitral Valve Prolapse

Cortney Gensemer, Reece Moore, Kelsey Moore, Lilong Guo, Tyler Beck, Christina Wang, Diana Fulmer, Russell Norris, College of Graduate Studies, Department of MCBP Regenerative Medicine, MUSC.

1:50 – 1:58 PM

81 Transcranial Magnetic Stimulation's Effects on Cognitive Function Measured Through the WinSCAT

Mary McElveen, Donna Roberts, College of Medicine (MD, PhD), Department of Radiology, MUSC.

Session 15	Postdoc / Resident / Fellow / Staff Scientist	ORAL

1:00 – 1:08 PM

82 Commensal Oral Microbiota Promotes Osteoimmune Response Effects that are Distinct from the Systemic Microbiota

Jessica Hathaway-Schrader, Johannes D. Aartun, Nicole Poulides, Megan Kuhn, Blakely Graham, Michael Chew, Emily Huang, Richard P. Darveau, Caroline Westwater, Chad Novince, College of Dental Medicine, Department of Oral Health Sciences, MUSC.

1:10 – 1:18 PM

83 Age-related loss of activity of low-spontaneous-rate auditory nerve fibers in humans

Carolyn McClaskey, James W. Dias, Richard A. Schmiedt, Judy R. Dubno, Kelly Harris, College of Medicine, Department of Otolaryngology - Head & Neck Surgery, MUSC.

1:20 – 1:28 PM

84 Neural re-organization after upper extremity rehabilitation therapy with sensory stimulation in chronic stroke survivors

Christian Schranz, Amanda Vatinno, Viswanathan Ramakrishnan, Na Jin Seo, College of Health Professions, Department of Health Profressions, MUSC.

1:30 – 1:38 PM

85 Age dependent effects of yeast derived complex dietary polysaccharide on gut microbiota composition, autoimmunity and type 1 diabetes incidence in non-obese diabetic mice

Harrison Taylor, , Chenthamarakshan Vasu, College of Medicine (MD, PhD), Department of Microbiology and Immunology, MUSC.

1:40 – 1:48 PM

86 Site-targeted complement inhibition halts progressive motor decline in a murine model of Amyotrophic Lateral Sclerosis (ALS)

Khalil Mallah, Davis M. Borucki, Marcelo Vargas, Stephen Tomlinson, College of Graduate Studies, Department of Microbiology and Immunology, MUSC.

1:50 – 1:58 PM

87 Complement Activation Contributes to Hydrocephalus Development following Germinal Matrix Hemorrhage

Mohammed Alshareef, Khalil Mallah, PhD; Ramin Eskandari, MD, MS, Stephen Tomlinson, College of Medicine, Department of Microbiology and Immunology, MUSC.

Session 16	Research Specialist / Technician	ORAL

1:00 – 1:08 PM

88 Antibiotic Disruption of the Indigenous Oral Microbiota has Catabolic Effects on Alveolar Bone

Amy Warner, Brooks A. Swanson, Jessica D. Hathaway-Schrader, Matthew D. Carson, Joy E. Kirkpatrick, Alexander V. Aleksenyenko, Caroline Westwater, J. Ignacio Aguirre, Chad Novince, College of Dental Medicine, Department of Oral Health Sciences, MUSC.

1:10 – 1:18 PM

89 Insulin and its effects on relative cerebral blood flow and cognition

Guadalupe Sanchez, , Catrina Robinson, College of Graduate Studies, Department of Neurology, MUSC.

1:20 – 1:28 PM

90 Physiological effects of ranitidine on renal function in salt-sensitive hypertension

Mark Domondon, Ryan Schibalski, Thelma Amoah, Mikhail Fomin, Tengis S. Pavlov, Sergey Arkhipov, Daria Ilatovskaya, College of Medicine, Department of Department of Medicine / Nephrology, MUSC.

1:30 – 1:38 PM

91 Emotional Activation and Attention During Avoidance and Escape Preparation: Parallel or Distinct Processes?

James Lopez, Holly H. Fleischmann, Lisa M. McTeague, Christopher Sege, College of Medicine (MD, PhD), Department of Sleep and Anxiety Division, MUSC.

1:40 – 1:48 PM

92 Transcutaneous Auricular Neurostimulation (tAN): a non-pharmacological adjuvant treatment in neonates suffering from opioid withdrawal

Georgia O'Leary, Naivd Khodaparast, PhD, Stephanie Washburn, Alejandro Covalin, PhD, Bashar W. Badran, PhD, Dorothea Jenkins, College of Medicine, Department of Pediatrics, MUSC.

1:50 – 1:58 PM

93 Does a pandemic bias all outcomes in ongoing depression treatment trials?

Sarah Huffman, Morgan Dancy, Xingbao Li, Truman Brown, Mark George, College of Medicine, Department of Psychiatry Brain Stimulation Lab, MUSC.

Special Session	Sigma Xi

11:00 – 11:08 AM Oral

55 Commensal Gut Microbiota: A Novel Regulator of Craniofacial Skeletal Development

Joy Kirkpatrick, Naoto Ohkura, Nan Hatch, Chad Novince, College of Dental Medicine (DMD, PhD), Department of Oral Health Sciences, MUSC.

11:10 – 11:18 AM Poster

39 Triazole-based reversible inhibitors of spermine oxidase and implications for amelioration of neuronal injury

Amelia Furbish, Houston, Aubree, Patrick Woster, College of Graduate Studies, Department of Drug Discovery and Biomedical Sciences, MUSC.

11:20 – 11:28 AM Poster

23 Design, synthesis, and validation of CD38 inhibitors as immuno-therapeutics against cancer

Thomas Benton, Catherine Mills Pieter Burger Yuri Peterson Patrick Woster, Patrick Woster, College of Graduate Studies, Department of Drug Discovery, MUSC.

11:30 – 11:38 AM Poster

26 Cell Type-specific Expression of Npas4 is Required for Cocaine-reinforced Learning and Memory

Brandon Hughes, Makoto Taniguchi, Christopher Cowan, College of Graduate Studies, Department of Neuroscience, MUSC.

11:40 – 11:48 AM Poster

2 Targeting Mitochondria as an Adjuvant Therapy for Cisplatin-Resistant Ovarian Cancer

Zachary Hough, Gyda Beeson, Robin Muise-Helmericks, College of Graduate Studies, Department of Department of Regenerative Medicine, MUSC.

Special Session	Interprofessional	POSTER

11:00 – 11:08 AM

98 First in-neonate use of non-invasive transcutaneous auricular vagus nerve stimulation: 18 months neurodevelopment and sensory follow up.

Turki Aljuhani, Patty, Coker-Bolt, Dorothea Jenkins, College of Health Professions, Department of College of Medicine, MUSC.

11:10 – 11:18 AM

14 A Novel Perfusate to Preserve Vascular Mechanical Capacity

Devin Mahon, Raj Patel, SarahRose Hall, Rupak Mukherjee, Demetri Spyropoulos, Jean Ruddy, College of Medicine, Department of Surgery, MUSC.

11:20 – 11:28 AM

97 HGF-induced activation of Nephrin and Neph1 serves as a novel mechanism for recovery of podocytes from injury

Ashish Solanki, Pankaj Srivastava, Ehtesham Arif, Christopher M. Furcht, Bushra Rahman, Pei Wen, Avinash Singh, Lawrence B Holzman, Wayne R. Fitzgibbon, Glenn Lobo, Joshua H. Lipschutz, Sang-Ho Kwon, Zhe Han, Matthew J Lazzara, Deepak Nihalani, College of Medicine, Department of Medicine, MUSC.

11:30 – 11:38 AM

21 Factor Analysis of a MUSC Telemedicine Provider Satisfaction Survey

Parker Rhoden, Jillian B. Harvey, MPH, PhD; James T. McElligott, MD, MSCR; Kit Simpson, DrPH;, Jillian Harvey, College of Health Professions, Department of Department of Healthcare Leadership and Management, MUSC.

Special Session	Interprofessional	ORAL

11:00 – 11:08 AM

102 Effect of hyperthermia method on drug delivery with thermosensitive liposomes

Krishna Ramajayam, A.Marissa Wolfe, Anjan Motamarry, Georges Nahas, John Yost, Mike Yost, Dieter Haemmerich, College of Medicine, Department of Pediatrics, MUSC.

11:10 – 11:18 AM

103 Feeding and Swallowing Disorders in Preterm Infants: Who Receives Early Feeding Interventions after Hospital Discharge?

Brooke Mulrenin, Megan Richmond, Annie Simpson, College of Health Professions, Department of Department of Health Care Leadership and Management; Department of Health Sciences and Research, MUSC.

11:20 – 11:28 AM

60 Predicting Individual Post-Stroke Upper Extremity Motor Recovery Using EEG

Amanda Vatinno, Christian Schranz, PhD, Viswanathan Ramakrishnan, PhD, Leonardo Bonilha, MD, PhD, Na Jin Seo, College of Health Professions, Department of Occupational Therapy, MUSC.

11:30 – 11:38 AM

93 Does a pandemic bias all outcomes in ongoing depression treatment trials?

Sarah Huffman, Morgan Dancy, Xingbao Li, Truman Brown, Mark George, College of Medicine, Department of Psychiatry Brain Stimulation Lab, MUSC.

11:40 – 11:48 AM

62 Can Noninvasive Brain Stimulation Improve Working Memory in Healthy Aging Adults? Insights from Electric Field Modeling

Kevin Caulfield, Aprinda Indahlastari, Nicole R. Nissim, James W. Lopez, Holly H. Fleischmann, Adam J. Woods, Mark George, College of Graduate Studies, Department of Psychiatry, MUSC.

Special Session	Ralph H Johnson VA Medical Center	POSTER

11:00 – 11:08 AM

105 Aging and Smoking Exacerbates Post-Stroke Complement Driven Neuroinflammation

Christine Couch, Ali Alawieh, E. Farris Langley, Stephen Tomlinson, College of Health Professions, Department of Department of Microbiology and Immunology, MUSC.

11:10 – 11:18 AM

99 Magnetic Resonance Imaging-Based Comparison of Temporal Changes in Brain Microstructure after Microemboli Injection in Control and Diabetic Rats: Relevance to Vascular Cognitive Impairment/Dementia

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

11:20 – 11:28 AM

35 SPARC by Bone Marrow-Derived Cells Contributes to Myocardial Fibrosis in Pressure-Overload

Lily Neff, Hannah Riley, Ryan Kelly, An Van Laer, Shaoni Dasgupta, Catalin Baicu, Lindsay McDonald, Amanda LaRue, Michael Zile, Amy Bradshaw, College of Graduate Studies, Department of Cardiology, Division of (Dept. of Medicine), MUSC.

11:30 – 11:38 AM

40 Sex Differences in Cognitive and Psychological Outcomes of Stroke: Impact of Diabetes

Victoria Wolf, Aunay Miller, Raghavendar Chandran, Weiguo Li, Adviye Ergul, College of Graduate Studies, Department of Pathology & Laboratory Medicine, MUSC.

11:40 – 11:48 AM

43 RAS inhibition limits neuroblastoma tumorigenesis and promotes Retinoic acid induced differentiation in a subset of NBL tumors

Vinodh Rajagopalan, , John O'Bryan, College of Graduate Studies, Department of Pharmacology, MUSC.

11:50 – 11:58 AM

100 Targeting Strategy for Localizing Alternative Pathway Inhibition in Age-related Macular Degeneration

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

Special Session	Ralph H Johnson VA Medical Center	ORAL

11:00 – 11:08 AM

86 Site-targeted complement inhibition halts progressive motor decline in a murine model of Amyotrophic Lateral Sclerosis (ALS)

Khalil Mallah, Davis M. Borucki, Marcelo Vargas, Stephen Tomlinson, College of Graduate Studies, Department of Microbiology and Immunology, MUSC.

11:10 – 11:18 AM

87 Complement Activation Contributes to Hydrocephalus Development following Germinal Matrix Hemorrhage

Mohammed Alshareef, Khalil Mallah, PhD; Ramin Eskandari, MD, MS, Stephen Tomlinson, College of Medicine, Department of Microbiology and Immunology, MUSC.

11:20 – 11:28 AM

69 The Effect of Complement Inhibition on Neuroinflammmation after Traumatic Brain Injury - A High Throughput Analysis

Amer Toutonji, Silvia Guglietta, Mamatha Mandava, Carsten Krieg, Stephen Tomlinson, College of Medicine (MD, PhD), Department of Microbiology and Immunology, MUSC.

11:30 – 11:8 AM

75 Delayed treatment with a site-targeted complement inhibitor reduces cognitive deficits following traumatic brain injury

Davis Borucki, Khalil Mallah, Christine Couch, Wenxue Wang, Shahid Husain, Baerbel Rohrer, Stephen Tomlinson, College of Graduate Studies (MSTP), Department of Microbiology & Immunology, MUSC.

Special Session	John Vournakis Innovation

11:00 – 11:08 AM Poster

95 Inhibition of RAS oncogenesis by identification and targeting a novel vulnerability in selected oncogenic mutants

Imran Khan, Akiko Koide, Mariyam Zuberi, Eric Denbaum, Gayatri Ketavarapu, Kai Wen Teng, Matthew Rhett, Russell Spencer-Smith, Ernest Ramsay Camp, Shohei Koide., John O'Bryan, College of Medicine, Department of Pharmacology, MUSC.

11:10 – 11:18 AM Poster

96 Identification and Characterization of a Small Molecule Inhibitor of KDM4B to Target Periodontal Disease

Kathleen Garrabrant, Kathleen A. Garrabrant, Joy E. Kirkpatrick, Pieter Burger, Jonathan M. Turner, Rachel E. Wilkinson, Patrick M. Woster, Patrick Woster, College of Graduate Studies, Department of Drug Discovery, MUSC.

11:20 – 11:28 AM Oral

66 Targeting Mek/Erk Signaling in the Treatment of Mitral Valve Prolapse

Tyler Beck, , Russell Norris, College of Graduate Studies (MSTP), Department of Regenerative Medicine and Cell Biology, MUSC.

Special Session	Health Humanities

11:00 – 11:08 AM Poster

18 Examining Racial Differences in Privilege and Social Class: Use of a Modified Privilege Walk to Promote Discussions on Racial Inequities

Aramis Gregory, Trevaris Morris, Elizabeth Brown, College of Health Professions, Department of Health Professions, MUSC.

11:10 – 11:18 AM Oral

68 Let's Hang Out!: A Live Online Group Play Intervention Addressing Clinical Socialization Gaps for Adolescents with Autism Spectrum Disorder during the COVID-19 Pandemic

Melanie G. Wiley, Danielle W. Lowe, Erin M. Hopper, James S. Truelove, Jennifer A. Warthen, McLeod F. Gwynette, College of Medicine (MD, PhD), Department of Department of Psychiatry and Behavioral Sciences, MUSC.

Special Session	Center on Aging	POSTER

11:00 – 11:08 AM

5 AGE:RAGE Signaling Pathway as a Target in Neuroendocrine Prostate Cancer

DeMarcus Woolfork, Bradley A Krisanits, Arabia Satterwhite, Lourdes M Nogueira, Ashley Evans-Knowell, David P Turner and Victoria J Findlay, Victoria Findlay, College of Graduate Studies, Department of Pathology and Laboratory Medicine, MUSC.

11:10 – 11:18 AM

94 Age and initial severity as predictors of treatment outcome in chronic post-stroke aphasia

Lorelei Phillip Johnson, Caitlyn Duffy, Alexandra Basilakos, Julius Fridriksson, College of Health Professions, Department of Communication Sciences and Disorders (USC), MUSC.

11:20 – 11:28 AM

42 Pain and Pain Catastrophizing as Predictors of Depression, Anxiety, and Opiate Misuse in Veterans and Veteran Family Members with Chronic Pain

Abagail Ault, Lester Shayla, Mappin Georgia, Santa Ana Elizabeth, Christon Lilian, Wedin Sharlene, Bottonari Kathryn, Balliet Wendy, Carter Lauren, Muzzy Wendy, McCauley Jenna, Imperatore Julia, George Mark, Jeffrey Borckardt, College of Medicine, Department of Psychiatry and Behavioral Sciences, MUSC.

11:30 – 11:38 AM

30 Tau-spiracy: A Developing Mechanism for Cardiac Dysfunction

Stephanie DiLucia, Rakez Kayed, Anna Ellsworth, Federica del Monte, College of Medicine (MD, PhD), Department of Department of Medicine, Division of Cardiology, MUSC.

Special Session	Center on Aging	ORAL

11:00 – 11:08 AM

72 Brain microvascular insulin receptor dysfunction may underly increased risk for early onset dementia during obesity

Luke Watson, Guadalupe Sanchez, Alexus S. Williams, Taylor Lowry, Catrina Sims-Robinson, College of Graduate Studies, Department of Neurology, MUSC.

11:10 – 11:18 AM

84 Neural re-organization after upper extremity rehabilitation therapy with sensory stimulation in chronic stroke survivors

Christian Schranz, Amanda Vatinno, Viswanathan Ramakrishnan, Na Jin Seo, College of Health Professions, Department of Health Profressions, MUSC.

11:20 – 11:28 AM

58 The Effect of Demographic, Stroke, and Clinical Characteristics on Neglect Severity Scores

Emerson Hart, Michelle Woodbury, Annie Simpson, Emily Grattan, College of Health Professions, Department of CHP OT & HRS, MUSC.

11:30 – 11:38 AM

101 Revisiting the Concept of Minimal Detectable Change for the Activities-Specific Balance Confidence Scale with Individuals Post-Stroke

Bryant Seamon, Craig A. Velozo, Steven Kautz, College of Health Professions, Department of Department of Health Sciences and Research, MUSC.

11:40 – 11:48 AM

57 Carbohydrate Binding Protein Galectin-3 and It's Role in Macrophage Activation and Chronic Cochlear Inflammation in Age Related Hearing Loss

Phillip Elvis, Junying Tan, Kenyaria Noble, Jeremy Barth, Hainan Lang, College of Medicine, Department of Pathology and Laboratory Medicine, MUSC.

11:50 – 11:58 AM

61 The Effect of Sensory Impairment Severity on TheraBracelet Efficacy

Jenna Blaschke, Amanda Vatinno, MS, OTR/L, Corey Morrow, MS, OTR/L, Na Jin Seo, College of Health Professions, Department of Occupational Therapy Department, MUSC.

LIST OF ABSTRACTS

1 High-fat diet impairs tactile discrimination memory and leads to problem solving deficits

Tyler Stone, Luke Watson, Alexus Williams, Catrina Robinson, College of Graduate Studies, Department of Neurology, MUSC.

High-fat diet (HFD) mice, a model of obesity, have deficits in working memory using tasks such as the novel object recognition task (NOR). In NOR, normal memory is evident by spending more time exploring the novel object. Mice use their vibrissae to explore the environment; however, it is not known whether deficits in NOR are due to HFD-induced sensory deficits or whether HFD mice exhibit deficits with problem solving. Our hypothesis is the HFD-induced obesity leads to non-sensory dependent cognitive deficits in both working memory and problem solving. To determine the potential impact of sensory deficits on working memory tasks, we modified the NOR, by replacing objects with sandpaper grits, to create the novel tactile recognition task (NTR). The NTR task is whisker dependent task evident by the inability to identify the novel sandpaper grit following bilateral whisker removal in mice on a standard diet (STD). Furthermore, the inability to determine the novel sandpaper grit in HFD mice compared with the STD, suggests that HFD mice have impairments in tactile recognition memory. To determine the potential impact of HFD on whisker sensitivity, mice were subjected to the corner task. HFD mice do not exhibit any deficits in the corner task compared with STD mice. To evaluate problem solving, STD and HFD mice were subjected to the Puzzle box, which consists of an open field and an enclosed dark box, connected by an escape door. Obstacles were placed in front of the escape door to create the problem solving task. Our data demonstrates that HFD mice have increased escape latencies compared to STD mice. Collectively, our data demonstrates that HFD leads to deficits in both working memory and problem solving, which are not due to sensory deficits. This work was supported by This work was supported by the National Institute of Health (NINDS 1R01NS099595).

2 Changes in Adolescent HIV Knowledge Following a Prevention Intervention

Declan Sykes, Nada M. Goodrum, Angela D. Moreland, April Borkman, Alyssa Rheingold, Carla Kmett Danielson, College of Medicine, Department of Department of Psychiatry and Behavioral Sciences, MUSC.

Introduction There is a growing body of literature regarding the value of HIV prevention programs for high risk youth, indicating that HIV knowledge may play an important role for prevention. For example, Sill (2017) showed higher engagement in risk behaviors for people with lower HIV knowledge, compared to those with more. Despite this foundation, effectiveness of increasing adolescent HIV knowledge through prevention-interventions remains understudied. Researchers call for additional study about the impact of prevention-interventions for adolescents. Methods The SAMHSA-funded EMPOWERR Program aims to reduce risk of substance abuse, HIV, and other sexually transmitted infections (STIs) among minority youth by delivering evidence-based prevention-intervention. Data from the EMPOWERR Program were collected from a total of 233 adolescents age 10-18 living in the Charleston (SC) Metropolitan area. Data were collected at three timepoints: baseline (n=197), post-intervention (n=136), and three-month follow-up (n=40). HIV knowledge was measured through self-report at each timepoint using nine true/false items, scored as correct (1) or

incorrect/don't know (0). Data were analyzed using repeated measures ANOVA in SPSS 25. Results On average, out of the 9 items, adolescents answered 4.84 (SD=2.46) HIV-related questions correctly at baseline, 6.46 (SD=2.05) at post-intervention, and 6.60 (SD=2.00) at follow-up. Results displayed a significant increase in HIV knowledge across time, $F(1.99, 45.57) = 16.13$, $p<.001$. Posthoc analyses revealed a statistically significant increase from baseline to post-intervention, with no significant change from post-intervention to follow-up, revealing a significant association between long-term increase in HIV knowledge and the prevention-intervention. Conclusions In this sample of adolescents, which included youth from high risk populations, there was a significant association between prevention-interventions and increased scores on an HIV knowledge scale. Youth who participated in the EMPOWERR program increased their HIV-related knowledge. This increase is encouraging given the well-established association between HIV knowledge and risky sexual behavior. This work was supported by Substance Abuse and Mental Health Services Administration (SAMHSA; grant 1U79SPO15156-01; PI: Carla Kmett Danielson).

3 Does Medication Reduce Alcohol Experimentation in Preadolescents with Attention-Deficit/Hyperactivity Disorder?

Briana Hunt, Alexis M. Garcia, Ph.D., Brittany N. McKenzie, B.S., Rachel L. Tomko, Ph.D., Brittany E. Bryant, D.S.W, Lindsay Squeglia, College of Medicine, Department of Psychiatry and Behavioral Sciences, MUSC.

Attention-deficit/hyperactivity disorder (ADHD) is the most common neurodevelopmental disorder in youth. For preadolescents, medication and/or evidence-based behavioral interventions are strongly recommended for treatment of ADHD. Medication can help increase concentration and reduce impulsiveness, while behavioral treatments help parents and teachers manage problematic behaviors in the context in which they occur. Early interventions for ADHD are important, as untreated ADHD increases the likelihood of externalizing behaviors, including substance use. The aim of this study was to examine the differences in early alcohol experimentation in preadolescents who are medicated vs. non-medicated for ADHD. Baseline data from the Adolescent Brain Cognitive Development (ABCD) Study were used for analyses. The ABCD Study is the largest long-term study of brain development in the United States, consisting of 21 sites and approximately 12,000 youth. Youth (ages 9-10) were categorized as meeting criteria for ADHD if either: (1) they met criteria for current ADHD through parent-reported Kiddie Schedule for Affective Disorders and Schizophrenia (K-SADS) or (2) if the parent reported a previous ADHD diagnosis. Parents provided information on the child's current medications. Non-religious alcohol sipping behaviors were reported by youth. Based on parent report, 2551 of the youth (21.5% of total sample; mean age= 9.48; 51.4% male) met criteria for ADHD, of which 221 children (8.6%) were medicated for ADHD. Within the medicated ADHD group, 14.5% of youth reported non-religious alcohol sipping, compared to 18.3% of the non-medicated ADHD group. After controlling for demographic, youth in the non-medicated ADHD group did not differ from the medicated group in terms of odds of non-religious sipping (OR= 1.29; 95% CI = .87 - 1.92). There were no significant differences in early alcohol experimentation between medicated and non-medicated youth with ADHD, though future research should examine older children for whom sipping may be more commonplace. This work was supported by NIH grant R25 DA020537, U01 DA041093 (Squeglia).

4 **Severity of Cannabis Use Disorder and Perceived Problems Due to Use in Adolescents with and without Depression or Anxiety**

Jenny Nankoua, Jade Tuttle, Erin McClure, Lindsay Squeglia, Kevin Gray, Rachel Tomko, College of Medicine, Department of Psychiatry and Behavioral Sciences, MUSC.

Abstract Withheld from Publication

5 **AGE:RAGE Signaling Pathway as a Target in Neuroendocrine Prostate Cancer**

DeMarcus Woolfork, Bradley A Krisanits, Arabia Satterwhite, Lourdes M Nogueira, Ashley Evans-Knowell, David P Turner and Victoria J Findlay, Victoria Findlay, College of Graduate Studies, Department of Pathology and Laboratory Medicine, MUSC.

Advanced Glycation End products, AGEs are non-enzymatically attached sugar metabolites that can contribute to prostate cancer development and progression. AGEs form when reducing sugars interact with amino acids, proteins, lipids, or nucleic acids under physiological conditions, and are categorized as either endogenous or exogeneous. Exogenous AGEs contribute to the body's total AGE pool and are responsible for increased AGE accumulation which facilitates interaction with the major AGE receptor, the Receptor for Advance Glycation End products, RAGE. RAGE is a transmembrane member of the Ig superfamily of cell surface molecules and is overexpressed in a variety of tumor types, including prostate cancer. Increased AGE accumulation upregulates RAGE expression, amplifying the signaling cascade with impacts on cytokinesis. This is relevant, as we have shown that both AGE and RAGE are significantly elevated in tumors from AA men when compared to EA men at the same stage. De novo neuroendocrine prostate cancer (NEPC) only constitutes 1% of all prostate cancers. However, recent studies have shown that individual cells within a prostate tumor can undergo a process termed neuroendocrine differentiation (NED) to become neuroendocrine-like. Studies have shown that androgen deprivation therapy (ADT) can drive NED, promoting development of the castrate resistant prostate cancer phenotype. Transformation to a neuroendocrine phenotype is one proposed mechanism of resistance to contemporary AR-targeted treatments and is associated with poor prognosis and short life expectancy. Due to increased application of ADTs, NEPC is thought to be on the rise, posing a significant health problem. Our studies show that AGEs can induce NED in AR-positive prostate adenocarcinoma cells in vitro with a concomitant loss of the AR. In addition, we observed AGEs promote more aggressive tumor growth in both syngeneic xenograft and spontaneous mouse models in vivo. Using shRNA and pharmacological inhibitors to RAGE, we show that AGE-mediated NED is RAGE-dependent.
This work was supported by NIH/NCI: R01 CA245143 NIH/NCI: U54 CA210962.

6 **Functional importance of renal histamine receptors and their signaling in the collecting ducts**

Mikhail Fomin, Anastasia Sudarikova, Ying Zhao, Morgan Spicer, Regina Sultanova, Mark Domondon, Daria Ilatovskaya, College of Graduate Studies, Department of Department of Medicine/Nephrology, MUSC.

The immunology of kidney disease is complex and involves factors from both the innate and the adaptive immune systems. Histamine is an important regulator of allergic inflammation, gastric acid secretion, neurotransmission and immunomodulation. Although an increase in histamine level and expression of histamine-metabolizing enzymes has been shown in the kidney, renal

pathological and physiological effects of histamine have not been clearly defined. We hypothesized here that histamine receptors, H1R-H4R, have functional importance in the CD cells. First, we tested HRs expression and localization in polarized mpkCCDc14 cells grown on permeable supports using immunocytofluorescence (ICF). All 4 receptors were found in these cells, further verified with Western Blotting and qPCR. H1R and H4R were localized apically, while H3R and H4R were diffusely distributed within the cells. H1R and H4R expression was significantly increased upon stimulation with histamine. Next, we showed in confocal imaging that lower micromolar histamine evokes a dose-dependent transient increase in intracellular calcium. In addition, we observed a dose-dependent increase in cAMP in the mpkCCDc14 cells post treatment with histamine. In short-circuit current studies aimed at measuring sodium reabsorption via the ENaC (epithelial sodium channel expressed in the CD), we observed an inhibition of the vasopressin-stimulated ENaC-mediated currents by histamine. This was further corroborated in ICF and qPCR, which showed a decrease in mRNA and protein expression for the alpha subunit of ENaC upon histamine treatment. In conclusion, we demonstrated that HRs are expressed in the cells of the collecting ducts, and histamine has dose-dependent effects on calcium handling and cAMP levels. Furthermore, histamine was able to modulate sodium reabsorption and ENaC expression in these cells. These data provide insight into the functional importance of histamine receptors in the CD, and suggest potential implications of histamine in inflammation-related renal diseases, such as diabetes. This work was supported by NIDDK R00 DK105160, R01HL148115, Dialysis Clinic Inc Reserve Fund, the MUSC SCTR support program via NIH/NCATS UL1TR001450, and the American Physiological Society awards (all to DVI).

7 Cause and Effect Relationships Between Glycation and the Ancestry Specific Tumor Stroma

Courtney Lloyd, Bradley A. Krisanits, Pamela Woods, Dion Foster, Lourdes M. Nogueira, Bria Sanders, Laura Spruill, Marvella E. Ford, Mahtabbudin Ahmed, Victoria J. Findlayand David P. Turner, David Turner, College of Graduate Studies, Department of Pathology, MUSC.

Advanced glycation end products (AGEs) are reactive sugar metabolites that our research has shown can increase cancer severity. AGEs are formed endogenously via a slow, nonenzymic reaction. However, high AGE levels associate with the same socioeconomic and environmental factors that contribute to cancer health disparity. Lack of exercise and modern dietary patterns represent cancer disparity factors that lead to the increased accumulation of AGEs. Our published research indicates that AGE levels are highest in prostate cancer patients with more aggressive disease and those with African Ancestry. An accumulation of AGEs in the body drives chronic inflammation which has an impact on the progression of diseases such as Alzheimer's, diabetes, and as we have recently shown cancer. Our unpublished data demonstrate that consumption of a diet high in AGEs increases the growth of prostate cancer in both syngeneic xenograft and spontaneous mouse models. Dietary-AGE mediated effects on prostate tumor growth were dependent upon the stromal expression of the receptor for AGE (RAGE) which led to the activation of fibroblasts. This work was supported by R01 CA245143 NIH/NCI, U54 CA210962 NIH/NCI.

8 **Combining Transcutaneous Auricular Vagus Nerve Stimulation (taVNS) with Transcranial Magnetic Stimulation (TMS) to Enhance Cortical Excitability**

Alex Kahn, Sean Thompson, Bashar Badran, College of Graduate Studies, Department of Institute of Psychiatry, MUSC.

Background: Transcranial Magnetic Stimulation (TMS) is a widely used tool to augment motor training used to facilitate function post-stroke. Although effective in increasing cortical excitability, the effects of TMS are transient and behavioral benefits are mild in rehabilitation paradigms. There is a need for noninvasive neuromodulatory techniques that can induce robust changes in cortical excitability to facilitate motor recovery after strokes and to enhance and accelerate the neuroplastic changes induced by rTMS. Transcutaneous auricular vagus nerve stimulation (taVNS) has emerged as a promising facilitator of neuroplasticity, and in this trial, we explore combining two forms of brain stimulation (taVNS and rTMS) to boost cortical excitability. Methods: Here we present on one of the planned 24 healthy participants enrolled into a four-visit, randomized, sham-controlled trial exploring various forms of neuromodulation on cortical excitability. First, we will use a validated motor evoked potential (MEP) paradigm to quantify resting baseline excitability. Participants will then receive 20 minutes of one of four different stimulation conditions (active TMS with sham taVNS, active taVNS with sham TMS, Paired taVNS + TMS, or unpaired taVNS + TMS). MEPs will be then recorded immediately after stimulation, and every 10 minutes following for 30 minutes to analyze the changes in excitability. Results: In subject 1, Active TMS/Sham taVNS condition induced a +114.9% increase in MEP amplitude compared to the baseline. Similarly, Active taVNS/Sham TMS condition induced a +82.4% increase in MEP amplitude compared to baseline (20 minutes post-stim). Both combinatory methods resulted in reductions in MEP amplitude compared to baseline at the 20 minute timepoint (Paired taVNS+TMS: -73.4%, Unpaired taVNS+TMS: -70.7%). Conclusions: These preliminary results suggest that combining two forms of brain stimulation is safe, feasible, and likely impacts cortical excitability. Furthermore these findings suggest there may be an interaction between the two administered simultaneous, rather than independently. This work was supported by NIH grant R25 DA020537, NIH grant P2CHD086844.

9 **Unna Boots and Dermatologic Disease: A retrospective review**

Gabriella Santa Lucia, Alan Synder, John Plante, Alexandra Ritter, Dr. Dirk Elston, College of Graduate Studies, Department of dermatology, MUSC.

Unna boots are a low risk, cost effective, comfortable and quality of live sparing treatment in wound management. The semi-solid gauze casting is saturated with anti-inflammatory zinc oxide, gum acacia, glycerol, castor oil and deionized water that increases compression promoting faster angiogenesis, reepithelization and wound granulation. Compression decreases the pro-inflammatory milieu while increasing anti-inflammatory cytokines. This duel synergism has shown succuss in the healing of venous ulcers, however, significant evidence is lacking on its effect in other dermatological inflammatory pathologies. We aim to measure Unna boots success and adverse events associated with wound healing on wide range of pathologies. A retrospective chart review was conducted with approval of the Institutional Review Board at the Medical University of South Carolina. 124 patients with 19 different dermatologic pathologies were collected. Treatment response was calculated on a scale of 0-4 with negative outcomes= 0, no outcomes=1, mild outcomes=2, significant outcomes=3, and completely healed=4. The patient profile consisted of 73% female and 26.6% male, with a mean age of 67.6 (range: 27-91)

years. Ten different body parts were measured with the left leg (22.6%) being the most common. The mean treatment duration was 5.46 weeks (range: 1d-22mo) with 4% of participants on Unna Boot treatment alone, and 96% on Unna Boot + adjunctive therapies. The overall positive outcomes of Unna Boots were 91% with 114 total positive outcomes. Two patients had no change and eight had negative outcomes. The adverse event rate was 5.6%, with pruritus being the number one complaint. The majority of the patients had mild (27%) significant (46%) or complete (18.5%) healing. Limitations of the study are its retrospective design and non-validated scale. The location and severity of the disease were not taken into consideration during treatment response. In conclusion, our findings support that clinicians should consider using UB in their treatment plans.

10 Neural reactivity in response to alcohol and trauma cues with depression severity as a moderator in patients with comorbid alcohol use disorder and posttraumatic stress disorder

Zahraa Atoui, Jane E. Joseph, Laura Lohnes, Kevin Gray, Elizabeth Santa Ana, Sudie E. Back, Amber Jarnecke, College of Medicine (MD, PhD), Department of Department of Psychiatry and Behavioural Sciences, MUSC.

Background: Patients with comorbid alcohol use disorder (AUD) and posttraumatic stress disorder (PTSD) experience severe impairments and are at increased risk for depressive symptomatology. The reward pathway, represented by dopaminergic projections from the ventral tegmental area to the nucleus accumbens (NAc), contains circuitry implicated in both AUD and PTSD. However, little is known about the neurobiological mechanisms underlying comorbid AUD/PTSD, and how neural circuits implicated in this comorbidity might be modulated by depression severity. The current study uses functional magnetic resonance imaging (fMRI) to examine blood-oxygen level dependent (BOLD) signal among individuals with AUD/PTSD while accounting for sex and depression severity. Methods: AUD/PTSD participants (N=24) were enrolled in a larger clinical trial. Participants listened to personalized imagery scripts (trauma, alcohol, and neutral cues) during a baseline fMRI scan. Voxel-wise general linear modeling characterized BOLD signal (threshold>3.1). Main effects for the group were modeled, as were effects for sex, depression severity, and the interaction of sex by depression severity. Results: In the alcohol versus neutral contrast, significant activation was found in the bilateral inferior frontal gyrus (IFC) (max $Z=6.4$, $p<.05$). In the trauma versus neutral contrast, significant activation was found in the middle/superior temporal gyrus (max $Z=6.5$, $p<.05$). There were no effects for sex, depression severity, or sex by depression severity in either contrast. Conclusion: Findings suggest that depression severity is not associated with a difference in NAc activity among individuals with AUD/PTSD, whether responding to an alcohol or trauma cue. Among individuals with AUD/PTSD, reactivity in the IFC, a region involved in response inhibition and attentional control, might indicate an anticipatory effect during a salient alcohol cue. The middle/superior temporal gyrus, which may play a role in dissociative states in PTSD, shows increased activity during a trauma cue. These neural regions might be particularly relevant treatment targets for AUD/PTSD. This work was supported by NIH grant DA020537 for the Drug Abuse Research Training (DART) at MUSC.

11 Interleukin-6 is necessary but not sufficient for abdominal aortic aneurysm development

Raj Patel Patel, SarahRose Hall, Nicholas Ward, Hayes Lanford, Tyler Grespin, Rupak Mukherjee, Jeffrey Jones, Jean Marie Ruddy, Jean Ruddy, College of Medicine, Department of Vascular Surgery, MUSC.

Introduction: The gene expression profile of interleukin-6 (IL-6) signaling through the STAT3 transcription factor distinguishes it as a potential effector of macrophage accumulation and abdominal aortic aneurysm (AAA) growth. This project aims to demonstrate that IL-6 is an integral component of aortic macrophage accumulation and AAA development. Methods: C57Bl/6 and IL-6 knockout (IL-6KO) mice underwent induction of AAA by the application of peri-adventitial CaCl2 (0.5M) +/- implantation of an osmotic mini-pump delivering IL-6 (4.36□g/kg/day x 21 days). At the terminal procedure, aortic diameters (AoDs) were measured by digital microscopy and represented as percent change from baseline (n=4-7). The infrarenal aorta was harvested for immunoblot (fold change in pSTAT3/STAT3; n=4-6) or flow cytometric analysis of macrophage content (percentage of CD11b+/F4-80+ cells; n=3-8). Results: IL-6 treatment or AAA induction alone significantly increased the AoD of C57Bl/6 mice, along with increased pSTAT3/STAT3 ratio (1.66+/-0.15 and 1.94+/-0.17 fold, respectively; $p<0.05$) and elevated accumulation of CD11b+/F4-80+ cells in the aorta (1.36%+/-0.03 and 1.88%+/-0.03, respectively vs C57Bl/6 control at 0.86%+/-0.03; $p<0.05$). In the IL-6KO mice, the change in AoD with AAA induction was attenuated, as was the change in pSTAT3/STAT3 ($p<0.05$). Macrophage accumulation in IL6-KO after pump or AAA treatments was mildly but significantly elevated ($p<0.05$). Furthermore, when compared to C57Bl/6 controls, there was no significant difference in macrophage accumulation ($p>0.05$). However, when IL-6 was restored in the IL-6KO mice and AAA was induced, the change in AoD matched that of C57Bl/6 mice, the pSTAT3/STAT3 ratio increased 3.74+/-0.37 fold ($p<0.05$ vs IL-6KO control), and more CD11b+/F4-80+ cells were accumulated (1.89%+/-0.12 vs 0.66%+/-0.02 in IL-6KO control, $p<0.05$). Conclusion: By employing dual therapy with IL-6 infusion and AAA induction in IL-6KO mice, this project has demonstrated that IL-6 is necessary but not sufficient for AAA development, thereby emphasizing the therapeutic value of targeting this cytokine signaling pathway.

12 Neuroanatomical networks associated with associative and taxonomic semantic errors during speech production in individuals with post-stroke aphasia.

Jesse Varkey, Leonardo Bonilha, College of Medicine, Department of Neurology, MUSC.

ABSTRACT Background: Semantic paraphasia, a common feature of post-stroke aphasia, are classified into subtypes such as associative and taxonomic semantic errors during clinical diagnosis. However, the neuroanatomical underpinnings of these subtypes and their response to treatment remain elusive, hindering the development of targeted treatment approaches. Methods: We obtained brain MRIs, language assessments and demographic data from 43 individuals with chronic left-hemispheric stroke who completed a 6 week-long language treatment. We performed region-based and connectome-based lesion symptom mapping analyses to determine the relationship between lesion locations to the grey and/or white matter and associative/taxonomic errors at baseline and their change from baseline to 1 month after treatment. Results: On average participants produced 3.05% associative and 1.92% taxonomic

errors before treatment, and 2.46% associative and 2.03% taxonomic errors after treatment. Baseline white mater integrity between the left angular gyrus and left middle temporal gyrus was independently associated with improvement in associative semantic errors after treatment (beta=-0.57, p=0.049). We did not find any neuroanatomical associations with taxonomic errors. Conclusions: In our study associative and taxonomic errors had a low prevalence. Further, we did not find a double dissociation between associative and taxonomic errors, suggesting that they do not occupy distinct brain regions. We believe that it may not be clinically worthwhile to diagnose and treat these error types differently, thus our results encourage a shift in the traditional clinical approach for diagnosing and treating anomia. This work was supported by This study was supported by research grants from the National Institutes of Health / National Institute on Deafness and Other Communication Disorders (NIDCD): DC014021 (PI: Bonilha), DC011739 (PI: Fridriksson), DC014664 (PI: Fridriksson), DC014435 (Traine.

13 Impact of Maternal and Child Vitamin D Supplementation during Lactation on Acute Infection: a Randomized Controlled Trial

Kari VanEvery, MPH, RD, John E. Baatz, Judith Shary, Myla D. Ebling, Carol Wagner, College of Medicine, Department of Neonatology, MUSC.

Objective: Examine whether maternal vitamin D (vitD) supplementation influences health among breastfed infants. Methods: In this RCT, mother/infant dyads enrolled at 4-6 weeks postpartum (baseline) were randomized to receive either 400 IU/400 IU (control), 2400 IU/placebo (low dose), or 6400 IU/placebo (high dose) vitD3/day for 6 months. Maternal serum vitamin 25(OH)D concentration was measured at baseline then monthly and infant values measured at baseline, 4 months, and 7 months. For this post hoc analysis, the primary outcome was acute infection (ARI, defined as a cold and/or ear infection) in offspring at baseline, 4 months, and 7 months. Student's t-test analyses were used to show difference in infant infection, mean maternal 25(OH)D, or mean infant 25(OH)D ($p<0.05$). Results: Lactating women (n=242) were randomized to control (n = 105), low-dose (n = 32), or high-dose (n = 105) vitD3 supplementation. 128 infants (53%) had ARI through six months. Infants in the high-dose group did not differ in illness profile or vitD status compared to those infants in the control group. Maternal 25(OH)D was significantly lower among infants who had an ear infection at visit 4 (44.2 v. 22.7 ng/mL 25-D, p=0.04). Conclusions: While infants in the 400- and 6400-IU groups had equivalent vitD status, mothers' vitD status differed. On the basis of maternal treatment group and 25(OH)D concentration, there were no differences in the incidence of ARI during the first six months of life. There was a difference, however, in maternal vitD of infants with acute ear infections at visit 4. Additional studies are needed to determine the role of maternal vitD status on infant immune status during lactation. This work was supported 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 MUSC, NIH/National Center for Advancing Translatinal Sciences grant UL1 TR000062.

14 A Novel Perfusate to Preserve Vascular Mechanical Capacity

Devin Mahon, Raj Patel, SarahRose Hall, Rupak Mukherjee, Demetri Spyropoulos, Jean Ruddy, College of Medicine, Department of Surgery, MUSC.

Introduction: Open infrainguinal bypass surgery is indicated in patients with critical limb ischemia (CLI) but successful limb salvage depends upon conduit efficacy. There are currently no cellularized, functional, biologic conduits available for infrainguinal bypass construction. A novel perfusate formulation 'SolnIX-SK' (SS) has been developed which is hypothesized to stabilize tissues to maintain cell viability and matrix architecture through freezing, storage, and thawing. This project compared mechanical properties of porcine superficial femoral artery (SFA) banked in the SS perfusate against vessels maintained in common alternative preservative solutions. Methods: SFA was harvested from Yorkshire swine (30-40kg) and tested as Fresh samples; stored at 4OC for 24 hours in Kreb's-Henseleit (KH), Hypothermosol® (HT), or SS; or frozen in Cryostor or SS. For compliance testing, 5mm vessel segments were mounted on the Radnotti tissue myograph and assessed at 2g increments of isometric tension. After allowing for equilibration, passive relaxation of the vessel was calculated to account for matrix compliance. Separate vessel segments of the same dimension were tested for contractility at 5g increments by treating with 100mM KCl and quantifying maximal increase in generated tension. At each tension increment, percent change values were compared by ANOVA. Results: When SFA vessel segments were harvested and assessed for compliance, those refrigerated in KH for 24 hours behaved the same as Fresh samples, but those in HT and frozen in CS or SS were significantly more stiff ($p<0.05$). At 8g tension and above, vessels in SS matched the compliance of the Fresh SFA segments. In contractility, refrigerated samples mirrored the Fresh vessels, but all frozen samples were significantly less contractile ($p<0.05$). Conclusions: Vessels refrigerated in the novel perfusate SS approximated mechanical activity of Fresh SFA, but frozen samples demonstrated decreased compliance and decreased contractility, suggesting that further investigation into the effect of this non-toxic preservative is warranted.

15 Differences in Bone Mineral Content and Bone Mineral Density of Infants Receiving Direct vs. Indirect Vitamin D Supplementation: A Randomized Controlled Lactation Study

Laura Andrews, Kristen Phlegar, Judith Shary, Myla Ebeling, John Baatz, Carol Wagner, College of Medicine, Department of Department of Neonatology, MUSC.

Background: Vitamin D (vitD) plays a significant role in the maintenance of bone mineral homeostasis. It is unknown if a difference in bone mineral content (BMC) and bone mineral density (BMD) exists between infants who receive direct vitD supplementation and those who receive vitD indirectly via their mother's breastmilk, while she received a high dose of vitD. It is hypothesized that there would be no differences in BMC or BMD based on treatment group. Design/Methods: Randomized, double-blind trial to compare BMC and BMD of infants who received direct vitD supplementation (400 IU vitD3/day) in addition to their mother receiving standard dosage (400 IU vitD3/day), versus infants whose mothers were their only source of vitD and were given high dose supplementation (2400 or 6400 IU vitD3/day). Participants were exclusively breastfeeding mothers and their singleton infant consuming only human milk. Infant BMC and BMD were measured by DXA scans of the infant's total body (Hologic Discovery A Densitometer and Infant software) at 1-, 4-, and 7- months of age. Data were analyzed by t-test and mixed regression models using SAS 9.4. Results: Infant BMC and BMD did not differ

significantly at 1-, 4-, or 7 months between direct and indirect supplementation arms. The mean difference in BMC from 1-7 months was 1.624 g and 1.464 g for the 400 IU and 6400 IU groups, respectively (p=0.5); the mean difference in BMD over this same period was 0.042 g/cm2 and 0.032 g/cm2 for the 400 IU and 6400 IU groups, respectively (p=0.2). Although some differences among races were observed, they did not reflect changes in bone growth between the treatment arms. Conclusion: As evidenced by similar infant BMC and BMD between treatment groups, high dose vitD supplementation of mothers provides a safe and effective alternative to direct supplementation of infants. This work was supported by National Institutes of Health (NIH) 5R01HD043921, NIH RR01070, Medical University of South Carolina Department of Pediatrics, The South Carolina Clinical & Translational Research (SCTR) Institute, with an academic home at the Medical University of South C.

16 Nursing swallow screens for cervical spine surgery patients: A systematic review

Janet Horn, Teri Lynn Herbert, Heather Bonilha, College of Health Professions, Department of Health Sciences and Research, MUSC.

Introduction: It is well-recognized that patients who undergo cervical spine surgery (i.e., anterior cervical discectomy and fusion (ACDF) or posterior cervical discectomy and fusion (PCDF)) are at increased risk for post-operative swallowing impairment (dysphagia) with the incidence reported as high as 79%. Studies also show that up to 48% of cervical spine surgery patients have pre-existing dysphagia. Given the potentially high incidence of (pre- and) post-operative dysphagia, implementing a nursing swallow screen prior to receiving oral intake for all post-ACDF/PCDF patients may be warranted to identify high risk patients prior to surgery, identify patients with new dysphagia after surgery, and facilitate appropriate referrals. Without nursing swallow screens, many dysphagic patients may not receive timely intervention, leading to poor outcomes; therefore, our purpose was to explore pre- and post-operative nursing swallow screens in patients undergoing ACDF/PCDF. Methods: We conducted a Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) systematic review. Initially, we searched for all relevant publications examining: 1) dysphagia in the setting of cervical spine surgery and 2) nursing swallow screens; however, this search yielded no results. Therefore, we divided our review into two separate searches further noted as "Dysphagia ACDF/PCDF" and "Nursing Swallow Screens," respectively. Results: Our results revealed no standardized, validated nursing swallow screen for cervical spine surgery patients, nor any evidence for commonly agreed upon dysphagia assessments, assessment time frames, or criteria to define and identify dysphagia in this patient population. Conclusions: This systematic review highlighted the necessity for additional research in this area to provide more concrete, consistent evidence of the risk of dysphagia and predictive risk factors for ACDF-/PCDF-related dysphagia with the goals of developing a nursing swallow screen for this patient population, improving patient swallowing safety, facilitating recovery of swallow function, and reducing adverse outcomes. This work was supported by NIDCD Institutional T32 Training Grant, Interdisciplinary Research Training in Otolaryngology and Communication Science (Trainee), NIH/NIDCD Institutional T32 Training Grant, DC014435 Site: MUSC Program Director: Judy R. Dubno, Ph.D..

17 Creating an Efficient Training Program for a New Post-Stroke Rehabilitation Device

Laura Judy, Corey Morrow, MOT, OTR/L, Amanda Vatinno, MS, OTR/L, Amanda Giles, OTD, OTR/L, Jillian Harvey, PhD, and Emily Johnson, PhD, Na Jin Seo, College of Health Professions, Department of Department of Health Professions, MUSC.

Background: Many rehabilitation devices do not translate into clinical practice. One of the barriers is therapist access to the initial training session. Therapists often have to bear the burden of time and cost for travel to training, in addition to missing or non-billable work hours. Difficulty in accessing training for new rehabilitation devices results in lost opportunity for improved patient outcomes. Objective: The purpose of this project is to create an efficient training program for a new rehabilitation technology device, TheraBracelet. Methods: First, we defined the learning objectives of the training: (1) Define main outcome of TheraBracelet on post-stroke patients, (2) Classify patients appropriate for TheraBracelet, (3) Summarize set-up of TheraBracelet, (4) Demonstrate use of TheraBracelet in treatment session. Second, a literature review was conducted for effective teaching approaches and theories including Bloom's taxonomy, adult learning theories, multi-modal approaches, spaced retrieval, and flipped classroom. We developed our training approaches based on the evidence. Third, we are currently interviewing occupational therapists to obtain their preference on training formats and logistics (e.g., training duration, time of day, pre-recorded vs. live for varying contents, in-person vs. zoom, group size). Content analysis will be used to determine specific training formats and logistics that are considered most efficient for therapists. Future steps include determining the effectiveness of our training program by training local therapists and assessing the success rate of mastery of the learning objectives. We will additionally obtain their feedback on the training program and refine the training as needed. Impact: This work is expected to result in an efficient training program for using a new rehabilitation device that is easy to implement with minimal burden for therapists, yet effective. Easier access to training is expected to increase adoption of new treatments, ultimately leading to improved patient outcomes in rehabilitation.
This work was supported by NIH/NCATS TL1-TR001451 NIH/NCATS UL1-TR001450 NIH/NIGMS P20GM109040 NIH/NICHD 1R01HD094731-01A1.

18 Examining Racial Differences in Privilege and Social Class: Use of a Modified Privilege Walk to Promote Discussions on Racial Inequities

Aramis Gregory, Trevaris Morris, Elizabeth Brown, College of Health Professions, Department of Health Professions, MUSC.

Systemic racism and discrimination regarding social determinants of health (SDOH) can lead to disparities within the infrastructures of the education system, economic opportunity, housing market, and food availability have long persisted. We examined racial disparities regarding socioeconomic status (SES) using a modified privilege walk (MPW) and total privilege score to have discussion about privilege and race. There were 38 participants. The majority were White (68.4%) or female (86.8%). The mean age for the total cohort was 31.3 years. White and minority students were not statistically different in-regards to age, sex, and ethnicity. There was a statistically significant difference between Whites and minorities for their total privilege score (16.5 v. 0.67, p=0.0002). Compared to White students, minority students were significantly more likely to skip meals or go hungry (OR 5.476, CI: 1.038, 28.878). Minority students were more likely to say they had a parent that did not graduate high school, or they moved due to not having enough money to pay rent; however, these findings were not significant. Racial

disadvantages related to parents' SES could negatively impact access to various resources, including healthy food options and stable housing. A lower total privilege score regarding SDOH could be indicative of poor health equity and quality of life. Current events exposing racial and health inequities have prompted discussions on SDOH. Thus, it is imperative health educators and researchers to prepare future health professionals are equipped to recognize the SDOH, privilege, and health inequities within their social and physical communities. This work was supported by N/A.

19 Maladaptive Reward Seeking Behavior Influenced by Changes in PVT to NAc Neurons After Heroin Use

Preston Siegler, Kelsey Vollmer, James Otis, College of Graduate Studies, Department of Neuroscience, MUSC.

Opioid use disorder is a serious issue plaguing the United States, as data from the CDC shows that approximately 128 people die from opioid overdose each day. When exposed to drug-associated cues, such as the environment or tools used to consume drugs, people with OUD are more likely to relapse despite knowing there may be negative consequences associated with consuming these substances. The mechanism in which drug-associated cues engage reward circuits in the brain to control maladaptive reward-seeking is still largely unknown. One brain region of interest for understanding this maladaptive reward seeking is the paraventricular nucleus of the thalamus. While others have shown that PVT is inhibited by natural reward-associated cues, it is unclear how PVT is engaged by opioid-associated cues for the control of maladaptive drug-seeking. Here, we aim to target PVT neurons which project to the nucleus accumbens, a major component of the brain's reward system. Previous studies done in our laboratory reveal that PVTNAc neurons express μ-ORs, suggesting that μ-OR signaling contributes to changes in this circuit. Using optogenetic viral techniques, we have manipulated PVTNAc neurons during sucrose or heroin self-administration to evaluate this circuit's role in adaptive and maladaptive reward-seeking, respectively. Mice were virally infused with either a cre-driven halorhodopsin, channelrhodopsin, or YFP in PVT, and a retro-cre in NAc. Animals were equipped with an IV catheter, and once recovered from surgery, underwent heroin or sucrose self-administration. Our viral strategy allowed us to manipulate the PVTNAc pathway after animals had extinguished sucrose or drug-seeking behaviors. Collectively, these experiments will bring better clarity as to how these brain circuits are affected by chronic opioid use and exposure to drug-associated cues. Determining how drug-associated cues can engage brain circuits for the control of drug-seeking behaviors is paramount to developing novel therapeutics to treat OUD. This work was supported by COCA 50, PREP R25.

20 Non-invasive brain stimulation as a tool to decrease chronic pain in current opiate users: a parametric evaluation of two promising cortical targets

Julia Imperatore, Daniel M. McCalley, Jeffery J. Borckhardt, Kathleen T. Brady, Colleen Hanlon, College of Graduate Studies, Department of Psychiatry and Behavioral Sciences; Neurosciences, MUSC.

Background: Poorly controlled chronic pain can lead to non-prescription use of opiates, which is a growing crisis in our communities. Transcranial magnetic stimulation (TMS) is a non-invasive therapeutic tool which has emerged as a potential treatment option for these patients. It is still

unclear, however, if the dorsolateral prefrontal cortex (DLPFC) or the motor cortex (MC) is a more effective treatment location. The purpose of this study was to directly compare the effects of DLPFC versus MC TMS on pain severity and the urge to use opiates among chronic pain patients. Methods: Twenty-two individuals with chronic pain currently using prescription opiates were randomized to receive 10, 3000 pulse sessions of 10 Hz repetitive TMS (rTMS) to the left DLPFC (110% resting motor threshold) or right MC (90% resting motor threshold). The effect of TMS on pain and opiate use was evaluated with a multivariate linear model, which included items from the Brief Pain Inventory (BPI) as well as subjective ratings of pain, distress, and the urge for opiates. Results: Twenty participants (91%) completed all 10 treatment sessions and follow up visits. There was a significant main effect of stimulation site on self-reported pain and opiate usage metrics ($F_{7,210}=3.742$, $p=0.001$). MC stimulation led to a significantly greater decrease in pain interference than DLPFC stimulation ($F_{1,216}=8.447$, $p=0.004$). While both sites had comparable effect sizes on stress, pain, and discomfort (Cohen's d: 0.5-0.8), MC stimulation had larger effects on pain interference (Cohen's d: 0.7) and urge to use opiates (Cohen's d: 0.5) than DLPFC stimulation. Conclusion: These preliminary data suggest that the MC may be a promising target for decreasing opiate dependence and pain interference among chronic pain patients.

21 Factor Analysis of a MUSC Telemedicine Provider Satisfaction Survey

Parker Rhoden, Jillian B. Harvey, MPH, PhD; James T. McElligott, MD, MSCR; Kit Simpson, DrPH;, Jillian Harvey, College of Health Professions, Department of Department of Healthcare Leadership and Management, MUSC.

Abstract Withheld from Publication

22 Role of Porphyromonas gingivalis in Mediating Ceramide-dependent Mitophagy in Oral Squamous Cell Carcinoma

Megan Sheridan, Dr. Özlem Yilmaz, Dr. Nityananda Chowdhury, Besim Ogretmen, College of Graduate Studies, Department of Biochemistry and Molecular Biology, MUSC.

Abstract Withheld from Publication

23 Design, synthesis, and validation of CD38 inhibitors as immuno-therapeutics against cancer

Thomas Benton, Catherine Mills Pieter Burger Yuri Peterson Patrick Woster, Patrick Woster, College of Graduate Studies, Department of Drug Discovery, MUSC.

Abstract Withheld from Publication

24 Role of IFNLR1 Receptor Dynamics and Plasticity in Regulating Cellular Response to Type-III Interferons

John Evans, Christiana S. Kappler, Ray Liu, Juliana D. Carten, Cody M. Orr, Sarah Stephenson, Paula Traktman, Stephen A. Duncan, Eric G. Meissner, Eric Meissner, College of Medicine (MD, PhD), Department of Medicine, MUSC.

Introduction: Cells produce a class of soluble cytokines known as interferons (IFNs) upon viral infection. Of the three main types of IFNs, the type-I and type-III systems are essential in generating antiviral programming by inducing expression of hundreds of interferon stimulated genes (ISGs). While most tissues are sensitive to type-I IFNs-due to the ubiquitous expression of its receptor complex (IFNAR1/2)-restriction of the type-III IFN receptor (IFNLR1) to tissues of epithelial origin limits its effects to the skin, lung, liver, and gut. Rationale: Type-I IFN receptor dynamics and plasticity-defined here as surface abundance, internalization, intracellular sorting, and expression of transcriptional variants-have been shown to be critically important in shaping cellular response to IFNs, leading to the adoption of a "receptor-centric" model of type-I IFN regulation. In stark contrast, the role of IFNLR1 dynamics and plasticity in regulating the type-III IFN response is largely unknown. As a specific, powerful component of innate immunity, understanding how the type-III IFN system is regulated could lead to the development of novel therapeutic targets and strategies to face a multitude of viral illnesses. Methods: To facilitate our investigation, we will generate doxycycline-inducible FLAG-tagged IFNLR1-expression plasmids representing all known transcriptional variants. These plasmids will allow us to: 1) Evaluate the effect of IFNLR1 surface abundance on the type-III IFN transcriptional profile and 2) Assess the extent of IFNLR1-FLAG co-localization with several notable intracellular structures using immunofluorescence, before and after stimulation with IFNL3. Results: We have successfully generated three IFNLR1-FLAG transcriptional variants and confirmed inducible-expression and function in vitro. We are currently assessing the role of surface abundance, internalization, differential isoform expression, and trafficking. Conclusions: By completing this study, we hope to provide a more nuanced understanding of the type-III IFN system, thereby exploring its therapeutic potential in the realm of infectious diseases. This work was supported by MUSC MSTP, MUSC TL1, K08AI121348 (NIAID), P20GM130457.

25 CD26 defines responsiveness to neoadjuvant checkpoint blockade

Hannah Knochelmann, Amalia Rivera-Reyes, Joshua Horton, Michael Bobian, Megan Wyatt, Carsten Krieg, Kent Armeson, Mark Rubinstein, Dongjun Chung, Chrystal Paulos, David Neskey, College of Graduate Studies (MSTP), Department of Otolaryngology -- Head and Neck Surgery, MUSC.

Immunotherapy targeting PD-1/L1 has revolutionized medicine by mediating durable responses in small cohorts of patients. Mechanisms permitting response remain incompletely understood, limiting ability to bolster efficacy for non-responsive cancers. We reported that CD26, a novel, multifunctional ectoenzyme, marks T cells with potent antitumor activity and posited that CD26 may correspond with response to checkpoint blockade. To address this, a Phase II single-arm trial of presurgical nivolumab for oral cavity squamous cell carcinoma (OCSCC) was conducted at MUSC. CD26 expression was evaluated in tumor-infiltrating lymphocytes (TILs) expanded ex vivo from surgical specimens. For mechanistic modeling, murine OCSCCs responsive (Moc22) and non-responsive (Moc2) to PD-1 blockade were used. Neoadjuvant nivolumab elicited a 44% overall response rate for stage one of the trial, where 4 of 9 patients demonstrated >30%

reduction in tumor size. Responding patients had higher frequencies of CD26+ TILs versus non-responders, while expression of PD-1, Tim3, and Lag3 did not correlate. TCRbeta sequencing revealed that responders had more profound clonotype overlap between blood and tumor compartments; therefore, we addressed whether CD26 corresponded with T cell chemotactic properties. Strikingly, chemokine receptor expression was highest in CD26+ TILs versus bulk T cells, highlighting superior chemotaxis as a potential response mechanism. In contrast to TIL, CD26 in the blood (evaluated via CyTOF) was similar among patients, indicating tumor-specificity of this effect. In mice, the frequency of CD26+ TILs was augmented by PD-1 therapy, but only in responding tumors; CD26+ TILs also produced substantially higher IFN-gamma upon stimulation relative to CD26- populations. In summary, CD26+ TILs correlate with response to PD-1 blockade in both clinical and preclinical OCSCC settings. CD26 marked highly functional, chemokine receptor-expressing T cells, thereby providing insight to antitumor efficacy. These findings should be validated in larger studies and have translational implications for designing therapies which promote immunity in patients. This work was supported by NCI F30 CA243307, NIH T32 GM08716 and DE017551, and AHNS Pilot Grant Award (HMK), NIDCR K08 DE26542 (DMN), and NIDCR R21 DE029592 to CMP and DMN. Funding for the trial was provided by BMS, who played no role in data collection or correlate analysis.

26 Cell Type-specific Expression of Npas4 is Required for Cocaine-reinforced Learning and Memory

Brandon Hughes, Makoto Taniguchi, Christopher Cowan, College of Graduate Studies, Department of Neuroscience, MUSC.

Hallmark features of substance use disorders include patterns of drug use, dependence, and compulsive seeking despite negative and/or harmful outcomes. During repeated drug use, persistent neuroadaptations develop in the nucleus accumbens (NAc), a brain region involved in reward learning and predominately composed of dopamine D1 receptor- and D2 receptor-expressing medium spiny neurons (MSNs). The progression from casual drug use to abuse is mediated in part by the strong associations formed between the euphoric effects of the drug and the environmental contexts and cues linked to drug use experiences. As such, these external cues can become powerful triggers for relapse. However, the molecular and cellular mechanisms underlying these powerful and enduring drug-context memories are poorly understood. One possible regulator of neuroadaptations responsible for drug reward-related learning is the activity-dependent transcription factor, neuronal PAS Domain Protein 4 (Npas4). In the forebrain, Npas4 regulates excitatory and inhibitory synapse balance and synaptic transmission in a cell type-dependent manner. We sought to examine the cell type-specific regulation and role of Npas4 in the rodent NAc during cocaine-reward learning. Following exposure to a drug-paired environment, we found that a small population of NAc neurons induce Npas4 and, of those, ~50% are D1R- or D2R-expressing MSNs. Npas4 knockdown in D2-, but not D1-, MSNs of the NAc caused a significant reduction in cocaine conditioned place preference, a behavioral task that measures drug-context memory. Our data also suggest that Npas4 regulates cocaine conditioned behaviors by modulating the excitatory/inhibitory balance of the NAc, whereby Npas4 knockdown is associated with hyperactivation of D2-MSNs. In addition, ongoing studies indicate a role for D2-MSN Npas4 in mediating relapse-like behaviors following cocaine self-administration. Together, these data support the hypothesis that NAc Npas4 plays a critical cell type-specific role in guiding circuit adaptations that are required for

the development of drug reward-context memories. This work was supported by F31 DA048557, T32 DA07288, R01 DA027664, R01 DA032708 , P50 DA046373.

27 Targeting Mitochondria as an Adjuvant Therapy for Cisplatin-Resistant Ovarian Cancer

Zachary Hough, Gyda Beeson, Robin Muise-Helmericks, College of Graduate Studies, Department of Department of Regenerative Medicine, MUSC.

Abstract Withheld from Publication

28 Cardiomyocyte death and fibrotic scarring in the infarcted neonatal mouse heart

Mary Mohr, Shuang Li, Patrick Roddy, Ge Tao, College of Graduate Studies, Department of Regenerative Medicine, MUSC.

Myocardial infarction (MI) is a leading cause of death in the United States resulting in severe public health burden. Following MI, the loss of healthy cardiomyocytes leads to decreased contractility and eventually heart failure. Mature mammalian cardiomyocytes have a low turnover rate at only 0.5-2% per year, insufficient for repopulating injured myocardium. However, recent research has shown that the neonatal mammalian heart exhibits regenerative capacity shortly after birth. Understanding the mechanisms underlying neonatal cardiomyocyte regeneration is imperative to developing potential therapeutic techniques in treating MI. In the current project we attempt to profile cell death and scar formation to gain insights into the predominant form of cardiomyocyte death in the regenerating heart. We induced MI in postnatal day 1 (P1, regenerative), and postnatal day 7 (P7, non-regenerative) mouse hearts by left anterior descending artery occlusion (LAD-O). The progressive scar formation was assessed using Masson's Trichrome staining at multiple timepoints up to 14 days after MI. At each time point, we profiled types of regulated cell death using immunofluorescent staining. To further investigate the role of ferroptosis in cardiomyocyte death, in vitro experiments were performed using an immortalized cardiomyocyte line, AC16, and a ferroptotic agent, erastin. We found that the scar formation was most dynamic between 2 and 3 days after MI and that the course of scar formation varied greatly between P1 and P7 hearts. Immunofluorescence of cell death markers reveal unique timing of cardiomyocyte death in P1 and P7 hearts. Lastly, we confirmed reports that cell density impacts extent of ferroptotic death in AC16 cardiomyocytes. Our results indicate that timing of scar formation and cardiomyocyte death is dynamic and differs in P1 regenerative and P7 non-regenerative mouse hearts. Interestingly, our results potentially implicate a pronounced role of ferroptotic cell death in the injured heart. This work was supported by National Heart Lung and Blood Institute.

29 Transcriptomic analysis of engineered, multicellular cardiac organoids reveals similarities to human myocardium

Charles Kerr, Dylan Richards, Ying Mei, Ying Mei, College of Graduate Studies, Department of Department of Regenerative Medicine and Cell Biology, MUSC.

Abstract Withheld from Publication

30 Tau-spiracy: A Developing Mechanism for Cardiac Dysfunction

Stephanie DiLucia, Rakez Kayed, Anna Ellsworth, Federica del Monte, College of Medicine (MD, PhD), Department of Department of Medicine, Division of Cardiology, MUSC.

Abstract Withheld from Publication

31 Evaluating the Influence of Individual Cerebral Architecture and Alcohol Cue-Reactivity Patterns on AUD Treatment Outcome

Daniel McCalley, Julia P. Imperatore, Ingrid E. Contreras, Colleen Hanlon, College of Graduate Studies, Department of Psychiatry and Behavioral Sciences; Neurosciences, MUSC.

Introduction: Transcranial Magnetic Stimulation (TMS) is a non-invasive neuromodulation tool which can decrease drinking and alcohol cue-reactivity among individuals with Alcohol Use Disorder (AUD). Two unique aspects of AUD, however, may impact TMS treatment efficacy: 1) alcohol-induced atrophy in the prefrontal cortex (affecting TMS-induced electric fields), and 2) unique spatial topographies of individual alcohol cue-reactivity. Objective: Evaluate the influence of individualized variables such as TMS-induced electric field and alcohol cue-reactivity patterns on treatment outcome in AUD. Methods: In the randomized, double-blind Parent Study, 45 individuals with AUD received 10 sessions of real or sham TMS targeting the medial-prefrontal cortex during an intensive outpatient program. Mood and drinking behaviors were measured throughout the study. Structural MRI was used to construct individualized electric fields (SIMNIBS v3.1). Functional MRI was used to determine individualized patterns of cue-reactivity to alcohol vs. non-alcoholic beverage cues. These patterns were overlaid with each individual's electric field map. If the two images overlapped, individuals were grouped as 'ideal' TMS-candidates (n=14), otherwise they were grouped as 'non-ideal' TMS-candidates (n=11). The sham group (n=20) was not categorized. Results: The 'ideal' TMS-candidate group had the highest retention throughout the 3-4 month experiment ($\chi^2(2, 45)=14.58$, $p=0.02$). A multivariate linear model including mood data throughout the experiment revealed a main effect of group ('ideal' vs 'non-ideal') ($F(3,64)=2.981$, $p=0.04$), wherein the 'ideal' group had a greater decrease in depression (Beck's Depression Inventory; $F(1,66)=5.016$, $p=0.028$) and anxiety (Spielberger's Anxiety Inventory; State - $F(1,66) =3.655$, $p=0.06$, Trait - $F(1,66)=7.746$, $p=0.007$) symptoms relative to the 'non-ideal' group. Conclusions: These data suggest that TMS targeting the loci of cue-reactivity may be a fruitful strategy in improving TMS-AUD treatment outcome. Ongoing analyses will determine relative contributions of TMS-induced electric field size and strength, magnitude and distribution of cue-reactivity, and the extent of overlap between these factors on treatment outcome. This work was supported by F31AA028426 (McCalley), R01DA036617 (Hanlon), R21DA0412244 (Hanlon), P50 AA010761 (Becker), T32 32AA00747-32 (Woodward).

32 Temporal Encoding of Cocaine Seeking and Refraining from Seeking in Different Neuronal Populations of the Nucleus Accumbens Core

Reda Chalhoub, Constanza Garcia-Keller, Rusty Nall, Jasper Heinsbroek, Ana-Clara Bobadilla, Peter Kalivas, College of Graduate Studies (MSTP), Department of Neuroscience, MUSC.

Abstract Withheld from Publication

33 Elucidating the Mechanism of PCBP1 Regulated Transcription at Cancer Gene Promoters

Joseph Karam, Bidyut Mohanty, Philip Howe, College of Graduate Studies, Department of Biochemistry and Molecular Biology, MUSC.

Abstract Withheld from Publication

34 Metabolic requisites for T cell protein translation in tumors

Megan Tennant, Katie E. Hurst, Alex M. Andrews, Lee R. Leddy, David M. Neskey,, Lauren E. Ball, and Jessica E. Thaxton, Jessica Thaxton, College of Graduate Studies, Department of Orthopedics and Physical Medicine, Microbiology and Immunology, Hollings Cancer Center, MUSC.

T cells are a secretory immune subset with the capacity to control solid tumors. Protein translation is of paramount importance in CD8 T cells, controlling proliferation, stimulation and lineage fate. We studied the ability of T cells to undergo protein translation in mouse and human tumors and found that canonical protein synthesis is restricted in endogenous CD8 tumor infiltrating lymphocytes (TILs) by the tumor microenvironment (TME). Proteomic analysis revealed that gluconeogenesis and □-oxidation of fatty acids (FAO) were upregulated in CD8 T cells under tumor stress but these metabolic sources were unable to support translation in the TME. Further, we discovered that glucose metabolism and mammalian target of rapamycin complex 1 (mTORC1) preferentially hinder protein synthesis in CD8 TILs. These data enabled the discovery that proteasomal protein degradation is the optimal source to fuel protein translation in T cells in the stress of solid tumors. We demonstrate that Rapamycin-primed T cells are preferentially powered by proteasomal proteolysis and are able to sustain protein translation in tumors and control tumor growth. Our data establish that canonical protein translation is subject to inhibition in the TME and promotion of protein catabolism is a new strategy to support antitumor immunity. We have leveraged these findings to benefit oral cavity cancer (OCC) patients as our preclinical data illustrate the breakthrough discovery that transient inhibition of mTORC1 in vivo promotes T cells able to eliminate established OCC when combined with standard immunotherapy. We are poised to rapidly translate these data to a clinical trial. This work was supported by T32 DE017551.

35 SPARC by Bone Marrow-Derived Cells Contributes to Myocardial Fibrosis in Pressure-Overload

Lily Neff, Hannah Riley, Ryan Kelly, An Van Laer, Shaoni Dasgupta, Catalin Baicu, Lindsay McDonald, Amanda LaRue, Michael Zile, Amy Bradshaw, College of Graduate Studies, Department of Cardiology, Division of (Dept. of Medicine), MUSC.

Heart failure with preserved ejection fraction (HFpEF) is a complex clinical condition associated with pressure overload (PO) and characterized by cardiac dysfunction, myocardial stiffness, and fibrosis. In a mouse model of cardiac fibrosis, left ventricular (LV) is induced by transverse aortic constriction (TAC). Previous research has demonstrated that Secreted Protein Acidic and Rich in Cysteine (SPARC) is necessary for the development of fibrosis and myocardial stiffness. However, previous studies have not elucidated the cellular sources of cardiac SPARC in LVPO. In the present study, full-body irradiation and bone marrow rescue was used to address cellular sources of SPARC in PO. Irradiated SPARC-null mice were transplanted with donor wild-type

(WT) bone marrow, whereas WT mice were transplanted with SPARC-null bone marrow. Following bone marrow transfer, mice were subjected to LVPO through TAC surgery. Analyses of collagen content and myocardial stiffness demonstrated that SPARC expression by bone-marrow derived cells was required for fibrotic deposition of collagen following PO. In addition, increases in myocardial macrophage numbers was dependent upon SPARC production by bone marrow-derived cells. To assess whether myocardial vasculature was affected by PO, platelet endothelial cell adhesion molecule (PECAM) staining was used to compare total vasculature between groups. No apparent differences between groups was detected in terms of average vessel size as assessed which suggested that neither cardiac angiogenesis nor rarefication after irradiation followed by PO had occurred. This work was supported by T32GM132055, 1 I01 CX001608.

36 ANP affects mitochondrial function in the renal cortex during salt-sensitive hypertension

Morgan Spicer, Regina Sultanova, Mark Domondon, Ryan Schibalski, Krisztian Stadler, Daria Ilatovskaya, Daria Ilatovskaya, College of Graduate Studies (MSTP), Department of Department of Medicine, Nephrology, MUSC.

Background: Natriuretic peptides (NPs) are involved in lipid oxidation and mitochondrial respiration in cardiac and adipose tissues; however, little is known about the effects of NPs on renal mitochondria. Atrial NP (ANP) level was suggested as a marker for salt-sensitivity (SS). Previous studies showed that in Dahl SS rats lacking ANP (SSNPPA-/-) renal disease is exacerbated when they are placed on a high salt (HS) diet, compared to SSWT (wild type) rats. We hypothesized that in SS hypertension ANP deficiency affects renal mitochondrial bioenergetics and thus contributes to end-organ damage. Methods: Hypertension was induced in male SSNPPA-/- and SSWT rats by a 21 day long high salt (HS, 4% NaCl) diet; control group received a normal (NS) 0.4% NaCl diet. We isolated renal cortical mitochondria and tested oxygen consumption rate (OCR), as well as mt (mitochondrial) membrane potential, superoxide, and H2O2 production via spectrofluorimetry. Electron micrographs (EM) of mitochondria were analyzed with FIJI. SOD activity was measured using a commercial assay. Results. We report a decrease in mt-membrane potential, and an increase in mtH2O2 production in SSNPPA-/- vs SSWT. SOD2 level and total SOD activity were found similar in all groups. Interestingly, we observed lower expression of Opa1, a mitochondrial fusion protein, in the SSNPPA-/- groups vs SSWT. We observed elevated respiration and spare OCR in cortical mitochondria isolated from SSNPPA-/- on HS, whereas in SSWT rats these parameters were reduced (vs NS). Analysis of EM in the collecting duct cells showed more numerous and dense mitochondria in SSNPPA-/- vs SSWT groups on HS diet. Conclusions: Our data suggest that renal cortical mitochondrial bioenergetics is affected by ANP. However, more research is needed to resolve the potentially differential effects in various nephron segments, and to firmly establish signaling cascades important for renal function. This work was supported by NIH R00 DK105160, R01HL148115, and Dialysis Clinic Inc Reserve Funds.

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

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

Recent studies have shown that genomic instability, oncogene expression, and high mutation rates in more than 50% of tumors can be attributed to 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 mechanism 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), a member of the Argonaute family of proteins and a key component of the piRNA processing pathway that is responsible for transposon silencing. piRNAs (PIWI-interacting RNAs) are a distinct class of small RNAs that bind to and are processed by PIWI proteins, resulting in concomitant transposon degradation. 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 epithelial cells, whereas this association is lost in cancer cells. Furthermore, our data show that E-cadherin depletion in well-differentiated breast epithelial MCF10A cells 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 transposons, as well as of γ-H2AX, an indicator of DNA double-stranded breaks, which could be an indication of increased retrotransposition. From these findings, we hypothesize that the adherens junctions recruit PIWIL2 and suppress transposon activity in differentiated cells to maintain genomic integrity and the normal epithelial phenotype. We are currently testing this hypothesis by examining regulation of transposons through adherens junctions-regulated piRNAs. Since both loss of junctional integrity and increased transposon activity are universal events in cancer, the study has the potential to further our understanding of the causes of tumorigenesis. This work was supported by NIH/NCI R21 CA246233-01A1, NIH/NIGMS P20 GM103499, TL1 TR001451, UL1 TR001450.

38 Cell-targeted collagen imaging proteomics in breast cancer

Denys Rujchanarong, Michael C Ostrowski Ph.D., Peggi Angel, College of Graduate Studies, Department of Department of Pharmacology, MUSC.

Breast stroma plays a significant role in breast cancer risk and progression yet remains poorly understood. Breast density, significantly correlated with increased collagen deposition, is a risk factor for breast cancer. Collagen is the most abundant protein expressed in the stroma and its increased deposition and alignment have been shown to contribute to breast cancer progression. Proper protein folding of collagen into fibril triple helical molecules is required for extracellular secretion and collagen stability. This process is primarily mediated by the collagen post-translational modification proline hydroxylation (HYP), which is catalyzed by prolyl hydroxylase enzymes. Previous studies have shown increased prolyl hydroxylase expression corresponds to increased collagen stiffness, deposition, and misalignment; in turn, tumor size and risk of metastasis increase. Additionally, tumor suppressor gene PTEN has been identified as an important regulator of the breast stroma and plays a role in collagen reorganization observed in breast cancer progression. From this, we hypothesized that specific collagen

sequence variants, including collagen types and their post-translational modifications, are regulated dependent upon stromal PTEN expression. To investigate how PTEN expression regulates collagen variants and localization, our lab used matrix assisted laser desorption/ionization imaging mass spectrometry (MALDI-IMS) to identify and quantify collagen sequence variants in stromal breast tissue based on cellular PTEN staining. From the acquired peak data, intensities of four collagen peaks were significantly different between areas of high and low PTEN staining and were putatively identified to contain site-specific HYP. Overall, identifying collagen sequence variants influenced by PTEN expression can provide insight on breast cancer risk, progression, and metastasis risk. Current studies focus on understanding PTEN-mediated collagen regulation in health disparities of breast cancer risk. This work was supported by NIH/NCI R01 CA253460, NIH/NCI 1R21 CA240148-01.

39 Triazole-based reversible inhibitors of spermine oxidase and implications for amelioration of neuronal injury

Amelia Furbish, Houston, Aubree, Patrick Woster, College of Graduate Studies, Department of Drug Discovery and Biomedical Sciences, MUSC.

Spermine oxidase (SMOX) is a highly inducible amine oxidase involved in the polyamine back-conversion pathway. SMOX catalyzes the conversion of spermine to spermidine, producing the toxic byproducts 3-aminopropanal (3-AP) and hydrogen peroxide. 3-AP undergoes spontaneous conversion to acrolein, a highly reactive aldehyde with the propensity to alkylate DNA and inactivate vital cellular proteins. Of these toxic metabolites, acrolein, which is most effectively produced by spermine oxidase, has been shown to exert the most significant effects on cell damage and cytotoxicity. Within the central nervous system, intracellular polyamines have the potential to act as radical scavengers in response to neuronal damage. Studies have linked the overexpression of SMOX with increased susceptibility to excitotoxic stress and neuronal injury. A small number of SMOX inhibitors have been described in the literature, however, currently available inhibitors lack selectivity for the enzyme and are associated with dose-limiting toxicity. Our group has recently described a series of triazole-based reversible inhibitors of SMOX (Holshouser et al. 2019). The purpose of the current project is to optimize our most promising inhibitors by structural modification, and to determine whether they can reduce oxidative damage in neuronal cells. Along these lines, we investigated the ability of hydrogen peroxide to induce SMOX expression in an SH-SY5Y neuroblastoma cell line. SMOX expression was quantified using western blot. We found that cellular SMOX protein increases in response to hydrogen peroxide exposure in a dose-dependent manner, indicating that this may be a viable cellular model for testing the efficacy of our experimental compounds. Finally, we used multiple medicinal chemistry techniques to synthesize a variety of novel triazole-based analogs as potential SMOX inhibitors. Our future aims include testing these compounds for potency and selectivity as SMOX inhibitors and analyzing the most selective and potent compounds in cellular models of neuronal injury. This work was supported by TL1 TR001451 & UL1 TR001450, NIH 1R01CA204345 (PMW).

40 Sex Differences in Cognitive and Psychological Outcomes of Stroke: Impact of Diabetes

Victoria Wolf, Aunay Miller, Raghavendar Chandran, Weiguo Li, Adviye Ergul, College of Graduate Studies, Department of Pathology & Laboratory Medicine, MUSC.

Diabetes increases risk and severity of post-stroke cognitive impairment (PSCI), a major cause of disability worldwide. While it is known that females suffer more from PSCI, psychological outcomes and underlying reasons are poorly understood. From a preclinical perspective, potential explanations include 1) use of otherwise healthy animals in experimental stroke research without integration of common comorbid diseases like diabetes into the study design, and 2) optimization of most behavioral tests for sensorimotor and cognitive functions using only male animal models. Our hypothesis is that post-stroke outcomes are sex and comorbid disease-dependent. To test this, we validated the Novel Object Recognition (NOR), Y-maze, and Passive Avoidance (PAT) behavioral paradigms in Ctrl and Diabetic (DM) male (M) and female (F) rats pre- and post-stroke (S) via 60 min. middle cerebral artery occlusion (MCAO). We tested the PAT paradigm with a multi-trial method where the animals were habituated to the dark/light chambers without foot shock and then trained in 3 trials where they received foot shock upon entering the dark. We then tested retention following MCAO for their memory of foot shock 2 weeks prior. Multitrial results suggested that there was no difference between groups in learning to associate the dark chamber with the shock, so we revised the multitrial method into a single-trial method for ongoing retention tests to compare the impact of stroke on shock memory recall. PAT revealed disease- and sex-dependent responses to aversive stimulus. NOR revealed that M-DM-S and F-DM-S rats have decreased exploration time, suggesting that they are unmotivated or depressed. Y-maze indicated that males displayed spatial memory recovery, while females remained impaired. In summary, we have observed numerous sex- and disease-dependent post-stroke outcomes with standard behavioral paradigms, causing us to carefully consider how we evaluate preclinical outcomes. This work was supported by VA Merit Award (BX000347), VA Senior Research Career Scientist Award, NIH awards (R01NS083559, PO1HL134604, and NS104573), and NIDDK Diabetic Complications Consortium Pilot & Feasibility Grant (DK076169 and DK115255), VW (NIHLBI T32 HL007260-44), AM (PRE.

41 Characterization of Human Temporomandibular Lateral Capsule-Ligament Complex Ultrastructure, Biochemistry and Biomechanics

Cherice Hill, Matthew Coombs, Daniel Bonthius, Sarah Cisewski, Marshall Wilson, Hai Yao, College of Dental Medicine, Department of Clemson-MUSC Bioengineering Program, Department of Oral Health Sciences, MUSC.

The human temporomandibular joint (TMJ), which allows for dependent rotation and translation between the cranium and mandible, is highly debated. Some describe the TMJ capsule as a fibrous capsule with distinct ligaments while others describe it as a ligamentous thickening that is part of the capsule. The LCL complex is also believed to both actively and passively reduce the motion of the mandibular condyle. Due to the uncertainty that surrounds the LCL complex, a baseline characterization of the LCL complex is needed to better understand the complex and its role in the anatomy. This study explores the ultrastructural arrangement, biochemical composition, and biomechanical tensile properties of the human LCL complex. Specifically, this study investigates region-specific differences to explore the presence of a distinct temporomandibular ligament and sex-specific differences to establish baseline values for evaluations of potential etiological mechanisms. There was no significant difference between

male and female samples for collagen fiber coherency or collagen fiber bundle size. There was also no significant difference between male and female samples for elastic fiber count, however, females trended higher. There were no significant differences between sexes or between regions for human LCL complex water content, collagen content, or sGAG content. There was a significant region effect on failure stress, with failure stress 1.1(0.7) MPa in the anterior region and 0.6(0.4) MPa in the posterior region. These significant regional differences confirm the presence of a mechanically distinct temporomandibular ligament or ligamentous thickening. This study's results have important biomechanical and clinical ramifications, providing critical baseline tissue material properties, imposing new requirements for the development of temporomandibular joint musculoskeletal models, and identifying new areas for etiologic investigations for temporomandibular disorders. This work was supported by This project was supported by NIH grants P20GM121342, R03DE018741 and R01DE021134, NIH K99 post-doctoral fellowship DE028358, NIH F32 post-doctoral fellowship DE027864, NIH T32 post-doctoral fellowship DE017551, and NIH F31 pre-doctoral fellowship DE02668.

42 Pain and Pain Catastrophizing as Predictors of Depression, Anxiety, and Opiate Misuse in Veterans and Veteran Family Members with Chronic Pain

Abagail Ault, Lester Shayla, Mappin Georgia, Santa Ana Elizabeth, Christon Lilian, Wedin Sharlene, Bottonari Kathryn, Balliet Wendy, Carter Lauren, Muzzy Wendy, McCauley Jenna, Imperatore Julia, George Mark, Jeffrey Borckardt, College of Medicine, Department of Psychiatry and Behavioral Sciences, MUSC.

Chronic pain patients are at a higher than average risk of suffering from psychiatric disorders including depression, anxiety, and opioid misuse. However, the relationship between chronic pain and psychiatric illnesses is not well understood. Pain catastrophizing, a set of negative emotions and cognitions in relation to painful stimuli, may be an important related factor. This study investigated the correlation of pain and pain catastrophizing in relation to depression, anxiety, and opioid misuse. 105 Veterans and veteran family members (21 female, average age 53.2[SD=11.1]) with chronic pain who met criteria for opioid misuse completed multiple measures of pain, and psychiatric symptoms prior to engaging in a randomized controlled trial for chronic pain treatment. The present study examined 4 self-report measures (Beck Anxiety Inventory (BAI), Beck Depression Inventory (BDI), Pain Catastrophizing Scale (PCS), Common Opioid Misuse Measure (COMM) and several items from the Brief Pain Inventory (BPI). Pearsons r correlations were carried out comparing predictive power of pain and pain catastrophizing on psychiatric outcomes. Pain catastrophizing had significant correlations with depression ($r=0.506$, $p<0.001$), anxiety ($r=0.491$, $p<0.001$), and opioid misuse (0.481, $p<0.001$). BPI item "Pain on average" was weakly correlated with anxiety ($r=0.203$, $p=0.038$) and unable to predict depression or opioid misuse. BPI items "Pain at it's worst in the last 24 hours," "pain at its least in the last 24 hours," and "pain right now" were not statistically correlated with any of the examined psychiatric outcomes. Furthermore, pain catastrophizing was at best only weakly correlated with each of the pain items ($r=0.186$-0.295, $p=0.002$-0.057). Pain catastrophizing was a better predictor of depression, anxiety, and opioid misuse than any measure of pain taken, and was only weakly related to actual pain. Further research should explore causal roots of pain catastrophizing to inform potential pain catastrophizing interventions for pain related psychiatric illness. This work was supported by Ralph H Johnson VA Medical Center, NIH.

43 RAS inhibition limits neuroblastoma tumorigenesis and promotes Retinoic acid induced differentiation in a subset of NBL tumors

Vinodh Rajagopalan, , John O'Bryan, College of Graduate Studies, Department of Pharmacology, MUSC.

Abstract Withheld from Publication

44 Stabilization of Gap and Tight Junctions Ameliorates Ischemia-Reperfusion Injury in a Porcine Model of Renal Transplantation

Leah Plumblee, Jane Kilkenny, MD; Kunal Patel, MD PhD; Patterson Allen; Herman Connor; Logan Langerude BS; Domonique Rivers; Satish Nadig, MD PhD, Carl Atkinson, College of Graduate Studies, Department of Microbiology and Immunology, MUSC.

Background: Renal transplant is an accepted therapy for end-stage renal failure. Chronic transplant dysfunction remains as the leading cause of long-term graft loss and is, in part, caused by ischemia reperfusion injury (IRI). Connexin proteins compromising gap and tight junctions, in particular Connexin43 (Cx43), govern many facets of endothelial cell functionality and play a pivotal role in the pathophysiology of IRI. Here we determine the therapeutic utility of Alpha Connexin carboxy-Terminal (aCT1), a novel Cx43-based peptide, which has been shown to stabilize gap junctions by modulating the molecular interaction between Cx43 and its C-terminal binding partners. Methods: Kidneys were harvested from 5 Yorkshire/Landrace pigs. The renal allografts were flushed with either aCT1 augmented UW solution (n = 4) or UW alone (n = 6). Kidneys were then subjected to 36 hrs of cold storage prior to 6 hrs of hypothermic pulsatile perfusion. On completion of kidney perfusion 200µm kidney sections were taken and organ cultures performed to stimulate ex-vivo graft IRI. The effect of UW aCT1 therapy on renal function was assessed during machine perfusion, and pathology, and pro-inflammatory gene transcription analyzed in organ culture tissues. Results: Augmentation of UW with aCT1 had no adverse effect on renal function as determined by physiological and biochemical assays. Ex-vivo organ cultures used to model IRI demonstrated a significant increase in pro-inflammatory (IL-6 and IL-8), adhesion molecule gene (P-selectin, ICAM, VCAM), and chemokine genes (MCP-1, IL-1β, TNF-α), key factors associated with IRI, which were all significantly reduced in aCT1 treated kidneys. Conclusions: Augmentation of standard of care UW solution with gap/tight junction modifying aCT1 significantly reduced ex-vivo kidney IRI and had no deleterious impact on graft function during hypothermic pulsatile perfusion. The addition of aCT1 to UW solution holds promise as a therapeutic augmentation in renal transplantation. This work was supported by NIH T32 HL007260 NIBIB K08EB019495.

45 Analytical methods for characterization of collagenous soft tissue

Glenn Hepfer, Peng Chen, Matthew Coombs, Hai Yao, College of Dental Medicine, Department of Oral Health Sciences, MUSC.

Introduction/rationale: Tissue preservation and engineering techniques strive to produce tissues that are readily available for transplantation. Soft connective tissues such as cartilage, heart valve, tendon, and cornea are composed mainly of a collagenous extracellular matrix (ECM). Characterization of the ECM of preserved and engineered tissue is critical to maintaining tissue function when developing processing and fabrication methods. The purpose of this study is to test the sensitivity of various techniques for measuring properties of ECM. Methods:

Cryopreserved porcine heart valves and human tendons were subjected to various levels of collagenase and heat treatment. Following treatment, biomechanical, electrical conductivity, viability, a collagen assay, and imaging techniques were used to assess the degree of damage. Based on each method's ability to detect damage, the sensitivities of the methods were evaluated. Results: For porcine heart valves subjected to enzymatic degradation with collagenase, biomechanical, conductivity, and viability tests were able to detect a statistically significant effect ($p \leq 0.02$). For heart valves subjected to thermal degradation, viability was the most sensitive test, followed by conductivity and the collagen assay. For human tendons, biomechanical tests were more sensitive for heat treated samples while conductivity tests were more sensitive for collagenase treated samples. Conclusion: A variety of techniques is necessary to fully characterize the properties and, thus, the function of collagenous soft tissue. Depending on the damage and tissue, electrical conductivity tests may complement traditional biomechanical and viability tests in evaluating processing and engineering methods for soft tissue grafts. This work was supported by NIH grants DE021134, DE018741, AR055775.

46 Serum and Glucocorticoid Inducible Kinase-1 Drives Aortic Macrophage Accumulation in Hypertension and Abdominal Aortic Aneurysms

SarahRose Hall, Tyler Grespin MS, Rupak Mukherjee PhD, Jeffrey A. Jones PhD, Jean Marie Ruddy, College of Medicine (MD, PhD), Department of Surgery, MUSC.

Introduction: Hypertensive aortic remodeling is driven by macrophage infiltration and a subset of these patients will also develop an abdominal aortic aneurysm (AAA). The serum and glucocorticoid inducible kinase-1 (SGK-1) is mechanosensitive and implicated in bypass graft remodeling. It is hypothesized that SGK-1 is upregulated under elevated tension to promote macrophage accumulation and contribute to AAA development. Methods: Aortic vascular smooth muscle cells (VSMCs) were subjected to 12% biaxial cyclic stretch for 3 hours with subsequent mRNA harvest and interleukin-6 (IL-6) expression quantification by QPCR (n=5). SGK-1 activity was blocked by the selective inhibitor EMD638683 (10□M). Hypertension (HTN) was induced in C57Bl/6 mice with Angiotensin-II (AngII) infusion via mini-osmotic pump (1.46mg/kg/dayx21days, n=4). Terminal procedure included blood pressure quantification by tail cuff plethysmography. Abundance of SGK-1, pSGK-1, and the mature macrophage marker F4/80, was determined by immunoblotting. AAA was induced in C57Bl/6 mice by peri-adventitial application of $CaCl_2$ with terminal procedure at 21 days for aortic diameter assessment and immunoblot quantification of target proteins (n=4). Results: Following VSMC cyclic stretch, IL-6 expression increased 1.8+/-0.3 fold compared to static conditions ($p<0.05$), and returned to baseline in EMD638683 treated cells, demonstrating tension-dependent activity of SGK-1. Mice receiving AngII infusion developed >40% elevation in systolic BP ($p<0.05$) with no change in aortic diameter. The activity of SGK-1 (evidenced by pSGK-1/SGK-1) and abundance of F4/80 were increased with HTN ($p<0.05$). Three weeks after AAA induction, aortic diameters were expanded by >60%, and SGK-1 activity as well as abundance of F4/80 ($p<0.05$) were again elevated ($p<0.05$, respectively), suggesting a positive biomechanical link between tension and macrophage content, mediated in-part by SGK-1 activation. Conclusions: External stimuli to elevate SGK-1 activity can increase IL-6 production to accumulate aortic F4/80 positive macrophages and contribute to aortic remodeling. Therefore, SGK-1 may represent a novel target to abrogate hypertensive AAA growth.

47 The Role of ER-alpha in the Transcription of Pro-Fibrotic Mediators

Alisa Savchenko Savchenko, Carol Feghali-Bostwick, DeAnna Baker Frost, College of Medicine, Department of Department Of Medicine, Division of Rheumatology, MUSC.

Systemic sclerosis (SSc) is an autoimmune disease characterized by fibrosis of the skin and internal organs. Important pro-fibrotic mediators in SSc includes transforming growth factor-beta 1 and 2 (TGFb1 and TGFb2) and fibronectin (FN). Although, SSc predominates in females, males have a more severe form of the disease. Since a sex-based disparity exists, hormonal influences may contribute to disease prevalence and severity. Estradiol (E2) is a form of estrogen with pro-fibrotic effects in the skin. Patients with SSc have high levels of E2, and unpublished data show E2 increases TGFb1 and TGFb2 in primary human dermal fibroblasts. E2 binds to its classical receptors, estrogen receptor alpha (ERa) or estrogen receptor beta (ERb), to cause cellular changes. ERa is the major receptor implicated in fibrosis. However, its role in E2-induced dermal fibrosis is undefined. We investigated how ERa affects TGFb1, 2 and FN transcription using primary mouse male and female dermal fibroblasts genetically lacking ERa (ERa-/-). ERa was silenced in human dermal fibroblasts through siRNA to measure TGFb1 and 2. There was a trend that knockdown of ERa using siRNA prevented TGFb1 and 2 induction. Similarly, in wild-type (WT) mouse dermal fibroblasts, E2-induced TGFb1 and 2 transcription, significantly. ERa-/- cells had a significant increase in TGFb1 and a trend in FN. Upon further inspection, female WT dermal fibroblasts had a significant increase in TGFb1 and FN transcripts with a trend for TGFb2. Yet, the same trend in female WT cells existed for ERa-/- male dermal fibroblasts. We conclude that E2-mediated dermal fibrosis occurs in part through ERa, since the lack of ERa causes a decrease in TGFb1 and 2 transcription. However, the decrease seems to be sex-specific, isolated to female mouse dermal fibroblasts. Future studies are needed to determine if manipulation of ERa signaling could be used to treat SSc. This work was supported by KL2 TR001452 & UL1 TR001450.

48 Compensatory Gain at The Brainstem Represents Increased Neural Recruitment in the Face of Age-Related Declines in Neural Synchrony

Lilyana Kerouac, Brendan J. Balken, James W. Dias, Carolyn M. McClaskey, Kelly Harris, College of Medicine, Department of Otolaryngology - Head and Neck Surgery, MUSC.

Aging is associated with robust deficits in auditory nerve function, including a decrease in the number of nerve fibers present and diminished neural synchrony. Despite these auditory nerve deficits, neural responses at higher levels of the auditory system are often preserved with age. Animal models suggest that this preservation is the result of central gain mechanisms, wherein decreased inhibitory function leads to greater neural responses to incoming auditory stimuli. However, it is unclear whether these central gain mechanisms are present in humans. Further, it is unknown if these mechanisms can compensate for deficits in neural synchrony and preserve auditory temporal information, important for auditory perception. We hypothesize that, in older adults, central gain is present at the auditory brainstem and results in preserved brainstem response amplitudes, but a loss of neural synchrony. Central gain effects were examined by comparing click-induced auditory neural responses from the auditory nerve (N1 of the compound action potential) and from the auditory brainstem (Wave V of the auditory brainstem response) in a large sample of younger and older adults with and without hearing loss. Despite robust and significant deficits in auditory nerve function, brainstem activity exhibited well-preserved response amplitudes but age-related deficits in neural synchrony. The results support

our hypothesis that central gain at the brainstem may arise from the recruitment of additional neurons and compensate for age-related auditory nerve loss. Despite the evidence for compensatory gain, the continued loss of neural synchrony may disrupt the coding of auditory temporal information and lead to auditory perceptual deficits. Amplification of the auditory evoked response without preserved neural synchrony at the brainstem may therefore be maladaptive and not beneficial to auditory processing. This work was supported by NIDCD RO1 DC014467, RO1 DC017916, P50 DC00422, T32 DC014435.

49 Sex differences in renal mitochondrial function of young healthy rats

Ryan Schibalski, Regina Sultanova, Mark Domondon, Allison McCrimmon, Krisztian Stadler, Daria Ilatovskaya, College of Medicine, Department of Medicine/Nephrology, MUSC.

Introduction. Sex differences in mitochondrial performance have been linked to many renovascular (RV) pathologies; premenopausal females are typically less prone to RV damage than males. Differences in the ability to manage mitochondrial function can mediate the progression of the RV diseases. Little is known about how sex-related dissimilarities may affect the performance of renal mitochondria. The goal of this study was to test the differences in renal mitochondrial function in healthy male vs female rats. Methods. Mitochondria were isolated from the kidneys collected from Sprague Dawley (SD) rats. Mitochondrial membrane potential, superoxide and H2O2 levels were measured with luminescent or fluorescent dyes, and seahorse assay was performed. Lipid peroxide radical formation was detected using electron spin resonance spectroscopy (ESR) with in vivo spin trapping. The SOD activity was measured by a commercial kit. Results. Kidneys from SD male (SDM) and female rats (SDF) were divided into cortex (SDMC, FC) and medulla (SDMM, FM). We report higher membrane potential in SDFM compared to SDMM ($p<0.001$). H2O2 levels were elevated in both the SDFC and SDFM mitochondria compared to SDM ($p<0.01$). Interestingly, superoxide production was increased in the medulla compared to the cortex for both SDM and SDF, while SOD2 expression was similar. Total SOD activity was increased in SDFC compared to all other groups ($p<0.01$). ESR showed similar lipid peroxide radical levels in all groups. Antioxidant capacity was reduced in SDFM tissues compared to other groups ($p<0.05$). Female mitochondria had decreased oxygen consumption rate (OCR) compared to males, and all OCR parameters were lower in medullary vs cortical mitochondria, independent of sex. Conclusions. We report robust sex-related differences in mitochondrial function in the kidneys of young healthy rats. Further studies are needed to establish the specific mechanisms that may affect the predisposition to kidney disease development later in life.

50 The Effects of Zero Gravity Parabolic Flight on Transcranial Magnetic Stimulation (TMS) Motor Threshold

Claire Cox, James W. Lopez, Holly H. Fleischmann, Kevin A. Caulfield, Jeffrey J. Borckardt, William H. DeVries, Philipp Summers, Suzanne Kerns, Colleen A. Hanlon, Lisa M. McTeague, Mark S. George, Bashar W. Badran, Donna Roberts, College of Medicine, Department of Radiology, MUSC.

Abstract Introduction: It is currently unclear how long-term exposure to zero gravity (0G) during spaceflight may alter brain physiology. In this study, we used transcranial magnetic stimulation (TMS) to test the effect of acute exposures to 0G during parabolic flight on neurophysiology.

Methods: In 10 healthy adults (5 women), TMS was applied over motor cortex and resting motor thresholds (rMTs) were acquired before, during, and after parabolic flight. We built custom helmets to keep the TMS coil in position during 0G periods. TMS was applied over the left motor cortex and electromyography (EMG) signals in the contralateral right hand were obtained. For each participant, we obtained three Earth rMTs pre- and post-flight, and three to five 0G rMTs over the course of 30 parabolas. We hypothesized that an upward shift of the brain in the 0G periods, similar to the brain shift which has been observed in NASA astronauts, would result in lower rMTs compared to pre- and post-flight MTs acquired on Earth at 1G. Results: TMS in 0G was safe and no participants experienced adverse events due to TMS. There was a significant main effect of gravity state on rMTs. Preflight, 0G, and post-flight, rMTs were, mean (SEM): 55.0 (3.6), 48.1 (2.4), and 55.4 (3.5). This equates to a 12.6% reduction in rMT that was independent of emotional arousal, age, gender, or rMT assessment number (Linear Mixed Model, $p = 0.0035$). Conclusions: We found that acute exposures to 0G alter rMTs.. Neurophysiological changes in 0G could be due to several reasons, including decreased distance between the scalp and cortex due to brain shift or changes in cerebrospinal fluid outflow due to body position, amongst others. Further studies are needed to clarify these findings prior to embarking on exploration-class missions to the Moon or Mars. This work was supported by Translational Research Institute for Space Health (TRISH).

51 Effects of atrial natriuretic peptide on mitochondrial bioenergetics in cortical collecting duct cells

Thelma Amoah, Yuliia Kashyrina, Mark Domondon, Ryan Schibalski, Mikhail Fomin, Regina Sultanova, Daria Ilatovskaya, College of Graduate Studies, Department of Nephrology, Division of (Dept of Medicine), MUSC.

Background. Atrial natriuretic peptide (ANP) is a hormone released from cardiomyocytes in response to cardiac wall stretching. ANP acts on the kidney by promoting sodium and water excretion. Direct application of ANP has been shown to reduce sodium reabsorption in the renal tubular cells. It has been discovered that ANP is involved in mitochondrial bioenergetics and respiration. Little is known about these pathways in the kidney. We hypothesized that ANP may be implicated in regulation of mitochondrial bioenergetics in the renal cortical collecting ducts (CCD). Methods. Mouse cortical collecting duct (mpkCCD) cells were treated with ANP (5 nM to 10 μM range) for 1 hour. Fluorescent dyes TMRM and Rhod123, CellRox Deep Red, AmplexRed, Rhod2 and Hoechst 33342 were used to label mitochondrial membrane potential (TMRM/Rhod123), production of cytoplasmic ROS or mitochondrial H_2O_2, calc ium, and nuclei in live cells, respectively. A Leica TCS SP5 confocal microscope or a BMG Labtech microplate reader were employed to monitor fluorescence intensity changes in response to ANP. Mitochondrial stress test assays were performed using a Seahorse XF96 Extracellular Flux Analyzer. One-way ANOVA (OriginPro) was used for statistical comparisons. Results. Fluorescence microscopy with TMRM showed a mild dose-dependent decrease in mitochondrial membrane potential in mpkCCD cells treated with low dose ANP (1 nM to 500 nM). These data were confirmed in a 96-well plate assay using Rhod 123. In addition, we observed an acute increase in cytoplasmic ROS and mitochondrial H_2O_2 production and mitochondrial calcium level in response to ANP. Preliminary seahorse analysis indicated that ANP decreases mitochondrial respiration in a dose-dependent manner. Conclusion. Decreased mitochondrial membrane potential is indicative of a disruption in the oxidative phosphorylation and potential

ROS leak. The reported mitochondria-mediated effects of ANP suggest a novel pathway through which ANP may regulate mitochondrial function in the collecting ducts. This work was supported by R25 GM113278, R01HL148115.

52 Role of CTA Surveillance in Managment of Endovascular Repair of Aortic Dissection

Brandon Sloan, Anna Lena Emrich, M.D., Marc Katz, M.D., U. Joseph Schoepf, M.D., Tilman Emrich, M.D., Sanford Zeigler, College of Medicine, Department of Department of Surgery, MUSC.

INTRODUCTION: Thoracic endovascular aortic repair (TEVAR) is considered the preferred modality to treat acute, complicated type B aortic dissection (TBAD). Albeit computed tomography angiography (CTA) is deemed the gold standard for follow-up after TEVAR, there is a lack of evidence concerning the optimal timing of surveillance. This study aims to investigate the role of early postoperative CTA following TEVAR for TBAD, defined as CTA performed within 30 days of the index operation. Endpoints include all-cause mortality and freedom from additional interventions. METHODS: Data on 70 patients who underwent TEVAR during a 3-year period from a single institution were retrospectively collected. The study participants were stratified based on those who had a post-operative CTA in the first 30 days after index intervention (early) vs. those who did not (late). The rates of reintervention and all-cause mortality between the two groups were investigated using Kaplan-Meier and Cox regression analysis. RESULTS: During a median follow-up time of 230 days, the primary endpoint (additional operation) was reached in 24/70 patients (34.3%) with no statistically significant difference between both groups (log-rank-test: $p = 0.886$). All-cause mortality was present in 14/70 (20%) patients, no statistically significant difference between both groups (log-rank-test: $p = 0.440$). Additionally, there were no significant differences in time to additional operation and death for both groups. Cox regression analysis revealed the presence of a chronic TBAD and underlying CTD as risk factors for the need of an additional operation and obesity as a protective factor for all-cause mortality. DISCUSSION: CTA surveillance within 30 days of the index operation, as currently recommended by the STS/SVS guidelines, did not significantly modify mortality or rate of re-intervention after TEVAR for TBAD. In contrast, the presence of underlying conditions influenced significantly the need for an additional operation. Surveillance recommendations should therefore be tailored to the initial indication. This work was supported by MUSC Department of Surgery.

53 Sociodemographic Factors Affecting Perceived Stress During Pregnancy and the Impact on Immune-Mediator Concentrations

Caroline McLeod, Myla D. Ebeling RA, John E. Baatz PhD, Judy R. Shary MS, Jennifer R. Mulligan, PhD, Carol Wagner, College of Medicine, Department of Neonatology, MUSC.

Background: Increased maternal stress during pregnancy is associated with adverse health outcomes for mother and baby. The objective of this study was to determine which sociodemographic factors are most associated with perceived stress during pregnancy. A secondary objective was to determine if an association exists between increased maternal perceived stress and plasma concentrations of specific immune mediators. We hypothesized that low-income level, single marital status, and increased concentrations of C-reactive protein and tumor necrosis alpha (TNF-a) would be positively associated with perceived stress.

Methods: In a prospective, randomized controlled trial of vitamin D (vitD) supplementation, participants were randomized to one of two vitD doses (400 vs 4400 IU/day) and completed health demographic questionnaires and a Perceived Stress Scale survey (PSS-10) during each trimester. Blood samples were collected from participants and were analyzed for 25(OH)D concentration (by RIA) and for 10 immune-mediators: interferon-gamma, interleukins (IL-) IL-1b, IL-2, IL-4, IL-6, IL-8, IL-10, IL-12p70, and IL-13, and TNF-a (R&D Elisa). The potential associations between PSS-10 scores, sociodemographic factors, and immune-mediator concentrations were assessed. Results: In bivariate analysis, participants who were not married and/or had higher risk pregnancies were more likely to have increased PSS-10 scores ($p < 0.05$). Increased PSS-10 scores also were significantly associated with higher serum concentrations of IL-2 and TNF-a, and decreased concentrations of IL-10 and 25(OH)D. In a mixed linear regression analysis, we found that single marital status, high-risk pregnancy, IL-2, and TNF-a all were independent predictors of PSS-10 scores. Conclusions: This study identifies specific sociodemographic factors that are associated with increased perceived stress during pregnancy. This study also provides evidence that increased perceived stress is associated with physiological changes as measured by changes in circulating IL-2, TNF-a, IL-10, and 25(OH)D concentrations. These findings can inform appropriate psychosocial risk assessment of pregnant women in order to improve health outcomes. This work was supported by Kellogg Foundation, SCTR, NIH/NCRR Grant Number 1UL1TR001450.

54 Plasma Sphingolipid Profiles Associated with Atherosclerosis in Systemic Lupus Erythematosus

Olivia Harden, Waleed Twal, Jim Oates, Samar Hammad, College of Medicine, Department of Regenerative Medicine and Cell Biology, MUSC.

Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease that involves multiple organs. SLE affects females more than males with African Americans developing more severe manifestation of the disease. SLE patients are at increased risk for cardiovascular disease (CVD), and SLE women 35-44 years old have 50 fold the incidence rate of CVD. Since SLE patients do not follow the normal age and gender pattern for CVD, but instead an accelerated disease course, the traditional biomarker of elevated LDL and total cholesterol levels do not accurately assess their CVD risk. Recently, Hammad et al. (PLoS One. 2019; e0224496) have identified certain sphingolipids as potential biomarkers related to SLE disease activity and associated CVD, and showed that plasma sphingolipid levels in SLE patients with CVD is dependent on race. In the current study, we sought to identify sphingolipid species as potential biomarkers that can predict or indicate atherosclerosis severity in African-American female SLE patients. Banked plasma samples from a group of African-American female SLE patients (n=39) with well-defined carotid atherosclerotic plaque burden were analyzed for the plasma sphingolipid profiles using mass spectroscopy. The data showed increase in the levels of one sphingomyelin species, and three ceramide species in SLE patients with atherosclerosis (n=31) compared with control patients without detectible atherosclerosis. Dihydrosphingosine 1-phosphate levels decreased in patients with atherosclerotic compared to controls; no significant differences were detected in lactosylceramides between the two groups. There was a statistically significant positive correlation between sphingolipids and plaque burden in five lactosylceramides, total lactosylceramide, two sphingomyelins, total sphingomyelin as well as three ceramide species Taken together, the data demonstrate that sphingolipidomics have the

potential to be used as an early diagnostic tool of atherosclerosis in SLE and may have an added benefit to the currently available tools in the diagnosis, prognosis, and treatment of the disease. This work was supported by This study was funded by College of Graduate Studies (CGS) to SMH, from South Carolina Clinical & Translational Research (SCTR) to JCO and Research Education Program for Minority Medical Students (REPMMS) to OCH. Sphingolipidomics analyses supported in pa.

55 Commensal Gut Microbiota: A Novel Regulator of Craniofacial Skeletal Development

Joy Kirkpatrick, Naoto Ohkura, Nan Hatch, Chad Novince, College of Dental Medicine (DMD, PhD), Department of Oral Health Sciences, MUSC.

Abstract Withheld from Publication

56 Effectiveness and Safety of Maternal Vitamin D Supplementation on Fetal Bone Mineral Density and Content

Kristen Phlegar, Laura Andrews, Myla Ebling, John Baatz, Judith Shary, Carol Wagner, College of Medicine, Department of Neonatology, MUSC.

Abstract Context: Infants with vitamin D (vitD) deficiency are at risk for rickets and other immune diseases. It is unknown if maternal vitD status affects later bone mineralization during infancy. Objective: Examine the effectiveness and safety of maternal vitD supplementation on the bone mineral density (BMD)/bone mineral content (BMC) of offspring through six months. Design/Methods: Participants were mothers with singleton pregnancies and their infants participating in a randomized clinical trial. Each maternal supplementation group received a standard prenatal vitamin containing 400 IU vitamin D each day and an additional supplement of either 0 IU, 1600 IU, or 3600 IU per day, based on treatment arm starting at 12-16 weeks' gestation taken through delivery, substratified by race (African American, Hispanic or white). Infant BMD and BMC were measured using whole body dual-energy Xray absorptiometry (DXA; Hologic 4500A or Discovery A Densometer and software). Measurements were taken at 2-4 weeks and six months, focusing on Region 1, spine; and Region 2, hip. Results: There was no significant differences in either BMD/BMC at baseline or at six months nor in the mean change of BMD or BMC between treatment groups (p=0.5). A statistically significant difference between racial/ethnic groups in mean change in BMC from baseline to 6 months was found: African American infants had a larger increase in BMC (p=0.005) and mean change in BMD (p=0.0003) during the 6 months compared to Hispanic infants. White/Caucasian infants had a greater increase in BMD from baseline to 6 months compared to Hispanic babies (p=0.0003). Conclusions: There were no differences in infant BMD/BMC on the basis of maternal treatment group but there were differences between racial/ethnic groups within each treatment group. Future research may expand upon our finding of racial/ethnic differences mediating the effect of vitD supplementation.

57 Carbohydrate Binding Protein Galectin-3 and It's Role in Macrophage Activation and Chronic Cochlear Inflammation in Age Related Hearing Loss

Phillip Elvis, Junying Tan, Kenyaria Noble, Jeremy Barth, Hainan Lang, College of Medicine, Department of Pathology and Laboratory Medicine, MUSC.

Presbyacusis, or age-related hearing loss, affects one in every two individuals over the age of 75 in the United States and is expected to grow as our population continues to age. Our present understanding is that multiple factors and pathways contribute to presbyacusis pathology, however, much of the mechanism remains unknown. Recently, more attention has been given to inflammation and its role in presbyacusis; this new immune-metabolic viewpoint for age-related degeneration has been termed inflammaging. Inflammaging is a chronic, low-grade inflammatory state observed systemically in the tissues of older patients. Our previous studies have found that activated macrophages were elevated in the aging cochlea, but little is known about the causes of this increase. Galectin-3 (Gal-3), a carbohydrate binding protein, has emerged as a key regulator of inflammation: 1) elevated levels of Gal-3 have been associated temporally with motor impairment in mouse models of Huntington's disease, and 2) knockdown of Gal-3 results in decreased microglia activation. We hypothesized that Gal-3 could be playing a role in the chronic inflammation and macrophage activation observed in the aging cochlea resulting in hearing loss. Transcriptomic analysis of aged CBA/CaJ mice found the expression of Gal-3 to be significantly increased in lateral wall tissues of aged animals. This increased expression was noted at 1.5 years and was found to be further elevated at 2.5 years. Immunofluorescence analyses confirmed that there was an increase in numbers of Gal-3 positive macrophages in aged mouse cochleae. When double stained for Gal-3 and IBA, a macrophage marker, Gal-3 was found to be restricted to a subset of the IBA-positive macrophages. These findings suggest that upregulation of Gal-3 in the auditory nerve and cochlear lateral wall may play an important role in the chronic inflammation and macrophage activation seen in age-related cochlear tissue degeneration and hearing loss. This work was supported by NIH/NIDCD Institutional Training Grant (T32 DC014435).

58 The Effect of Demographic, Stroke, and Clinical Characteristics on Neglect Severity Scores

Emerson Hart, Michelle Woodbury, Annie Simpson, Emily Grattan, College of Health Professions, Department of CHP OT & HRS, MUSC.

Introduction: Neglect is a post-stroke condition consisting of a lack of awareness of one side of space or the body and has consistently been difficult to measure. Several studies have attempted to identify clinical and demographic characteristics that may be associated with neglect and have demonstrated inconsistent findings. However, these studies have used less sensitive paper-and-pencil assessments rather than functional assessments. In this study, we are evaluating the effect of demographic (age, race, gender), stroke (stroke severity), and clinical (motor and cognitive abilities) characteristics on neglect severity as measured by four functional neglect assessments to identify populations that may be at higher risk for neglect. Methods: This study is a retrospective cohort analysis of secondary questions from a prospective cross-sectional neglect assessment study. The 47 participants include a convenience sample from an academic medical center seen post-stroke. We used linear regression modeling with scores on the functional neglect assessments as outcomes (Catherine Bergego Scale, Naturalistic Action Test, Behavioral Inattention Test, and Virtual Reality

Lateralized Attention Test) and patient characteristics as potential predictors (age, gender, race, stroke severity, motor function, and cognitive function). Results: Of patient characteristics we assessed, only stroke severity had an effect on all four neglect assessments. Patients with more severe stroke were more likely to receive scores indicating more severe neglect on all 4 assessments, ranging from a 2 point change out of 81 potential points on the BIT to a 0.3 point change out of 20 potential points on the VRLAT (all p-values <0.05). Race, gender, motor, and cognitive function had various effects on some but not all assessments, while age had no effect on any assessment. Conclusions: Our results challenge previous findings that used paper-and-pencil assessments, suggesting that some patient characteristics may affect neglect when more sensitive functional assessments are utilized, or vice versa. This work was supported by This work was supported by a T32 grant number T32 DC0014435 (PI: Dubno, J.) from the NIH/NIDCD; an Institutional Development Award (IDeA) from the National Institute of General Medical Sciences of the National Institutes of Health under grant number P20GM.

59 Determining the Effects of TheraBracelet on Upper Extremity Deficits: Reaching vs Grasping

Allison Pennington, Amanda Vatinno, MS, OTR/L, Corey Morrow, MOT, OTR/L, Na Jin Seo, College of Health Professions, Department of Occupational Therapy, MUSC.

Background: Reaching and grasping are the primary motions that serve upper limb function. Stroke survivors experience impairments in both motions, resulting in diminished abilities for activities of daily living. These two motions recover at different times, thus therapists focus on one or the other depending on the patient status/progress. TheraBracelet is a wearable device providing sensory stimulation to upper extremity to facilitate neuronal communication during therapy for greater neuroplasticity and recovery. TheraBracelet has been shown to have promising effects on improving general upper limb function in chronic stroke survivors (Seo et al. 2019). However, it is currently unknown which upper limb motion TheraBracelet is most effective in improving. Objective: The objective of this study is to determine whether TheraBracelet leads to greater improvements in reaching or grasping motions. Methods: Retrospective analysis of data from 3 studies that used TheraBracelet during upper limb therapy. The 3 studies had sample sizes of 12, 11, and 4, therapy durations of 2, 4, and 6 weeks, and 2 triple-blind pilot randomized controlled trials and 1 single-group intervention trial. For all 3 studies, upper extremity motor function was assessed using the Box and Block Test (BBT) at baseline, every 2 weeks during intervention, and post-intervention. In the present study, we will employ the motion time analysis for the BBT video recordings (Slota et al. 2014) to quantify the speed of reaching and grasping separately. Repeated measures ANOVA will be used to determine relative effects of TheraBracelet on reaching vs. grasping speed, while accounting for intervention durations and group. Impact: The results of this study will elucidate the specific motion that TheraBracelet is most effective in treating. This information is expected to guide therapists in choosing a targeted treatment approach for individual patients, thereby improving efficacy and outcomes of rehabilitation of the upper limb following stroke. This work was supported by NIH/NIGMS P20GM109040, NIH/NIGMS U54-GM104941, NIH/NICHD 1R01HD094731-01A1, NIH/NCATS TL1-TR001451, NIH/NCATS UL1-TR001450.

60 **Predicting Individual Post-Stroke Upper Extremity Motor Recovery Using EEG**

Amanda Vatinno, Christian Schranz, PhD, Viswanathan Ramakrishnan, PhD, Leonardo Bonilha, MD, PhD, Na Jin Seo, College of Health Professions, Department of Occupational Therapy, MUSC.

Uncertain prognosis presents a challenge for therapists in determining the efficient course of treatment for individual patients. Sensorimotor network connectivity may have prognostic utility because the integrity of the communication between sensorimotor cortices forms the basis for neuroplasticity and motor recovery. We hypothesize that patients with greater ipsilesional connectivity will have greater motor recovery with therapy. In addition, we hypothesize that use of sensory stimulation intended to increase neural communication (i.e. TheraBracelet) may assist recovery for patients with reduced ipsilesional connectivity. The objective is to investigate if EEG connectivity predicts upper extremity motor recovery. Retrospective analysis was performed for data from a pilot randomized controlled trial (n=12 stroke survivors). All participants underwent 2-week task-practice therapy while receiving TheraBracelet stimulation for the treatment group and no stimulation for the control group. Recovery was quantified as change in Box and Block Test (ΔBBT) from baseline to post-therapy. Ipsilesional connectivity was obtained, in addition to contralesional/interhemispheric for comparison, using EEG pre-intervention. In particular, alpha connectivity was obtained for its involvement in sensory processing, attention allocation, and motor planning/execution. Conventional predictors (age, time post-stroke, lesion volume) were also investigated. The association between EEG and ΔBBT was examined using regression, controlling for group. The association between ipsilesional connectivity and ΔBBT differed by group ($p=0.05$). In the control group, greater ipsilesional connectivity was associated with greater recovery ($r=0.44$). In the treatment group, patients with greater ipsilesional connectivity had the same extent of improvement as the control group, while patients with lower initial connectivity had greater recovery ($r=-0.57$). In contrast, lower contralesional/interhemispheric connectivity was associated with greater recovery ($p=0.02$). Conventional predictors were not significant ($p>0.05$). Pre-intervention sensorimotor connectivity may predict individual patients' upper extremity motor recovery. In addition, patients with lower connectivity with less potential to recover may benefit from use of TheraBracelet that facilitates neural communication. This work was supported by NIH/NCATS TL1-TR001451, NIH/NCATS UL1-TR001450, NIH/NIGMS P20-GM109040.

61 **The Effect of Sensory Impairment Severity on TheraBracelet Efficacy**

Jenna Blaschke, Amanda Vatinno, MS, OTR/L, Corey Morrow, MS, OTR/L, Na Jin Seo, College of Health Professions, Department of Occupational Therapy Department, MUSC.

Background: TheraBracelet is a wrist-worn device that stimulates mechanoreceptors during upper extremity movement therapy to improve neural communication for hand tasks and ultimately increase motor outcomes in stroke survivors. While the efficacy of TheraBracelet has been shown in a group of chronic stroke survivors with moderate upper extremity motor impairment, characteristics of patients who respond well to TheraBracelet are unknown. In particular, the level of sensory impairment is of interest, because (1) TheraBracelet uses the sensory pathway to impact motor recovery; (2) sensory impairment significantly hinders motor function, execution of daily activity tasks, and motor recovery; and (3) 50-85% of chronic stroke survivors have sensory impairment. This study aims to determine if the extent of motor recovery with TheraBracelet depends on sensory impairment level of individual stroke survivors.

Methods: Retrospective analysis of data from 3 studies that used TheraBracelet during therapy. The 3 studies had sample sizes of 12, 7, and 4, therapy durations of 2, 4, and 6 weeks, and 2 triple-blind pilot randomized controlled trials and 1 single-group intervention trial. For all 3 studies, the upper extremity motor function score was assessed at baseline, every 2 weeks during intervention, and post-intervention. Motor recovery was quantified as change in the motor score from the baseline. The level of sensory impairment was assessed using the Monofilament test and the sensory threshold for TheraBracelet stimulation at baseline. Regression analysis will be used to determine the relationship between sensory impairment and motor recovery, accounting for group and differences in intervention duration. Impact: The results of this study may serve to establish criteria for determining optimal candidates for using TheraBracelet. This study is expected to contribute to personalized rehabilitation treatment by utilizing the level of sensory impairment as a prognostic and prescriptive tool for using TheraBracelet with stroke survivors. This work was supported by NIH/NIGMS U54-GM10494 NIH/NIGMS P20-GM109040 NIH/NCATS TL1-TR00145 NIH/NCATS UL1-TR001450.

62 Can Noninvasive Brain Stimulation Improve Working Memory in Healthy Aging Adults? Insights from Electric Field Modeling

Kevin Caulfield, Aprinda Indahlastari, Nicole R. Nissim, James W. Lopez, Holly H. Fleischmann, Adam J. Woods, Mark George, College of Graduate Studies, Department of Psychiatry, MUSC.

Background: Transcranial direct current stimulation (tDCS) for working memory is an enticing treatment, but with mixed evidence to date. In this study, we tested the effects of electric field strength from uniform 2mA dosing on working memory change from pre- to post-stimulation. Secondly, we statistically evaluated a reverse-calculation method of individualizing tDCS dose and its effect on normalizing electric field at the cortex. Methods: We used electric field modeling on MRI brain scans in 28 healthy aging adults (15 women, mean age = 73.7, SD = 7.3) who received 10 sessions of active 2mA tDCS (N = 14) or sham tDCS (N = 14) applied over bilateral dorsolateral prefrontal cortices (DLPFC) in a triple-blind design. We evaluated the relationship between electric field strength and working memory change on an N-back task in conditions of above-median, high electric field from active 2mA (N = 7), below-median, low electric field from active 2mA (N = 7), and sham (N = 14) at regions of interest (ROI) at the left and right DLPFC. We then calculated the individualized reverse-calculation dose to produce the group average electric field, and measured the electric field variance between uniform 2mA doses vs. individualized reverse-calculation doses at the same ROIs. Results: Working memory improvements from pre- to post-tDCS were significant for the above-median electric field from active 2mA condition at the left DLPFC (mixed ANOVA, $p = 0.013$). Furthermore, reverse-calculation modeling significantly reduced electric field variance at both ROIs (Levene's test; $p < 0.001$). Conclusions: Higher electric fields from uniform 2mA doses appear to drive working memory improvements from tDCS. Individualized doses from reverse-calculation modeling significantly reduce electric field variance at the cortex. Taken together, using reverse-calculation modeling to produce normalized electric fields at the cortex may produce more effective future tDCS treatments for working memory. This work was supported by NIH K01AG050707, NIH R01AG054077, NC NM4R, MUSC COBRE.

63 **Heart Failure Symptom Clusters: An Integrative Review**

Alexandra Ruppe, Gayenell Magwood, Sarah Miller, Alexandra Ruppe, College of Nursing, Department of College of Nursing, MUSC.

Abstract Withheld from Publication

64 **NF-κB mediates resistance to cell stressors in epithelial and hematological cancers but not rhabdomyosarcoma (RMS)**

Alexander Oles, Denis Guttridge, College of Graduate Studies (MSTP), Department of Pediatrics, MUSC.

Abstract Withheld from Publication

65 **In Situ Intraepithelial Localizations of Opportunistic Pathogens, Porphyromonas gingivalis and Filifactor alocis, in Human Gingiva**

Jaden Lee, Ralee Spooner, Nityananda Chowdhury, Bridgette Wellslager, Zachary Evans, Ozlem Yilmaz, College of Dental Medicine (DMD, PhD), Department of Department of Oral Health Sciences, MUSC.

Abstract Withheld from Publication

66 **Targeting Mek/Erk Signaling in the Treatment of Mitral Valve Prolapse**

Tyler Beck, , Russell Norris, College of Graduate Studies (MSTP), Department of Regenerative Medicine and Cell Biology, MUSC.

Abstract Withheld from Publication

67 **PLEKHA7 is an intrinsically disordered protein that phase separates and binds RNAs at the adherens junctions of epithelial cells**

Mary Bridges, Alyssa Risner, Valentina Ortega, Jensen Tomberlin, Kathleen Garrabrant, Joyce Nair-Menon, Antonis Kourtidis, College of Graduate Studies, Department of Regenerative Medicine and Cell Biology, MUSC.

The adherens junctions (AJs) are essential architectural elements of epithelial tissues. Recently, we identified a novel mechanism whereby the AJ component, PLEKHA7, recruits the RNAi machinery, mRNAs, and miRNAs, to suppress pro-tumorigenic cell transformation. While PLEKHA7 is essential in recruiting this machinery at the AJs, it is unclear whether RNA localization occurs via direct or indirect PLEKHA7 binding. Although PLEKHA7 does not contain a RNA-binding domain, our bioinformatic analyses predict that PLEKHA7 contains large intrinsically disordered regions (IDRs). IDRs typically consist of conserved proline-rich sequences and negatively charged residues, which promote RNA binding; indeed, our bioinformatic analysis shows that PLEKHA7's IDRs contain multiple, highly-conserved, proline-rich sequences. Thus, we hypothesize that PLEKHA7 recruits RNAs to the AJs by direct RNA binding. A hallmark property of IDRs is that they promote liquid-liquid phase separation (LLPS), a physiological process through which key non-membranous ribonucleoprotein condensates

form in the cell either under homeostatic conditions, such as P-bodies, or under stress stimuli, such as Stress Granules (SGs). Utilizing immunofluorescence and confocal microscopy, we demonstrate that PLEKHA7 undergoes LLPS and localizes to SGs, as indicated by co-localization with SG markers such as G3BP1, EDC4, following heat shock in multiple colon epithelial cell lines. Treatment with 1,6-hexanediol, which dissolves LLPS condensates, confirms the liquid-like property of these PLEKHA7-containing granules. Furthermore, PLEKHA7 UV-CLIP followed by qRT-PCR demonstrates direct binding to mRNAs such as MYC, SOX2, and JUN, which we have previously shown that are regulated by PLEKHA7. Ongoing studies using recombinant PLEKHA7 aim into verifying that this protein forms LLPS droplets in in vitro crowding assays, whereas mutational studies are under way to determine the minimum IDR domain required for phase separation and RNA binding. In summary, our work uncovers a novel function of cell-cell adhesion components in directly recruiting ribonucleoprotein complexes through an IDR- and LLPS-based mechanism. This work was supported by NIH grants P20 GM130457-01A1, R21 CA246233-01A1, and P30 DK123704-01; NIH training grants TL1 TR001451 and UL1 TR001450.

68 Let's Hang Out!: A Live Online Group Play Intervention Addressing Clinical Socialization Gaps for Adolescents with Autism Spectrum Disorder during the COVID-19 Pandemic

Melanie G. Wiley, Danielle W. Lowe, Erin M. Hopper, James S. Truelove, Jennifer A. Warthen, McLeod F. Gwynette, College of Medicine (MD, PhD), Department of Department of Psychiatry and Behavioral Sciences, MUSC.

Introduction: Social skills training is a mainstay of therapy for individuals with Autism Spectrum Disorder. However, most graduates of these courses fail to reinforce and strengthen these skills due to a lack of practice opportunities in a safe environment. The COVID-19 pandemic added an additional challenge of not having opportunities to socialize safely in-person. The authors developed an unstructured play therapy group called Hangout to fill the gap between social skills training and real-world use of social skills, allowing participants to further develop skills amongst familiar peers during the summer months. The hangout was adapted to an online-only format during summer 2020 to provide a safe option for socializing. Methods: Hangout was developed as an unstructured play program including games, creative supplies, and sensory items with staff supervising and encouraging social interactions between youth. The Virtual Hangout included group play sessions with games and discussions led by staff. De-identified demographics, autism questionnaires, and parent feedback were collected to characterize the participant population for the both the virtual hangout and previous in-person hangout sessions. Results: Twenty-five adolescents with moderate-severe social skill deficiencies participated in the first two years of the in-person Hangout program. Participants attended on average four sessions, and the average number of participants in attendance per week was ten. The Virtual Hangout had a total of 26 participants over the course of 12 weeks with an average of 8 participants per week. Parent and staff feedback was extremely positive, and the program was well received by both youth and their parents. Conclusion: As an unstructured play group, the Hangout complemented and added value to the existing social skills training courses offered. It was simple and inexpensive to implement both in-person and online. Future study of this intervention, delivered in both clinical and non-clinical settings is warranted. This work was supported by N/A.

69 The Effect of Complement Inhibition on Neuroinflammmation after Traumatic Brain Injury - A High Throughput Analysis

Amer Toutonji, Silvia Guglietta, Mamatha Mandava, Carsten Krieg, Stephen Tomlinson, College of Medicine (MD, PhD), Department of Microbiology and Immunology, MUSC.

The complement system consists of 3 effector pathways that in the context of injury or infection lead to immune cell activation, phagocytosis and cell lysis. Animal studies in models of Traumatic Brain Injury (TBI) suggest robust activation of complement proteins that lead to chronic neurologic deficits, both motor and cognitive. Our lab has previously shown that pharmacological inhibition of all complement effector pathways promotes significant histological and neurological recovery. This is in contrast to inhibiting only the cell lysis pathway, which leads only to a partial histological and a short-lived neurological recovery compared to full inhibition. This gap in recovery between both modalities of treatment suggests a important role for the other effector pathways in TBI, namely immune cell activation. Hence, in this study, we use high-throughput mass cytometry to identify 13 cell types in TBI-injured mouse brain at 3, 7 and 28 days after TBI. Along with studying the effect of complement inhibition on the abundance of these cell types at different timepoints, we also look at changes in the phagocytic profiles of the cells by assessing for differential expression of more than 10 phagocytic receptors. Finally, we identify subpopulations of each cell type that are enriched in injury and that are more susceptible to treatment with complement inhibitors. Interestingly, we found that complement inhibition reduces the number of all immune cells infiltrating the injured brain without changing their relative frequencies. We also found that the phagocytic profiles and the relative frequencies of specific subpopulations are significantly changed at different timepoints after TBI and with complement inhibition. While there are numerous insights to be derived from the data, the main conclusion is that all cell types are affected by complement inhibition and that specific "emergent" cellular and phagocytic phenotypes are more susceptible to treatment. (Study Funding: Ralph Johnson VAMC). This work was supported by VA (I01BX004256), AHA Predoctoral Fellowship (19PRE34450105).

70 Mechanoregulation of the Adherens Junction - associated RNAi machinery through cross-talk with the Extracellular Matrix

Amanda Daulagala, John Yost, Amirreza Yeganegi, Catherine Bridges, Joyce Nair-Menon, William J. Richardson, Michael Yost., Antonis Kourtidis, College of Graduate Studies, Department of Regenerative Medicine and Cell Biology, MUSC.

Abstract Withheld from Publication

71 Physical Activity Negates the Oncogenic Effects of Lifestyle-associated Advanced Glycation End-Products

Bradley Krisanits, Pamela M. Woods, Lourdes M. Nogueira, Laura Spruill, Marvella E. Ford, Victoria J. Findlay, David Turner, College of Graduate Studies, Department of Pathology and Laboratory Medicine, MUSC.

Lifestyle factors such as a sedentary lifestyle, obesity and a western diet high in protein, fat, and processed foods, contribute to the accumulation of advanced glycation end-products (AGEs). The pathogenic effects of AGEs are mediated through protein modification, genetic fidelity, and

cellular signaling pathways promoting pro -inflammatory and -oxidant effects. However, the role of dietary AGEs in cancer progression and the potential impact of physical activity (PA) is largely unknown. We propose that a diet high in AGEs can accelerate prostate cancer progression and severity that can be reversed by physical activity. Xenograft and spontaneous prostate cancer mouse models were utilized to assess the effects of AGEs on prostate cancer progression and severity with and without daily PA on an animal treadmill (1 hr, 5 days/week). Tumor and prostate tissue were collected for histology, IHC, qPCR and western blot analysis. PBMCs were isolated from pre-PA and endpoint mice for flow cytometry to assess changes in immune phenotypes. Consumption of AGEs resulted in a 3-fold increase in tumor growth in xenograft mice with decreased expression of AR, increased expression of MYC, RAGE, AGE, and cellular proliferation. Consumption of AGEs in the spontaneous model resulted in increased progression towards high grade PIN and metastatic potential when compared to regular fed control mice. Increased progression correlated with increased recruitment of macrophages and cellular proliferation of lesions, as well as elevated AGE, RAGE levels. Of note, PA resulted in reduced tumor growth, progression, metastasis and negation of immunohistochemical changes. Our studies support the premise that AGEs as a biological consequence of lifestyle promote cancer progression and that PA can alleviate these effects. This may have the greatest impact in African American populations who have worse outcomes in prostate cancer and where a lack of PA, poor diet, and high obesity rates are more prevalent. This work was supported by Hollings Cancer Center Pre-Doctoral Fellowship, Graduate Assistance in Areas of National Need (GAANN) Fellowship, U54 CA21096.

72 Brain microvascular insulin receptor dysfunction may underly increased risk for early onset dementia during obesity

Luke Watson, Guadalupe Sanchez, Alexus S. Williams, Taylor Lowry, Catrina Sims-Robinson, College of Graduate Studies, Department of Neurology, MUSC.

Introduction- Obesity impacts 40% of Americans and is a significant risk factor for dementia disorders. While epidemiological data relates midlife obesity and dementia, the underlying mechanistic links remain elusive. Previous reports suggest that both obese individuals and dementia disorders patients are insulin resistant, and that both groups exhibit high levels of circulating insulin but low levels of central nervous system (CNS) insulin; this is a problem given insulin's critical role in maintaining brain health longevity. Given that insulin must be transported into the CNS, this indicates a lack of transport across the blood-brain barrier. Herein, we sought to investigate the impact of chronic hyperinsulinemic treatment on the blood-brain barrier microvascular insulin receptor, given that this is implicated as the major transporter for insulin into the CNS. My hypothesis is that chronic hyperinsulinemia leads to changes in the blood-brain barrier microvascular insulin receptor function, expression, and variation, leading to impaired receptor internalization. Methods- In this current study, primary brain microvascular endothelial cells were incubated in hyperinsulinemic conditions and assessed for insulin receptor dysfunction. Through a cell impermeant biotinylation labelling strategy, we quantified both the membrane associated insulin receptor levels, and their ability to internalize. Finally, we assessed receptor splice variation via molecular approaches. Results- Our results indicate that hyperinsulinemia impairs the insulin receptor functioning within this cell type by impairing its ability to trans-phosphorylate key residues involved with internalization. This corresponded with decreased receptor internalization rates. Molecular techniques revealed hyperinsulinemia's

influence on receptor mRNA splicing. Conclusions- Hyperinsulinemic treatment of these cells induced receptor dysfunction that related with reduced ligand-induced internalization. Given that receptor internalization is the primary step following ligand interaction during transcytosis, this has potential implications for CNS-insulin delivery. The variations exhibited following hyperinsulinemia may lead to further understanding of the breakdown in this process. This work was supported by 4T32HL007260-40, 1R01NS099595-02S1, 1R01NS099595-01A1, 5K01NS079461, AARGD-16-440893.

73 STAT3 in Cancer-Associated Fibroblasts Promotes an Immunosuppressive Tumor Microenvironment in PDAC

Julia Lefler, Katie MarElia, Blake E. Hildreth III, Katie A. Thies, Maria C. Cuitino, Michael Ostrowski, College of Graduate Studies, Department of Biochemistry and Molecular Biology, MUSC.

One of the features of pancreatic ductal adenocarcinoma (PDAC) is a dense stroma comprised of cancer associated fibroblasts (CAFs) and immune cell populations. This stroma is immunosuppressive and contributes to therapeutic resistance. 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 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. The stromal-specific function of the IL-6/STAT3 signaling axis 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. Loss of fibroblast STAT3 also resulted in a significant decrease in ECM deposition in the pancreas. We also observed an increase in overall T cell infiltration and decrease in regulatory T cell populations in the STAT3 deleted cohort. Further, STAT3 deletion resulted in an increased ratio of M1 to M2 macrophages within the PDAC stroma, suggesting CAF STAT3 signaling is important to maintaining an immune microenvironment conducive to tumor progression. These preliminary results suggest STAT3 signaling in PDAC CAFs contributes to an overall survival disadvantage, an immunosuppressive tumor microenvironment, and an increase in ECM deposition.

74 Identification of a novel potential therapeutic target for liver fibrosis

Nour Hijazi, Zengdun Shi, Don Rockey, College of Graduate Studies (MSTP), Department of Medicine, MUSC.

Abstract Withheld from Publication

75 Delayed treatment with a site-targeted complement inhibitor reduces cognitive deficits following traumatic brain injury

Davis Borucki, Khalil Mallah, Christine Couch, Wenxue Wang, Shahid Husain, Baerbel Rohrer, Stephen Tomlinson, College of Graduate Studies (MSTP), Department of Microbiology & Immunology, MUSC.

Abstract Withheld from Publication

76 Induction of fibrosis in lung tissues and fibroblasts results in decreased free anti-fibrotic proteins with a corresponding increased packaging in extracellular vesicles.

Joe Mouawad, , Carol Feghali-Bostwick, College of Medicine (MD, PhD), Department of Professor, MUSC.

Fibrosis is characterized by the excessive accumulation of connective tissue components which form the extracellular matrix (ECM). Pulmonary involvement in fibrotic diseases, like Idiopathic Pulmonary Fibrosis (IPF) and Systemic Sclerosis (SSc), results in high morbidity and mortality. Lung fibroblasts have long been implicated in the progression of pulmonary fibrosis through their activation into myofibroblasts and secretion of excessive ECM. Recently, extracellular vesicles (EV) have been implicated in several diseases. However, characterization of EV during myofibroblast activation in fibrosis has yet to be delineated. We show that activation of primary human lung fibroblasts (phLF) with the profibrotic cytokine Transforming Growth Factor beta (TGF-b) reduces the release of EV while increasing their protein content. Similarly, lung tissues from donors whose lungs are not used for transplantation showed a reduction in EV release coupled with an increase in their protein cargo in response to TGF-b. Interestingly, in both lung fibroblasts and tissues, there was no significant change in average diameter of EV released with TGF-b treatment compared to control. To begin characterizing the cargo of EV, we compared levels of a lysosomal cysteine peptidase, Cathepsin L (CTSL), with anti-fibrotic properties in the supernatants of fibroblast and in EVs. We report that despite a significant downregulation of CTSL expression and a corresponding decrease in CTSL secreted levels in the supernatants, TGF-b-activated myofibroblasts increase packaging of CTSL into EVs. This suggests that activated myofibroblasts package CTSL into EV in a paracrine endeavor to inhibit progression of fibrosis and maintain homeostasis. Our future goals include understanding the functional implications of this phenomenon. Our findings provide insights into EV paracrine signaling in the lung and will pave the way for development of EV-mediated delivery of targeted antifibrotic therapies for fibrotic lung diseases. This work was supported by SmartState and Kitty Trask Holt endowment.

77 The design and synthesis of immunomodulatory CD38-PROTAC molecules for the treatment of neuroblastoma

Catherine Mills, Thomas Benton, Pieter Burger, Yuri Peterson, Patrick Woster, College of Graduate Studies, Department of Drug Discovery and Biomedical Sciences/Pharmacy, MUSC.

Abstract Withheld from Publication

78 **Reactive oxygen species regulate HDAC5 function: implications for drug addiction**

Daniel Wood, Ethan Anderson, Makoto Taniguchi, Joachim Uys, Christopher Cowan, College of Graduate Studies (MSTP), Department of Neuroscience, 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. Our data indicate that this shuttling is regulated by the dynamic interplay of HDAC5 phosphorylation status and signaling events initiated by reactive oxygen species (ROS), enigmatic signaling molecules produced by virtually all drugs of abuse. Using immunofluorescent techniques we find that oxidative conditions regulate HDAC5 subcellular localization in vitro. This likely occurs through the oxidation of two conserved cysteines within HDAC5's c-terminal region, which form a disulfide bond following exposure to oxidative conditions. Preliminary data using an HDAC5 redox mutant suggest that oxidation of these cysteines may take precedence over HDAC5 phosphorylation status in governing subcellular localization. Together, our data point toward a critical role of redox signaling in HDAC5 functional regulation. Future studies will investigate the effects of heroin-induced ROS on HDAC5 function in vivo and the redox modulation of HDAC5 on drug-seeking behaviors. This work was supported by P50 DA046373, Project One T32 DA007288 T32 GM008716.

79 **Minocycline-Induced Dysbiosis of Gut Microbiota Disrupts Metabolism and Post-Pubertal Skeletal Development**

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

Abstract Withheld from Publication

80 **Myocardial Fibrosis in Mitral Valve Prolapse**

Cortney Gensemer, Reece Moore, Kelsey Moore, Lilong Guo, Tyler Beck, Christina Wang, Diana Fulmer, Russell Norris, College of Graduate Studies, Department of MCBP Regenerative Medicine, MUSC.

Mitral valve prolapse (MVP) is a common cardiac valve disease affecting 1 in 40 individuals. Current effective treatment options for MVP are restricted to surgical intervention, indicated by

severity of mitral regurgitation (MR). Roughly 20% of patients with MVP develop left ventricular remodeling, significant myocardial fibrosis (MF), associated arrythmias and heart failure. Mitral valve repair (MVr), the treatment of choice for patients with MVP, is highly effective for MR but often leaves residual fibrosis and LV-dysfunction. This underscores the importance for studying the progression of MVP and mechanisms of fibrosis in both patients and our genetically accurate murine model of MVP. Left ventricular and septal biopsies were obtained from surgical MVP patients and analyzed by immunohistochemsitry and histology. The fibrosis observed in both the human and mice was only found within regions of the LV that are under enhanced mechanical stress from the prolapsing valve. These fibrotic regions also exhibited increased inflammation in both the human and mouse biopsies as well as a loss of mechanosensing primary cilia in ventricular fibroblasts. These data demonstrate that mitral valve prolapse likely results in increased mechanical tension on the papillary muscles resulting in inflammation and regionalized fibrosis. This mechanically-induced fibrosis may be exacerbated by the loss of mechanosensing primary cilia. These data suggest that early surgical intervention for MVP, prior to the development of MF may prevent long term consequences of collagen deposition and heart failure.

81 Transcranial Magnetic Stimulation's Effects on Cognitive Function Measured Through the WinSCAT

Mary McElveen, Donna Roberts, College of Medicine (MD, PhD), Department of Radiology, MUSC.

Abstract Withheld from Publication

82 Commensal Oral Microbiota Promotes Osteoimmune Response Effects that are Distinct from the Systemic Microbiota

Jessica Hathaway-Schrader, Johannes D. Aartun, Nicole Poulides, Megan Kuhn, Blakely Graham, Michael Chew, Emily Huang, Richard P. Darveau, Caroline Westwater, Chad Novince, College of Dental Medicine, Department of Oral Health Sciences, MUSC.

Abstract Withheld from Publication

83 Age-related loss of activity of low-spontaneous-rate auditory nerve fibers in humans

Carolyn McClaskey, James W. Dias, Richard A. Schmiedt, Judy R. Dubno, Kelly Harris, College of Medicine, Department of Otolaryngology - Head & Neck Surgery, MUSC.

Auditory function declines with age, which can impede successful communication for older adults, particularly in noisy environments. These challenges present a significant barrier to social interaction, potentially diminishing health outcomes and quality of life. Declines in auditory function may arise partly from an age-related loss or inactivity of low-spontaneous-rate (SR) auditory nerve (AN) fibers - a subgroup of neurons known to be important for processing moderate to higher level sounds and sounds in noise - but evidence in humans is lacking. The current study takes advantage of the forward-masked recovery function paradigm, an electrophysiologic method of estimating the relative proportions of low-SR and high-SR AN fibers. This method was developed in animal models to exploit the slower recovery times of low-

SR fibers. In this paradigm, AN responses are elicited by a brief signal that is preceded by another "conditioner" signal by some time interval, delta-t. The minimum delta-t required for the conditioned AN response amplitude to approximate the unconditioned AN response amplitude (delta-t recovery point) is quantified, and indicates the relative proportions of low- and high-SR fibers. That is, an AN with a shorter delta-t recovery point is comprised of a lower proportion of low-SR fibers than an AN with a longer delta-t recovery point. To test the hypothesis that low-SR fiber activity declines with age, we assessed recovery functions in 35 older adults (aged 56-86 years) and 18 younger adults (aged 19-30 years). Older adults show a shorter delta-t recovery point than younger adults, consistent with the theorized age-related loss of activity of low-SR fibers. This study is the first to successfully assess forward-masked recovery functions in both younger and older adults and provides important insights into the functional changes occurring in humans at the level of the auditory nerve with increasing age. This work was supported by NIH/NIDCD (R01 DC014467, R01 DC017916, P50 DC000422, T32 DC014435). NIH/NCRR (UL1 RR029882, C06 RR014516).

84 Neural re-organization after upper extremity rehabilitation therapy with sensory stimulation in chronic stroke survivors

Christian Schranz, Amanda Vatinno, Viswanathan Ramakrishnan, Na Jin Seo, College of Health Professions, Department of Health Profressions, MUSC.

Background: Knowledge on the neural mechanism of motor recovery post stroke is limited. This study aims to investigate the impact of stimulation-added therapy on cortical sensorimotor mechanism. Methods: Twelve chronic stroke survivors underwent two-weeks upper extremity task-practice therapy, while wearing a vibrator on their paretic wrist. They were randomized to either a treatment group that received imperceptible vibratory stimulation, or control group with no stimulation during therapy. EEG during paretic hand grip was measured at pre-intervention, post-intervention, and follow-up (3-weeks). Specifically, EEG connectivity between and power of premotor, precentral and postcentral regions of both hemispheres were examined. Change was evaluated through multifactorial ANOVA. Results: Significant group by time interactions were observed for both connectivity and power ($p<0.05$). Posthoc analysis showed, that the treatment group increased connectivity between the premotor and contralateral premotor, precentral and postcentral areas bilaterally from pre- to post-intervention. Connectivity returned to baseline at follow-up. In addition, the treatment group reduced power modulation at post-intervention, which was maintained at follow-up. On the contrary, the control group showed no change in connectivity or power. Conclusions: Addition of stimulation to therapy increased connectivity and reduced power modulation in the bilateral sensorimotor cortices at post-intervention. The increased connectivity may indicate cortical reorganization specific to motor learning. Reduced power modulation may indicate lessened effort for gripping with the paretic hand. At follow-up, retention of learned motor skills but without further motor learning was expected, which is reflected by the retained lower power modulation without changed connectivity from pre-intervention. The therapy-only group showed no cortical changes. Cortical changes coincided with clinical changes (reported in Seo et al. 2019) in which the treatment group significantly improved BBT at post-intervention and follow-up while the control group did not. These findings suggest EEG is a viable surrogate for motor improvement and potential neural targets for therapy. This work was supported by NIH/NIGMS P20GM109040.

85 **Age dependent effects of yeast derived complex dietary polysaccharide on gut microbiota composition, autoimmunity and type 1 diabetes incidence in non-obese diabetic mice**

Harrison Taylor, Chenthamarakshan Vasu, College of Medicine (MD, PhD), Department of Microbiology and Immunology, MUSC.

Complex dietary polysaccharides (CDPs) such as β-glucans (BG) are widely used for their anti-inflammatory properties. Our previous work has found that oral treatment of adult non-obese diabetic (NOD) mice with Baker's yeast β-glucan (YBG) can alter the composition of gut microbiota and suppress the incidence of type 1 diabetes (T1D). Because gut microbiota is more prone to changes at younger age, we sought to investigate the age-dependent impacts of YBG treatment on the gut microbiota maturation and autoimmune progression. NOD mice aged 2 weeks (infant) or 8 weeks (adult) were administered YBG daily by oral gavage for 7 (short-term) or 30 (long-term) days. Changes in the composition of fecal microbiome were analyzed through 16S rRNA gene sequencing and quantitative PCR (qPCR), immune phenotypes of small and large intestines were assessed by qPCR, and disease incidence was determined through monitoring blood glucose levels. Although short-term treatment with YBG did not significantly alter the ratio of Bacteroidetes to Firmicutes compared to controls, prolonged treatment caused a significant increase ($p<0.01$) in in the abundance of Bacteroidetes. Cytokine expression profiles revealed a significant upregulation of the anti-inflammatory cytokine IL10 and a shift in immune response toward Th17 type in the large intestine. Prolonged pretreatment with YBG beginning at infancy significantly delayed the onset of hyperglycemia. These observations suggest that oral consumption of CDPs such as YBG at infancy can shape gut microbiota composition more effectively and promote protection of T1D susceptible mice from autoimmunity.

86 **Site-targeted complement inhibition halts progressive motor decline in a murine model of Amyotrophic Lateral Sclerosis (ALS)**

Khalil Mallah, Davis M. Borucki, Marcelo Vargas, Stephen Tomlinson, College of Graduate Studies, Department of Microbiology and Immunology, MUSC.

Abstract Withheld from Publication

87 **Complement Activation Contributes to Hydrocephalus Development following Germinal Matrix Hemorrhage**

Mohammed Alshareef, Khalil Mallah, PhD; Ramin Eskandari, MD, MS, Stephen Tomlinson, College of Medicine, Department of Microbiology and Immunology, MUSC.

Introduction Germinal matrix hemorrhage (GMH) is a devastating neonatal neurologic injury that results in sequalae such as post-hemorrhagic hydrocephalus (PHH) and periventricular leukomalacia (PVL). The complement cascade has been implicated as an actor in secondary injury and subsequent development of gliosis. However, the lack of an appropriate murine model has hindered research on the role of complement. We investigate the impact of complement activation on GMH using a novel GMH murine model with high rates of PHH. Methods A neonatal GMH model was developed by injecting collagenase into the subventricular zone on various days post-natal. A control (injured) group was compared to

animals treated with a complement inhibitor (CR2-Crry). Neurocognitive motor function and survival analysis was obtained on all animals up to 90 days of life. Histologic and immunofluorescent (IF) comparisons were performed at various time points, with a focus on inflammation (GFAP, Iba-1, C3 deposition) and neuroprotection (NeuN, MAP2). Results Animals treated with CR2-Crry, complement inhibitor, had significantly higher weight gain compared to vehicle, with an overall improved motor and cognitive function. There was a 60% hydrocephalus rate in GMH control animals, which was reduced to 6% following CR2-Crry treatment. IF showed a significant reduction in perilesional C3, GFAP and Iba-1 deposition with a concurrent increase in NeuN and MAP2 in treated animals. Conclusion There are currently no treatments for GMH, a pathology in which we demonstrate a role for complement. Understanding the associated inflammation is essential for development of a therapeutic to mitigate effects of secondary injury after GMH. We describe a novel model for GMH with associated PHH. We utilized this model to show a role for complement-dependent inflammation in the development of secondary injury. The model will provide a valuable tool for expanded pre-clinical studies of GMH. This work was supported by AANS/CNS Section on Pediatric Neurological Surgery & NREF 2020-21 Research Fellowship Grant, VA supplemental grant: BX004256.

88 Antibiotic Disruption of the Indigenous Oral Microbiota has Catabolic Effects on Alveolar Bone

Amy Warner, Brooks A. Swanson, Jessica D. Hathaway-Schrader, Matthew D. Carson, Joy E. Kirkpatrick, Alexander V. Aleksenyenko, Caroline Westwater, J. Ignacio Aguirre, Chad Novince, College of Dental Medicine, Department of Oral Health Sciences, MUSC.

Abstract Withheld from Publication

89 Insulin and its effects on relative cerebral blood flow and cognition

Guadalupe Sanchez, , Catrina Robinson, College of Graduate Studies, Department of Neurology, MUSC.

Abstract Withheld from Publication

90 Physiological effects of ranitidine on renal function in salt-sensitive hypertension

Mark Domondon, Ryan Schibalski, Thelma Amoah, Mikhail Fomin, Tengis S. Pavlov, Sergey Arkhipov, Daria Ilatovskaya, College of Medicine, Department of Department of Medicine / Nephrology, MUSC.

Histamine is a regulatory component of the local immune response that is involved in the allergic response, neurotransmission, and gastric acid secretion. Elevated histamine levels and increased expression of histamine metabolizing enzymes have been reported in kidney disease. The goal of this study was to provide insight into the physiological importance of the histamine-related pathways in salt-sensitive hypertension (SSH), a disease accompanied with inflammation-driven kidney damage. Methods. SSH was induced in Dahl salt-sensitive rats (DSS) by a 3-week long high salt diet challenge (HS, 4% NaCl). Before the switch to a HS diet, and at the end of the HS challenge, the animals received single daily i.p. injections of histamine

receptor 2 (HR2) antagonist ranitidine (RAN, 25mg/kg in saline) or saline (VEH), for 3 consecutive days. Urine and water consumption were assessed in metabolic cages during hours 0-8 (acute), and 8-24 post-injections. At the end of the protocol, GFR was measured, and tissues were collected for further examinations. Renal IHC revealed that expression of histamine receptor 2 (HR2) was pronounced in the apical region of collecting duct (CD) cells; HR2 expression was downregulated in the CDs of HS diet fed rats. RAN rats exhibited an acute (8-hr) decrease in urine production on day 1 of injections both before and after HS challenge (NS, p=0.02155; HS, p=0.15235). We observed trends for an increase in Na+ and Cl- excretion, and a significant increase in the excretion of K+ with ranitidine vs vehicle 8 hours post-injection on day 1 (310±31 vs 187±16 uMoles/8hr, respectively, p=0.006). GFR between the groups was found similar on day 3 post-injection. Our data show that histamine has unexpected effects on renal function in SSH; more in-depth research is required to discern the downstream molecular pathways, and assess the role of specific receptors in renal pathophysiology.

91 Emotional Activation and Attention During Avoidance and Escape Preparation: Parallel or Distinct Processes?

James Lopez, Holly H. Fleischmann, Lisa M. McTeague, Christopher Sege, College of Medicine (MD, PhD), Department of Sleep and Anxiety Division, MUSC.

Affective engagement varies during avoidance vs. escape preparation - thus, reflexive blink reactions to startle probes presented during coping response preparation are inhibited when coping avoids (i.e. prevents) aversive stimuli whereas they are somewhat enhanced if coping merely escapes (i.e. shortens) such stimuli. Here we examine event-related potential (ERP) for startle probes presented during coping preparation to determine if cortical processing of and reflexive reaction to such probes are modulated differently, as has been shown in other (e.g., picture viewing) contexts. Cues signaled that a button press would terminate (escape), completely prevent (avoid), or have no effect on (uncontrollable) subsequent presentation of an aversive scene. Brief acoustic probes were presented throughout the cue interval, and startle blink magnitude and ERP amplitude for each probe were measured in 40 healthy adults. During coping preparation, blinks were potentiated during uncontrollable anticipation, somewhat reduced during escape preparation, and further reduced during avoidance preparation, $F(2,37) = 9.5$, $p < .001$. A different pattern was found for probe ERP, $F(2,33) = 7.3$, $p = .002$, with modulation apparent in a window from 175-225ms post-probe onset, such that amplitude was similarly reduced during escape and avoidance preparation relative to aversive anticipation. These data suggest that startle and ERP are modulated by different processing dimensions during coping preparation, such that startle reflects certainty of aversive exposure whereas probe ERP is modulated by action. This work was supported by CRDF.

92 Transcutaneous Auricular Neurostimulation (tAN): a non-pharmacological adjuvant treatment in neonates suffering from opioid withdrawal

Georgia O'Leary, Naivd Khodaparast, PhD, Stephanie Washburn, Alejandro Covalin, PhD, Bashar W. Badran, PhD, Dorothea Jenkins, College of Medicine, Department of Pediatrics, MUSC.

Introduction: Neonatal Opioid Withdrawal Syndrome (NOWS) is a condition that occurs in newborns who are exposed to opioids in utero via maternal transmission. NOWS symptoms

include: high-pitched crying, tremors, gastrointestinal dysfunction, hypertonicity and sleep disturbances. Unfortunately, maternal opioid use rates have quadrupled from 1999 to 2014, increasing NOWS cases with limited advancements in treatment options. The primary treatment for NOWS is opioid replacement (oral morphine administration). Morphine, however is neurotoxic and has developmental consequences in infants. There is a need for non-opioid treatments for NOWS and in this study, we explore the use of neurostimulation as an adjuvant to morphine to reduce the duration of morphine treatment. Using a novel wearable ear stimulation system known as Transcutaneous Auricular Neurostimulation (tAN), we predict we may accelerate the weaning of morphine treatment and reduce the opioid burden in newborns with NOWS. Methods: Four newborns (2 Female, 2 Male, Mean GA: 36.9□2.3 weeks) with NOWS received tAN as an adjuvant to morphine therapy one hour before scheduled morphine dose, four times per day for up to 12 days. Withdrawal symptoms were assessed by nurses using the Finnegan Neonatal Abstinence Scoring Tool (FNAST) every three hours. Primary outcomes of safety (using the Neonatal Infant Pain Scale and physiology) and duration of oral morphine treatment were measured. Results: tAN was well-tolerated with no unanticipated adverse events occurring in 131 sessions. The median LOT from the start of administering oral morphine was 10d (range 9-18d), and the median LOT after starting tAN was 7□1.1d (range 6-8d). Four morphine rescue doses were administered. Conclusion: tAN as an adjuvant to oral morphine therapy allowed for successful weaning of morphine within 8 days of tAN onset in the four infants with NOWS. tAN may become a promising treatment option for infants with NOWS and large-scale clinical trials are warranted. This work was supported by NIH NIDA R43 DA050360-01.

93 Does a pandemic bias all outcomes in ongoing depression treatment trials?

Sarah Huffman, Morgan Dancy, Xingbao Li, Truman Brown, Mark George, College of Medicine, Department of Psychiatry Brain Stimulation Lab, MUSC.

In double-blind randomized trials the goal is to control for confounds so that causal inferences regarding the efficacy of the intervention can be made. However, the COVID-19 epidemic has introduced massive stress and lifestyle confounds which are particularly relevant for ongoing depression trials. Our group has been conducting an NIH funded double-blind rTMS depression trial before and during the COVID-19 pandemic and we were interested to see if rTMS remains an effective treatment for depression when the population served is restricted from their normal routine (e.g., grocery shopping, gym, social gatherings). Without breaking the blind, we compared overall outcomes of all patients entered into the trial before the onset of the pandemic (n=9) with those who have been treated during the pandemic (n=5). The overall percentage of patients responding or remitting has not changed significantly during COVID (88.9%) compared to pre-COVID (80.0%). Using a chi-square test, we examined the relationship between overall patient response or remission rate pre-COVID and during COVID and we found no significant difference, $X2(1, N=14) = 0.27$, $p=.649$. We note that this is a small sample size and thus not particularly well-powered, however it suggests that we have yet to see reduction in the efficacy of rTMS treatment for treating depression during the pandemic. This work was supported by NIH.

94 Age and initial severity as predictors of treatment outcome in chronic post-stroke aphasia

Lorelei Phillip Johnson, Caitlyn Duffy, Alexandra Basilakos, Julius Fridriksson, College of Health Professions, Department of Communication Sciences and Disorders (USC), MUSC.

Demographical and stroke-related factors have been investigated in multiple treatment studies to determine which are most useful for determining prognosis in post-stroke aphasia. While initial aphasia severity and lesion factors often prove to be good predictors of outcome, there have been mixed results in terms of demographical factors including age (e.g. Ellis & Urban, 2016; Johnson et al., 2019; Plowman et al., 2011). A retrospective analysis of three treatment studies was undertaken to investigate the role of age and initial aphasia severity on outcome. Study one (N=30) consisted of two weeks of intensive language treatment. Study two consisted of three weeks of computerized naming treatment plus active or sham transcranial direct current stimulation (tDCS) (N=74). Study three consisted of six weeks of treatment (N=76). The aphasia quotient of the Western Aphasia Battery - Revised (WAB-R; Kertesz, 2007) was used as a measure of initial severity and the Philadelphia Naming Test (PNT; Roach et al., 1996) was used to measure change. Maximal proportional gain was calculated by dividing the raw improvement in correct naming by the room for improvement (number of items named correctly subtracted from total items). Spearman's rho was calculated to determine the relationship between predictor variables (age at assessment and initial severity). Initial severity was a significant predictor of outcome in all three studies with individuals who were less severe at baseline demonstrating more improvement post-treatment (Study1: $r=.712$, $p<.001$; Study2: $r=.195$, $p=.049$; Study3: $r=.459$, $p<.001$) Age was significantly correlated with outcome for only one study with younger people with aphasia demonstrating greater improvements post-treatment (Study3: $r=-.232$, $p=.022$). Overall, these results suggest that taking age and initial severity into account when determining a patient's clinical prognosis can be helpful, but more research is needed to further clarify these relationships. This work was supported by NIH/NIDCD DC008355 (PI: Fridriksson), NIH/NIDCD DC011739 (PI: Fridriksson), NIH/NIDCD DC014664 (PI: Fridriksson), NIH/NIDCD DC014435 (Trainee: Johnson).

95 Inhibition of RAS oncogenesis by identification and targeting a novel vulnerability in selected oncogenic mutants

Imran Khan, Akiko Koide, Mariyam Zuberi, Eric Denbaum, Gayatri Ketavarapu, Kai Wen Teng, Matthew Rhett, Russell Spencer-Smith, Ernest Ramsay Camp, Shohei Koide., John O'Bryan, College of Medicine, Department of Pharmacology, MUSC.

Introduction: RAS GTPases are the most commonly mutated oncogenes in human cancers. However, RAS-specific inhibitors remain elusive. To identify vulnerabilities in oncogenic RAS, we employed Monobody technology. Monobodies are high affinity tool biologics that can be used as intracellular reagents to inhibit their target. We recently developed a high affinity Monobody, termed NS1, that selectively inhibited HRAS and KRAS, but not NRAS. Here, we describe a new RAS Monobody, termed R15, that inhibits signaling and transforming activity of selected oncogenic RAS mutants. Methods: Apo-RAS specific Monobody called R15 was screened by biopanning from phage library. Next, we engineered R15 as genetically encodable reagent in cells to assess its effects on oncogenic RAS function as measured by MAPK/PI3K signaling, growth transformation, anchorage-independent growth, tumor growth in athymic nude mice and patient derived xenografts (PDXs) Results: R15 inhibited signaling and oncogenic

activity of RAS mutants that exhibit high spontaneous release of nucleotides called fast exchange mutants (G13D, Q61Land A146T) but not slow exchange mutants (G12V) or downstream oncogenic kinases [BRAF(V600E) and MEK(DD)]. Surprisingly, R15 also bound and inhibited KRAS(G12D), the most common oncogenic KRAS mutation in pancreatic cancer. R15 did not impair signaling in RASless MEF's highlighting the lack of "off target" effects. Finally, inducible expression of R15 selectively inhibited the growth of tumor cells lines, tumor xenografts and PDXs driven by fast exchange (G12D) but not slow exchange mutants (G12V). Conclusion: These data reveal that selected oncogenic RAS mutants, i.e., fast exchange mutants, can be inhibited by targeting the apo state of RAS. Thus, in contrast to conventional wisdom, it is possible to target the nucleotide state of RAS despite its high affinity for nucleotide and the high levels of GTP/GDP in cells. Thus, we have established a new opportunity to selectively inhibit RAS mutants by targeting the apo state with drug-like molecules. This work was supported by NIH, VA.

96 Identification and Characterization of a Small Molecule Inhibitor of KDM4B to Target Periodontal Disease

Kathleen Garrabrant, Kathleen A. Garrabrant, Joy E. Kirkpatrick, Pieter Burger, Jonathan M. Turner, Rachel E. Wilkinson, Patrick M. Woster, Patrick Woster, College of Graduate Studies, Department of Drug Discovery, MUSC.

Periodontal diseases (PD) are extremely prevalent, affecting over 47% of Americans. None the less, current treatments are not effective in reducing the inflammation and bone loss associated with the disease. PD is caused by bacterial buildup in the oral cavity, bacterial lipopolysaccharide (LPS) prompts a persistent inflammatory immune response and causes tissue damage ultimately leading to bone loss. Most currently available PD treatments focus on targeting this damage via root planing and mechanical debridement, despite the fact that the bone and tissue damage directly results from the inflammatory host immune response. Previous data generated in our laboratories demonstrates that the microenvironment of PD can lead to epigenetic changes, in particular increased lysine demethylase 4B (KDM4B) activity and decreased lysine-specific demethylase 1 (KDM1A) activity. Both KDM4B and KDM1A contain a catalytic domain that acts to cleave methylated lysine at specific histone locations. An increase in KDM4B activity not only down regulates KDM1A, but also leads to a pro-inflammatory state that is reversible in the presence of a KDM4B small molecule inhibitor. High throughput and phenotypic screening recently completed in our laboratories have resulted in the identification of a novel benzamidobenzoic acid scaffold for optimization as therapeutically useful KDM4B inhibitors. We have now identified and synthesized a small library of compounds that correlate well with our pre-existing QSAR data. These compounds have been synthesized using facile route involving boronic acid starting materials. In vitro phenotypic immunosuppression screening has revealed differences in pro-inflammatory cytokine expression for these compounds when compared to the parent molecule ML324 following stimulation with LPS. Our ongoing studies will focus on understanding the precise mechanism of action for these immunosuppressive compounds. This work was supported by NIH 1R01DE029637.

97 HGF-induced activation of Nephrin and Neph1 serves as a novel mechanism for recovery of podocytes from injury

Ashish Solanki, Pankaj Srivastava, Ehtesham Arif, Christopher M. Furcht, Bushra Rahman, Pei Wen, Avinash Singh, Lawrence B Holzman, Wayne R. Fitzgibbon, Glenn Lobo, Joshua H. Lipschutz, Sang-Ho Kwon, Zhe Han, Matthew J Lazzara, Deepak Nihalani, College of Medicine, Department of Medicine, MUSC.

INTRODUCTION: The extracellular domains of podocyte proteins NEPHRIN and NEPH1 serve as the building blocks for slit diaphragm, which are critical components of the glomerular filtration barrier. Although these are signaling proteins, the activation mechanisms for these proteins have never been described. Here, we present a novel concept showing that apart from structural organization, NEPHRIN and NEPH1 constitute a receptor-based function, where these proteins can be activated in a ligand-induced fashion. METHODS: Proteomics, Cloning, protein expression and purification using baculovirus-systems, SPR (surface-plasma-resonance), Co-IP, ELISA, Immunofluorescence. RESULTS: The ability of NEPHRIN and NEPH1 to interact with tyrosine phosphatase SHP-2 in a phosphorylation-dependent manner prompted us to investigate whether ligands that induce PTPN11 stimulation also induced activation of NEPHRIN and NEPH1. The screening of multiple ligands identified HGF as a prominent inducer of both NEPHRIN and NEPH1 phosphorylation. To further establish HGF as a ligand, we used baculovirus expression system to generate purified NEPHRIN and NEPH1 proteins and confirmed not only a direct interaction between HGF and the extracellular domains of NEPHRIN and NEPH1, but also, the ligand-induced phosphorylation of these proteins. In addition to their ligand-induced activation, we demonstrate that SHP-2 can directly dephosphorylate these proteins, thus presenting for the first time an activation and deactivation mechanism for these proteins. Since HGF has a protective role in podocytes and NEPHRIN and NEPH1 phosphorylation participates in actin cytoskeletal reorganization, we hypothesize that HGF-induced activation of these proteins is critical for recovery of podocytes from injury when the podocyte actin cytoskeleton needs to be repaired. Indeed, when HGF was added to injured podocytes, their recovery was significantly enhanced in a NEPHRIN and NEPH1-dependent fashion, suggesting that NEPHRIN and NEPH1 activation participates in the recovery mechanisms of podocytes. Conclusions: We provide compelling evidence that ligand-induced activation of NEPHRIN and NEPH1 by HGF is a component of podocyte recovery. This work was supported by NIH RO1.

98 First in-neonate use of non-invasive transcutaneous auricular vagus nerve stimulation: 18 months neurodevelopment and sensory follow up.

Turki Aljuhani, Patty, Coker-Bolt, Dorothea Jenkins, College of Health Professions, Department of College of Medicine, MUSC.

PURPOSE: Feeding is a very complex task that infants are required to do at very early stage. Feeding required infant's to coordinate a complex and rapid sequence of sucking, swallowing, and breathing. Infants discharged with g-tube are more likely to have lower scores in all neurodevelopment outcomes than full feed infants. A non-invasive application of VNS, transcutaneous auricular VNS (taVNS), stimulates the auricular branch of the vagal nerve. Yet, application of taVNS, the long-term impact remains unknown. DESIGN: Prospective cohort study with a convenience sample of infants enrolled at the Medical University of South Carolina (MUSC). All infants were at a high risk of developmental delays and all were scheduled for g-

tube procedure before the start of treatment. METHOD: Data were analyzed using descriptive data analysis of means, standard deviation, and independent t-test. RESULTS: Eleven children have complete follow-up data to date (6 responders, 5 non-responders). Infants who responded to early taVNS feeding treatment showed greater avg. Bayley III scaled scores than non-responders in the Cognition (+1.6), Receptive Language (+0.3), Fine Motor (+0.7), and Gross Motor (+1.6) domains, although differences were not statistically significant. SP2 forms were completed for 7 children (4 responders, 3 non-responders) and showed that all children in the non-responders group had an atypical sensory performance, while only one child in the responder group showed atypical sensory performance. In the 4 quadrants sensory patterns, a total of 7 atypical sensory patterns were noted in the non-responders group, while there were only 4 atypical quadrant scores in infants who responded to taVNS treatment. CONCLUSION: Early findings from this study reveal that responders to taVNS treatment (attainment of full oral feeds), on average, had higher scaled Bayley-III scores when compared to non-responders and demonstrated more typical sensory processing patterns. This work was supported by Funded by the National MUSC Center of Neuromodulation for Rehabilitation (NC NM4R) and COBRE for Stroke Recovery, The National Center of Neuromodulation for Rehabilitation (NC NM4R) is supported by the Eunice Kennedy Shriver National Institute of Child Health & Human Development of the National Institutes of Health under award number P2CHD086844 and P20GM109040.

99 Magnetic Resonance Imaging-Based Comparison of Temporal Changes in Brain Microstructure after Microemboli Injection in Control and Diabetic Rats: Relevance to Vascular Cognitive Impairment/Dementia

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

Diabetes doubles the risk of vascular cognitive impairment and dementia (VCID) but underlying reasons remain unclear. We reported that diabetic animals are more prone to microemboli (ME)-mediated tissue damage/demyelination and progressive cognitive decline. The goal of the current study was to determine the temporal and spatial changes in cerebral blood flow (CBF) and brain structure after ME injection using MRI. At 10 weeks after onset of diabetes, control and diabetic rats received cholesterol crystal ME (40-70 μm) injection. MRI scans were performed at baseline, weeks 8 and 12 post-ME. Behavioral tests including novel object recognition (NOR) and Y-maze for cognitive function and gait analysis with CatWalk were conducted at same time points as well as week 16. Diabetic animals had baseline deficits in certain cognitive domains and progressively worsened. ME injection caused infarction in two of the diabetic animals (n=6) but were not detected in controls (n=8). Diffusion Tensor Imaging (DTI) metrics showed lower axial diffusivity (DA) in the cortex of diabetic animals, indicating a degree of axonal damage. Post ME, radial diffusivity (DR) was increased while fractional anisotropy (FA) was decreased in the cortex at week 12. At the dorsal hippocampus, mean (MD), DA and DR were all significantly increased by week 12. These changes may reflect loss of tissue integrity and edema in the cortex and loss of axons and myelin damage in the hippocampus of diabetic animals after ME injection. Diabetic animals also showed a significant increase of CBF at week 8 particularly at the dorsal hippocampus and thalamus, which returned to normal by week 12. These results suggest that ME injury and associated cognitive deficits

are greater in diabetes, which also causes cerebrovascular dysfunction, and strategies to improve vascular function can be a preventive and therapeutic strategy for VCID. This work was supported by Adviye Ergul: VA Merit Award, VA SRCS Award and NIH Awards (R01NS083559 and NS104573), Weiguo Li: NIDDK DiaComp Pilot and Feasibility Grant.

100 Targeting Strategy for Localizing Alternative Pathway Inhibition in Age-related Macular Degeneration

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

Introduction: Age-related macular degeneration (AMD) is the leading cause of vision loss in the United States for people over sixty. Neovascular AMD (nAMD) is a consequence of new blood vessel growth breaching the posterior eye, bruch's membrane (BrM) and retinal pigment epithelium (RPE), into the subretinal space causing vision loss. This space accumulates vascular endothelial growth factor (VEGF) and complement activation components, predominantly contributed by the alternative pathway (AP), that drive nAMD. Treatments are monthly intraocular anti-VEGF injections. Injections can cause retinal detachment, infection, cataracts, or drug resistance. We propose a one-time sub-retinal injection of adeno-associated virus serotype 5 (AAV5) containing an inducible promoter under oxidative stress conditions (complement C3 promoter, pC3) that drives expression of therapeutic protein; complement receptor 2 (CR2) fused to the inhibitory domain of factor H (fH) (CR2-fH). The CR2 domain localizes fH to cells opsonized with complement activation product, opsonin C3d. Here we test if pC3-CR2-fH is active in RPE cells and if AAV5-pC3-CR2-fH can be used as a therapeutic in a mouse model. Material and Methods: ARPE-19 cells were co-transfected with pC3-mCherry and CMV-GFP. Complement-mediated stress was triggered by H2O2 or H2O2 + normal human serum (NHS), with or without inhibitors N-acetylcysteine (NAC) or CR2-fH, respectively. mCherry expression was evaluated by imaging. AAV5-pC3-mCherry and AAV5-pC3-CR2-fH were injected subretinally in mouse, over a range of doses. Results: mCherry expression was increased in H2O2 or H2O2 + NHS treated cells, and effects were mitigated the presence of NAC or CR2-fH, respectively. Subretinally injected mice were evaluated for dose safety using fundus photography, and electroretinography. Efficacy was evaluated in nAMD (laser-induced choroidal neovascularization; CNV) animal models. Conclusion: Proof of concept that pC3 can inducibly drive downstream production of mCherry in a complement-mediated manner. Additionally, we hypothesize that AAV5-pC3-CR2-fH mitigates AP activation in nAMD pathology as needed. This work was supported by Smart State Endowment From the State of SC, National Institutes of Health Grants EY019320, Department of Veterans Affairs Awards RX000444, T32 Support DC014435.

101 Revisiting the Concept of Minimal Detectable Change for the Activities-Specific Balance Confidence Scale with Individuals Post-Stroke

Bryant Seamon, Craig A. Velozo, Steven Kautz, College of Health Professions, Department of Department of Health Sciences and Research, MUSC.

Precision care in stroke rehabilitation requires an accurate evaluation of an individual's change over time. Current change thresholds, like the Minimal Detectable Change (MDC) index, are used to establish a measurement tool's sensitivity for change. However, the MDC is based on

group-level information and assumes that measurement error is consistent across an entire scale. We sought to show how a conditional Minimal Detectable Change (cMDC) index can produce an individualized threshold for determining detectable change by accounting for error fluctuations within a measurement tool. We used Activities-specific Balance Confidence (ABC) scale response data from a retrospective sample of 406 individuals 2-months post-stroke who participated in the Locomotor Experience Applied Post-Stroke Trial. Rasch analysis generated a standard error (SE) associated with each score on the ABC scale. SE data was used to calculate a cMDC index for each possible initial and final score combinations across the scale (cMDC=[SEscore1+SEscore2]/2*1.96*sqrt(2)). We also calculated the MDC index using group summary information (MDC=1.96*sqrt(2)*Standard Deviation of scores*sqrt(1-Internal Consistency)). We visually compared the MDC and cMDC by plotting all possible change thresholds for three initial scores representative of low, moderate, and high balance confidence. The cMDC produced a U-shaped curve illustrating how increased error towards the extreme ends of the scale inflates the required threshold for detectable change. The lower error associated with the middle of the scale decreased the threshold for detectable change below the MDC indicating the MDC could miss a detectable change. This effect was amplified when individuals had initial and final scores near the middle of the scale. Relying on the MDC index can result in an individual patient's change on the ABC Scale being misclassified. We recommend using a cMDC index based on an individual's initial and final scores to make more sensitive evaluations of change and enhance decision making precision. This work was supported by US Department of Veterans Affairs (1I01RX001935, 1IK6RX003075), National Institutes of Health (NIH P20 GM109040, R01 NS050506), Foundation for Physical Therapy Research (Promotion of Doctoral Studies Level I Scholarship).

102 Effect of hyperthermia method on drug delivery with thermosensitive liposomes

Krishna Ramajayam, A.Marissa Wolfe, Anjan Motamarry, Georges Nahas, John Yost, Mike Yost, Dieter Haemmerich, College of Medicine, Department of Pediatrics, MUSC.

Objective: Thermosensitive liposomes (TSL) are stimuli responsive nanoparticles that release encapsulated drug on hyperthermic temperatures (>40˚C). However, the effect of different hyperthermia (HT) methods on TSL based drug delivery is not well understood. The current study evaluates the impact of different hyperthermia (HT) methods on tumor drug uptake with TSL encapsulated doxorubicin (TSL-DOX). Methods: We developed three dimensional (3D) coupled computer models that simulated TSL- DOX based delivery in tumors based on actual mouse hind limb geometry. TSL-DOX based drug delivery was simulated in a computer model and investigated in vivo with three hyperthermia methods (thermistor (T), laser (L) and water bath (WB), for 15 min and 60 min. In vivo whole body fluorescence imaging was performed to visualize the tumor drug uptake in nude mice carrying subcutaneous Lewis lung carcinoma. Results: The computer model predicted that the maximum drug concentration (µg/g) at the tumor surface was 18.5 (T, 15 min), 36.8 (T, 60 min), 17.5 (L, 15 min), 28.9 (L, 60 min), 9.6 µg/g (WB, 15 min), and 8.6 (WB, 60 min). In vivo whole body fluorescence imaging suggested that tumor fluorescence was enhanced 2.6 fold (T) and 1.6 fold (L) with the increase in HT duration from 15 min to 60 min, with no change for water bath. The pharmacokinetic analysis from the computer model and in vivo blood sampling confirmed that water bath HT caused rapid depletion of TSL-DOX in the systemic circulation, which explains the lesser tumor drug uptake. Furthermore, results indicate that focused heating methods (T, L) provide better drug delivery.

Conclusion: Large volumetric heating depletes the systematically available encapsulated TSL-DOX resulting in poor tumor drug uptake. The computational models described here corroborate the in vivo findings and can aid in design of optimal drug delivery approaches. This work was supported by This work was supported by NIH Grant Number RO1CA181664. Part of this work was conducted in a facility constructed with support from the National Institutes of Health, C06 RR015455 and Grant Number C06 RR018823. This work was supported by the flow cytometry shared resource at the Hollings Cancer Center, Medical University of South Carolina (P30 CA138313).

103 Feeding and Swallowing Disorders in Preterm Infants: Who Receives Early Feeding Interventions after Hospital Discharge?

Brooke Mulrenin, Megan Richmond, Annie Simpson, College of Health Professions, Department of Department of Health Care Leadership and Management; Department of Health Sciences and Research, MUSC.

Introduction: Preterm birth often leads to a range of developmental sequelae, including feeding and/or swallowing disorders. Prospective studies have shown that early feeding intervention (occupational and/or speech therapy (henceforth: "OT/SLP")) improve outcomes for preterm infants. However, it is widely believed that many infants who could benefit from these early OT/SLP services do not receive them. Retrospective data analysis provides an opportunity to examine the proportion of these infants receiving OT/SLP services after hospital discharge. Additionally, it allows for better understanding of patient characteristics that influence whether OT/SLP services are received. Methods: Using Marketscan Medicaid administrative records from 2013 and 2014, we retrospectively examined a cohort of 7183 infants who were born preterm (<37 weeks gestation) and diagnosed with feeding and/or swallowing disorders (henceforth: feeding problems) during their birth hospitalization. We aimed to determine who received OT/SLP services after hospital discharge. Using ICD-9 diagnosis and procedure codes, we identified OT/SLP services received and examined patient characteristics known to impact feeding and swallowing development (e.g. birth weight, gestational age at birth). We also examined the length and cost of birth hospitalization. Results: In the first 6 months after hospital discharge, only 6 percent of preterm infants with feeding problems received OT/SLP services. This increased to 8.5 percent in the 12 months after that. Factors that increased the likelihood that an infant would receive OT/SLP services after hospital discharge included: born extremely preterm, extremely low birth weight, and longer more expensive birth hospitalization. Discussion: Many preterm infants with feeding problems continue to face feeding challenges throughout childhood. Infant feeding problems that are qualitative in nature (e.g. uncoordinated or slow feeding) often become more pronounced as purees and solid foods are introduced. To enhance feeding development throughout childhood, we must ensure that preterm infants with feeding problems receive early feeding intervention after hospital discharge. This work was supported by T32 DC014435 Predoctoral Training Grant.

104 Determining factors that influence adoption of new post-stroke physical rehabilitation devices

Corey Morrow, Emily Johnson, Austin Hayes, Na Jin Seo, College of Health Professions, Department of College of Health Professions/Occupational Therapy, MUSC.

Objectives: Rehab device efficacy alone does not lead to adoption into clinical practice. The objective of this work was to increase understanding of the landscape for clinical adoption of post-stroke physical rehabilitation devices. Specifically, the focus was on the type of devices that aim to increase neuroplasticity for recovery, since they are the majority of rehab devices in current research and development. Method: We retrospectively analyzed field notes of interviews with 105 stakeholders including patients who have had strokes, rehab directors, and physical/occupational therapists to understand their viewpoints for adopting new rehabilitation devices. Results: Care settings whose therapy goals are best aligned with increasing neuroplasticity for restoration of function are found to be outpatient rehab, followed by inpatient rehab. Therapists are the major influencers of adoption since they typically introduce new rehab devices to patients. Therapists' use rate of a rehab device primarily influences a rehab director's decision to acquire the device for their rehab facility. Main drivers and barriers for each stakeholder including the influencer (therapists), decision maker (rehab directors) and beneficiary (patients) are identified, along with interactions between stakeholders, for clinic adoption of rehab devices. In addition, drivers and barriers for home adoption of rehab devices by patients are identified. Conclusions: Best settings for introducing restorative rehab devices to stroke rehabilitation are deemed to be outpatient and inpatient rehab facilities based on the treatment goals of these settings. Rehab device development should consider the roles of stakeholders and their drivers and barriers for successful adoption. This work was supported by National Center for Advancing Translational Sciences of the National Institutes of Health under Grant Numbers TL1 TR001451 & UL1 TR001450. NIH 3R41HD090792-01A1S1, NIH R41HD090792-01A1, COBRE funding NIH/NIGMS P20GM109040.

105 Aging and Smoking Exacerbates Post-Stroke Complement Driven Neuroinflammation

Christine Couch, Ali Alawieh, E. Farris Langley, Stephen Tomlinson, College of Health Professions, Department of Department of Microbiology and Immunology, MUSC.

Introduction: Following stroke, complement-dependent neuroinflammation exacerbates secondary injury and worsens acute and chronic outcomes. We have shown that an injury site-targeted complement inhibitor (B4Crry), that targets specifically to the ischemic brain, inhibits complement activation leading to improved outcomes. Stroke comorbidities have been shown to promote a pro-inflammatory environment in the brain and systemically, and to exacerbate inflammatory responses after injury. We investigated the impact of age and smoking on acute outcomes after stroke and assessed whether increased complement activation contributes to the worsening outcomes with these stroke comorbidities. Methods: Mouse brain endothelial cells (bEnd3) were exposed to hypoxia followed by exposure to serum that was derived from either cigarette smoke (CS)-exposed mice or naïve mice, and IgM and C3d deposition assessed. Adult (12 weeks) and aged (1 year) mice were subjected to 1h transient middle cerebral artery occlusion. Animals were exposed to CS for 3-6 months (5hr/day, 5days/week) by burning 3R4F cigarettes using a smoking machine. Animals were treated with B4Crry or vehicle intravenously 2h post-MCAO. Survival analysis and neurological deficit scores were performed up to 7 days. Brains were extracted for histological and molecular analyses. Results: Following

hypoxia, bEnd3 cells exposed to serum from CS-exposed mice had higher C3d and IgM deposition compared to naïve serum. Older and CS-exposed mice had significantly worse neurological deficits and mortality compared to younger adults post-MCAO. B4Crry reduced mortality and motor deficits in young, old and old+CS mice with a higher effect size in comorbid animals. Age and/or CS exposure resulted in larger infarct volumes, and increased levels of C3d deposition and microglial activation compared to young adults, but aged/CS animals treated with B4Crry fared comparable to young adults. Conclusion: The pro-inflammatory effects of aging and smoking contribute to worse stroke outcomes, and these effects can be successfully mitigated by injury. This work was supported by NCATS through TL1 TR001451 and UL1 TR001450, Department of Veterans Affairs Merit Award RX001141.

106 LC3-C-Associated Selective Autophagy is Induced under the Control of HSp27 during P. gingivalis Infection of Human Primary Epithelial Cells

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

Abstract Withheld from Publication

107 The Impact of Nurse Navigation on Timeliness to Treatment for Benign Breast Pathology

Catherine Shirer, Catherine Chung MD, Rupak Mukjerjee PhD, Julie B. Siegel MD, David J. Cole MD, Mark A. Lockett MD, Nancy Klauber-Demore MD, Andrea Abbott, College of Medicine, Department of Surgery, MUSC.

Background: Benign high-risk breast pathology is a risk factor for the development of breast cancer and time to treatment is crucial. Nurse navigation programs, a multi-disciplinary approach to cancer care at many centers, have been shown to eliminate delays in care and alleviate anxiety among cancer patients. This study evaluated the effect of nurse navigation on timeliness to care for patients with benign, high-risk breast pathology undergoing surgery. Methods: A single-institution, retrospective review of patients with benign high-risk breast pathology undergoing lumpectomy between January 2017 and June 2019 was analyzed. Patients were stratified into two cohorts based on time periods with and without nurse navigation. Preoperative and postoperative time to care variables as well as demographics and tumor characteristics were compared using univariate and multivariate analysis. Results: There were 29 patients without nurse navigation and 100 patients with nurse navigation. In univariate analysis, nurse navigation significantly reduced time to care from referral to first appointment from 13 days to 8 days ($p<0.01$), referral to date of surgery from 49 to 32 days ($p<0.01$), and first appointment to day of surgery from 35 to 23 days ($p=0.04$). In multivariate analysis, nurse navigation remained the predominant variable associated with reductions in time to care that reduced time from referral to first appointment ($p<0.05$), referral to day of surgery ($p<0.05$), and first appointment to day of surgery ($p<0.06$). The overall percent of patients that were upstaged to cancer on final surgical pathology was approximately 20% and was not significantly different between the two groups. Conclusion: The implementation of nurse navigation significantly decreased time to care for patients with benign, high-risk breast pathology undergoing lumpectomy. We recommend the use of a nurse navigation program as part of a comprehensive approach to breast health for patients with high-risk breast pathology.

108 NF-kB regulates local muscle inflammation that associates with impaired regeneration and muscle wasting in cancer cachexia

Benjamin Pryce, Erin Talbert, David Wang, Mary E. Dillhoff, Carl R. Schmidt, David C. Evans, Amy Webb, Denis Guttridge, College of Medicine, Department of Pediatrics, Hollings Cancer Center, MUSC.

Cachexia is observed in most cancer patients and is due in large part to the wasting of skeletal muscle. The effects of cachexia include increased mortality rates, decreased quality of life, and reduced tolerance to frontline therapies. In pancreatic cancer, which has a 5-year survival rate of less than 10%, as many as 90% of patients will experience some form of cachexia. Therefore, understanding the mechanisms of muscle wasting in cancer has the potential to lead to the discovery of novel therapies which could greatly improve disease outcomes in these patients. Recently, we determined that the muscle microenvironment (MME) plays a key role in the pathology of muscle wasting of cancer patients, with muscle damage leading to subsequent activation of muscle progenitor cells (MPCs). Interestingly, MPCs in cachectic muscle are unable to commit to differentiation due to sustained activity of NF-kB. Here, we demonstrate that cachectic muscles show increased expression of inflammatory chemokines, as well as an increase in CD11b+ cells. Inhibition of NF-kB in MPCs reduced the expression of inflammatory chemokines in cachectic muscle as well as the level of macrophages within the MME. Furthermore, data suggest that ablation of macrophages using clodronate treatment in tumor bearing mice partially rescued muscle differentiation. Collectively, these results imply that NF-kB activity in MPCs functions to regulate a local skeletal muscle inflammatory environment to limit muscle repair and in turn drive muscle wasting in cancer cachexia.

109 Trigeminal Nerve Stimulation to Selectively Target Sensory Triggers Associated with Olfactory Sensitivity

Elise Gruber, Bernadette Cortese, Lisa McTeague, Sarah Huffman, Bashar Badran, College of Medicine, Department of Brain Stimulation Lab, MUSC.

Olfactory Sensitivity (OS) has been largely recognized as an important factor and trigger for anxiety, stress-related, attention deficit hyperactivity, and obsessive compulsive-related disorders. Approximately 11-33% of the population is identified as having OS, however, despite its prevalence, there are no established, effective treatments. Prior studies have indicated that OS triggers are preferentially sensed through the trigeminal nerve, thus, tempering odor detention of the trigeminal pathway specifically is optimal, especially considering the association of complete odor dysfunction with depression and neurodegenerative disorders. This study aims to determine whether direct activation of the trigeminal nerve via trigeminal nerve stimulation (TNS) and transcranial direct current stimulation (tDCS) may impact odor detection and sensitivity. 20 healthy participants were recruited in this 3 visit, sham controlled, double-blinded crossover trial. During each visit, a baseline odor sensitivity threshold was conducted, followed by one of three neurostimulation modalities (active TNS, sham TNS, or tDCS. Post-stimulation odor thresholds were conducted as well as pre-post mood and cognitive testing. An interim analysis on blinded data (n=8) suggests that two of three conditions modulate odor sensitivity to olfactory and trigeminal odorants. Olfactory sensitivity (PEA odorant) increased by 10% from baseline in Condition C, whereas only 4% in conditions A and B. Trigeminal sensitivity (GUA odorant) increased by 20% and 12% following conditions C and A respectively, whereas only 3% in condition B. Although these data are still blinded, our interim findings suggest that two of

the three stimulation conditions are likely biologically active and effective in modulating the trigeminal nerve system as measured by changes in sensitivity to the trigeminal-activating odorat GUA. If positive, these findings may help create new treatments for individuals with olfaction disorders. This work was supported by MUSC Internal Funding -.

110 Barriers and Facilitators to School-Based Interventions addressing Physical Activity and Healthy Eating Behaviors: Perspectives of School Administrators and Personnel

Logan Camp-Spivey, Susan D. Newman, PhD, RN, CRRN; Robert Stevens, PhD, MS; Michelle Nichols, PhD, RN, Logan Camp-Spivey, College of Nursing, Department of College of Nursing, MUSC.

Introduction: In South Carolina (SC), nearly 37% of youth are overweight or obese. Behaviors that lead to excess weight gain include inadequate participation in physical activity (PA) and consumption of high-calorie, low-nutrient foods. School-based interventions have been shown to improve PA and healthy eating behaviors. There is a notable gap in the literature on system-wide barriers and facilitators regarding awareness, selection, and implementation of these school-based interventions from the perspectives of SC school administrators and the needs of SC school personnel. There is also limited information on COVID-19's effects on school-based initiatives. Methods: Using a multi-methodological approach, guided by the social ecological model and aspects of the Steps in Quality Intervention Development model, we will conduct semi-structured interviews with SC school administrators and distribute a needs assessment survey to SC school personnel (teachers, school nurses) to accomplish two main specific aims. Aim 1 - Describe actual and perceived barriers and facilitators school administrators and personnel encounter regarding awareness, selection, and implementation of school-based PA and healthy eating interventions. Aim 2 - Identify greatest challenges and supports, priority focal areas, and interventions that have been implemented along with their outcomes. Progress to Date: The study has received IRB approval and recruitment and data collection have begun. The PI has interviewed 28 school administrators, and qualitative data analysis is underway. There are 1285 responses to the needs assessment survey in REDCap. Next Steps: To address both Aims 1 and 2, the PI will continue analysis of interviews to identify common themes. Quantitative data analysis will also be completed using univariate and bivariate descriptive statistics to recognize most common barriers and facilitators and compare responses based on school district classifications, academic levels, and roles in schools. Findings will inform future intervention mapping to adapt and implement school-based interventions that account for barriers and facilitators. This work was supported by Sigma Theta Tau International Honor Society of Nursing: Mu Rho Chapter.

111 The Effect of Body Mass Index on High Energy Acetabular Fracture Patterns

Andrew Moore, Chad Richardson, harris slone, College of Medicine, Department of orthopaedics, MUSC.

Obesity is a growing public health concern affecting 42% of US adults and confers increased risk of infection, thromboembolic disease, longer operative times, increased blood loss, and longer hospital stay after acetabular fracture (fx) surgery. There are well known variations in fx pattern between high and low energy traumas, however, there is a lack of information regarding the effect of BMI on acetabular fx patterns. Acetabular fxs are categorized using the Letournel

classification system into Elementary and Associated groups. Given obesity's implication on surgical intervention, we investigated the effects of obesity and acetabular fxs. Hypothesis: Acetabular fx pattern is dependent on BMI at time of injury. Methods: Patients were pulled from an institutional database from 2014 to 2018 based on CPT codes. Data collected includes BMI at time of injury, fx patterns, mechanism of injury, demographics, and length of stay. Only high energy fxs were analyzed, which includes falls over 1 meter, motor vehicle accidents and other high impac traumas. Pathological fxs and low energy fxs were excluded from data analysis (fragility fxs, falls <1 meter). Pearson chi-square test was utilized to determine if Letournel fx pattern (Elementary vs. Associated) was independent of BMI. Statistical analysis was performed with BMI in 2 groups (<30 vs. >=30) as well as 4 groups (normal<25, overweight 25-29.9, obese 30-40, morbidly obese>40). Results: 208 high energy subjects were included, with 80 elementary fxs and 128 associated; other demographics: 28% female, 39% African American, 56% white, with a median age of 38, and median length of hospital stay 9 days. Pearson chi-square test for independence revealed no relationship between BMI and fracture pattern ($p=0.156$ for 4 BMI groups and $p=0.280$ for 2 BMI groups). However, notable observed differences in 4 BMI group: 61% of overweight fxs were elementary and 70% of obese fxs were elementary.

112 Advancing peptide siRNA-carrier designs through stereochemistry and D-amino acid modifications to enhance gene silencing

Charles Holjencin, Colton Feinberg, Travis Hedrick, Robert Williams, Priya Patel, Evan Biles, James Cummings, Chance Wagner, Andrew Jakymiw, College of Dental Medicine (DMD, PhD), Department of Oral Health Sciences, 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. These modifications were also found to affect cellular uptake and intracellular localization patterns of siRNA cargo, with one particular variant capable of mediating binding of siRNAs to specific cellular projections, identified as filopodia. Interestingly, this variant also exhibited the most enhanced gene silencing in comparison to the parent 599 peptide, thus, suggesting a possible connection between filopodia binding and enhanced gene silencing. 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 grants R21DE027231 and T32DE01755, MUSC Summer Health Professions Research Program, MUSC Summer Undergraduate Research Program, US Government Federal Work-Study Program.

113 Gender Differences in Outcomes of Interdisciplinary Pain Rehabilitation

Julia Rodes, Taylor Crouch, Ph.D, Kelly Barth, College of Medicine, Department of Associate Professorr, MUSC.

Background: Gender differences exist in pain experiences. A systematic literature review discovered reported gender differences in outcomes of interdisciplinary pain rehabilitation, with women generally demonstrating greater outcomes. We hypothesized gender differences exist in outcomes of the MUSC interdisciplinary pain rehabilitation program. Methods: A retrospective cohort study was conducted on participants in the 3-week MUSC Pain Rehabilitation Program from 2018-2020 (N=36). Patients reported measures at baseline and discharge. To accurately compare genders, male subjects (n=18) were matched to female subjects using an innovative matrix of sociodemographic and diagnostic variables: (1) age (10 years), (2) race, (3) ethnicity, (4) primary pain diagnosis, (5) Medicaid enrollment. Statistical analyses were performed using SPSS version 25. Within-subject changes were examined using paired sample t-tests. Change scores in treatment variables were compared between groups using independent samples t-tests. Results: Statistically significant differences were found. Differences in baseline and discharge variables were found. Pain Interference (BPI) differences were significant at discharge ($t(35) = 1.57$, ($p < .05$), along with a trending difference in change scores between genders ($t(35) = 1.33$, ($p < .05$), with women showing a greater reduction in pain interference. There were significant differences in Pain Willingness (CPAQ) change scores ($t(36) = 10.33$, ($p < .05$) and discharge scores ($t(36) = 9.22$, ($p < .05$) with women showing greater change in willingness. The change score for Anxiety (BSI) between genders was significant ($t(36) = 3.277$, ($p < .05$), with women showing larger reduction in anxiety. Helplessness (PCQ) was significantly different at baseline ($t(35) = -16.52$, ($p < .05$) but not at discharge, with a significant change score of ($t(35) = 4.50$, ($p < .05$). Discussion: Both genders showed improvements and the results demonstrated statistically significant gender differences in outcomes. Women showed significantly greater change in regard to anxiety, pain catastrophizing, and pain acceptance. This work was supported by Supported by the NIDA-Funded Drug Abuse Research Training (DART) Program, R25, DA020537.

114 Improved Auditory-Visual Superadditivity Compensates for Age-Related Declines in Heard and Lipread Speech Intelligibility

James Dias, Carolyn McClaskey, Kelly Harris, College of Medicine (MD, PhD), Department of Otolaryngology - Head and Neck Surgery, MUSC.

Cross-sensory speech information can improve upon the perception of speech available from only a single sense. For example, heard speech can be more accurately identified when listeners also see the speaker's articulating face. These cross-sensory effects can be superadditive to unisensory speech processing such that audiovisual speech identification is better than the sum of auditory-only and visual-only (lipread) speech identification. It has been hypothesized that age-related declines in auditory and visual speech processing are concomitant with improved cross-sensory speech processing, but little evidence exists to support this. Past studies have been primarily concerned with assessing how information available from one sense (auditory or visual) influences perception of audiovisual speech, and have found that these cross-sensory influences do not change with age. However, these studies did not consider the multisensory (auditory and visual) superadditive benefit in audiovisual speech. The current investigation evaluated age-related changes in multisensory speech

processing, employing metrics of cross-sensory influence previously found to exhibit no age-related changes and a metric of multisensory superadditivity. Normal-hearing normal-sighted younger and older adults identified words in auditory noise that were heard (auditory-only), seen (visual-only), and heard and seen (audiovisual). Replicating previous findings, older participants had greater difficulty identifying auditory-only and visual-only speech, but performed similarly to younger adults when identifying audiovisual speech. Similar to past reports, metrics quantifying the auditory or visual influence on audiovisual speech identification did not differ between age groups. However, older participants did exhibit improved auditory-visual superadditivity over younger participants. The results suggest that age-related declines in auditory and visual speech identification are accompanied by an improved auditory-visual superadditivity that can preserve audiovisual speech perception. We discuss why metrics for cross-sensory influence fail to exhibit age-group differences and the value of using a metric of multisensory superadditivity when investigating age-related changes in multisensory processing. This work was supported by NIDCD R01 DC014467, R01 DC017619, P50 DC000422, T32 DC014435.

115 Generation of a new immortalized human lung pericyte cell line: a promising tool for human lung pericyte studies

Pengfei Li, Yan Wu, Andrew J. Goodwin, Perry V. Halushka, Carole, L Wilson, Lynn M Schnapp., Hongkuan Fan, College of Medicine, Department of Department of Pathology and Laboratory Medicine; Department of Regenerative Medicine and Cell Biology, MUSC.

Pericytes are uniquely apposed to the capillary endothelium and are known to stabilize and promote endothelial integrity. Recent studies indicate that lung pericytes play a prominent role in lung physiology, and they are involved in the development of various lung diseases, including lung injury in sepsis, pulmonary fibrosis, asthma, and pulmonary hypertension. Accordingly, human lung pericyte studies are important for understanding the mechanistic basis of lung physiology and pathophysiology, however, they can only be cultured for a few passages and no immortalized human lung pericyte cell line has been established to date. Our present study aimed to establish an immortalized human lung pericyte cell line using transfection of SV40 large T antigen lentivirus. Immortalized pericytes exhibited sustained proliferation and significantly higher telomerase activity compared to normal human lung pericytes. SV40T expression was also detected by western blot in immortalized pericytes but not in normal pericytes. In addition, the immortalized cells retained pericyte characteristics, marked by similar morphology, and expressed pericyte cell surface markers such as PDGFRβ, NG2, CD44, CD146, CD90 and CD73. Furthermore, immortalized pericytes exhibited "reactive" features in response to different stimuli, similar to control pericytes. Our previous data showed that friend leukemia virus integration 1 (Fli-1), a member of the ETS transcription factor family, is a key regulator that modulates inflammatory responses in mouse lung pericytes. We found that Fli-1 regulated inflammatory responses in immortalized human lung pericytes as measured via IL-6 levels. To summarize, we successfully established a new immortalized human lung pericyte cell line, which serves as a promising tool for in vitro pericyte studies to further our understanding of human lung pericyte physiology and pathophysiology. This work was supported by National Institute of General Medical Sciences grants 1R01GM113995 (HF), 1R01GM130653 (HF), 1K23HL135263-01A1 (AG), and UL1TR001451 (PVH).

116 The splanchnic mesenchyme during fetal development is the major source of pancreatic cancer associated fibroblasts

Lu Han, Yongxia Wu, Sean Sweeney, Ulyss Roesner, Khushbu Patel, Melodie Parrish, Xuezhong Yu, Cynthia Timmers, Gustavo Leone, Michael Ostrowski, College of Medicine, Department of Biochemistry, MUSC.

Pancreatic ductal adenocarcinoma (PDAC) is one of most lethal cancers due to lack of effective treatments. In PDAC, cancer associated fibroblasts (CAFs) are a major cell type in the desmoplastic stroma and play complex roles in the tumor microenvironment. However, the tissue origin(s) of CAFs are unknown and genetic tools to robustly target them in vivo are lacking. Here we aimed to examine three potential tissue sources of CAFs: the pancreatic epithelium (through epithelium-to-mesenchyme transition), the bone marrow (through migration via the circulation), and the tissue resident fibroblasts (TRFs) in the normal pancreas (through proliferation). We utilized a genetically engineered mouse model of PDAC, where Kras and p53 mutations were engineered in the pancreatic epithelium using an Flp-Frt system. To determine whether the pancreatic epithelium gives rise to CAFs, we permanently labeled the pancreatic epithelium and their descendants with a GFP reporter. We found that GFP expression was rarely identified in CAFs. To determine whether the bone marrow gives rise to CAFs, we transplanted GFP-positive donor bone marrow to GFP-negative recipient mice. We found that only a small proportion of pancreatic CAFs were tagged with GFP. Lastly, to genetically label TRFs with a Tomato reporter, we used an inducible CreER-Loxp system to activate Tomato expression in the splanchnic mesenchyme during mid-gestation. Tomato expression was subsequently identified in the majority of both pancreatic TRFs and CAFs. In summary, we identified the splanchnic mesenchyme as the fetal origin of pancreatic TRFs, which expand to contribute to the vast majority of CAFs in PDAC. The bone marrow contributes to a small proportion of CAFs, and the pancreatic epithelium contributes even less. This provides approaches to robustly target CAFs in vivo to further investigate their heterogeneity and function in PDAC. This work was supported by NIH/NCI T32 CA193201, NIH/NCI F32 CA254238.

117 Long-term impact of acute restraint stress on heroin self-administration, reinstatement, and stress reactivity

Jordan Carter, Angela Kearns, Kelsey Vollmer, Constanza Garcia-Keller, Rachel Weber, Nathanial Baker, Peter Kalivas, Carmela Reichel, College of Graduate Studies (MSTP), Department of Neuroscience, MUSC.

Epidemiologic studies have repeatedly confirmed the strong comorbid relationship between post-traumatic stress disorder (PTSD) and substance use disorder (SUD). Of the substances used by individuals with PTSD, prescription (e.g., oxycodone) and non-prescription (e.g., heroin) opioids are the second most commonly abused; and one-third of people dependent on opioids have probable comorbid PTSD. Concerningly, opioid use by those with PTSD has increased alongside the worsening opioid epidemic in the USA. Here, we combined acute restraint stress (ARS) and contingent heroin self-administration (SA) in rodents to study stress and opioid use comorbidity and to identify changes in anxiety-like behaviors following stress and/or heroin in response to a stress-conditioned cue. We used a 2-h ARS paired with an odor stimulus to condition a stress cue (CS) for testing effects of stress reactivity on extinction and reinstatement of heroin seeking and a burying task. Additionally, rats were tested for social place preference for measures of social reward. Blood samples were taken at various time points during the study

to measure plasma corticosterone levels. Stress rats exhibited numerous disrupted behaviors, including enhanced acquisition of heroin intake as well as potentiated reinstatement and delayed extinction in response to the stress CS. All rats developed a social place preference, but stress rats spent more time in nose-to-nose contact with the unfamiliar rat while heroin rats spent time exploring the chamber. In the burying task, stress shortened latencies to bury the CS and increased burying and immobility relative to sham rats. Corticosterone levels were significantly elevated 15min into ARS and immediately following the burying task. These findings demonstrate that ARS results in development of anxiety-like behaviors and that a stress-associated cue is sufficient to reinstate extinguished heroin seeking. Further work on this project has the potential to elucidate the complex relationship between stress/PTSD and SUD. This work was supported by NIDA P50 DA016511, U54 DA016511, T32 DA728823, CofC Honors SEG, R25 DA033680.

118 TLR9-activated B cells empower adoptively transferred CD8+ T cells with enhanced persistence and tumor immunity

Aubrey Smith, Hannah Knochelmann, Megan Wyatt, Connor Dwyer, Guillermo Rangel Rivera, Amalia Rivera Reyes, David Neskey, Jessica Thaxton, Eric Bartee, Mark Rubinstein, Bei Liu, Chrystal Paulos, College of Graduate Studies, Department of Microbiology and Immunology, MUSC.

Adoptive cell transfer (ACT) therapy can be more effective than traditional therapies for late-stage melanoma, but with only 20% of patients achieving long-term regression-free survival, more potent cell therapies are needed. Preconditioning patients via chemo- or radiotherapy prior to ACT is a critical step in ACT as it provides several benefits to the transferred T cells. One benefit is the systemic activation host immune cells via the release of Toll-like receptor (TLR) ligands from the injured gut. TLR-activated host cells then potentiate the transferred T cells' antitumor ability. TLR ligands injected to the host alongside ACT also results in better outcomes, but may lead to toxic side effects. Thus, we hypothesized that TLR agonists could be used in an alternative way - in the ex vivo propagation of potent T cells for ACT. To address this question, we added the TLR9 agonist, CpG, during the ex vivo expansion of tumor-reactive T cells. We found that CpG-generated T cells elicited potent immunity against melanoma in vivo. T cells expanded with CpG exhibited an IL-2Ra-high, ICOS-high and CD39-low surface phenotype and a unique proteome ex vivo and engrafted robustly in vivo. In culture, B cells, not DCs or macrophages, were essential for imprinting T cells with this phenotype and potent tumor immunity. Further, B cell-activating, not DC-activating, TLR9 agonists improved CD8+ T cell antitumor immunity. Purified B cells mediated similar CpG-associated changes in CD8+ T cells, suggesting that in this context B cells do not require CD4+ T cell help to improve CD8+ T cell therapy. These findings reveal a previously underappreciated role for B cells in the generation of powerful antitumor CD8+ T cells and imply that the B cell/T cell axis should be harnessed to produce novel cell-based therapies for patients with cancer.This work was supported by RO1 CA175061 (NCI), RO1 CA208514 (NCI) (C.M. Paulos), Hollings Cancer Center Graduate Fellowship (A.S. Smith), Hollings Cancer Center Proteomics Pilot Award (A.S. Smith and C.M. Paulos).

119 Futility Analysis Utilizing Conditional Power Boundaries from Popular Error Spending Functions in Randomized Control Trials

Corinne McGill, Jonathan Beall, Valerie Durkalski-Mauldin, College of Graduate Studies, Department of Department of Public Health Sciences, MUSC.

Nearly all clinical trials are longitudinal, which, in some cases, presents the need for interim monitoring prior to trial conclusion. In the case of trials with lengthy follow-up periods, it may be wise to consider an interim look for a variety of reasons including but not limited to: early harm detection, insurance of patient safety, sooner benefit in the case of overwhelming efficacy, and prevention of wasted resources in the case of no treatment effect. An interim look with the latter case in mind is referred to as a futility analysis. One common method utilized in determining early stopping rules for futility is conditional power. This method is prediction-based, as it refers to the probability that the null hypothesis will be rejected at the trial's conclusion based on the fraction of data available at the time of interim analysis. When utilizing a conditional power boundary for futility, this interim look can take place at any time throughout the trial. Typically, conditional power thresholds for futility range from 0.10-0.30 and are static throughout studies. We found that these standard boundaries are very conservative, particularly when a study has reached the halfway point. Spending functions that account for the inflation of type II error and approximate time-varying boundaries for futility are an alternative to conditional power. We conducted a simulation study to examine the properties of conditional power and to determine the optimal threshold depending on the amount of information collected. The conditional power threshold for futility should change throughout the study depending on the amount of information accumulated at the time of interim analysis. Therefore, we identified boundaries in the conditional power setting that are equivalent to those of popular error spending functions and applied them to two currently running randomized controlled trials.

120 Augmentation of Graft Preservation Solution with a Targeted Complement Inhibitor Promotes Protection from Brain Death Induced Ischemia Reperfusion Injury

M. Mahdi Sleiman, Biao Lei, Qi Cheng, Zhenxiao Tu, Peng Zhu, Martin Goddard, Paulo N. Martins, Satish Nadig, Carl Atkinson, Stephen Tomlinson, College of Graduate Studies (MSTP), Department of Microbiology and Immunology, MUSC.

Donor brain death (BD) is an inherent component of vascularized composite allograft (VCA) transplantation and is thought to be a key contributor to ischemia-reperfusion injury (IRI). Complement is activated and deposited within solid organ grafts as a consequence of BD and has been shown to exacerbate IRI, although the role of BD and complement in VCA transplantation and the role it plays in IRI and graft rejection has not been studied. Here we investigate the role of BD and complement in VCA IRI in the context of a therapeutic and clinically relevant paradigm involving the delivery of a complement inhibitor to the VCA pre-transplant. BD was induced in Balb/c donors, and the VCA perfused prior to graft procurement with UW solution augmented with CR2-Crry, a complement inhibitor that target sites of complement activation. Following perfusion, donor VCAs where cold stored for 6 hours before transplantation into C57BL/6 recipients. Donor VCAs from living donors (LD) were also procured and similarly stored. Compared to LD VCAs, BD donor VCAs had exacerbated IRI as determined by increased histopathological injury and immune cell infiltration, and BD donor VCAs rejected earlier. Pretransplant perfusion of the graft with CR2-Crry resulted in a significant reduction in IRI as compared to vehicle-treated BD donors, and returned IRI severity and graft

rejection times of BD VCAs to that seen for LD VCAs. In vivo fluorescent imaging of labeled CR2-Crry confirmed graft retention of CR2-Crry following cold storage and transplantation. Following a single pre-transplant perfusion, CR2-Crry was detected bound in the graft at the end of cold ischemia and at 6 hours post transplantation. This work was supported by NIH NIAID, Lee Patterson Allen Foundation Award, DOD, AHA.

121 Cognitive, affective, and behavioral moderators and mediators in a randomized controlled trial of tDCS-augmented in vivo exposure therapy for specific fears

Adam Cobb, Patrick O'Connor, Eric Zaizar, Kevin Caulfield, Francisco Gonzalez-Lima, Michael J. Telch, Lisa McTeague, College of Medicine (MD, PhD), Department of Psychiatry and Behavioral sciences, MUSC.

Background: Several forms of non-invasive brain stimulation have demonstrated potential to enhance evidence-based treatments for affective disorders. We recently reported that transcranial direct current stimulation (tDCS) targeting prefrontal regions enhanced in vivo exposure across a range of specific fears. This report extends these efforts to probe whether (and how) tDCS may operate through modifying online mental and emotional processes by applying advanced moderation and mediation analytic techniques. Methods: In a double-blind, placebo-controlled trial, contamination- and animal-phobic participants (N = 49) were randomized to active tDCS (1.7 mA, 20 min.; n = 27), or sham tDCS (1.7mA, 30 sec.; n = 22), followed by 30 min. of in-vivo exposure. Active tDCS targeted excitation of the left mPFC and inhibition of the right dlPFC; polarity was counterbalanced for controls. Before and after tDCS (20 min.), but prior to in vivo exposure (30 min.), participants completed measures of (a) attentional engagement and disengagement with phobogenic images; (b) working memory; and (c) state affect. Attentional biases were assessed again, along incidental contextual memory for the extinction context 1-month later. Results: Active tDCS promoted attentional and behavioral engagement towards feared targets, which emerged as the only significant mediators of tDCS-augmentation effects among those evaluated from a battery spanning emotional, cognitive, physiological, and behavioral domains. Conclusions: Our results suggest that our previously observed tDCS-augmentation effects were at least partly accounted for by promoting attentional and behavioral engagement with feared targets, whereas other patterns of effects of tDCS on cognition and affect were not found to mediate the augmentation effects on reductions in peak fear during in vivo exposure. These results are consistent with evidence-based treatment guidelines with respect to the need to promote engagement with feared targets, particularly among those with the strongest tendencies to resist doing so, and those with elevated negative prognostic indicators. This work was supported by The study design and implementation was supported by an internal Graduate Research Fellowship at the University of Texas at Austin. Analyses and manuscript preparation were supported by the PI's NIMH T32 postdoctoral fellowship (MH18869) at the National Crime Victims Research and Treatment Center within the Department of Psychiatry and Behavioral Sciences at the Medical University of South Carolina.

122 Using longitudinal data to build a better prediction model for transplant-free survival after acute liver failure

Sherry Livingston, Valerie Durkalski-Mauldin, College of Graduate Studies, Department of Public Health Sciences, MUSC.

Introduction: Liver transplantation can greatly reduce the risk of death for acute liver failure (ALF) patients, but not all ALF patients are able to receive a transplant. To aid clinicians in decisions regarding transplant, a number of prognostic models have been built to predict transplant-free survival (TFS). The ALF Prognostic Index is the most recently validated model, using admission lab values, clinical factors, and etiology to predict TFS. In this setting, however, lab values continue to be measured daily, and can change dramatically in the first days or weeks after ALF. We aim to develop a method for using repeated lab values taken over time to build a robust prediction model for TFS in ALF patients. Methods: The Acute Liver Failure Study Group maintains a database of more than 2000 ALF patients with daily lab values taken up to seven days after enrollment. These lab values are used to build prognostic models predicting TFS. While existing prognostic models use lab values taken at a single time-point as predictors, we also look at models that use the totality of available information post-admission either as a single value or summary measure: last value, worst value, best value, mean, median, and change score. Results: Prognostic models incorporating information taken over time have better fit and better prediction accuracy than models built using only information from a single day when predicting TFS in ALF patients. Conclusions: The incorporation of data taken at multiple time-points in predictor variables can lead to better prediction models, even in the case of using simple summary measures. More complex methods (such as functional data analysis or latent trajectory analysis) that use repeated measures of independent variables to build models for prediction of a binary outcome are currently limited, but potentially could provide more robust prediction accuracy and precision. This work was supported by Supported in part by a grant from the NIDDK to the Acute Liver Failure Study Group (U01 DK058369).

123 MEF2C, a neurodevelopmental disorder-linked gene, regulates PCDH17 expression to control cortical synapse density

Yongjoo Cho, Adam J Harrington, Aram Raissi, Carly Hale, Ahlem Assali, Jennifer Darnell, Kimberly Huber, Christopher Cowan, College of Medicine (MD, PhD), Department of Department of Neuroscience, MUSC.

The MEF2C transcription factor regulates gene expression during development and in adulthood, and mutations or deletions of the MEF2C gene cause a syndromic form of autism termed MEF2C Haploinsufficiency Syndrome, which is characterized by common symptoms such as intellectual disability, language deficits, seizures, and motor abnormalities. MEF2C is expressed at high levels in forebrain excitatory neurons during brain development, and genetic deletion of Mef2c in these populations (Emx1 Mef2c cKO) produced a marked decrease in structural and functional glutamatergic synaptic transmission and behavioral phenotypes, including deficits in social interaction, ultrasonic vocalizations, and learning and memory, and increases in repetitive and hyperactive motor activity. The decrease in glutamatergic synapse density was rescued by expression of a dominant-repressor form of MEF2C, suggesting that it functions as a repressor on key target genes to regulate glutamatergic synapse elimination or weakening. However, the identity of MEF2C's critical downstream targets remain unclear. Using RNA-seq analysis of cortical tissue from Emx1 Mef2c cKO mice, we detected a ~2.5-fold

increase in protocadherin 17 (Pcdh17) mRNA. In the somatosensory cortex, there is an inverse relationship between Mef2c and Pcdh17 mRNA, suggesting that MEF2C might repress expression of Pcdh17 in a cortical layer-specific manner. Interestingly, in cultured cortical neurons, overexpression of Pcdh17 is sufficient to reduce cortical spine density, similar to the effects of MEF2C loss-of-function, and Pcdh17 mRNA associates with the RNA-transporter, Fragile X Mental Retardation Protein, which is required for MEF2-induced synapse remodeling. To examine the role of PCDH17, we recently generated a floxed Pcdh17 mouse to perform critical in vivo loss-of-function studies to explore the functional relationship between MEF2C and PCDH17. Together, our data suggest an important role for PCDH17 in MEF2C-regulated synapse elimination and developmental synaptic physiology with implications for mechanistic insights into autism, intellectual disabilities, and other common neurodevelopmental disorders. This work was supported by Simons Foundation SFARI Grant (CWC), NIH/NIMH R01MH111464 (CWC).

124 Membranous Septum Length is Not Associated with a Need for Permanent Pacemaker Implantation Following TAVR at MUSC

Davis Leaphart, Nicholas Amoroso MD, Sanford Zeigler MD, Marc Katz MD, Daniel Steinberg, College of Medicine, Department of Medicine, MUSC.

Introduction Transcatheter aortic valve replacement (TAVR) has become an important intervention for high risk surgical patients suffering from aortic stenosis. However, post implant electrical disturbances such as complete heart block requiring permanent pacemaker (PPM) implantation are common. Recent studies have shown that short membranous septum (MS) length is an anatomical risk factor for PPM following TAVR. As part of a quality improvement project, MUSC Structural Heart and Valve Center looked at PPM implants following TAVR that was performed utilizing a tailored approach based on MS length. Methods A retrospective cohort of all patients, n=157, undergoing TAVR at MUSC between September 2019 to June 2020 were included in this study. 66 patients were excluded due to lack of MS measurements and 10 already had a PPM. An additional 5 patients were excluded due to perioperative mortality or conversion to open repair due to implant complications. Pre-procedure MS lengths were measured using 3mensio structural heart imaging software, and patients were placed in either the high-risk group (MS < 6cm) or low-risk group (MS >6 cm). Chi-square testing was utilized to compare the groups. PPM implantation had to occur within 30 days following TAVR. Results A total of 76 patients were included in the statistical analysis, 62 of which were considered high risk. There were 7 PPM implants following TAVR, 6 in the high-risk group. There was no statistical difference between high and low risk groups for PPM implant based on MS length X^2 (1, n=76) = 0.088, p=0.77. All PPM implantations occurred prior to discharge. Conclusion Shorter MS lengths was not associated with a higher number of PPM implantation following TAVR at MUSC. Current use of preprocedural MS length measurements allows for individualized risk prediction in large studies, but did not translate to this patient sample. Further investigation is warranted to explore this discrepancy.

125 Feasibility of a Self-Directed Home Therapy Program for People Post-Stroke.

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

Rehabilitation of hand function post-stroke can require extensive amounts of therapy. Maximized outcomes are more likely to be achieved when individuals practice therapy independently at home in addition to regular therapy sessions. The objective of this study was to determine feasibility of a self-directed home therapy component of a rehabilitation program for individuals post-stroke. Data from 2 separate home interventions of upper extremity task-specific practice were evaluated for this study. A total of 13 participants with chronic stroke recorded their home performance of prescribed therapeutic activities 4 days per week for a period of 4-6 weeks. Additionally, 9 participants recorded the time that they wore an investigational TheraBracelet stimulation device 5 days per week for 6 weeks. An occupational therapist monitored therapy progress and met with participants to collaboratively select therapy tasks and help address barriers to therapy adherence. Adherence was calculated as the percentage of prescribed repetitions (200-300 repetitions of selected functional tasks and at least 5 attempts at completing challenging activities using the paretic hand) completed as well as the percentage of prescribed duration (8 hours) that the TheraBracelet was worn. Relationships between adherence and baseline characteristics were examined using Pearson correlations. The home program was feasible, as average adherence was 66% for functional tasks, 74% for challenging activities, and 86% for wearing TheraBracelet. Adherence varied by participant, with a strong, negative correlation between adherence and baseline arm use measured by the Motor Activity Log, indicating that that participants with less functional use of their affected arm prior to the study were more adherent to exercise recommendations. Clinical implications of this finding are that self-directed home therapy is feasible for people post-stroke, particularly those with decreased use of their affected arm. Future direction includes determining mechanisms to increase adherence by all participants. This work was supported by NIH/NIGMS P20GM109040, NIH/NIGMS U54-GM104941, NIH/NCATS TL1-TR001451, NIH/NCATS UL1-TR001450.

126 Differentiating Between Avoidance and Escape in Anxiety Disorder Treatment Seeking Individuals: An Autonomic and Reflex Physiology Analysis

Holly Fleischmann, James W. Lopez, Lisa M. McTeague, Christopher Sege, College of Medicine, Department of Psychiatry and Behavioral Sciences, MUSC.

Avoidance is a central target of all frontline treatment for anxiety, trauma-related, and obsessive-compulsive disorders. Avoidance is often presented as a unitary construct in clinical manuals, but animal studies have shown that proactive avoidance and reactive escape behaviors have different neural mechanisms and physiological concomitants. Here, we examine how clinically elevated anxiety affects autonomic and reflex physiological concomitants of preparing to avoid or escape aversive stimuli. Participants completed a task in which visual cues signaled whether an upcoming aversive picture could be avoided (by quickly pressing a button prior to picture onset), escaped (by quickly pressing a button immediately after unpleasant picture onset), or not controlled. In 17 treatment-seeking subjects and 19 non treatment-seeking controls, heart rate and skin conductance physiology were measured throughout each cue, and startle reflex reactivity was also probed via presentation of brief acoustic probes. Consistent with our prior study in an analogue sample, clinically anxious individuals and controls each showed

enhanced heart rate deceleration and skin conductance responding during avoidance and escape preparation, with no differences across groups. Conversely, clinically anxious individuals showed exaggerated startle reactivity specifically in an escape context, whereas all individuals showed startle inhibition during avoidance preparation (Group X Context $F[2, 33] = 9.9$, $p < .001$). These data suggest that clinically exaggerated fear appears when aversive stimuli can be escaped, but not necessarily when they can be avoided. Thus, these behaviors may be treated more effectively by more targeted interventions.

Index of Presenters and Mentors

Index of Presenters and Mentors