Perry V Halushka
MUSC 2019 Research Day
54th Annual

November 1, 2019

MUSC
College of Graduate Studies

Sigma Xi, The Charleston Chapter

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

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

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

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

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

Send the completed form to:
Dr. Karen Burnett, Membership Chair
Charleston Chapter of Sigma Xi
Hollings Marine Laboratory
331 Fort Johnson Road
Charleston, SC 29412
Phone: 843-725-4826
E-mail: burnettk@cofc.edu

Questions? Contact:
Dr. Joe Carson, President
Charleston Chapter of Sigma Xi
Associate Professor, Dept. of Physics & Astronomy
College of Charleston
66 George Street
Charleston, SC, 29424
Phone: 843-953-3643; E-mail: carsonjc@cofc.edu

Perry V Halushka 2019 MUSC Research Day

will be held

Friday, NOVEMBER 1, 2019

Keynote Speaker: Suzanne Topalian, M.D.

12:00 PM, DD 110

Professor of Surgery and Oncology, Johns Hopkins Medicine
Associate Director, Bloomberg-Kimmel Institute for Cancer Immunotherapy

"PD-1 pathway blockade: a common denominator for cancer therapy"

8:00-11:30 AM	Poster Session	Harper Center Gym
12:00 – 1:00 PM	Keynote Presentation	DD 110
1:30 – 4:30 PM	Oral Sessions	Education Library
5:00 – 6:00 PM	Awards Ceremony	DD 110

Information about poster and oral presentations can be found by following the Research Day link on the College of Graduate Studies home page

Please direct any questions regarding MUSC Research Day 2019 to Dr. Steven Kubalak at: kubalaks@musc.edu

INFORMATION FOR PARTICIPANTS

Poster Presentation Sessions:

Poster sessions will be held in the **Harper Student Center Gym**. Presenters are encouraged to view the posters currently on display on the walls of the Basic Science Building and at other locations around campus for examples of poster layout, design and size. For assistance with poster design and content, contact the MUSC Center for Academic Excellence. Most poster support boards are approximately 3' 6" tall by 5' 6" wide.

Poster boards will be available Friday morning for:

Group A	Set up poster: **7:30 and 8:00 AM**	Session time: **8:00 – 9:30 AM**
Group B	Set up poster: **9:30 and 10:00 AM**	Session time **10:00 – 11:30 AM**

with numbers corresponding to the abstract numbers in this program.

Group A should take their posters down at 9:30 AM so Group B be can put their posters up. Judging begins at 8:00 AM for Group A and at 10:00 AM for Group B. Group B can take their posters down at 11:30 AM. Presentations should be no more than **10 minutes** followed by 5 minutes of question by the judges. **Please note that unless notified otherwise, you will have 3 judges for the regular sessions visit your poster – they may visit all together, in pairs, or they may come one at a time. Judges for the regular sessions will be wearing red nametags. Please do not leave your poster until you have presented it to all three regular session judges**. Special session judges are in addition to the regular session judges.

Oral Presentation Sessions:

Most, if not all of the oral sessions will be in the **Colbert Education Center and Library** in various rooms on the first floor. Please check the program for specific room assignments. Computer projection using a PC platform will be available. It is suggested that you save your presentation on thumb drive, etc. Ensure that your presentation loads and runs correctly before you save it. Download your presentation to the desktop of the computer in the room where you will be presenting; do this **BEFORE** the start time of your session on Friday, November 1st. Oral presentation time slots are 15 minutes. An oral presentation should last no more than **10 minutes** with the remaining time for questions. The 15-minute time slot will be strictly adhered to by the session judges – you will receive a warning at minus 3 minutes. Remember that question handling is one of the criteria being evaluated and if you leave no time for questions, you will lose points.

Judging:

Teams of 3 judges will evaluate presentations in each of the sessions. Judges will be wearing red nametags. Presentations will be scored on a scale of 1 to 10 in ten categories (see next page for a sample judges' sheet). The scores for the ten categories (max 100 points) from each judge in that session will be used to compute a ranked score. 1st and 2nd place prizes will be awarded to the presentations in your session with the highest and next highest mean ranked scores respectively. We have tried to assign judges so as to avoid possible conflicts of interest. Scores and evaluation sheets will be emailed to presenters by responding to the message from Dr. Kubalak indicating the score sheets have been compiled. Please note, the judges selecting presentations for prizes in the following categories: Sigma Xi, Interprofessional Research, Ralph H Johnson VA Research, Innovation, Health Humanities, and Aging Research will be operating as separate teams. If you selected that you wanted to be considered for these and your presentation qualifies for further judging, you will be visited by these additional judges.

Breaks:

Coffee, doughnuts and soft drinks will be available from 9:30 am – 11:30 pm in the Harper Center Gym. There will be a MUSC-catered lunch for presenters and other student attendees in the Harper Center Gym at 10:30 AM.

Awards Ceremony:

The Awards Ceremony will begin at 5:00 pm in the Drug Discovery Auditorium (Rm 110) on Friday, November 1st. In each session there will be a 1st place prize of $500 and a 2nd place prize of $200. The special awards listed above have their own cash prizes that are in addition to the regular session prizes.

Poster and Oral Presentation Program

POSTER PRESENTATIONS - Harper Wellness Center Gym

Group A - 8:00 am - 9:30 am

		Abstracts
Session 1:	Undergraduate – I	001-011
Session 2:	Clinical / Professional / Masters – I	012-019
Session 3:	Clinical / Professional / Masters – II	020-029
Session 4:	Clinical / Professional / Masters – III	030-040
Session 5:	*** no abstracts in Group A ***	
Session 6:	PhD – II	041-050
Session 7:	Postdoc / Resident / Fellow / Staff Scientist – I	051-057
Session 8:	Postdoc / Resident / Fellow / Staff Scientist – II	058-064
Session 9:	Research Specialist / Technician – I	065-074

Group B - 10:00 am - 11:30 am

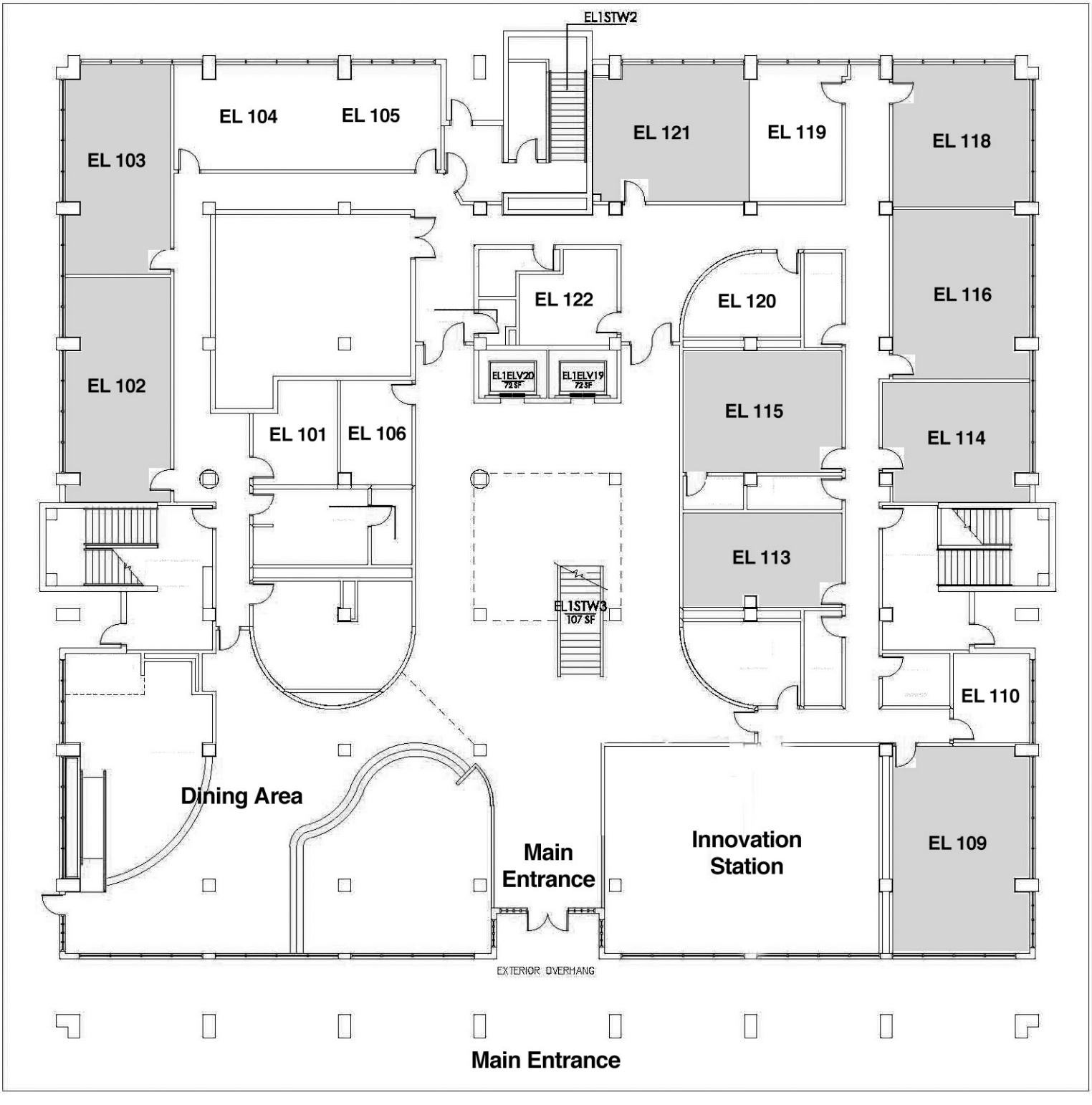
		Abstracts
Session 1:	*** no abstracts in Group B ***	
Session 2:	*** no abstracts in Group B ***	
Session 3:	Clinical / Professional / Masters – II	075-084
Session 4:	Clinical / Professional / Masters – III	085-096
Session 5:	PhD – I	097-106
Session 6:	PhD – II	107-115
Session 7:	Postdoc / Resident / Fellow / Staff Scientist – I	116-123
Session 8:	Postdoc / Resident / Fellow / Staff Scientist – II	124-131
Session 9:	Research Specialist / Technician – I	132-142

ORAL PRESENTATIONS - Colbert Education Center and Library

		Room	Time	Abstracts
Session 10:	Undergraduate – II	EL 113	1:30 - 2:45	143-147
Session 11:	Clinical / Professional / Masters – IV	EL 103	1:45 - 3:45	148-154
Session 12:	Clinical / Professional / Masters – V	EL 102	1:30 - 4:15	155-164
Session 13:	PhD – III	EL 114	1:30 - 4:00	165-173
Session 14:	PhD – IV	EL 118	1:30 - 4:15	174-183
Session 15:	PhD – V	EL 109	1:30 - 4:15	184-193
Session 16:	Postdoc / Res / Fellow / Staff Sci – III	EL 116	1:30 - 4:00	194-202
Session 17:	Postdoc / Res / Fellow / Staff Sci – IV	EL 121	1:30 - 4:15	203-212
Session 18:	Research Specialist / Technician – II	EL 115	1:30 - 2:45	213-217

EL = Colbert Education Library

LOCATION OF ORAL PRESENTATIONS



JAMES W. COLBERT EDUCATION CENTER & LIBRARY

FIRST FLOOR PLAN

HORSESHOE SIDE OF BUILDING

ACKNOWLEDGEMENTS

The Perry V. Halushka Research Day Endowment

In 2006, in recognition of the many years of service given by their father, Dr. Perry V. Halushka, to the Medical University, Francine Halushka Katz, Marc Halushka, M.D., Ph.D., and Suzanne Friedman and their families have established, through the MUSC Foundation, **The Dr. Perry V. Halushka Research Day Endowment.** This endowment will help to support the activities of Student Research Day in perpetuity. Specifically, the endowment will enable the University to:

- Provide monetary awards for outstanding research presentations
- Attract world-class scientists as guest keynote speakers
- Provide funds to support the annual MUSC Research Day event

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MUSC Research Day Committee would like to thank the following for their support:

Lawrence Olanoff, MD, PhD
Eric James, PhD
Marine Polymer Technologies (John Vournakis, PhD) www.marinepolymer.com
Charleston Research Institute https://www.charleston.va.gov
MUSC Foundation for Research Development http://academicdepartments.musc.edu/frd/
VA Medical Center www.charleston.va.gov

The MUSC Research Day Committee

Steven Kubalak	College of Medicine (Chair)	Regenerative Medicine & Cell Biology
Eric Bartee	College of Medicine	Microbiology & Immunology
Victoria Findlay	College of Medicine	Pathology and Laboratory Medicine
Brett Froeliger	College of Medicine	Neurosciences
Vamsi Gangaraju	College of Medicine	Biochemistry & Molecular Biology
Teri-Lynn Herbert	Education Library Center	Academic Affairs Faculty
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Mariana Pehar	College of Medicine	Cell & Mol Pharm & Exper Therap
Susan Reed	College of Medicine	Pediatrics/Neonatology/Stomatology
Michelle Woodbury	College of Health Professions	Health Sciences Research
Stephanie Brown-Guion	College of Graduate Studies	Administrative Assistant
Kelsey Moore	College of Graduate Studies	Student Representative
Connor West	College of Graduate Studies	Student Representative
Charlie Kerr	College of Graduate Studies	Student Representative

Session 1 Undergraduate I Harper Center Gym

Group A 8:00 – 9:30 AM

1 The Effect of Daily Stressors on Neuroendocrine and Subjective Reactivity Following a Psychosocial Stress Paradigm in Cocaine Dependent Individuals.
Raquelle Bourgeois, Kathleen T. Brady, Brian Sherman, Aimee Mcrae-Clark, Medicine, Department of Psychiatry and Behavioral Sciences, MUSC.

2 An ex-vivo comparison of Alzheimer amyloid-beta plaque species and the cerebrovasculature.
Rob Aldrin Robino, David Hartmann, Maricel Soliven, and Sangeeta Mohanty., Narayan R. Bhat, Medicine, Neuroscience, MUSC.

3 Behavioral tasks that assess recognition memory are useful tools to assess cognitive deficits in preclinical models.
Tyler Stone, Alexus Williams, Luke Watson, and Dominique Williams, Catrina Robinson, Graduate Studies, Neurology, MUSC.

4 BMP-Notch signaling interaction in AV endocardial cushion coordinately regulates AV valvulogenesis
Haleigh Ferro, Maria Gonzalez, Patrick. G. Smith, Miriam M. Atteya, Sarah Suber, Jeremy L. Barth, Yukiko Sugi, Medicine, Regenerative Medicine, MUSC.

5 Role of Sox9 gene in the development of the AV mesenchymal complex in embryonic mice hearts
Renelyn Wolters, Raymond Deepe, Andy Wessels, Graduate Studies, Department of Regenerative Medicine and Cell Biology, MUSC.

6 Is the Relationship between Conservatism and Climate Change Attitudes Moderated by Right Wing Authoritarianism and Social Dominance Orientation?
Brittany McKenzie, Stephen Short, Graduate Studies, Psychology - College of Charleston, MUSC.

7 The synergy of CD36 and Scleraxis in the activation of intestinal fibroblast "Potential Role in Fibrosis"
Samuel Kirsch, Andrea Nillas and Michael P. Czubryt, Titus Reaves, Medicine, Regenerative Medicine and Cell Biology, MUSC.

8 Disrupted DNA binding and autistic-like behaviors in a mouse model of syndromic autism.
Kayla Blankenship, Adam Harrington, Acadia Thielking, Christopher Cowan, Medicine, Neuroscience Department, MUSC.

9 Dietary fat intake and the comorbidities of pregnancy: a post-hoc analysis of two cohorts
Shellie Davis, Elliott Lyles, Judy Shary, Myla Ebeling, Carol Wagner, Carol Wagner, Health Professions, Neonatologist and Associate Director of SCTR's Research Nexus, MUSC.

10 Examining Changes in Depression and Anxiety Symptoms in Adolescent Smokers During a 12-Week Pharmacotherapy Trial
Iris Sakamoto, Jennifer Dahne, PhD, Rachel L. Tomko, PhD, Kevin M. Gray, MD, Erin McClure, Medicine, Department of Psychiatry and Behavioral Sciences, Addiction Sciences Division, MUSC.

11 Cognitive Behavioral Therapy for Chronic Pain and Shared Decision Making to Reduce Prescription Opioid Use and Misuse in Pregnant Women
Marinna Smith, Edie Douglas, Tonya Cassaday, Lisa Boyars, Constance Guille, Medicine, Department of Psychiatry and Behavioral Sciences, MUSC.

Group B 10:00 – 11:30 AM

No Group B abstracts

Session 2 Clinical / Professional / Masters I Harper Center Gym

Group A 8:00 – 9:30 AM

12 Use of a Modified "Privilege Walk" to Teach Undergraduate Pre-Health Professionals at an Academic Health Center: A Pilot Project Examining Personal Privilege as a Social Determinant of Health
Aramis Gregory, Lauren Gellar, PhD, MS, MCHES, Brandi M. White, PhD, MPH, Elinor Borgert, PhD, MS, Elizabeth Brown, Health Professions, Department of Health Professions, MUSC.

13 taVNS treatment: relationship to motor abilities and neuroimaging in at-risk infants
Shelby Davis, Hannah Haskin, Amy Reiner, Hunter Moss, Bashar Badran PhD, Mark George MD, Dorothea Jenkins MD, Turki Aljuhani MA, Patty Coker-Bolt PhD, OTR/L, FAOTA, Patricia Coker-Bolt, Health Professions, Occupational Therapy, MUSC.

14 A Program Evaluation of the Medical University of South Carolina's Presidential Scholars Program
Parker Rhoden, Dayan Ranwala, Donna Reinbeck, Debora Brown, Masahiro Kono, Michelle Ziegler, Bryant A. Seamon, Jillian Harvey, Health Professions, Department of Healthcare Leadership & Management, MUSC.

15 Living with neglect: A qualitative analysis of patient perspectives
Nicholas Dean, Katie Dry, OTS, Brianna Eberl, OTS, Hannah Hooks, OTS, Lindsay Manning, OTS, Stacie McLamb, OTS, Emerson Hart, OTR/L, and Michelle Nichols, PhD, R.N., Emily Grattan, Health Professions, Division of Occupational Therapy, Department of Health Sciences and Research, and Ralph H. Johnson VA Medical Center, MUSC.

16 Tracking the Rising Trend of Student-Run Pro-Bono Clinics in Occupational Therapy Programs
Chandler G. Nash, Britt Harris, Melissa Nettle, Sanica Bendre, Julianne Robertson, Amanda Giles, Patty Coker-Bolt, Tambra Marik, Craig Velozo, Sara Kraft, Gretchen Seif, Karen Wager, Amanda Giles, Health Professions, Occupational Therapy, MUSC.

17 Improving Quality of Life for Children with Cerebral Palsy in Vietnam: Implementation of Intensive Models of Rehabilitation
Caitlin Weatherhead, Chandler G. Nash, Rebekah Wade, Sarahjane Zablow, Stephanie Deluca, PhD, Megan Price and Miranda Gerrard, Johan Baudewigns, Patty Coker-Bolt, Health Professions, Occupational Therapy, MUSC.

18 Duck-Duck-Punch: a Rehabilitative Video Game Designed to Improve Recovery of Upper Limb Coordination Post-Stroke
Allison Wheeler, Melissa Nettle, OTS; Morgan Hesse, OTS; Austen Hayes, CEO, Recovr LLC.; Larry Hodges, CFO, Recovr LLC.; Kevin Jett, Software Engineer; Recovr LLC., Christian Finetto, PhD, MUSC; Scott Hutchison, OTD, MUSC, Michelle Woodbury, Health Professions, Occupational Therapy, MUSC.

19 "There is no 1-800 number to fix it.": A qualitative study capturing views of stroke survivors. Amber Linnen, Brittany Pinson, Samantha Brophy, Michelle Nichols, Michelle Woodbury, MUSC.
Amber Linnen, Samantha Brophy, Brittany Pinson, Michelle Woodbury, Michelle Nichols, Health Professions, College of Nursing, MUSC.

Group B 10:00 – 11:30 AM

No Group B abstracts

Session 3 Clinical / Professional / Masters II Harper Center Gym

Group A 8:00 – 9:30 AM

20 Alginate-RGD hydrogel and bioactive glass: mechanical properties and cellular properties
Dustin Mueller, Qing Hong, Brian Gibson, Brittany Moore, Douglas Beals, Elizabeth Hull, Alireza Moshaverinia, John Mitchell, Dental Medicine (DMD, PhD), College of Dental Medicine, Midwestern University, MUSC.

21 Analytical Insights into the Use of Collagen Volume Fraction and Endothelial Markers as Diagnostic Tools in Heart Failure Histomorphometry
Adegboyega Adewale, Amy Bradshaw, Medicine (MSTP, MD years), Gazes Cardiac Research Institute; Ralph H. Johnson VA Medical Center; Department of Medicine, MUSC.

22 Impact of Pharmacist Led Diabetes Education and Management at a Federally Qualified Health Center
Ryan Rosenblatt, Samuel Mcgee, Erin Weeda, James Sterrett, Pharmacy, College of Pharmacy, MUSC.

23 Community-Based Experiential Learning: Using an Interprofessional Student-Run Free Clinic to Enhance Student Collaboration and Critical Thinking
Emily Harrison, Megan Lebov, Stacie McLamb, Tambra Marik, Karen Wager, Patty Coker-Bolt, Craig Velozo, Sara Kraft, Gretchen Seif, Amanda Giles, Health Professions, Department of Occupational Therapy, MUSC.

24 Survival Outcomes of Donation After Cardiac Death Kidney Transplant: Is it Worth It?
Allison Kuhn, Faisal Alanazi, Nicole Pilch, Pharmacy, College of Pharmacy, MUSC.

25 Can Pre-Clinical Students Correctly Identify Pain Mechanisms and Apply Pain Neuroscience Education while Treating a Patient in a Student-Run Free Clinic? Yes!
Courtney Mason, Spencer Cowen, Gretchen Seif, Health Professions, Department of Physical Therapy, MUSC.

26 Literature Review of Blood Flow Restriction Resistance Training
Mitchell Tanner, Stephanie McGowan, Health Professions, Assistant Professor in the Department of Health Professions, MUSC.

27 Transcutaneous Electrical Stimulation Therapy in Obstructive Sleep Apnea
Young Jae Byun, Flora Yan, Shaun Nguyen, Eric Lentsch, Medicine, Department of Otolaryngology - Head and Neck Surgery, MUSC.

28 Are Ankle Motor Control and Balance Post Stroke Related?
Rebecca Angles, John H Kindred PhD, Jesse C Dean PhD, Mark Bowden, Health Professions, College of Health Professions, MUSC.

29 Determinants and Distractors in Gauging Surgical Skill in Mastoidectomy
Andrew Rowley, Joshua Lee, Michaela Close, Yuan Liu MD, Mitchell Isaac MD, Ted Meyer MD PhD, Ted Meyer, Medicine, Otolaryngology, MUSC.

Group B 10:00 – 11:30 AM

75 Analysis of statin use for modulation of cardiovascular disease risk in HIV patients in a southern academic medical center
Miranda McGee, Anupha Mathew, Richard Lueking, Eric G. Meissner, James New, Stephanie Kirk, Emily Ware, Pharmacy, MUSC Pharmacy Ambulatory Care, MUSC.

76 Sex-specific auditory functional deficits in a mouse model of autism
Josef Blaszkiewicz, Junying Tan, Kenyaria Noble, Ahlem Assali, Christopher Cowen, Hainan Lang, Medicine (MSTP, MD years), Department of Pathology and Laboratory Medicine, MUSC.

77 Characterization of the Angiogenic Factor SFRP2 in Papillary Thyroid Cancer
Wyatt Wofford, Julie Siegel, Rupak Mukherjee, Denise Garcia, Eleanor Hilliard, Patrick Nasarre, Nancy Klauber-DeMore, Mahsa Javid, Medicine, Department of Surgery, MUSC.

78 DCHS1 Regulated miRNA Processing and Its Effects on Valve Endocardium Stabilization
Mary Rumph, Kelsey Moore, Rebecca Stairley, Diana Fulmer, Reece Moore, Janiece Glover, Joyce Nair-Menon, Amanda Daulagala, Courtney Gensemer, Lilong Guo, Christina Wang, Antonis Kourtidis, and Russell Norris, Russell Norris, Graduate Studies, Cell Biology and Regenerative Medicine, MUSC.

79 Prospective surveillance of infectious disease with application to SC seasonal influenza data
Joanne Kim, Andrew Lawson, Graduate Studies (MSTP, PhD years), Public Health Sciences, MUSC.

80 Big Gaps for Little People: A Scoping Review of Access to Rehabilitation Services for Children with Down Syndrome
Jacquelyn Ross, Morgan Callahan, OTS; Caroline Walsh, OTS; Grace Grantland, OTS; Emily Patten, OTS; Cristina Reyes Smith, OTD, OTR/L; Addie Middleton, PhD, DPT; Elizabeth A. Brown, PhD, MPA; Joni Nelson, PhD, MS; Heather Shaw Bonilha, PhD, CCC-SLP, Cristina Smith, Health Professions, MUSC CHP Division of Occupational Therapy, MUSC.

81 Influence of hospital encounters for falls on potentially inappropriate medication use among older patients
Yara Salem, Maha Assadoon, Matthew Hebbard, Erin Weeda, Pharmacy, MUSC- Department of Clinical Pharmacy & Outcomes Sciences, MUSC.

82 Program Evaluation of CARES Therapy Clinic: Barriers and Facilitators for Using Standardized Outcome Measures
Shelly Law, Hattie Johnson, Megan Lebov, Emily Lievsay, Meghan Martin, Maddi Wever, Tambra Marik, Craig Velozo, Health Professions, Department of Health Professions/Division of Occupational Therapy, MUSC.

83 The Effect of TheraBracelet and In-Home Therapy on Neural Plasticity and Hand Function
Emma McCarthy, Nicole Bradford, Julia Campbell, Amanda Vatinno, Will DeVries, Andrew Fortune, Michelle Woodbury, Viswanathan Ramakrishnan, Leonardo Bonilha, Na Jin Seo, Health Professions, Department of Health Professions, MUSC.

84 Medication Adherence to Rivaroxaban and Dabigatran in Patients with Non-valvularAtrial Fibrillation: a Meta-analysis
Irene Ruiz, Ashley Prentice, Erin Weeda, Pharmacy, MUSC College of Pharmacy, MUSC.

Session 4 Clinical / Professional / Masters III Harper Center Gym

Group A 8:00 – 9:30 AM

30 ADAMTS5-mediated cleavage is required for subchondral bone formation in the mandibular condyle
Alexandra Rogers-DeCotes, Sarah C. Porto, Christine Kern, Dental Medicine (DMD, PhD), Regenerative Medicine and Cell Biology, MUSC.

31 Open Reduction Internal Fixation of Distal Radius Fractures: Retrospective Cohort Analysis of the Geriatric Population using the NSQIP Database
Narayan Raghava, Anna Skochdopole BS, Brian Mailey MD, Sami Taribishy MD, Steven Hermiz MD, Fernando A Herrera MD, Medicine, Division of Plastic and Reconstructive Surgery, MUSC.

32 Diagnosis, treatment, follow up, and persistence of Trichomonas vaginalis in women over age forty-five according to HIV status: a ten-year retrospective cohor
Allyson Hill, Tarleton Jessica, Soper David, Gwenth Lazenby, Medicine, OBGYN, MUSC.

33 Germ Busters: Environmental Care for the Prevention of MBI CLABSIs in pediatric oncology patients
Stephanie Gehle, Jessica Howard, Brooke Criddle, Corinne Corrigan, Elizabeth Mack, Medicine, Pediatrics, MUSC.

34 Breastfeeding among Women with Systemic Lupus Erythematosus (SLE)
Erin Hynd, Jim C. Oates, MD, Gary S. Gilkeson, MD, Diane L. Kamen MD, MSCR, Diane Kamen, Medicine, Rheumatology and Immunology, MUSC.

35 taVNS for oromotor infant feeding I. Development of a closed loop delivery system
Sean Thompson, Daniel Cook, Morgan Dancy, William H. DeVries, Georgia Mappin, Philipp Summers, Marom Bikson, Sarah Huffman, Sasha Stomberg-Firestein, Mark S. George, Dorothea D. Jenkins, Bashar Badran, Medicine, Psychiatry, MUSC.

36 Publishing Trends in Velopharyngeal Insufficiency
Charles Poff, Joshua Horton MD, Ryan Boerner MD, Alex Marston MD, Shaun A. Nguyen MD, David White, Medicine, Otolaryngology, MUSC.

37 Adolescents Proceeding to Weight Loss Surgery Have Higher Parent and Self-rated Quality of Life
William Head, Aaron Lesher MD, Molly Jones RD, Sharlene Wedin PsyD, ABPP, Lillian Christon PhD, Nina Crowley, Medicine, MUSC Health Bariatric Surgery Program, MUSC.

38 Understanding the Preventability of our Pediatric Readmissions
William Cornwell, Elizabeth Mack, Medicine, Pediatric Critical Care, MUSC.

39 Birthing Experience of Obese Parturients: Quality of Care During Pregnancy, Labor and Delivery
Matthew Turner, Zeiler Lydia, Joel Sirianni, Medicine, Anesthesiology, MUSC.

40 Long-term Effects of Thyroid Procedures on Weight Change
Parker McDuffie, Reece Moore, Paige Broadley, Dr. Carneiro-Pla, Mahsa Javid, Medicine, Surgical Oncology, MUSC.

Group B 10:00 – 11:30 AM

85 Instillation of povidone-iodine ophthalmic solution onto the eye surface causes a decrease in respiratory rate in spontaneously breathing children under general anesthesia undergoing strabismus surger
Melanie Rubin, Bethany Jacobs Wolf, PhD , Alexandra Ritter, BS , Christopher L. Heine, MD , Tracy E. Wester, MD , Cory M. Furse, MD, MPH, FAAP, Michelle Rovner, Medicine, Department of Anesthesia & Perioperative Medicine, Medical University of South Carolina, MUSC.

86 Observational Study of Patients Demographics in Those Presenting with Acute ST-Elevated Myocardial Infarction: a 5-Year Review at a High-Volume Institution
Alexander Canova, Katrina Bidwell, Billy Joe Mullinax, Valerian Fernandes, Medicine, Cardiology, MUSC.

87 Correlating pre-operative Mini-Cog screening scores with post-operative delirium
Brenton Davis, Benjamin Kalivas, Medicine, Department of Medicine, MUSC.

88 Role of T cell Subsets in Glaucoma
Alexa DeMaio, Singh Sudha, Mehrotra Shikhar, Shahid Husain, Medicine, Ophthalmology, MUSC.

89 Diagnostic Efficacy of Computed Tomography in detecting Radiographic Extranodal Nodal Extension (rENE) in Head and Neck Squamous Cell Carcinoma (HNSCC): A Systemic Review & Meta-Analysis
Flora Yan, Young Jae Byun, Shaun Nguyen, Medicine, Otolaryngology, MUSC.

90 Evaluation of the Accuracy of Multiple Digital Impression Systems on a Fully Edentulous Maxilla
Madison Hoover, Walter Renne, Zachary Evans, Mark Ludlow, Griffin Revell, Anthony Mennito, Dental Medicine, College of Dental Medicine - Department of Oral Rehabilitation, MUSC.

91 Predictive Value of Hormones in Sperm Retrieval Surgery
Nicholas Major, Kent Edwards, Kit Simpson, Marc Rogers, Medicine, Assistant Professor, Urology, MUSC.

92 A comparison of a new fast brain MRI protocol to CT scans in pediatric trauma
Chelsea Shope, Mohammed Alshareef, Vittoria Spampinato, Tyler Vasas, Ramin Eskandari, Medicine, Neurosurgery, MUSC.

93 Effect of Malnutrition on Hearing Loss in Children
Joshua Van Swol, Michaela Close, Charmee Mehta, Josh Van Swol, James Dornhoffer, Yuan Liu, Shaun Nguyen, Teddy McRackan, Ted Meyer, Ted Meyer, Medicine, Otoloaryngology, MUSC.

94 Two Cases in Pediatric Neurology
Matthew Roberts, Kerry Roberts, Dan Williams, Medicine, Pediatrics, MUSC.

95 Rib-based anchors can induce proximal translational deformity in Early Onset Spinal Deformity patients undergoing growth-friendly surgical treatment
Connor Burke, Brett Goodloe, John Hughes, William Barfield, James Mooney, Robert Murphy, Medicine, Pediatric Orthopaedics, MUSC.

96 Sphingosine Kinase 1 Inhibition Attenuates Hypertension-Induced Left Ventricular Hypertrophy
Matthew Bridges, Katherine A. Robinson, Rupak Mukherjee, Hesham El-Shewy, Medicine, Medicine, MUSC.

Session 5 PhD I Harper Center Gym

Group A 8:00 – 9:30 AM

No Group A Abstracts

Group B 10:00 – 11:30 AM

97 Assessment of Impairment Following Oral and Vaporized Cannabis Administration in Infrequent Users
Erin Martin, Tory Spindle, Megan Grabenauer, Michael Milburn4, Ryan Vandrey, Graduate Studies, Johns Hopkins University School of Medicine, Department of Psychiatry, MUSC.

98 A Novel Method of Individualizing Transcranial Direct Current Stimulation Dosage Using Reverse-Calculation Electric Field Modeling
Kevin Caulfield, Bashar W. Badran, William H. DeVries, Philipp M. Summers, Emma Kofmehl, Xingbao Li, Jeffrey J. Borckardt, Marom Bikson, Mark George, Graduate Studies, Psychiatry, MUSC.

99 E2F8 tumor suppressive role in nonalcoholic Steatohepatitis
Shaaron Ochoa-Rios, Lindsey Kent, Julian M Clouse, Yannis Hadjiyannis, Gustavo Leone, Graduate Studies, Department of Biochemistry and Molecular Biology, MUSC.

100 Generation and Validation of a Novel Model for Mitral Valve Prolapse Based on Human Familial Mutations
Cortney Gensemer, Christina Wang, Diana Fulmer, Lilong Guo, Kelsey Moore, Tyler Beck, Mary Kate Rumph, Janiece Glover, Annette Krzyzanski, Reece Moore, Rebecca Stairley, Michael Borger, Robert Levine, Russell Norris, Graduate Studies, Regenerative Medicine and Cell Biology, MUSC.

101 Sex Differences in Cognitive and Psychological Outcomes of Stroke: Impact of Diabetes
Aunay Miller, Raghavendar Chandran, Adviye Ergul, Graduate Studies, Pathology and Lab Science, MUSC.

102 Glutamatergic modulation recovers multiple behavioral deficits in a model of AUD/PTSD comorbidity
Heyam Saleh, Cora E. Smiley, Justin T. McGonigal, Samantha Melton, Thomas Valvano, Justin Gass, Graduate Studies, Neuroscience, MUSC.

103 Placental cardiovascular gene expression in preeclampsia and diabetes: Defining subpopulations of a prevalent disease of pregnancy
Kelsey Tjen, Kelsey Tjen, Kymbreana Coley, Clare Kelley, Misti Leyva, Mary Starrett, Eugene Y. Chang, Timothy J. Lyons and Kyu-Ho Lee, Kyu-Ho Lee, Medicine (MSTP, MD years), Pediatrics (Cardiology), MUSC.

104 Development of Wearable Stimulation App to Increase Hand Functional Recovery in Patients with Neurological Movement
Corey Morrow, Andrew Fortune, Changki Kim, Viswanathan Ramakrishnan, Na Jin Seo, Health Professions, Department of Health Professions, MUSC.

105 Refining hotspot identification methods in the lower extremities using a double-cone TMS coil post stroke: MEP amplitude vs. latency
Jessica Ergle, John H Kindred, Charalambos C Charalambous, Elizabeth C Wonsetler, Mark Bowden, Health Professions, College of Health Professions, MUSC.

106 Donor Lung Beta 2 microglobulin deficiency delays the onset of acute rejection
Dorian Frazier, Changhai Li, Zhenxiao Tu,Jerec Ricci, Dianna Nord, Carl Atkinson, Graduate Studies, Microbiology and Immunology, MUSC.

Session 6 PhD II Harper Center Gym

Group A 8:00 – 9:30 AM

41 Role of Porphyromonas gingivalis in Mediating Ceramide-dependent Mitophagy in Oral Squamous Cell Carcinoma
Megan Sheridan, Dr. Nityananda Chowdhury, Dr. Ozlem Yilmaz, Dr. Besim Ogretmen, Besim Ogretmen, Graduate Studies, Biochemistry and Molecular Biology, MUSC.

42 Fibroblast Derived STAT3 Promotes PDAC Tumorigenesis by Fostering an Immunosuppressive Tumor Microenvironment
Julia Lefler, Katie MarElia, Blake E. Hildreth III, Katie A. Thies, Maria C. Cuitino, Sudarshana Sharma, Samuvel Devadoss, Stacey Kneeshaw, Michael Ostrowski, Graduate Studies, Biochemistry and Molecular Biology, MUSC.

43 Novel non-canonical mechanisms by which ErbB3/HER3 contributes to MPNST tumorigenesis.
Laurel Black, Steven Carroll, Graduate Studies, Pathology, MUSC.

44 Development of Inhibitors of KDM4B as a Therapeutic Strategy for Periodontal Disease
Joy Kirkpatrick, Rachel Wilkinson, Jonathan Turner, Jessica Hathaway-Schrader, Chad Novince, Patrick Woster, Dental Medicine (DMD, PhD), Drug Discovery and Biomedical Sciences, MUSC.

45 The role of paxillin in the pathogenesis of liver fibrosis
Nour Hijazi, Don Rockey, Graduate Studies (MSTP, PhD years), Chairman, MUSC.

46 Alcohol cue-reactivity in treatment seeking individuals with Alcohol Use Disorder
Daniel McCalley, Ingrid E Contreras, Julia P Imperatore, Logan T Dowdle, Josh P Smith, Sarah W Book, Colleen Hanlon, Graduate Studies (MSTP, PhD years), Neuroscience, MUSC.

47 Long-Term Treatment Strategy via AAV Delivery of an Inducible Vector Containing CR2-fH in a Murine Model of Choroidal Neovascularization
Nathaniel Parsons, Bärbel Rohrer, Graduate Studies, Ophthalmology, MUSC.

48 Cellular Specificity of Matrix Metalloproteinase Activation on Accumbens Medium Spiny Neurons During Cued Heroin Seeking
Vivian Chioma, Peter Kalivas, Graduate Studies (MSTP, PhD years), Neuroscience, MUSC.

49 Feasibility of an Animated Video Combined with Standard Radiation Therapy Education for Patients with Breast Cancer: Breast RAdiotherapy Video Education, BRAVE
Michelle Pembroke, Julie Bradley, Marina Mueller, Michelle Mollica, Lynne Nemeth, Lynne Nemeth, Nursing, College of Nursing, MUSC.

50 Transcription is Suppressed by Replication-Coupled Histone De-Acetylation
Colleen E. Quaas, John K. Barrows, David Long, Graduate Studies, Biochemistry and Molecular Biology, MUSC.

Group B 10:00 – 11:30 AM

107 Targeted Kappa Opioid Receptor Antagonist Treatment in the CeA or BNST Attenuates Stress-Potentiated Alcohol Consumption.
Harold Haun, Logan Manusky, William Griffin, Marcelo Lopez, Howard Becker, Graduate Studies, Psychiatry and Behavioral Sciences, Neuroscience, and VAMC, MUSC.

108 Improving identification of hub genes and gene sub-networks through data integration with the stochastic block model
Carter Allen, Dongjun Chung, Graduate Studies, Public Health Sciences, MUSC.

109 Improved survival with immune checkpoint inhibitors in the SEER-Medicare population
Ashley Howell, Kelly Hunt, Mulugeta Gebgregziabher, Bruce Thiers, Chrystal Paulos, John Wrangle, Kristin Wallace, Graduate Studies (MSTP, PhD years), Public Health Sciences, MUSC.

110 Difluoromethylornithine and Checkpoint Blockade/Oncolytic Virotherapy Combination Treatment in a Murine Melanoma Model
Parker Dryja, Thomas Benton, Patrick Woster, Eric Bartee, Graduate Studies, Microbiology & Immunology, MUSC.

111 Interaction of the Extracellular Matrix with the Cell-cell Junction Associated RNAi Machinery in Colon Cancer
Amanda Daulagla, Mary C. Bridges, John Yost, Lauren Rutledge, Joyce Nair-Menon, Michael Yost, Antonis Kourtidis. , Antonis Kourtidis, Graduate Studies, Regenerative Medicine and Cell Biology, MUSC.

112 Speech Pathology and Occupational Therapy Feeding Interventions Impact Health Outcomes and Health Care Costs for Preterm Infants with Feeding Problems: A Retrospective Analysis
Brooke Mulrenin, Megan Richmond, Cindy Dodds, Annie Simpson, Health Professions, Healthcare Leadership and Management, MUSC.

113 Complement Driven Auto-Reactive Antibodies in Lung Transplantation
Alexander McQuiston, Kunal Patel, Changhai Li, Zhenxiao Tu, Carl Atkinson, Graduate Studies, Department of Microbiology and Immunology, MUSC.

114 Kynurenine, an Endogenous AhR Agonist, Upregulates CXCL12- and Hdac3-Targeting miRNAs Inhibiting Osteogenesis
Ahmed Elmansi, Nada Eisa, Dmitry Kondrikov, Galina Kondrikova, Sadanand Fulzele, Meghan mcGee-Lawrence, Mark Hamrick, Carlos Isales, William Hill, Graduate Studies, Department of Pathology and Laboratory Medicine, MUSC.

115 Analysis of High-Dimensional Neuroimaging Data in Characterizing Alzheimer's Disease Progression
Daniel Baer, Brandon Vaughn, Jane Joseph, Andrew Lawson, Graduate Studies, Public Health Sciences, MUSC.

Session 7 Postdoc / Resident / Fellow / Staff Scientist I Harper Center Gym

Group A 8:00 – 9:30 AM

51 Diabetic Rats are More Susceptible to Infarction and Cognitive Decline in a Microemboli Based Model of Vascular Cognitive Impairment and Dementia (VCID)
Raghavendar Chandran, Weiguo Li, Lianying He, Yasir Abdul, Sarah Jamil, Maria de Fatima Falangola, Adviye Ergul, Medicine, Pathology and Laboratory Medicine, MUSC.

52 Treatment with FK506 promotes noise-induced hearing loss through inhibition of calcineurin and activation of autophagy
Zuhong He, Song Pan, Hongwei Zheng, Shan Xu, Qiaojun Fang, Suhua Sha, Medicine, Pathology and Lab Medicine Research, MUSC.

53 Coronary Artery Calcification on Computed Tomography in Patients with ST-elevation Myocardial Infarction
Mohamed Faher Almahmoud, Umair, Malik., Jasjeet, Khural., Katrina, Bidwell., Sandra, Coons, Valerian Fernandes, Medicine, Cardiology, MUSC.

54 Screening of non-electrophilic Bach1 inhibitors in in vitro and in vivo model of neuroprotection
Manuj Ahuja, Navneet Ammal Kaidery, Irina Gaisina, Kazuhiko Igarashi, Otis C. Attucks, Sudurshana Sharma, Thomas Bobby, Medicine, Pediatrics, Neuroscience, Drug Discovery, MUSC.

55 miR-145a regulates pericyte function and outcomes of a murine model of sepsis
Yan Wu, Pengfei Li, Andrew J. Goodwin, James A. Cook, Perry V. Halushka, Hongkuan Fan, Medicine, Department of pathology and lab medicine research, MUSC.

56 Normalizing altered finger force direction post stroke: randomized controlled study protocol
Changki Kim, Corey Morrow, Christian Finetto, Parker Rhoden, Jillian Harvey, Viswanathan Ramakrishnan, Derek Kamper, Na Jin Seo, Health Professions, Ralph H. Johnson VA Medical Center, Department of Health Professions, MUSC.

57 Analytical methods for characterization of transplantable collagenous soft tissue
Glenn Hepfer, Peng Chen, Kelvin Brockbank, Alyce Jones, Zhen Chen, Elizabeth Greene, Lia Campbell, Gregory Wright, Amanda Burnette, Hai Yao, Dental Medicine (DMD, PhD), Oral Health Sciences, Clemson Bioengineering, MUSC.

Group B 10:00 – 11:30 AM

116 Reverse Phase Protein Array Reveals Differential Basal and Adaptive Protein Expression Profiles in BMSCs Cultured in Normoxic vs. Chronic Physiologically Relevant Bone Marrow Low Oxygen Conditions
Nada Eisa, Ahmed Elmansi, Dmitry Kondrikov, Brian Volkman, Louis Luttrell, Carlos Isales, Mark Hamrick, Meghan McGee-Lawrence, Sudanand Fulzele, Jie Chen, William Hill, William Hill, Medicine, Pathology and Laboratory Medicine, MUSC.

117 Identification and targeting of novel vulnerability in RAS for tumor inhibition
Imran Khan, Akiko Koide, Eric Denbaum, Mariyam Zuberi, Matthew Rhett, Kai Wen Teng, Russell Spencer-Smith, Shohei Koide, John O'Bryan, Medicine, Department of Cell and Molecular Pharmacology & Experimental Therapeutics, MUSC.

118 Circulating exosomes contribute to acute respiratory distress syndrome development in patients with sepsis
Pengfei Li, Andrew J. Goodwin, James A. Cook, Perry V. Halushka, Hongkuan Fan, Medicine, Department of Pathology and Laboratory Medicine, MUSC.

119 Evaluation of aspirin platelet inhibition assay in LVAD population
Eva Morgan, Dr. Jaclyn Hawn, Dr. Holly Meadows, Dr. Brian Houston, Johana Fajardo, Caroline Perez, Pharmacy, Pharmacy, MUSC.

120 SARM1 Mediates Dopaminergic Neurodegeneration in a Mouse Model of Parkinson's Desease
Navneet Ammal Kaidery, Rebecca Banerjee., Lichuan Yang, Noel Y Calingasan, Aihao Ding, Carl F Nathan, Flint Beal, Anatoli Starkov, Bobby Thomas, Medicine, Pediatrics, Neuroscience and Drug Discovery, MUSC.

121 S-Nitrosoglutathione invokes beneficial eNOS activity in a mouse model of experimental stroke
Pavan Kumar, Qiao Fei, Avtar K. Singh, Inderjit Singh, Mushfiquddin Khan, Medicine, Pediatrics, MUSC.

122 Differential effects of iron chelation with deferoxamine on post-stroke neurovascular inflammation: Disease and sex interactions
Victoria Wolf, Weiguo Li, Yasir Abdul, Guangkuo Dong, Rebecca Ward, Sarah Jamil, Lianying He, Susan C Fagan, Adviye Ergul, Graduate Studies, Pathology & Laboratory Medicine, MUSC.

123 Voltage Dependent Anion Channels Regulate Proliferation of Cancer Stem Cells
Amandine Rovini, Elizabeth Hunt, Kareem Heslop, Monika Gooz,Sheghuin Qin, Gavin Wang, Eduardo Maldonado, Pharmacy, Drug discovery and Biomedical Sciences, MUSC.

Session 8 Postdoc / Resident / Fellow / Staff Scientist II Harper Center Gym

Group A 8:00 – 9:30 AM

58 Investigating the role of EPHB2 in autism and autism-associated behaviors
Ahlem Assali, Chris Cowan, Graduate Studies, Neuroscience, MUSC.

59 GATA6 is required for chromatin reorganization and modification during human definitive endoderm formation and specification
James Heslop, Stephen Duncan, Medicine, Regenerative Medicine and Cell Biology, MUSC.

60 Motor protein MYO1C participates in retinal function by regulating STRA6 trafficking
Ashish Solanki, Glenn Lobo, Ehtasham Arif, Pankaj Shrivastava, Bushra Rahman, Deepak Nihalani, Medicine, Medicine, MUSC.

61 Workflow for Immune Monitoring during Clinical Trials by using unsupervised high dimensional augmented intelligence assisted analysis
Alessandra Metelli, Silvia Guglietta, Luis Cardenas, John Wrangle, Mark Rubinstein, Mark Robinson, Zvi Fridlender, Carsten Krieg, Medicine, Immunology an Microbiology, MUSC.

62 Towards a Model of Methylmalonic Acidemia using Human Induced Pluripotent Stem Cells
Behshad Pournasr, Stephen Duncan, Medicine, Regenerative Medicine and Cell Biology, MUSC.

63 Suboptimal ER stress Induced Autophagy Regulates Anti-Tumor T Cell Response
Paramita Chakraborty, Shilpak Chatterjee, Danh T. Tran, Dosung Kim, Satish N. Nadig, Carl Atkinson, Hongjun Wang, J. Alan Diehl, Shikhar Mehrotra, Health Professions, Surgery, MUSC.

64 An iPSC derived Hepatocyte Platform to Investigate the Mechanism and Treatment of Mitochondrial DNA Depletion Syndromes
James Corbett, , Stephen Duncan, Graduate Studies, Regenerative Medicine and Cell Biology, MUSC.

Group B 10:00 – 11:30 AM

124 Insulin-like Growth Factor (IGF)-II- Mediated Fibrosis in Pathogenic Lung Conditions
SM Garrett, Eileen Hsu, Justin Thomas, Joseph Pilewski, Carol Feghali-Bostwick, Medicine, Medicine, MUSC.

125 Age-related hearing loss and the potential role of disinhibition and neural synchrony in the recovery of auditory-evoked cortical responses
Carolyn McClaskey, James W. Dias, Kelly Harris, Medicine, Otolaryngology - Head & Neck Surgery, MUSC.

126 Mechanical Activation of the Angiotensin II Type I Receptor (AT1R) Promotes Abdominal Aortic Aneurysm Formation in Spontaneously Hypertensive Mice
Nicholas Ward, Armaan Amin-Javaheri, Hayes Lanford, R. Tyler Grespin, Christine Couch, Rupak Mukherjee, Jeffrey A. Jones, Jean Ruddy, Medicine, Department of Surgery, MUSC.

127 Heparin Administration in the Emergency Department for ST-Elevation Myocardial Infarction and Culprit Vessel Patency
Katrina BIdwell, Katrina Bidwell, MD, Jasjeet Khural, MD, Umair Malik, MD, Mohammed Almamoud, MD, Sandra Coons, RN BSN, Valerian Fernandes, Medicine, Cardiology, MUSC.

128 Modified cochlear surface preparation in the adult mouse
Shan Xu, Qiao-Jun Fang, Fan Wu, Suhua Sha, Graduate Studies, Pathology and Laboratory Medicine, MUSC.

129 Elevated LVEDP in STEMI presentation does not guide use of temporary mechanical circular support systems.
Jasjeet Khural, Mohamed Almahmoud, Umair Malik, Katrina Bidwell, Valerian Fernandes, Medicine, Internal Medicine, MUSC.

130 **A screen using human iPSC-derived hepatocytes to identify novel drugs for the treatment for hypercholesterolemia**
Jui Tung Liu, Mary Paige Lamprecht, Yuri K. Peterson, Steven L. Holshouser, Patrick M Woster, Duncan Stephen, Medicine, Regenerative Medicine and Cell Biology, MUSC.

131 **Structural basis of cephalosporins resistance in N. gonorrhoeae Penicillin-Binding protein 2**
Avinash Singh, Robert A Nicholas, Christopher Davies, Medicine, Biochemistry and Molecular Biology, MUSC.

Session 9 Research Specialist / Research Assistant I Harper Center Gym

Group A 8:00 – 9:30 AM

65 **Dose Dependent Effects of tDCS on Post-operative Pain**
Georgia Mappin, Jeffery Borckardt, Medicine, Psychiatry, MUSC.

66 **Therapeutic Concentrations of Statins Hyperpolarize Mitochondria and Inhibit Cell Proliferation Without Promoting Cell Death in Human Hepatocarcinoma Cells**
Elizabeth Hunt, Diana Fang, Amandine Rovini, Charleston Christie, Kareem Heslop, Eduardo Maldonado, Graduate Studies, Department of Drug Discovery & Biomedical Sciences, MUSC.

67 **Characteristics and Behavior of Primary Mouse Cardiac Fibroblasts on Tissue Culture Plates of Varying Stiffness**
Tiffany Dean, Yuhua Zhang, Amy Bradshaw, Graduate Studies, Division of Cardiology, MUSC.

68 **Discrete populations of enteric progenitor cells revealed by cell lineage analysis in mice.**
Meagan Branch, Takako Makita, Graduate Studies, Pediatrics, MUSC.

69 **Inventing and testing a new, open-source 3D-printed transcranial magnetic stimulation coil tracker holder for MRI-guided neuronavigation studies**
James Lopez, Kevin A. Caulfield, Claire E. Cox, Donna R. Roberts, Lisa McTeague, Graduate Studies, Brain Stimulation Laboratory, Department of Psychiatry, Medical University of South Carolina, Charleston, SC USA, MUSC.

70 **Activity-regulated cytoskeleton-associated protein (arc/arg3.1) regulates addiction-related behavior via action in the nucleus accumbens.**
Dalia Martinez, Sarah Barry, Rachel Penrod, Christopher Cowan, Christopher Cowan, Graduate Studies, Neuroscience, MUSC.

71 **Impact of Industry, Age, and Gender on Incidence, Rate, and Days Lost from Work for Workplace Foot and Ankle Injuries**
Alexander Caughman, , Christopher Gross, Medicine, Orthopaedics, MUSC.

72 **Motor-Activated Auricular Vagus Nerve Stimulation (MAAVNS) to Restore Upper Limb Function in Chronic Stroke Patients**
Andrew Fortune, Scott Hutchison, Sean L. Thompson, Steve Kautz, Mark S. George, Bashar Badran, Health Professions, Psychiatry, MUSC.

73 **Epigenetic Therapy for Sickle Cell Disease**
Steven Holshouser, Joy Kirkpatrick, Hyacinth Hyacinth, Patrick Woster, Graduate Studies (MSTP, PhD years), Drug Discovery, MUSC.

74 **Combination of tumor localized PD1 blockade and IL-12 (p70) results in potent systemic antitumor efficacy**
Carrie Fisher, Cody Gowan, Mee Bartee, Eric Bartee, Graduate Studies, Microbiology and Immunology, MUSC.

Group B 10:00 – 11:30 AM

132 Can We Noninvasively Stimulate Deep Brain Structures? An Initial Study Using Low Intensity Focused Ultrasound Pulsation (LIFUP) of the Anterior Thalamus To Modulate Pain
Sasha Stomberg-Firestein, Kevin A. Caulfield, Philipp M. Summers, Matthew T. Savoca, Scott Henderson, Xingbao Li, Logan T. Dowdle, Christopher Austelle, Baron Short, Mark S. George, Bashar Badran, Medicine, Brain Stimulation Laboratory, MUSC.

133 Cancer immunotherapy findings of T cell behavior in responsive or non-responsive melanoma models
Amalia Rivera Reyes, Amalia M. Rivera Reyes, Megan M. Wyatt, Connor J. Dwyer, Hannah M. Knochelmann, Aubrey S. Smith, Guillermo O. Rangel Rivera, Dimitrios C. Arhontoulis, Nicholas P. Restifo, Chrystal Paulos, Graduate Studies (MSTP, PhD years), Department of Microbiology and Immunology, MUSC.

134 Females have decreased CD8 T-cell survival and exosome release after activation
Sarah Pippin, Miguel Troncoso, Kristine DeLeon-Pennell, Medicine, Cardiology, MUSC.

135 Investigating the Interaction between Vimentin and DZIP1 in Mitral Valve Prolapse
Christina Wang, Janiece Glover, Russell Norris, Graduate Studies, Regenerative Medicine, MUSC.

136 Alterations in Posterior Cingulate Cortex Resting-State Connectivity Specific to PTSD Patients with Comorbid Substance Use Disorder
Madeline Hohmeister, Jane Joseph, Graduate Studies, Neuroscience, MUSC.

137 taVNS for Oromotor Infant Feeding III. Does doubling the dose matter?
Sarah Huffman, Daniel Cook, Morgan Dancy, William H. DeVries, Georgia Mappin, Sean Thompson, Philipp Summers, Marom Bikson, Mark S. George, Bashar W. Badran, Dorothea Jenkins, Medicine, Department of Pediatrics, MUSC, MUSC.

138 Sex differences in posterior cingulate cortex connectivity in amnestic Mild Cognitive Impairment
Shaquanda Ross-Simmons, Madeline Hohmeister, Andreana Benitez, Ph.D, Jane Joseph, Medicine, Neuroscience, MUSC.

139 Unique Inflammatory Signatures in Response to Viral Dosage of Myxoma
Erica Flores, Mee Bartee, Eric Bartee, Graduate Studies, Microbiology & Immunology, MUSC.

140 Preliminary results of 60-min vs 90-min Prolonged Exposure sessions with active duty personnel.
Gabrielle Frook, Stephanie Hart MPH, Ron Acierno PhD, Wendy Muzzy, Nursing, College of Nursing, MUSC.

141 The effects of low dose sacubitril and/or valsartan on renal disease progression in salt-sensitive hypertension
Mark Domondon, Iuliia Polina, Rebecca Fox, Mikhail Fomin, Daria Ilatovskaya, Medicine, Medicine/Nephrology, MUSC.

142 Attenuation of thoracic aortic aneurysm development by inhibition of membrane type-1 matrix metalloproteinase activity
Isis Thomas, Xiong, Y., Stroud, R.E., Nadeau, E.K., Mukherjee, R., Jeffery Jones, Graduate Studies, Surgery, MUSC.

Session 10 Undergraduate II EL 113

1:30 - 1:45 PM

143 **Blood vessel atrophy and macrophage dysfunction in age-related hearing loss**
Tyreek Jenkins, Kenyaria Noble, Hainan Lang, Graduate Studies, Pathology and Laboratory Medicine, MUSC.

1:45 - 2:00 PM

144 **Effects of maternal supplementation and vitamin D binding protein polymorphisms on vitamin D status in breastfed infants**
Simran Paintlia, Danforth A. Newton, Manjeet K. Paintlia, John E. Baatz, Renee Washington, Judy R. Shary Carol Wagner, Medicine, Pediatrics, MUSC.

2:00 - 2:15 PM

145 **Post-hoc Analysis of NICHD Vitamin D Pregnancy Cohort and The Role of Functional Vitamin D Deficiency in Pregnancy**
Elliott Lyles, Shelly Davis, Judy R. Shary, Myla Ebeling, Bruce W. Hollis, Carol Wagner, Medicine, Neonatology, MUSC.

2:15 - 2:30 PM

146 **Frequency and severity of medication side effects and causes of noncompliance in Kidney transplant patients**
Anushka Fernandes, David Taber, Pharmacy, Department of Transplant Surgery, MUSC.

2:30 - 2:45 PM

147 **Th17 Cells Uniquely Induce IL-6 and Possess Potent Antitumor Activity**
Reilley Chamness, Hannah M Knochelmann, Chrystal Paulos, Graduate Studies, Microbiology and Immunology, MUSC.

Session 11 Clinical / Professional / Masters IV EL 103

1:45 - 2:00 PM

148 **Chronic Consumption of Dietary Advanced Stage Glycation End-Products (AGE)s Activates Mammary Fibroblasts in vivo**
Reid Schuster, David Turner, Lourdes Nogueira, Bradley Krisanits, Victoria Findlay, Graduate Studies, Pathology, MUSC.

2:00 - 2:15 PM

149 **Non-peptidic Galectin-1 Inhibitor OTX008 Suppresses Glioblastoma Growth**
Wayne Glore, David Cachia, William A. Vandergrift III , Scott M. Lindhorst, Abhay K. Varma, Sunil J. Patel, Arabinda Das, Graduate Studies, Department of Neurosurgery, MUSC.

2:15 - 2:30 PM

150 **Noise-induced loss of sensory hair cells is triggered by ROS/p-AMPK-alpha pathway**
Fan Wu, Hao Xiong, Suhua Sha, Medicine (MSTP, MD years), Pathology and Laboratory, MUSC.

2:30 - 2:45 PM

151 **Associations Between Parent Psychopathology and Youth Mental Health and Early Alcohol Use Behaviors**
Alexis Garcia M.S., Michaela Hoffman, Ph.D., Rachel Tomko, Ph.D., Lindsay Squeglia Ph.D, Graduate Studies (MSTP, PhD years), Psychiatry and Behavioral Sciences, MUSC.

2:45 - 3:00 BREAK

3:00 - 3:15 PM

152 **Histamine receptors and sodium reabsorption in the Cortical Collecting Ducts**
Mikhail Fomin, Anastasia Sudarikova Regina Sultanova Mark Domondon, Daria Ilatovskaya, Graduate Studies, Department of Medicine/Nephrology, MUSC.

3:15 - 3:30 PM

153 **Mitochondrial respiration and biogenesis in the glomeruli of Dahl SS rats**
Regina Sultanova, Mark Domondon, Anna Nikiforova, Iuliia Polina, Mikhail Fomin, Krisztian Stadler, Daria Ilatovskaya, Medicine, Department of Medicine/Nephrology, MUSC.

3:30 - 3:45 PM

154 Oral Antibiotic Therapy Critically Regulates Osteoimmune Response Effects and Skeletal Homeostasis in the Alveolar Bone Complex

Brooks Swanson, Jessica Hathaway-Schrader, Amy Warner, Matthew Carson, Joy Kirkpatrick, Alex Alexseyenko, Sakamuri Reddy, Chad Novince, Graduate Studies, Department of Oral Health Sciences, MUSC.

Session 12 — Clinical / Professional / Masters IV — EL 102

1:30 - 1:45 PM

155 Analyzing Safety in a Phase I trial on Boswellia, an extract from Frankincense, for breast cancer primary tumors

Ingrid Bonilla, Abbott, Andrea, MD, Garcia, Denise, MD, Spruill, Laura, MD, Cole, David, MD, Hill, Elizabeth, PhD, Lockett, Mark, MD, Nancy DeMore, Medicine, Surgery, MUSC.

1:45 - 2:00 PM

156 Dchs1 and the septin cytoskeleton: a molecular and developmental etiology underlying mitral valve prolapse

Reece Moore, Kelsey Moore, Rebecca Stairley, Diana Fulmer, Lilong Guo, Russel Norris, Medicine, Department of Regenerative Medicine and Cell Biology, MUSC.

2:00 - 2:15 PM

157 Mechanism of action and antibacterial activity of alkynyl bisbenzimidazoles

Jordan Chamberlin, Sandra Story, Nihar Ranjan, Geoffrey Chesser, Dev Arya, Medicine, Chemistry, MUSC.

2:15 - 2:30 PM

158 Commensal Microbiota Regulates Skeletal Development through C3aR/C5aR-Mediated Complement Signaling

Megan Kuhn, Amy J. Warner, Brooks A. Swanson, Matthew D. Carson, Andrew Reynolds, Jessica D. Hathaway-Schrader, Chad Novince, Dental Medicine, Oral Health Sciences, MUSC.

2:30 - 2:45 PM

159 Accuracy of Intraoral Scanning Systems in an Edentulous Maxilla with Implants and Scan Bodies

Griffin Revell, Walter Renne, Dental Medicine, College of Dental Medicine, MUSC.

2:45 - 3:00 BREAK

3:00 - 3:15 PM

160 taVNS for Oromotor Infant Feeding II: Overall Clinical Outcomes in the First 14 Subjects

Daniel Cook, Sean Thompson, Morgan Dancy, William DeVries, Georgia Mappin, Sarah Huffman, Philip Summers, Marom Bikson, Mark S. George, Bashar W. Badran, Dorothea Jenkins, Medicine, Pediatrics, MUSC.

3:15 - 3:30 PM

161 The Need for ED Based Primary Care: A Study of the Socioeconomic Factors Leading Patients to Consider the ED to be their Medical Home

Cameron Weekley, Berlene Shipes, Ryan Wolf, Dr. Renee Martin, Steven Saef, Medicine, Department of Emergency Medicine, MUSC.

3:30 - 3:45 PM

162 The Need for Emergency Department Based Primary Care: A Descriptive Study of Patients Who Seek Preventive Care in the Emergency Department

Ryan Wolf, Virginia Shipes, Cameron Weekley, Renee Martin, Steven Saef, Medicine, Emergency Department, MUSC.

3:45 - 4:00 PM

163 Determining specific chemical modification dependence on nanocarrier characteristics of a 599 peptide carrier-siRNA complex

Chance Wagner, Travis Hedrick, Charles Holjencin, Yanping Liu, Jeremy Gilbert, Andrew Jakymiw, Dental Medicine, Department of Oral Health Science, MUSC.

4:00 - 4:15 PM

164 **The effects of sexual dimorphisms and temporomandibular disorder on mandibular morphometrics**
Linda Thomas, Dr. Matthew Coombs, Shuchun Sun, James Grant, Hai Yao, Dental Medicine, Clemson-MUSC Bioengineering Program, MUSC.

Session 13 PhD III EL 114

1:30 - 1:45 PM

165 **Investigating the role of LINE-1 retrotransposons in genomic instability of autophagy deficient ovarian cancer**
Christian Jones, Joe Delaney, Graduate Studies, Biochemistry, MUSC.

1:45 - 2:00 PM

166 **Characterizing hnRNP E1's function in genome stability and DNA transactions at cancer gene promoters**
Joseph Karam, Bidyut Mohanty, Breege Howley, Simon Grelet, Philip Howe, Graduate Studies, Biochemistry and Molecular Biology, MUSC.

2:00 - 2:15 PM

167 **IL-6 fuels durable memory for Th17-mediated responses to tumors**
Hannah Knochelmann, Connor Dwyer, Aubrey Smith, Jacob Bowers, Megan Wyatt, Michelle Nelson, Guillermo Rangel Rivera, Joshua Horton, Carsten Krieg, Gregory Lesinski, Zihai Li, Mark Rubinstein, Kent Armeson, Chrystal Paulos, Graduate Studies (MSTP, PhD years), Microbiology & Immunology, Dermatology & Dermatologic Surgery, MUSC.

2:15 - 2:30 PM

168 **Protein-based targeted complement inhibition ameliorates experimental autoimmune encephalomyelitis, a mouse model of multiple sclerosis**
Davis Borucki, M Mahdi Sleiman, Bärbel Rohrer, Stephen Tomlinson, Graduate Studies (MSTP, PhD years), Microbiology & Immunology, MUSC.

2:30 - 2:45 PM

169 **Specific Commensal Gut Bacterium Critically Regulates Alveolar Bone Homeostasis**
Matthew Carson, Jessica Hathaway-Schrader, Joy Kirkpatrick, Amy Warner, Brooks Swanson, Sakamuri Reddy, Caroline Westwater, Chad Novince, Graduate Studies, Oral Health Sciences, MUSC.

2:45 - 3:00 BREAK

3:00 - 3:15 PM

170 **Regular physical activity can prevent the oncogenic effects of lifestyle-associated advanced glycation end products**
Bradley Krisanits, Pamela M. Woods, Dion Foster, Lourdes M. Nogueira, Laura Spruill, Marvella E. Ford, Victoria J. Findlay, David Turner, Graduate Studies, Pathology and Laboratory Medicine, MUSC.

3:15 - 3:30 PM

171 **Feasibility of and Adherence to a Home-Based Duck Duck Punch Protocol**
Emerson Hart, Austen Hayes, Larry Hodges, Kevin Jett, Christian Finetto, Scott Hutchison, Michelle Woodbury, Health Professions, CHP Occupational Therapy, CHP Health Science and Research, MUSC.

3:30 - 3:45 PM

172 **EEG as a Predictor of Post-Stroke Recovery: A Systematic Review and Meta-Analysis**
Amanda Vatinno, Viswanathan Ramakrishnan, PhD, Annie Simpson, PhD, Heather Bonilha, PhD, CCC-SLP, Na Jin Seo, Health Professions, Occupational Therapy, MUSC.

3:45 - 4:00 PM

173 **READ-TV - Open Source, Interactive, Visualization Software of Surgical Work Flow Disruptions. A tool to Improve Patient Safety in OR Settings**
John Del Gaizo, Kenneth Catchpole, Alexander Alekseyenko, Graduate Studies, Biomedical Informatics Center, MUSC.

Session 14 PhD IV EL 118

1:30 - 1:45 PM

174 Bayesian Latent Pattern Models

Jonathan Beall, Dr. Elizabeth Hill, Dr. Hong Li, Dr. Bonnie Martin-Harris, Elizabeth Hill, Graduate Studies (MSTP, PhD years), Department of Public Health Sciences, MUSC.

1:45 - 2:00 PM

175 Comparison of minimal sufficient balance and minimization for subject randomization in clinical trials with a binary endpoint

Steven Lauzon, Viswanathan Ramakrishnan, Paul J. Nietert, Jody D. Ciolino, Michael Hill, Wenle Zhao, Viswanathan Ramakrishnan, Graduate Studies, Public Health Sciences, MUSC.

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176 How to account for transplant when examining survival in acute liver failure research

Sherry Livingston, Bethany Wolf, Valerie Durkalski, Graduate Studies, Public Health Sciences, MUSC.

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177 Common gamma chain cytokines modulate metabolism and tumor immunity of T cells in ACT

Guillermo Rangel Rivera, Connor J. Dwyer, Hannah M. Knochelmann, Aubrey Smith, Megan M. Wyatt, Chrystal Paulos, Medicine (MSTP, MD years), Microbiology & Immunology, MUSC.

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178 CD8+ T cells break tolerance to tumors in a B cell-dependent manner

Aubrey Smith, Hannah Knochelmann, Connor Dwyer, Megan Wyatt, Guillermo Rangel Rivera, Dimitrios Arhontoulis, Amalia Rivera-Reyes, Mark Rubinstein, Eric Bartee, Jessica Thaxton, Bei Liu, Chrystal Paulos, Graduate Studies, Microbiology and Immunology, MUSC.

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179 Elucidating components of novel MyoD co-repressor complex on stemness genes

Alexander Oles, Denis Guttridge, Graduate Studies (MSTP, PhD years), Pediatrics, MUSC.

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180 Antibody Panel Based N-glycan Imaging of Patient Serum for Discovery of Hepatocellular Carcinoma Biomarkers

Alyson Black, Peggi Angel, Richard Drake, Anand Mehta, Graduate Studies, Cell and Molecular Pharmacology, MUSC.

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181 Localized regulation of RNAi-lncRNA interactions by epithelial adherens junctions

Mary Bridges, Joyce Nair-Menon, Antonis Kourtidis, Antonis Kourtidis, Graduate Studies, Reg Medicine and Cell Biology, MUSC.

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182 Human Cardiac Organoids for Cardio-Oncology

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

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183 DCHS1 based cell adhesions direct the septin cytoskeleton during critical stages of mitral valve disease inception

Kelsey Moore, Reece Moore, Diana Fulmer, Lilong Guo, Cortney Gensemer, Rebecca Stairley, Mary Kate Rumph, Janiece Glover, Tyler Beck, Christina Wang, Russell Norris, Graduate Studies, Regenerative Medicine and Cell Biology, MUSC.

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184 **Identification of penicillin-binding protein 2 (PBP2) inhibitors as agents against penicillin- and cephalosporin-resistant strains of Neisseria gonorrhoeae**
Jonathan Turner, Samantha Zygmont, Patrick M Woster, Christopher Davies, Graduate Studies (MSTP, PhD years), Biochemistry & Molecular Biology, MUSC.

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185 **Dissociating drug reward from contextual cues: The cell type-specific role of nucleus accumbens NPAS4**
Brandon Hughes, Makoto Taniguchi, Christopher Cowan, Graduate Studies, Neuroscience, MUSC.

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186 **Neuroimmine Dysfunction in a Mouse Model of MEF2C Haploinsufficiency Syndrome**
Catherine Bridges, Adam J. Harrington, Stefano Berto, Ahlem Assali, Yongjoo Jennifer Cho, Christopher Cowan, Graduate Studies (MSTP, PhD years), Psychiatry and Neuroscience, MUSC.

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187 **Inhibition of insulin signaling in the brain adversely impacts cognition in mice.**
Crystal Smith, Catrina Robinson, Graduate Studies (MSTP, PhD years), Neurology, MUSC.

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188 **taVNS for Oromotor Infant Feeding IV: Microstructural diffusion MRI changes before and after Treatment in Neonates with Feeding Failure**
Hunter Moss, Jens H. Jensen, Bashar W. Badran, Daniel Cook, Morgan Dancy, William H. DeVries, Georgia Mappin, Sean Thompson, Philipp Summers, Marom Bikson, Mark S. George, Dorothea Jenkins, Graduate Studies, Neonatalogy, MUSC.

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189 **Hyperinsulinemia induced brain microvessel insulin resistance correlates with reduced insulin transport**
Luke Watson, Crystal Smith, Alexus Williams, Catrina Sims-Robinson, Graduate Studies, Neurology, MUSC.

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190 **Host ectonucleotidase-CD73 and the opportunistic pathogen Porphyromonas gingivalis cross-modulation underlies a new homeostatic mechanism for chronic bacterial infection in human epithelial cells**
Jaden Lee, Nityananda Chowdhury, JoAnn Roberts, Ozlem Yilmaz, Dental Medicine (DMD, PhD), Oral Health Sciences, MUSC.

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191 **Alpha-conotoxin activity on nicotinic acetylcholine receptor subtypes**
Meghan Grandal, Clare Stokes, Roger Papke, Frank Mari, Graduate Studies, DDBS, MUSC.

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192 **The Role of R-Ras Family Signaling in Malignant Peripheral Nerve Sheath Tumor Progression**
Shannon Weber, Amanda Pretchl, Nicole Brossier, Stephanie Byers, Steven Carroll, Graduate Studies (MSTP, PhD years), Pathology, MUSC.

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193 **Rib-hook Construct for Pediatric Hyperkyphosis and Kyphoscoliosis**
Daniel Bonthius, Hai Yao, Graduate Studies (MSTP, PhD years), Oral Health, MUSC.

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194 **Incidence and trends of head and neck rhabdomyosarcoma versus non-rhabdomyosarcoma in adult and pediatric patients**
Vincent Desiato, Catherine Loftus, Eric Lentsch, Medicine, Department of Otolaryngology - Head and Neck Surgery, MUSC.

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195 **Impact of post-LVAD Ventricular Arrhythmia & Heart Failure on Re-admissions and Overall Mortality: A Retrospective Review**
Nagarajan Muthu, Jeffery A. Jones, Rupak Mukherjee, Steven Lauzon, Viswanathan Ramakrishnan, Lucian Lozonschi, Medicine, Cardiothoracic Surgery, MUSC.

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196 **Heated tumor volume decides effectiveness of drug delivery with thermosensitive liposomes**
Krishna Ramajayam, Marissa Wolfe, Anjan Motamarry, John Yost, Mike Yost, Dieter Haemmerich, Graduate Studies, Pediatrics, MUSC.

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197 **Using a Site-Targeted Complement Inhibitor as a Therapeutic Approach for Cognitive Decline Post Chronic Traumatic Brain injury.**
Khalil Mallah, Ali Alawieh, Reda Chalhoub, Farris Langley, Mikeala York, Henry Broome, Stephen Tomlinson, Graduate Studies, Microbiology and Immunology Department, MUSC.

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198 **Fretting Mechanics in Modular Total Hip Arthroplasty: Si3N4 vs CoCrMo Femoral Head on Ti-6Al-4V Trunnion**
Piyush Khullar, Jeremy Shealy Dongkai Zhu, Jeremy Gilbert, Medicine, Orthopaedics and Physical Medicine, MUSC.

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199 **Role of the Glycolytic Enzyme Enolase-1 in Fibrosis**
Shailza Sharma, Tomoya Watanabe, Carol Feghali Bostwick, Medicine, Medicine, MUSC.

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200 **ST Elevation Myocardial Infarction Presentation and Management Trends at the Medical University of South Carolina**
Umair Malik, Mohamad Almahmoud, Jasjeet Khural, Katrina Bidwell, Alexander Conavo, Valerian Fernandes, Medicine, Medicine, MUSC.

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201 **Predicting stroke recovery using neural networks**
Barbara Marebwa, Julius Fridriksson, Chris Rorden, Leonardo Bonilha, Medicine, Neurology, MUSC.

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202 **Embryonic Mesenchymal Programs Persist in the Adult Pancreas during Physiology and Cancer**
Lu Han, Gustavo Leone, Medicine, Biochemistry, MUSC.

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203 **The role of infralimbic cortical perineuronal nets in fear memory extinction after adolescent intermittent ethanol exposure**
Kristin Marquardt, Lawrence Judson, Medicine (MSTP, MD years), Neuroscience, MUSC.

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204 **Visual Enhancement of Auditory Speech Identification is Predicted by Individual Differences in Frontal-Occipital Fasciculus Microstructure**
James Dias, Carolyn McClaskey, Kelly Harris, Medicine, Otolaryngology, MUSC.

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205 **Single but not dual blockade of PI3K delta and PI3K gamma promotes robust CD8+ T cell responses to solid tumors**
Connor Dwyer, Dimitrios C. Arhontoulis, Hannah M. Knochelmann, Aubrey S. Smith, Guillermo O. Rangel Rivera, Megan M. Wyatt, Amalia M. Rivera Reyes, Chrystal Paulos, Medicine, Microbiology and Immunology/Dermatology, MUSC.

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206 **Neuronal dysfunction underlies autism-related behaviors in a mouse model of MEF2C haploinsufficiency syndrome**
Adam Harrington, Kayla Blankenship, Ahlem Assali, Stefano Berto, Benjamin Siemsen, Yongjoo Jennifer Cho, Evgeny Tsvetkov, Acadia Thielking, Michael Scofield, Christopher Cowan, Christopher Cowan, Medicine, Neuroscience, MUSC.

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207 **Residual brain white matter integrity predicts aphasia severity and recovery in patients with chronic left hemispheric stroke**
Janina Wilmskoetter, Barbara Marebwa, Alexandra Basilakos, Julius Fridriksson, Chris Rorden, Brielle C. Stark, Lisa Johnson, Gregory Hickok, Argye E. Hillis, Graham Warner, Leonardo Bonilha, Medicine, Neurology, MUSC.

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208 **GABAergic Neuronal Deficiency and Type 2 Potassium-Chloride Cotransporter Immaturity in Human Focal Cortical Dysplasia**
Peng Cheng Han, Cynthia T Welsh, Michael T Smith, Robert E Schmidt, Steven Carroll, Medicine (MSTP, MD years), Pathology and Laboratory Medicine, MUSC.

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209 **Comparative Enhancement of Motor Function and BDNF Expression Following Different Brain Stimulation Approaches in an Animal Model of Ischemic Stroke**
Serena-Kaye K.C. Sims, Aitana Rizzo, Kern Howard, Ariana Farrand, Heather Boger, DeAnna Adkins, Graduate Studies, National Institute of Health, Neuroscience, MUSC.

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210 **Commensal Oral Microbiota has Distinct Osteoimmunomodulatory Effects Driven by Induction of MHC-II Antigen Presentation and Toll-Like Receptor Mediated Immunity**
Jessica Hathaway-Schrader, Johannes D. Aartun, Nicole Poulides, Megan Kuhn, Blakely Graham, Michael Chew, Emily Huang, Richard P. Darveau, Caroline Westwater, Chad Novince, Dental Medicine, Oral Health Sciences, MUSC.

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211 **Outcomes of Inter-facility Helicopter Transportation in Acute Stroke Care**
Eyad Almallouhi, Christine Holmstedt, Medicine, Neurology, MUSC.

4:00 - 4:15 PM

212 **Dendritic Cells Regulate the Immunological Landscape of Breast Tumors**
Stephen Iwanowycz, Yingqi Li, Christopher Koivisto, Soo Ngoi, Bei Liu, Medicine, Microbiology and Immunology, MUSC.

Session 18 — Research Specialist / Research Assistant I — EL 115

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213 **CD26 enzymatic activity modulates efficient migration of adoptively transferred cancer-specific T cells to solid tumors**
Megan Wyatt, Stefanie Bailey, Michelle Nelson, Hannah Knochelmann, Aubrey Smith, Connor Dwyer, Dimitrios Arhontoulis, Guillermo Rangel Rivera, Amalia Rivera Reyes, Chrystal Paulos, Medicine, Microbiology and Immunology, MUSC.

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214 The Rising Incidence of Pediatric Head and Neck Cancers in the United States

Catherine Loftus, Avigeet Gupta BS; Clarice Clemmens MD; Shaun A. Nguyen MD, Eric Lentsch, Medicine, Otolaryngology, MUSC.

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215 Exosome-mediated long-range communication in stressed retinal pigment epithelial cell mono layers - focus up-take mechanisms.

Crystal Nicholson, Navjot Shah, Masakii Ishii, Bala Annamalai, Carlene Brandon, Tamara Nowling, Baerbel Rohrer, Graduate Studies, Department of Ophthalmology, MUSC.

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216 Minocycline-Induced Dysbiosis of Gut Microbiota Alters Normal Osteoimmune Processes in Post-Pubertal Skeletal Development

Amy Warner, Matthew Carson, Jessica Hathaway-Schrader, Joy Kirkpatrick, Brooks Swanson, Alex Alekseyenko, Jose Aguirre, Chad Novince, Dental Medicine, Oral Health Sciences, MUSC.

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217 MicroRNA-204 as a driver of the neuroendocrine phenotype through direct negative regulation of the Androgen Receptor

Lourdes Nogueira, Arabia Satterwhite, Sean Cosh, Michael Lilly, David P Turner, Ashley-Knowell and Victoria Findlay, Victoria Findlay, Graduate Studies, Pathology and Lab Medicine, MUSC.

LIST OF ABSTRACTS

1 The Effect of Daily Stressors on Neuroendocrine and Subjective Reactivity Following a Psychosocial Stress Paradigm in Cocaine Dependent Individuals.

Raquelle Bourgeois, Kathleen T. Brady, Brian Sherman, Aimee Mcrae-Clark, Medicine, Department of Psychiatry and Behavioral Sciences, MUSC.

Background: Chronic cocaine use induces long-term effects on neuroendocrine pathways in the brain. Notably, there is a high co-morbidity between cocaine misuse and stress-related disorders. While prior research has established past traumatic events as a predictor of relapse, recent evidence suggests that daily stressors may have a greater impact on psychological functioning. The current study used a human laboratory paradigm to examine the relationship of negative daily stressors on neuroendocrine (i.e. cortisol) and subjective (i.e. craving, stress, anxiety) reactivity to a social stress task in cocaine-dependent individuals. Methods: Secondary data analysis was conducted from a parent study of the therapeutic role of oxytocin on stress reactivity in cocaine-dependent individuals. Participants (N=97) reported baseline levels of daily hassles and their severity and were randomized to receive either intranasal oxytocin (40 IU) or placebo prior to completing the Trier Social Stress Task (TSST). Levels of cortisol, cocaine craving, anxiety, and perceived stress were recorded at baseline, 5 minutes pre-TSST, immediately post-TSST, and 10, 30, and 60 minutes post-TSST. Linear mixed-effects models were used to examine the effects of daily hassles on neuroendocrine and subjective reactivity. Results: There was a significant main effect of the frequency of daily hassles and the mean severity of hassles across all subjective measures in response to the TSST (Hassles-Frequency: craving, $p<0.001$; stress, $p<0.001$; anxiety, $p=0.042$; Hassles-Severity: craving, $p<0.001$; stress, $p=0.001$). There was an interaction between the frequency and severity of daily hassles and treatment (treatment x frequency, $p<0.001$; treatment x severity, $p<0.001$) on craving. There was no effect of daily hassles on neuroendocrine reactivity. Conclusion: Results suggest that response to treatment with oxytocin may depend on an individual's experience of daily stressors. Findings may inform future treatments aimed at decreasing the risk of relapse in cocaine-dependent individuals who experience stress in their daily lives. This work was supported by NIH grant R25 DA020537, NIH grant P50 DA016511.

2 An ex-vivo comparison of Alzheimer amyloid-beta plaque species and the cerebrovasculature.

Rob Aldrin Robino, David Hartmann, Maricel Soliven, and Sangeeta Mohanty., Narayan R. Bhat, Medicine, Neuroscience, MUSC.

Alzheimer's disease (AD) is the most common cause of dementia. Although the cause of AD is unknown, all AD patients by definition exhibit the pathological hallmarks of beta-amyloid aggregates ("plaques"), and phosphorylated tau protein ("tangles"). However, many individuals with high pathological burden of plaques and tangles are cognitively healthy, and several recent trials that reduced plaque burden failed to improve cognitive function. This has led many to believe that certain species of plaque, such as "diffuse" plaque, or plaque around blood vessels, might be more relevant for cognitive deterioration. Here we identify new fluorescent dyes capable of highlighting these specific types of plaque. In this study, we use immunohistochemistry in transgenic (Thy-SwDI strain) mice brain to identify patterns of distribution of plaque species among brain structures and the cerebrovasculature. We characterize two widely-used dyes that cross the blood-brain barrier (Methoxy-X04 and FSB), using a commonly-used ABeta-specific antibody as a reference (82e1). Our results to date show that Methoxy-X04 labels larger, compact parenchymal and arteriole plaques. In contrast, FSB labels more varieties of plaque, most interestingly the smaller, diffuse plaque found adjacent to capillaries that were invisible using Methoxy-X04 labeling. We confirm the spatial relationship between FSB and capillaries in 3-dimensional optically-cleared brain sections. This study better characterizes two widely-used fluorescent amyloid dyes, which will enable better interpretation of previous studies, and future use of FSB to identify plaque situated on capillaries. Perhaps in the future, derivatives of these dyes can be used as PET ligands to identify if capillary-associated plaque or diffuse plaques correlate with cognitive deficits. This work was supported by NIH 5R21AG059422-02

3 Behavioral tasks that assess recognition memory are useful tools to assess cognitive deficits in preclinical models.

Tyler Stone, Alexus Williams, Luke Watson, and Dominique Williams, Catrina Robinson, Graduate Studies, Neurology, MUSC.

Obesity is associated with cognitive deficits in working memory and problem solving. 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 activity 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 the National Institute of Health (NINDS 1R01NS099595)

4 BMP-Notch signaling interaction in AV endocardial cushion coordinately regulates AV valvulogenesis

Haleigh Ferro, Maria Gonzalez, Patrick. G. Smith, Miriam M. Atteya, Sarah Suber, Jeremy L. Barth, Yukiko Sugi, Medicine, Regenerative Medicine, MUSC.

Valvuloseptal defects are among the most common and serious of congenital heart defects (CHDs). Mesenchymalized endocardial cushions undergo maturation and remodeling into ventricular membranous septum and atrioventricular (AV) valves. Our recent studies have shown that lack of BMP2 in the endocardial lineage consistently results in membranous ventricular septal defects and AV valve dysplasia, indicating the requirement of BMP2 in the endocardial lineage. Because our data indicate that BMP2 ligand and receptors, as well as Notch ligands and receptors, are expressed in the AV endocardial cushion mesenchyme, and that BMP2 induces Notch pathway effectors in endocardial cushion cell cultures, we propose the novel hypothesis that BMP signaling intermediates interact with Notch signaling components to coordinately regulate differentiation of AV endocardial cushion cells into normal prevalvular fibroblasts. We use in vitro culture assays and in vivo genetically engineered mouse models to test our hypothesis. In our present study, we assessed the effect of combining up-regulated BMP signaling and down-regulated Notch signaling in vivo via genetic activation of Smad-dependent BMP signaling by conditionally activating Alk3 using caAlk3 and disrupting the key Notch transcription factor, RBPJ, using RBPJflox/+ with an endocardial lineage specific Nfatc1Cre driver line. By our morphological analyses, we found that the double mutant, caAlk3; RBPJflox/+ ; Nfatc1Cre mice exhibited mitral valve dysplasia and aberrant deposition of extracellular matrix (ECM) components at 8 weeks old. Transcriptomic analysis further revealed that genes linked to leukocyte, macrophage and immune response functions were significantly affected in mutant mouse mitral valves. We have further performed RT-quantitative PCRs to verify these changes in gene expression. Our data indicate that degenerative mitral valve phenotypes found in the caAlk3; RBPJflox/+ ; Nfatc1Cre mice are associated with alteration of ECM deposition and an increase in infiltration of leukocytes /macrophages in AV mitral valves. This work was supported by AHA 18TPA34170356, NIH/NIGMS P20 GM103499BIPP, NIH/NIGMS P20 GM103499DRP

5 Role of Sox9 gene in the development of the AV mesenchymal complex in embryonic mice hearts

Renelyn Wolters, Raymond Deepe, Andy Wessels, Graduate Studies, Department of Regenerative Medicine and Cell Biology, MUSC.

Previous studies have shown that inhibition of Sox9 contributes to atrioventricular septum defects (AVSDs), heart malformations that affect 1 in every 2,000 live births. The development of the AV mesenchymal complex, a structure comprised of the mesenchymal cap, superior AV cushion, inferior AV cushion, and the dorsal mesenchymal protrusion (DMP), is crucial in the formation of a normally septated heart. To better understand how Sox9 is involved in the development of the AV mesenchymal complex, Tie2-cre and Mef2c-cre mice were used to delete Sox9 from the endocardial cell lineage and from the second heart field (SHF). The development of the AV mesenchymal complex structures was assessed by determining the number of cells in each component using one knockout and one control 11.5 ED embryo of each cre-mouse line. AMIRA reconstructions were then created to determine size and volume. Results showed that the number of mesenchymal cells in the endocardial derived structures were significantly reduced in the T2Sox9 knockout. The superior and inferior cushions were both reduced by 52%; however, the M2Sox9 cushions were only reduced by 20% and 4% respectively. Both knockouts experienced over a 50% reduction in the mesenchymal cap, a structure derived from the endocardium that closely interacts with the DMP, a SHF derived structure. No significant change was observed in the DMP in either cre-knockouts despite earlier indications that it may play a role in the pathogenesis of AVSDs. These findings suggest that the DMP is not the only contributor to AVSDs, and that the mesenchymal cap may play a bigger role in the development of the AV mesenchymal complex than initially anticipated. This work was supported by RO1 HL 122906, MUSC Bridge Fund

6 Is the Relationship between Conservatism and Climate Change Attitudes Moderated by Right Wing Authoritarianism and Social Dominance Orientation?

Brittany McKenzie, Stephen Short, Graduate Studies, Psychology - College of Charleston, MUSC.

Past research demonstrates that conservatism negatively predicts climate change attitudes. Right-wing authoritarianism (RWA) and social dominance orientation (SDO) are also correlated positively with conservatism and negatively with climate change attitudes. The current study investigates whether RWA and SDO moderate the effect of conservatism on climate change attitudes. A sample of undergraduate college students (n =138) completed a survey containing measures of conservatism, RWA, SDO, and beliefs, intentions, doubts, and experiences with climate change. Multiple regression and simple slopes analyses were used to test the hypotheses that RWA and SDO would moderate the strength of the relationship between conservatism and climate change attitudes. We hypothesized that individuals higher in RWA and SDO would display a stronger negative relationship between conservatism and climate change attitudes. Our analyses found that neither RWA nor SDO significantly moderated the strength of the relationship between conservatism and climate change attitudes. RWA was found to reduce the strength of the relationship between conservatism and environmental concern, a finding that was in opposition to our original hypotheses. Additional analyses are being conducted to investigate other relationships among these variables, including potential mediation models. Results from these analyses will help future researchers understand which facets of political ideology influence one's attitudes toward climate change.

7 The synergy of CD36 and Scleraxis in the activation of intestinal fibroblast "Potential Role in Fibrosis"

Samuel Kirsch, Andrea Nillas and Michael P. Czubryt, Titus Reaves, Medicine, Regenerative Medicine and Cell Biology, MUSC.

Fibrosis can be defined as dysregulated deposition of excessive and aberrant extracellular matrix proteins, principally collagen. While fibrosis is organ specific, it is a multisystem process. Intestinal fibrosis typically follows Crohn's Disease (CD); described as idiopathic transmural inflammation that can emerge anywhere in the gastrointestinal tract from mouth to anus. Such inflammation can result in intestinal fistulas and bowel obstructions. We investigate CD36 and scleraxis for their effects on the activation of intestinal fibroblasts. CD36 is a scavenger and membrane bound protein that has a variety of effect on cells. In particular, it's an indicator of inflammation, interacts with TLRs 2,4,6, and is a receptor for collagen. Scleraxis was originally identified as a transcription protein involved in the release of collagen leading to the production of tendon and bone. One gene codes for two proteins. More recent studies show that scleraxis is involved in several diseases, including cardiac fibrosis. Thus, we examine intestinal fibroblasts for a connection between CD36 and scleraxis. In vivo, CD36 deficient mice show reduced expression of scleraxis. In vitro studies using siRNA also show that when CD36 is reduced, scleraxis is also reduced. Immuno-purification studies revealed that both proteins are connected. Moreover, under inflammatory conditions (DSS colitis) scleraxis appears

further reduced. When both proteins are uncoupled scleraxis deficient cells are not as adherent compared to normal and CD36 deficient cells. Results suggests that CD36 may be involved in adhesion and scleraxis involved in migration in intestinal fibroblasts.

8 Disrupted DNA binding and autistic-like behaviors in a mouse model of syndromic autism.

Kayla Blankenship, Adam Harrington, Acadia Thielking, Christopher Cowan, Medicine, Neuroscience Department, MUSC.

MEF2C is a transcription factor that binds to DNA to regulate expression of target genes. Mutations in the MEF2C gene are associated with multiple neurodevelopmental disorders such as autism spectrum disorder (ASD), intellectual disability (ID), and schizophrenia (SCZ). MEF2C Haploinsufficiency Syndrome (MCHS) is a syndromic form of autism in humans that occurs when only one copy of MEF2C is deleted or mutated. This leads to autistic-like behaviors, including reciprocity deficits, language deficits, repetitive motor movements, and severe intellectual disability. Through a collaboration with Greenwood Genetic Center, we identified single nucleotide variants (SNVs) specific to patients with MCHS. Based on this information, we introduced a select number of these SNVs, in addition to others previously identified in literature, into Mef2c through site directed mutagenesis by PCR. These include the missense mutations G27A, K30N, L38Q, and I46T, as well as the duplication mutation, D40-C41 dup. These constructs were cloned into an expression vector (pA1T7α) and expressed in 293T (human embryonic kidney) cells. The proteins were then isolated from the cells and evaluated through western blotting and the electrophoretic mobility shift assay (EMSA). We find that these mutations do not significantly alter protein stability as determined by western blotting. However, we show that all of these MCHS mutations disrupt the DNA-binding function of MEF2C using EMSA. Next, we generated a DNA-binding deficient Mef2c heterozygous mouse and examined brain morphology and MCHS-relevant behaviors. Interestingly, mice missing one copy of Mef2c displayed reduced vocalizations, reduced social interactions, and altered anxiety, as well as a significantly thicker corpus callosum than their wildtype counterparts. Together, our studies suggest that MCHS mutations disrupt DNA binding of MEF2C and that behavioral and morphological changes are observed in our mouse model of MCHS. This work was supported by NIH grant MH111464, Brain and Behavior Research Foundation NARSAD Young Investigator Award, NIH 5 R25 DA 33680-7 grant

9 Dietary fat intake and the comorbidities of pregnancy: a post-hoc analysis of two cohorts

Shellie Davis, Elliott Lyles, Judy Shary, Myla Ebeling, Carol Wagner, Carol Wagner, Health Professions, Neonatologist and Associate Director of SCTR's Research Nexus, MUSC.

Evidence shows considerable variations in diet and in birth outcomes among women of different races. Black women suffer the greatest risk, with higher rates of preterm birth, small for gestational age infants (SGA), and bacterial vaginosis (BV). Black women also tend to be the highest consumers of fat. This post hoc analysis investigates the association between dietary fat intake and the pregnancy comorbidities-BV, preterm birth, preeclampsia, gestational diabetes, gestational hypertension, and SGA infants as a function of race. A post-hoc analysis of pregnant women participating in vitamin D supplementation trials was conducted to ascertain the role of total dietary fat intake on pregnancy outcomes. Among 923 study participants from the Kellogg and NICHD pregnancy studies, those who delivered, completed a food frequency questionnaire (FFQ), and fell within the 10th-90th percentile for caloric intake were included in the current analysis: 388 participants met inclusion criteria: 76 Black, 153 Hispanic, and 156 White women. Complications of pregnancy were analyzed and defined as any one of the following: hypertensive disorders of pregnancy; gestational diabetes; bacterial vaginosis or any infection; and/or preterm birth. No significant associations were found between total dietary fat and any of the comorbidities of pregnancy. A significant association between dietary fat intake and marital status was found, with those unmarried individuals having greater fat intake than married individuals. Black women demonstrated the highest mean value of dietary fat intake (84.1 grams/day), followed by White women (76.4 grams/day), and Hispanic women (74.8 grams/day). These trends were not found to be significant. When examined by race, saturated and trans fats were not found to have a significant association with any of the comorbidities of pregnancy analyzed. Despite racial and ethnic differences, neither total dietary fat, nor saturated or trans fat specifically, was directly associated with any of the common comorbidities of pregnancy.

10 Examining Changes in Depression and Anxiety Symptoms in Adolescent Smokers During a 12-Week Pharmacotherapy Trial

Iris Sakamoto, Jennifer Dahne, PhD, Rachel L. Tomko, PhD, Kevin M. Gray, MD, Erin McClure, Medicine, Department of Psychiatry and Behavioral Sciences, Addiction Sciences Division, MUSC.

Background: Approximately 90% of smokers began smoking before the age of 18. Adolescent smokers are 1.5-2 times more likely to experience depression and anxiety than non-smokers, and those with elevated depression and anxiety symptoms are twice as likely to develop nicotine dependence. Thus, adolescence is a critical time for smoking prevention and cessation. Varenicline is the most efficacious monotherapy for adult smoking cessation, but little is known about its efficacy and potential secondary effects on depression and anxiety in adolescents. The parent study was a clinical trial evaluating the efficacy and tolerability of varenicline in adolescent smokers. The goal of the present study is to evaluate changes in depression and anxiety symptoms during smoking cessation treatment. Methods: In this randomized, double-blind, placebo-controlled clinical trial, 157 treatment-seeking adolescent smokers (40.1% Female, Age M(SD) = 19.1(1.5), 76.4% White, Cigarettes per day = 11.5(6.8)) were randomized to 12 weeks of varenicline (n=77) or placebo (n=80). Participants meeting criteria for psychiatric illness were excluded. Depression and anxiety symptoms were measured at baseline and weekly using the Hospital Anxiety and Depression Scale (Baseline Anxiety M(SD) = 4.9(3.4), Depression = 2.9(2.5)). Generalized estimating equations were used to examine the main effects of treatment and time on depression and anxiety symptoms, and the interaction between treatment and time, while adjusting for sex and baseline anxiety/depression. Results: During treatment, there were no significant differences in anxiety or depression symptoms between treatment groups ($ps<0.7$), and no interaction between treatment and time ($ps<0.4$). There was a significant main effect of time for anxiety symptoms ($p<0.01$), but not for depression ($p=0.2$). Conclusion: Although results should be interpreted with caution as this study was not powered for this secondary analysis, these results preliminarily suggest that varenicline did not alter anxiety or depressive symptoms during treatment among adolescent smokers as compared to placebo. This work was supported by This work was supported in part by NIH grants R25 DA020537 (Back) and U01 DA031779 (Gray)

11 Cognitive Behavioral Therapy for Chronic Pain and Shared Decision Making to Reduce Prescription Opioid Use and Misuse in Pregnant Women

Marinna Smith, Edie Douglas, Tonya Cassaday, Lisa Boyars, Constance Guille, Medicine, Department of Psychiatry and Behavioral Sciences, MUSC.

Background: Prescription opioid (PO) misuse during pregnancy has greatly increased in the past decade, posing a significant risk to maternal and newborn health. Women that misuse POs are at high risk for an opioid use disorder (OUD), but to date there are no non-pharmacological evidence-based treatment options to help pregnant women reduce the use and misuse of POs. The purpose of this pilot was to determine if combined Cognitive Behavioral Therapy for Chronic Pain (CBT-CP) and Shared Decision Making (SDM) for opioid tapering can help reduce PO use and misuse in pregnancy. Methods: Open-label prospective cohort study of 20 adult, pregnant women ≤28 weeks gestation who were misusing POs and willing to consider a PO dose reduction were invited to take part in an 8-week CBT-CP/SDM study. Women with OUD were excluded. Women participated in weekly 60-90 minute CBT-CP/SDM sessions for 8 weeks. The main outcome measure was the Current Opioid Misuse Measure (COMM). A secondary outcome was Morphine Equivalent Dose (MED) and percent of women not using POs at 8 weeks of treatment. Results: 90.9%[20/22] of eligible women agreed to take part in the study. On average women were 30.1[SD±3.28] years old, enrolled at 19[SD±2.98] weeks gestation and primarily Caucasian [86.4%[17/20]]. Mean years of PO use was 6.2[SD±3.20], mainly for low back pain [77.3%[15/20]]. There was a significant reduction in the mean COMM [baseline 16.5[SD±3.21] vs. 8 weeks 7.38[SD± 3.11]; $p < 0.05$]. Mean MED was lower at 8 weeks compared to baseline [baseline 133.5[SD± 60.96] vs. 6.78[SD±11.95]]. At week 8, 80%[16/20] of participants discontinued their PO. Conclusion: These results suggest that CBT for chronic pain and SDM are feasible and potentially beneficial treatments for decreasing PO use and misuse in pregnant women. Future studies, with longer follow-up are needed to determine if women continue cessation from opioid use. This work was supported by NIDA K23 DA039318-01, NIDA R25 DA020537

12 Use of a Modified "Privilege Walk" to Teach Undergraduate Pre-Health Professionals at an Academic Health Center: A Pilot Project Examining Personal Privilege as a Social Determinant of Health

Aramis Gregory, Lauren Gellar, PhD, MS, MCHES, Brandi M. White, PhD, MPH, Elinor Borgert, PhD, MS, Elizabeth Brown, Health Professions, Department of Health Professions, MUSC.

There is an increasing call to teach pre-health professionals about social determinants of health (SDOH). We examined personal privilege as a SDOH to increase awareness about privilege. Our pilot project measured the effect of a modified "Privilege Walk" (MPW) assignment on student awareness of personal privilege as a SDOH, change their attitudes about privilege, and determine if students identified certain SDOH with better privilege. Undergraduate pre-health professionals at the Medical University of South Carolina completed a pre-survey prior to the MPW assignment and a post-survey immediately after the MPW assignment. Nonparametric tests were used to determine the impact of the MPW assignment on privilege outcomes centered on SDOH, particularly race and socioeconomic status. Data included 18 matched pre- and post-surveys. The MPW assignment resulted in a statistically significant improvement of 1.5 points in recognition of parents' education as a privilege ($p=0.047$). There were similar improvements regarding the recognition of disability status (1.1 points, $p=0.0938$), parents' profession (0.94 points, $p=0.2412$), and race (0.94 points, $p=0.1519$), but findings were not statistically significant. Student responses showed a decline in guilt about personal privilege (-0.11 points, $p=0.7656$). On average, students agreed the MPW assignment made them more aware of their own personal privilege and positively impacted how they will interact with future patients who may be underprivileged. The pre- and post-survey identified SDOH that students, on average, felt gave them more privilege. Parents' education and profession can be linked to socioeconomic status, which could provide more privilege or resources that improve health or quality of life. This pilot project illustrates the need to teach about SDOH and include frank discussions about personal privilege as one component of SDOH. These discussions about privilege may increase quality of healthcare, create more empathetic healthcare providers and leaders, and increase advocacy from pre-health professionals for underserved populations.

13 taVNS treatment: relationship to motor abilities and neuroimaging in at-risk infants

Shelby Davis, Hannah Haskin, Amy Reiner, Hunter Moss, Bashar Badran PhD, Mark George MD, Dorothea Jenkins MD, Turki Aljuhani MA, Patty Coker-Bolt PhD, OTR/L, FAOTA, Patricia Coker-Bolt, Health Professions, Occupational Therapy, MUSC.

Vagal nerve stimulation (VNS) has been shown to promote neuroplasticity and improve motor function in adults post stroke when paired with a motor task. A non-invasive application of VNS, transcutaneous auricular VNS (taVNS), stimulates the auricular branch of the vagal nerve. In a first-in-neonates application, infants who failed to improve oromotor feeding received 2-3 weeks of daily taVNS-paired with bottle feeding at MUSC. With taVNS, 58% successfully attained full oral feeds (responders) vs. 42% who received gastrostomy feeding tube (non-responders). For a secondary outcome, we investigated the relationship of oromotor dysfunction to early global motor skills in taVNS treated babies. Our hypothesis is that the Specific Test of Early infant motor Performance (STEP) and brain neuroimaging before and after treatment may show taVNS treatment effect. Our aims are to determine: 1) the change in total STEP scores in taVNS responders vs non-responders, 2) the change in STEP items of head control which may relate to feeding success in taVNS responders vs non-responders; and 3) whether high or low performance on STEP items of head control relate to diffusion kurtosis imaging (DKI) in infants receiving taVNS. Data for both pre & post STEP assessment and DKI (n=13), and post-STEP assessment and DKI (n= 18) were analyzed using independent sample t-test and Tract Based Spatial Statistics for DKI. While change in total STEP scores were not different between responders and non-responders, scores for head movements in three positions - supine, rolling supine to sidelying, and supported sitting improved significantly in responders to taVNS treatment vs. non-responders. Infants with lower scores on STEP items prone extension and head control in supported sitting had significantly lower values of axonal integrity (fractional anisotropy, FA) in major white matter tracts related to sensorimotor integration and motor control when compared to higher scoring infants ($p<0.05$). This work was supported by the National Center of Neuromodulation for Rehabilitation (NC NM4R), supported by the Eunice Kennedy Shriver National Institute of Child Health & Human Development, and the Pilot project program of the Center of Biomedical Research Excellence (COBRE) in Stroke Recovery supported by the National Institutes of Health under P2CHD086844 and P20GM109040, which were awarded to the Medical University of South Carolina

14 A Program Evaluation of the Medical University of South Carolina's Presidential Scholars Program

Parker Rhoden, Dayan Ranwala, Donna Reinbeck, Debora Brown, Masahiro Kono, Michelle Ziegler, Bryant A. Seamon, Jillian Harvey, Health Professions, Department of Healthcare Leadership & Management, MUSC.

The Medical University of South Carolina (MUSC) developed the Presidential Scholars Program (PSP) in 2001 to facilitate interprofessional collaboration among students from the six colleges and the Charleston School of Law. Participants engage with faculty and alumni scholars as mentors to develop short-term projects to address complex healthcare issues affecting South Carolina communities. We conducted a program evaluation to assess the PSP. Students from the 2016, 2017, and 2018 cohorts were administered a REDcap survey with 19 questions assessing student perceptions of various aspects of the PSP at the conclusion of their experience. Students were asked to respond using a 10-point Likert scale (1=strongly disagree and 10=strongly agree). Descriptive statistics were used to summarize student responses. Composite scores were created by grouping similar questions by theme to assess the following PSP programmatic goals: teamwork/leadership, community engagement, mentorship, interprofessionalism, and education. Open-ended text boxes provided free responses to strengths and weaknesses of the program. A total of 163 students responded to the survey over a span of three student cohorts. The proportion of responses from each student population represented is as follows: Charleston School of Law (12%), Dental Medicine (10%), Graduate Studies (9%), Health Professions (23%), Medicine (17%), Nursing (10%), Pharmacy (20%). Results from this assessment indicate that students felt a greater sense of community engagement (8.6/10) and the PSP better prepared them to work in an interprofessional environment (8.5/10). Responses indicate the following areas can be improved: advancing scholars' leadership skills (7.9/10); ability to work as a team (7.9/10); and the mentorship role of alumni scholars (7.5/10). The interprofessional nature of the PSP was frequently cited as a major strength of the program. In conclusion, the PSP provides a unique opportunity for students to engage in interdisciplinary teamwork across traditional educational silos aligning with MUSC's core values and IMAGINE 2020.

15 Living with neglect: A qualitative analysis of patient perspectives

Nicholas Dean, Katie Dry, OTS, Brianna Eberl, OTS, Hannah Hooks, OTS, Lindsay Manning, OTS, Stacie McLamb, OTS, Emerson Hart, OTR/L, and Michelle Nichols, PhD, R.N., Emily Grattan, Health Professions, Division of Occupational Therapy, Department of Health Sciences and Research, and Ralph H. Johnson VA Medical Center, MUSC.

Neglect is a common impairment after stroke and is characterized by a lack of attention to one side of the person's body or space. There is a lack of existing research exploring the negative impact of neglect on patient independence in activities of daily living, participation, safety awareness, perceived quality of life, and caregiver burden. Current neglect assessments do not provide sufficient information on these topics and do not capture the extent of challenges stroke survivors face. Our aim is to explore ways individuals with neglect experience daily life following stroke, and to identify key themes shared by stroke survivors with neglect. We conducted semi-structured interviews with stroke survivors with neglect using an established interview guide. Interviews were audio recorded and transcribed via Verbalink. Data were analyzed using latent trait content analyses by condensing the text and using abstraction to identify themes. We used investigator triangulation throughout the process. We will report the findings of the initial four interviews conducted as data collection and data analyses are ongoing. Preliminary themes that have emerged include: lack of education, safety concerns, and loss. This work was supported by a Career Development Award-2 grant number 1 IK2 RX002420-01A2 (PI: Grattan, E.) from the U.S. Department of Veterans Affairs, VA Office of Research and Development, Rehabilitation Research and Development, Ralph H. Johnson VA Medical Center, NIH/NCATS grant number UL1TR001450, and an Institutional Development Award (IDeA) from the National Institute of General Medical Sciences of the National Institutes of Health under grant number P20GM109040 (PIs: Kautz, S. & Adams, R.).

16 Tracking the Rising Trend of Student-Run Pro-Bono Clinics in Occupational Therapy Programs

Chandler G. Nash, Britt Harris, Melissa Nettle, Sanica Bendre, Julianne Robertson, Amanda Giles, Patty Coker-Bolt, Tambra Marik, Craig Velozo, Sara Kraft, Gretchen Seif, Karen Wager, Amanda Giles, Health Professions, Occupational Therapy, MUSC.

ISSUE TO BE ADDRESSED: Pro-bono clinics are growing in popularity due to the healthcare benefits to the underserved community and the experiential learning benefits to students. The purpose of this project was to collect information about the number and types of pro-bono clinics that include occupational therapy (OT) as a service, as this has not been identified in the literature. METHOD: OT schools in the United States were contacted via phone using a standardized set of survey questions. OUTCOMES: The following data will be presented regarding OT schools that use a pro bono clinic as part of their educational program: (1) organizational structure, (2) number of patients treated, (3) patient population, (4) faculty/clinician involvement, (5) resources including clinic space and equipment, (6) challenges and solutions, (7) years of operation, and (8) contact information. CONCLUSION: Access to a database with the above information provides (1) instrumental resources to faculty and students who are looking to develop a new pro-bono clinic as part of the curriculum and (2) a guide to new and existing SRFC to promote problem solving and collaboration.

17 Improving Quality of Life for Children with Cerebral Palsy in Vietnam: Implementation of Intensive Models of Rehabilitation

Caitlin Weatherhead, Chandler G. Nash, Rebekah Wade, Sarahjane Zablow, Stephanie Deluca, PhD, Megan Price and Miranda Gerrard, Johan Baudewigns, Patty Coker-Bolt, Health Professions, Occupational Therapy, MUSC.

Constraint Induced Movement Therapy (CIMT) is one of the most widely used treatments for children with cerebral palsy (CP). While CIMT is common treatment in western countries, there is minimal literature on how CIMT is implemented in low-and-middle-income countries. Vietnamese therapists desire to implement evidence-based interventions, but it is unclear how they will deliver CIMT within the context of their healthcare system. Study aims: 1) to determine if two models of pediatric CIMT can be delivered with acceptable fidelity in two rehabilitation settings in Vietnam and 2) to determine if Vietnamese children who receive CIMT will show improved outcomes of motor capacity and performance. This prospective non-randomized study examined the delivery of CIMT in partner hospitals in Vietnam. Therapists at the Hanoi Rehab Hospital delivered a low dose (30 hours) CIMT protocol while therapists in Ho Chi Minh City Children's Hospital delivered a high dose (72 hours) CIMT protocol to 20 children diagnosed with hemiplegic CP. Fidelity to CIMT protocols was determined via video analysis of sessions using a CIMT fidelity measure. Assessments included the ABILHAND-Kids, Pediatric Motor Activity Log (PMAL), Box and Blocks, and the Goal Attainment Scale (GAS) administered at baseline, pre-CIMT, and post-CIMT. Clinicians at the Hanoi Rehab hospital delivered high quality CIMT with acceptable fidelity (n=93 videos); analysis of the Ho Chi Minh City videos is on-going (n=148

videos). Both low and high dose CIMT groups showed a statistically significant difference in ABILHAND Kids and PMAL ($p<0.05$) pre and post-CIMT. Both groups met or exceeded goals (GAS t-scores of 62.7 low dose, 52.8 high dose). This study was the first to examine implementation of high quality CIMT in Vietnam using newly validated outcomes measures. These results will greatly impact the delivery of evidence-based therapy in Vietnam and other middle-income countries. This work was supported by Humanity and Inclusion, USAID Grant,

18 Duck-Duck-Punch: a Rehabilitative Video Game Designed to Improve Recovery of Upper Limb Coordination Post-Stroke

Allison Wheeler, Melissa Nettle, OTS; Morgan Hesse, OTS; Austen Hayes, CEO, Recovr LLC.; Larry Hodges, CFO, Recovr LLC.; Kevin Jett, Software Engineer; Recovr LLC., Christian Finetto, PhD, MUSC; Scott Hutchison, OTD, MUSC, Michelle Woodbur , Health Professions, Occupational Therapy , MUSC.

INTRODUCTION: Stroke survivors have impaired arm coordination characterized by abnormal trunk movement and pairings of joint motions. Recovery of premorbid arm coordination is critical for long-term function. Duck-Duck-Punch (DDP) is a therapeutic video game designed to promote premorbid arm reaching patterns. The purpose of this study is to test effects of a DDP rehabilitation program in promoting premorbid shoulder, elbow, and trunk coordination. METHODS: Secondary analysis of existing data from a large RCT. N=33 subjects >6 months post-stroke were instructed to play DDP 60min/day for 18 days (3 days/week, 6 weeks, 1080 minutes total). Measurements of arm and trunk ranges of motion were taken prior to and immediately after intervention in a Motion Capture research laboratory. RESULTS: Subjects played an average of 15.55 days and 906.79 minutes, although 14/33 (42%) participants exceeded the 18 days and 17/33 (52%) exceeded the 1080 minutes of play. Stroke subjects showed decreased shoulder flexion, decreased elbow extension, and increased trunk displacement prior to treatment as compared to normative values (m=99.6 degrees, sd=37.4; m=128.1 degrees, sd=19.8; m=54.7 degrees, sd=41.4). Post-treatment shoulder, elbow, and trunk values did not show significant changes (m=105.5 degrees, sd=37.3; m=127.4 degrees, sd= 21; m=56.2 degrees, sd= 54.2). Prior to treatment, subjects showed decreased arm inter-joint coordination (m=0.91, sd=0.18), but values did not change post-treatment (m=0.91, sd=0.16) ($p=0.955$). Results show a significant inverse post-treatment arm-trunk inter-joint coordination correlation ($r = -0.742$, $p<0.01$). CONCLUSION: The effect of treatment was statistically insignificant. However, there was a significant correlation between arm and trunk coordination which is consistent with our expectation that recovery of normal movement is functionally advantageous. The data suggests that the time spent playing DDP is not enough to produce significant treatment-induced coordination improvements. We found no evidence that solely using DDP as a rehabilitation tool improves recovery of post-stroke arm coordination. This work was supported by NIH/NINDS Direct to Phase II Small Business Initiated Research (SBIR) Award, #R44NS097061, NCT03053492, mPIs: ML. Woodbury and A. Hayes., NIH/NIGMS Institutional Development Award (IDeA), P20GM109040, PI: S. Kautz.

19 "There is no 1-800 number to fix it.": A qualitative study capturing views of stroke survivors. Amber Linnen, Brittany Pinson, Samantha Brophy, Michelle Nichols, Michelle Woodbury, MUSC.

Amber Linnen, Samantha Brophy, Brittany Pinson, Michelle Woodbury, Michelle Nichols, Health Professions, College of Nursing , MUSC.

Each year, ~795,000 people have a stroke and 84% report reduced quality of life (QoL) at 2 years post stroke. The factors contributing to reduced QoL are not clear, thus there are few interventions to improve long term QoL. The purpose of this study is to identify specific unmet needs of stroke survivors from the perspectives of survivors, caregivers and providers in order to create new therapy and/or public health interventions. A qualitative analysis of existing data collected during a federally funded stroke rehabilitation community engagement project. In 1:1 interviews, stroke survivors (n=3, average age of 41, 1-10 years post stroke), a caregiver (n=1), and therapists (n=2) responded to stroke-related semi structured interview questions about the recovery process, changes, and ongoing unmet needs. Interviews were transcribed and then analyzed using content analyses methods to determine recurring themes. The analyses revealed 12 sub-themes which were then grouped into 6 themes indicating patient, therapist, and caregiver frustrations that occur during the stroke recovery process. Themes included financial counseling, stable support systems, recovering social identity, insurance plans, and community and public health education. The unmet needs expose a deficiency in treatment methods and thus provides an opportunity for intervention implementation in future research efforts. Stroke recovery differs among all survivors, but commonalities of struggle were found. The interviews gave participants the opportunity to speak candidly and voice suggestions for improvements in treatment approaches in the future. Incorporating stroke caregivers and therapists yields a new perspective. Insight was gained on the importance of therapist- client relationships, advocacy, and positivity in stroke recovery. Findings can be used to assist with the implementation of new interventions addressing unmet needs, specifically, assignment of specialized financial advisors and public health initiatives to increase stroke education and awareness. This work was supported by PCORI Pipeline to Proposal Tiers I-III Awards, NIH/NIGMS Institutional Development Award

20 Alginate-RGD hydrogel and bioactive glass: mechanical properties and cellular properties

Dustin Mueller, Qing Hong, Brian Gibson, Brittany Moore, Douglas Beals, Elizabeth Hull, Alireza Moshaverinia, John Mitchell, Dental Medicine (DMD, PhD), College of Dental Medicine, Midwestern University, MUSC.

Bone graft materials are commonly used in the dental field to fill extraction sites, periodontal defects, dental trauma sites, and as sinus augmentation materials to name a few. Bone grafting is important to maintain facial structure after such an event as the bone will start to recede from the site. There are a few forms of bone grafting materials and one is the alloplastic bone graft. These are synthetic materials. Alginate-RGD and bioactive glass (BAG) are two alloplastic bone graft materials. Alginate-RGD is a hydrogel material that allows for encapsulation of cells and growth factors. This may provide the site with mesenchymal stem cells (MSCs) which can differentiate into osteoblasts and allow for improved healing. BAG has the ability to corrode to form hydroxylapatite, while releasing calcium and phosphate ions into the local environment. The ion concentration and the subsequent change in pH also provide antimicrobial properties to the local environment. These two materials are currently being researched independently. This project aimed to find the optimal concentration of bioactive glass to add into the alginate-RGD hydrogel to promote growth and differentiation of encapsulated mesenchymal stem cells. This project also accomplished preliminary work in establishing a model to test this novel construct's antibacterial properties. To determine the optimal concentration this project tested the mechanical properties of mixtures, measured proliferation and viability differences and finally looked at the differentiation potential of the BAG/alginate-RGD hydrogel. We hypothesized that there was an optimal amount of bioactive glass that can be added to allow for injectability and without affecting the viability of the encapsulated mesenchymal stem cells. Bioactive glass is expected to increase the modulus of the hydrogel because the glass will increase the viscosity. The combination of these materials

has the potential to speed healing and increase the density of the bone. This work was supported by Midwestern University, College of Health Sciences

21 Analytical Insights into the Use of Collagen Volume Fraction and Endothelial Markers as Diagnostic Tools in Heart Failure Histomorphometry

Adegboyega Adewale, , Amy Bradshaw, Medicine (MSTP, MD years), Gazes Cardiac Research Institute; Ralph H. Johnson VA Medical Center; Department of Medicine, MUSC.

Background and Objectives: Heart failure with preserved ejection fraction (HFpEF) is a significant cause of morbidity and mortality in the general population and is associated with increased amounts of myocardial collagen. In response to myocardial injury, such as infarction, circulating monocytes adhere to activated endothelium, infiltrate tissues, and mature to macrophages that contribute to increased collagen deposition. The role of monocyte/macrophages in HFpEF progression however, is less characterized although increased numbers of macrophages are associated with tissue sections from patients with HFpEF. The distribution of endothelial adhesion proteins, serving as markers of activated endothelium, coupled with quantification of collagen deposition in tissue biopsies might provide valuable insight into cellular mechanisms of disease. Methods: Tissue sections from three healthy and three heart failure subjects were processed for immunohistochemical staining with antibodies generated against intercellular adhesion molecule 1 (ICAM-1), a marker of activated endothelium. Left ventricular biopsies from five subjects with heart failure and healthy controls were processed for collagen volume fraction analysis with picrosirius red staining. Collagen volume fraction and ICAM-1 immunoreactive vessels in human tissue sections were quantified. Results: In comparison with healthy controls, levels of ICAM-1 positive vessels were greater in sections from subjects with heart failure ($P<0.05$). In addition, the total area of ICAM-1 staining was significantly greater in the heart failure group ($P <0.005$). A linear regression analysis model showed a linear relationship between ICAM-1 antigen count and total area of ICAM-1 expression on the slide ($R2=0.79$, $P <0.0001$). Ordinary one-way ANOVA showed a significant difference in collagen volume fraction among healthy controls and heart failure ($P <0.05$). Conclusions: Histomorphometric analyses of molecular staining patterns in tissue sections from patients with HFpEF is a useful tool for studying molecular marker distribution to aid in the elucidation of cellular mechanisms of heart failure and potentially as diagnostic tools. This work was supported by VA Merit Award: 1 I01 CX001608 (AD Bradshaw); NIH TPMS 2T32GM008716-21 (AT Adewale)

22 Impact of Pharmacist Led Diabetes Education and Management at a Federally Qualified Health Center

Ryan Rosenblatt, Samuel Mcgee, Erin Weeda, James Sterrett, Pharmacy, College of Pharmacy, MUSC.

Introduction: The most recent CDC reports on diabetes statistics show that 8.5% of adults in the United States were diagnosed diabetes in 2016. This compares to 11.5% in the state of South Carolina and 9.5% in Charleston County, South Carolina over the same period. The CDC also reports that 86% of adult South Carolinians with diabetes visited a health care provider for a diabetes visit in 2015 and even less attended preventative services like a diabetes self-management class or had two or more A1c checks in a year, 54% and 69.2% respectively. Pharmacists have shown during the Asheville project that they may provide diabetes education and management services to patients that result in significant positive outcomes like decreased healthcare expenditures, decreased hospitalizations, and improved A1c. The primary objective of this work is to evaluate the impact a pharmacist led diabetes education program can have on the population at a Federally Qualified Healthcare Center in Charleston County, South Carolina. Methods: Single center, retrospective, cohort study of adult patients with diabetes mellitus type 2 who had at least one diabetes education visit between January 1, 2018 and February 1, 2019 and who had at least one A1c value recorded before and after the visit. Data collection occurred retrospectively through electronic medical record reporting. Results: 193 patients were included in the study of the 290 participating in diabetes education programming. The median (IQR) beginning A1c was 10.1% (8.9 to 11.8%) and the median (IQR) ending A1c was 8.7% (7.6 to10.3) which is a 1.4 point decrease (p value <0.001). Conclusions: Pharmacist led diabetes education and management services at a federally qualified healthcare center contributed to a significant reduction in patient A1c to levels. This work was supported by DUKE ENDOWMENT

23 Community-Based Experiential Learning: Using an Interprofessional Student-Run Free Clinic to Enhance Student Collaboration and Critical Thinking

Emily Harrison, Megan Lebov, Stacie McLamb, Tambra Marik, Karen Wager, Patty Coker-Bolt, Craig Velozo, Sara Kraft, Gretchen Seif, Amanda Giles, Health Professions, Department of Occupational Therapy, MUSC.

ISSUE TO BE ADDRESSED: Student-Run Free Clinics (SRFC) are a rising trend in health professions education that bridge the gap between the classroom and the clinic. The CARES SRFC is a well-established, non-profit, SRFC that has been offering physical therapy and occupational therapy services to uninsured and underserved individuals for over nine years. The purpose of this study was to collect student perceptions of the impact of participation in the CARES SRFC. METHOD: Occupational therapy (OT) and physical therapy (PT) students completed an anonymous, online survey related to the benefits of participation in the SRFC as well as areas for improvement. OUTCOMES: Survey responses were analyzed using descriptive statistics and thematic content analysis to reveal student perceptions on the impact of participation in the CARES SRFC on confidence, documentation, leadership, clinical reasoning, interprofessional collaboration, and understanding of the health care needs of the underserved population. Specific areas for improvement were also recognized. CONCLUSION: Participation in a SRFC can improve student clinical skills needed for future practice through hands-on treatment with patients in need of therapy services. This work was supported by N/A Program Evaluation

24 Survival Outcomes of Donation After Cardiac Death Kidney Transplant: Is it Worth It?

Allison Kuhn, Faisal Alanazi, Nicole Pilch, Pharmacy, College of Pharmacy, MUSC.

Introduction: Donation After Cardiac Death (DCD) increases warm ischemia time which may result in increased delayed graft function. In this study, we evaluated the impact of DCD kidney donors, recipients, and transplant characteristics on recipient outcomes. Study design: A retrospective, single center, cohort analysis evaluating the outcomes of DCD kidney transplantation in adult patient. Methods: The donor's baseline characteristics were obtained from the Standard Transplant Analysis and Research (STAR) file and the recipient data was collected from electronic medical records at the Medical University of South Carolina for all DCD transplants from 1/1/2017 to 6/30/2019. Data was

collected and adjudicated to the cut-off point of day-90 eGFR of 30 ml/min evaluating graft function. Appropriate tests were used to analyze the data utilizing the SPSS software package. Results: A total of 97 DCD kidney recipients were analyzed. Group 1, patients with a day- 90 eGFR <30ml/min, encompassed 19.5% (n=19/97) of the cohort. Group 2, patients with a day-90 eGFR > 30 ml/min, encompassed 80.5% (n=78/97). Overall, there was a total of 190 re-admissions within the first year and only 4% (n=4/97) had rejection. Group 1 had a significantly higher mean Kidney Donor Profile Index (KDPI) scores, need for dialysis up to day-30 post-transplant, and average Cold Ischemia Time (CIT) (52.3% vs 40.5%, p=0.022), (21.1% vs 3.8%, p=0.026) and (20.7 hrs vs 17.4 hrs, p=0.025) respectively. Specifically, a CIT of more than 24 hrs was more frequent in group 1 (31.6% vs 11.5%, p=0.03). Conclusion: Salient donor characteristics have not been identified to explain decreased kidney function measured at day 90. From a value proposition aspect, the value of accepting a DCD kidney remains uncertain when considering increased number of hospital re-admissions and overall burden for some patients.

25 Can Pre-Clinical Students Correctly Identify Pain Mechanisms and Apply Pain Neuroscience Education while Treating a Patient in a Student-Run Free Clinic? Yes!

Courtney Mason, Spencer Cowen, Gretchen Seif, Health Professions, Department of Physical Therapy, MUSC.

Background/Purpose: Current literature indicates that pain neuroscience education (PNE) is a useful tool in the treatment of patients with nociplastic pain and that pre-clinical students can correctly distinguish between pain mechanisms. However, the extent to which pre-clinical students can apply PNE to the treatment of a patient with nociplastic pain is not established. The purpose of this study is to describe the evaluation and treatment of a patient with persistent pain provided by pre-clinical students at a student-run free clinic. Case Description: The patient was referred to a student-run free clinic with a history of persistent, global pain. The students hypothesized that the patient had symptoms consistent with nociplastic pain. The students used a multifaceted treatment approach to reduce pain, improve overall fitness, and equip the patient with healthy coping techniques. Treatments included aerobic and strength training, manual therapy, relaxation exercises, lateralization training, and pain neuroscience education to address patient's concerns about memory and emotional changes due to her pain, allodynia, and hyperalgesia. All care was supervised by a licensed physical therapist. Outcomes: At initial visit, the patient stated on a Likert Pain Scale that her worst pain was 10/10 and best pain was 5/10. At discharge she reported a clinically meaningful change of 8/10 and 2/10, respectively (MCID=2). A body chart was administered at the fifth visit; the patient marked 32 painful sites and only 15 sites at discharge. After 10 sessions, the patient believed herself to be "moderately better." Discussion/Conclusion: This case study demonstrates that pre-clinical students can correctly identify the pain mechanism and apply PNE in the treatment of a patient with nociplastic pain. Future, more robust research is needed to demonstrate the viability of this approach as a model for preclinical student education in treating patients with nociplastic pain.

26 Literature Review of Blood Flow Restriction Resistance Training

Mitchell Tanner, Stephanie McGowan, Health Professions, Assistant Professor in the Department of Health Professions, MUSC.

Blood flow restriction resistance training (BFR-RT) is a process where a blood pressure cuff applies pressure to the distal portion of either upper or lower extremities to improve physiological deficits. The goal of the pressure is to be at a percentage where venous return is limited but arterial flow is still permitted. Effectively the individual participating in BFR-RT can place minimal strain on their musculoskeletal structures while still making strength and hypertrophic gains. Blood flow restriction resistance training (BFR-RT) at low loads has been linked to gains in muscular strength, hypertrophy, and power [7, 9, 10, 11, 12] that are comparable to those with traditional high-load resistance training and has also shown positive effects for pain management. There has been research surrounding BFR that examines training effects and cellular pathways. However, definitive clinical guidelines have not been established. A search was performed on PubMed and Scopus with the key phrase "blood flow restriction" and additionally the following terms: anterior cruciate ligament, strength, hypertrophy, knee, ankle, and rehabilitation. The purpose of performing this research allowed for examination of the current state of knowledge as well as subsequent gaps in the current understanding of BFR. Recognizing these deficits will allow for future research to be conducted so that clear clinical guidelines may be established.

27 Transcutaneous Electrical Stimulation Therapy in Obstructive Sleep Apnea

Young Jae Byun, Flora Yan, Shaun Nguyen, Eric Lentsch, Medicine, Department of Otolaryngology - Head and Neck Surgery, MUSC.

Objective: To evaluate the treatment efficacy of transcutaneous electrical nerve stimulation (TENS) in patients with obstructive sleep apnea (OSA). Methods: Systematic review was conducted by querying databases (PubMed, Scopus, OVID, and Cochrane Library) for primary articles published through July 2019. The search identified randomized controlled trial, randomized comparison, or observational studies pertaining to TENS treatment for OSA. Meta-analysis was performed on pre- and post-treatment apnea-hypopnea index (AHI), mean oxygen saturation (SaO2), nadir oxygen saturation (LSAT), and arousal index (AI). Results: Literature search identified 10 studies that reported sufficient outcome measures to be considered for analysis. A total of 198 patients were identified with a mean age of 50.9 years with male to female ratio of 1.6:1. Average body mass index (BMI) of the cohort was 29.8 kg/m2. Treatment with TENS demonstrated reduction in AHI by 12.9 points [95% CI -22.3 to -3.43] (p = 0.008). Some improvements were observed in SaO2, LSAT, and AI but mean differences in these parameters did not reach statistical significance. Conclusion: The TENS treatment of upper airway dilator muscles resulted in reduction of AHI in OSA patients. However, its effect on SaO2, LSAT, and AI were equivocal. Its impact on patient's quality of life could not be assessed due to heterogeneity in outcome measures. Future randomized controlled trials with generalizable standardized outcome measures are needed to assess the efficacy and compliance of TENS.

28 Are Ankle Motor Control and Balance Post Stroke Related?

Rebecca Angles, John H Kindred PhD, Jesse C Dean PhD , Mark Bowden, Health Professions, College of Health Professions, MUSC.

Purpose: The purpose of this study is to investigate the role ankle motor control plays in balance. Our current hypothesis is that individuals post-stroke who have poor ankle motor control will perform worse on dynamic balance tests. Methods: Five healthy controls (age 27.5years SD 6.8, ht. 68.0 in SD 3.3, wt. 159.0 lbs SD 33.2) and two with chronic stroke (age 58.5years SD 3.5, ht. 63.5in SD 3.5, wt 196.5lbs SD 18.5) have so far completed testing. Participants performed a seated plantarflexion/dorsiflextion motor control task in during which they were

provided with visual feedback of their ankle angle. Participants were told to match their ankle position to projected sine wave set to 0.2, 0.3, and 0.6 Hz. Balance was assessed with the sensory organization test (SOT) performed on a computerized posturography device under six different conditions. Results: Average motor control error was worse in the stroke group at all three levels (0.2Hz, Healthy 2.9 SD 0.8, Stroke 5.0 SD 5.0; 0.3Hz, Healthy 2.9 SD 0.9, Stroke 4.9 SD 1.6; 0.6Hz, Healthy 5.1 SD 1.0, Stroke 9.4 SD 2.3). Balance composite scores were also worse in the stroke group (Healthy 84.2 SD 3.6, Stroke 46 SD 11). In the stroke group, the visual component of the composite score was found to be less in the individual with the greater motor control error (stroke participant 1: visual score 72, motor control error 4.5 degrees; stroke participant 2: visual score 25, motor control error 8.4 degrees). Conclusions: In the stroke group, the individual with a lower balance composite score and visual sub-score had more motor control error than the individual with a higher balance composite score and visual sub-score. These findings indicate a potential association between ankle motor control and balance. Further testing is required and is ongoing.

29 Determinants and Distractors in Gauging Surgical Skill in Mastoidectomy

Andrew Rowley, Joshua Lee, Michaela Close, Yuan Liu MD, Mitchell Isaac MD, Ted Meyer MD PhD, Ted Meyer, Medicine, Otolaryngology, MUSC.

Rationale: Assessment of surgical skill has primarily been a subjective measure. Recent interest has been exhibited on developing objective means to measure a surgeon's skill. We aimed to determine if surgical skill during a mastoidectomy could be assessed using animated videos that showed only the burr head of the drill and removed other aspects of the surgery. Methods: 24 intra-operative videos of 12 surgeons performing mastoidectomies were sampled during the second minute of drilling. Using 5-second clips, 3 experts (1 fellow, 2 residents) made quantitative measurements of drill movements, qualitative judgments of surgical technique, and rated the surgeons' training level. The same assessment was then performed using animated videos which showed only the path of the burr head as dots against a white background. Results: The estimated level of the surgeon was highly correlated between the original and animated videos ($r=0.60$, $p<0.01$). Ratings of surgeon efficiency in the original videos were significantly correlated with the surgeon's true level ($r=0.63$, $p<0.01$), estimated level on the original video ($r=0.71$, $p<0.001$), and estimated level on the animated videos ($r=0.66$, $p<0.001$). The number of strokes on the original and animated videos were significantly correlated with the surgeon's estimated levels ($r=0.45$, $p<0.03$; $r=0.51$, $p<0.01$). Conclusions: Animated videos of the drill head provide similar results as recorded surgical videos when used in making quantitative measurements of drill movements, qualitative judgments of surgical technique, and rating surgeons' training levels. In the future, perhaps a computer program could adequately capture and quantify characteristics of surgical performance, opening the possibility for new objective methods of surgical evaluation.

30 ADAMTS5-mediated cleavage is required for subchondral bone formation in the mandibular condyle

Alexandra Rogers-DeCotes, Sarah C. Porto, Christine Kern, Dental Medicine (DMD, PhD), Regenerative Medicine and Cell Biology, MUSC.

Abstract Withheld from Publication

31 Open Reduction Internal Fixation of Distal Radius Fractures: Retrospective Cohort Analysis of the Geriatric Population using the NSQIP Database

Narayan Raghava, Anna Skochdopole BS, Brian Mailey MD, Sami Taribishy MD, Steven Hermiz MD, Fernando A Herrera MD, Medicine, Division of Plastic and Reconstructive Surgery, MUSC.

Purpose: Distal radius fractures (DRF) are the most common upper extremity fractures and account for up to 18% of fractures in the geriatric population. The purpose of our study was to identify the influence of patient age on 30-day postoperative outcomes while adjusting for patient demographics and comorbidities. Methods: The NSQIP database was queried for all patients having undergone open reduction internal fixation (ORIF) of DRFs. CPT codes, 25607, 25608, 25609 between the years of 2007 to 2016 were collected and analyzed. Patients were divided into 2 groups based on age; Group 1: 18-64 years; Group 2: 65 years and older. Patient demographics, preoperative, perioperative, and postoperative variables, and complications were recorded and analyzed. Results: A total of 5894 patients were identified; Group 1 included 4056 patients between the ages of 18-64 and Group 2 consisted of 1838 patients ages 65 and older. Total complication rate was 2.7% for all patients, 2.2% for Group 1, and 3.4% for Group 2. The most common complications included; superficial surgical site infection for Group 1 and UTI for Group 2. Univariate analysis demonstrated association between age ≥65 and complication (HR 1.55, 95% CI [1.12 – 2.14], $p=0.009$). However, after controlling for statistically significant clinicopathologic factors, age was not an independent predictor for complications (HR 0.92), 95% CI: [0.62 – 3.44], $p=0.685$). Admission status, ASA classification, total operative time, renal failure requiring dialysis, and bleeding disorders were independent predictors of 30-day complications across all patients. Conclusion: Age is not an independent risk factor for postoperative 30-day complications. Our data suggests that patients 65 and older with an optimal risk profile should not be contraindicated from undergoing surgery for ORIF of DRF. Further, preoperative variables can serve as valuable predictors of complication for patient/family counseling and clinical decision-making regardless of age.

32 Diagnosis, treatment, follow up, and persistence of Trichomonas vaginalis in women over age forty-five according to HIV status: a ten-year retrospective cohor

Allyson Hill, Tarleton Jessica, Soper David, Gwenth Lazenby, Medicine, OBGYN, MUSC.

Trichomonas is the most common treatable sexually transmitted infection among older women. Persistent Trichomonas infection after treatment is common among women with HIV. We sought to determine if HIV negative women were as likely as women with HIV to have persistent Trichomonas infection. We performed a retrospective cohort study of women > 45 years of age with Trichomonas infection. We evaluated differences in persistent Trichomonas infection according to HIV status using chi-square analysis. We performed regression analyses to describe factors associated with persistent and recurrent infection in older women. Over a ten-year study period, we identified 282 women with Trichomonas, 46 with HIV. Most women (240, 85%) were treated in accordance with 2015 CDC STD treatment guidelines. Half of women (144, 53%) had a repeat Trichomonas test 90-365 days after treatment, and one-third had persistent infection (39/125, 31%). Persistent infection was similar between women with HIV and HIV negative women treated according to CDC recommendations (17% vs

33%, p=0.3). When adjusting for age and incidental diagnosis, tobacco use was associated with an increased risk of > 1 or recurrent Trichomonas infection during the study period (aOR 2.8, 95% CI 1.5-4.9). HIV status did not affect persistent Trichomonas infection in women > 45 years of age. Given over one-third of women have a positive test within a year following recommended treatment, we recommend repeat testing in women > 45 treated for Trichomonas.

33 Germ Busters: Environmental Care for the Prevention of MBI CLABSIs in pediatric oncology patients

Stephanie Gehle, Jessica Howard, Brooke Criddle, Corinne Corrigan, Elizabeth Mack, Medicine, Pediatrics , MUSC.

Pediatric hematology/oncology patients are at high risk for central line bloodstream infection (CLABSI) due to immunosuppression, high device utilization, and mucosal barrier injury (MBI) related to chemotherapy. We aim to achieve 90% compliance with adjunct CLABSI prevention bundles (daily care, oral care, environmental care) in the pediatric hematology/oncology population in an effort to reduce CLABSI. We began a series of plan-do-study-act cycles aimed at improving compliance with the adjunct CLABSI bundles for pediatric oncology patients. In October 2016, our quality team began monthly meetings with bedside nurse champions, oncologists, environmental services, infection prevention, and nurse techs to identify system barriers. In May 2017 we implemented oral care and daily care bundles on the unit, including toothbrushing, mouthwash, lip balm, daily chlorhexidine treatments, linen and clothing change. In February 2018 an order set including adjunct bundles was implemented. In summer 2018 we conducted daily real-time audits and provided the team with feedback to improve compliance. We began auditing routine and terminal room cleaning using GloGerm on high-touch surfaces to share data feedback with environmental services. In November 2018 our oncologist implemented levofloxacin prophylaxis. In December 2018 we implemented prompts in the electronic health record for each adjunct bundle element. In June 2019 we began to track terminal cleans and 30-day room changes in the EHR and alert charge nurses when patients are approaching the 30-day limit so they can be moved to a clean room. We have had one MBI CLABSI in 1/1/18 - 5/31/19 (Figure 1). Compliance with deep clean and high touch surfaces has improved with HAC documentation and robust team feedback using GloGerm and EHR monitoring of room changes for terminal cleans (Figures 2, 3). We demonstrate preventability of MBI CLABSIs in this immunocompromised population concurrent with an increase in environmental care bundle compliance.

34 Breastfeeding among Women with Systemic Lupus Erythematosus (SLE)

Erin Hynd, Jim C. Oates, MD, Gary S. Gilkeson, MD, Diane L. Kamen MD, MSCR, Diane Kamen, Medicine, Rheumatology and Immunology, MUSC.

Background: Systemic lupus erythematosus (SLE) is a chronic autoimmune condition which disproportionately affects childbearing age women. Aspects of both the disease and the medications required to treat the disease can impact the likelihood of a successful pregnancy and the ability to breastfeed. Our hypothesis is that women with SLE are less likely to breastfeed compared to non-SLE controls, and that women with SLE have a shorter duration of breastfeeding when compared with non-SLE controls. Methods: Data was obtained from an ongoing longitudinal registry of patients with SLE and non-SLE population-matched controls. Information on demographics, medical, social, pregnancy and breastfeeding history, and SLE characteristics (if applicable) was gathered from in-person interviews. Chart review and telephone follow-up was done for missing values. Males and children were excluded from the study population. Pearson's chi-squared testing was performed for categorical measures. Results: Our study included a total of 789 women who had at least one live birth (374 with SLE and 415 controls) and 362 women with SLE with no history of a live birth. With the exception of renal disorder, none of the classification criteria used to characterize SLE significantly differed in prevalence between women based on breastfeeding history or history of live birth. Women with SLE and a history of renal disorder were significantly less likely to be mothers (57.8% vs 42.3%, $p<0.01$) and were less likely to have breastfed although not statistically significant (60.7% vs 39.3%, p=NS). Conclusion: In our study of women with SLE, a history of renal disorder (lupus nephritis) was a major factor influencing the likelihood of a successful pregnancy and appears to influence subsequent breastfeeding, although sample size was limited. We continue to investigate further into aspects of lupus nephritis, including modifiable risk factors, influencing pregnancy and breastfeeding outcomes. This work was supported by Funding for this project was made possible by the National Institutes of Health under award numbers: NIAMS P30 AR072582 (Gilkeson, Oates), NIAMS K24 AR068406 (Kamen), and NCRR UL1 RR029882 to MUSC. There are no other relevant financial disclosures.

35 taVNS for oromotor infant feeding I. Development of a closed loop delivery system

Sean Thompson, Daniel Cook, Morgan Dancy, William H. DeVries, Georgia Mappin, Philipp Summers, Marom Bikson, Sarah Huffman, Sasha Stomberg-Firestein, Mark S. George, Dorothea D. Jenkins, Bashar Badran, Medicine, Psychiatry, MUSC.

Vagus nerve stimulation (VNS) delivered during specific behaviors facilitates neuroplasticity Cervically implanted VNS is expensive and invasive. Transcutaneous auricular vagus nerve stimulation (taVNS) is a new non-invasive alternative. We have piloted it to enhance learning oromotor suck-swallow skills in neonates with brain injury or brain dysmaturation. This was initially manually-triggered. In order to make it more efficient, we developed and adjusted a novel, closed-loop, motor-activated, auricular VNS (MAAVNS) rehabilitation system. MAAVNS senses feed-related engagement of facial muscles via EMG and delivers taVNS during the suck-swallow. We compared the manual versus closed loop taVNS setup, in terms of the number of pulses delivered, length of an average train of pulses, heart rate changes, side effects, as well as clinical outcomes. For this analysis we present results from infants who were clinically determined to require g-tubes in this prospective, open-label phase-0 trial. We delivered taVNS concurrently with daily bottle feeding, triggered manually (n=5) or by buccinator muscle electromyography (EMG, n=13). Pulses were delivered via left ear electrode at 0.1mA less than perceptual threshold, frequency 25Hz, pulse width 500µs. For the manual operation, current was delivered with suck-swallow, off with rest, or, if the baby was continuously feeding, up to 2 minutes followed by 15 second rest. After using MAAVNS on 4 infants, we adjusted the train length from 3 to 10 seconds to more closely approximate the suck-swallow motor sequence and the dose delivered manually. For the 9 infants receiving MAAVNS with 10sec train, total number of pulses delivered per feeding session were not significantly different (20,220±6,242 pulses manual, 15,359±3,422pulses MAAVNS, p=0.16). No differences were found in terms of heart rate changes for safety or tolerability. A MAAVNS system is accurate and simplifies the technology for widespread acceptance in clinical settings. Automated taVNS-paired motor rehabilitation appears safe in neonates. This work was supported by Funding: The National Center of Neuromodulation for Rehabilitation (NC NM4R) NICHD, NIH P2CHD086844; SC Center for Stroke Recovery, COBRE, P20 GM109040. Industry Collaboration

36 Publishing Trends in Velopharyngeal Insufficiency

Charles Poff, Joshua Horton MD, Ryan Boerner MD, Alex Marston MD, Shaun A. Nguyen MD , David White, Medicine, Otolaryngology, MUSC.

Objective: This study seeks to describe publishing trends for VPI over a 33-year span with regard to treating specialty, methods of assessment, related diagnoses, and methods of treatment for each specialty. Methods: A PubMed search was performed on "velopharyngeal insufficiency" using medical subject headings terms from 1985-2017. Publisher specialty, method(s) of VPI assessment, associated diagnosis/diagnoses, and method(s) of VPI treatment per specialty and combined across specialties were analyzed. Respective publications were totaled in 11-year intervals and two-way analysis of variance was used to compare change over time within specialties and across specialties. Results: 763 publications were included for analysis. The total number of publications on VPI increased from a total of 6 in 1985 to a peak of 67 in 2015. The specialties that showed the largest increase in relative frequency of publication were Otolaryngology ($p<0.001$), Plastic Surgery ($p<0.001$), and Multidisciplinary ($p <0.001$). Publications on endoscopic ($p<0.001$) evaluation of VPI have significantly increased over time relative to magnetic resonance imaging and lateral cephalometry. Across all specialties, publications that feature pharyngoplasty ($p<0.001$), palatoplasty ($p<0.001$), and pharyngeal flap ($p<0.001$) as methods of VPI treatment have significantly increased over time. Conclusion: There is a trend towards endoscopy for diagnostics and a multidisciplinary approach when managing patients with VPI. The specialty that showed the largest increase in the relative frequency of publication was Otolaryngology. Surgical methods of treatment continue to be described at increasing frequency relative to more conservative treatments.

37 Adolescents Proceeding to Weight Loss Surgery Have Higher Parent and Self-rated Quality of Life

William Head, Aaron Lesher MD, Molly Jones RD, Sharlene Wedin PsyD, ABPP, Lillian Christon PhD, Nina Crowley, Medicine, MUSC Health Bariatric Surgery Program, MUSC.

BACKGROUND: Among adolescents with severe obesity, earlier intervention with weight loss surgery (WLS) has been associated with better long term outcomes. It is unclear if quality of life (QOL) plays a role in successful completion of WLS. METHODS: Adolescents seeking WLS (M age=15.7±1.4 years; BMI=52.49±6.12 kg/m2; 68% traditional school; 29% parent had WLS; 39% male; 54% African American, 39% Caucasian, 7% other race/ethnicity) at an academic medical center's Bariatric Program from 6/2017-1/2019 were included (N=28). As part of a comprehensive pre-surgical psychosocial evaluation, patients/parents completed the Pediatric Quality of Life Inventory (PedsQLTM 4.0 Teen and Parent Report for ages 13-18) to measure QOL in the core areas of physical, psychosocial, emotional, social and school functioning. Patients/parents were asked a single General Self-Rated Health Question (GSRH) (1=poor; 5=excellent). RESULTS: Half of those evaluated went on to have WLS (N=14). Surgery completers had higher self (M=79.2 vs 56.7, p=0.010) and parent-rated school QOL (M=76.8 vs. 52.9, p=0.012). There were no differences between groups on GSRH, but surgery completers had significantly higher scores on parent assessment of their GSRH (M=2.71 vs. 1.88, p=0.31). CONCLUSION: Results suggest that WLS-seeking adolescents with less perceived impairment (higher school QOL and higher parent-rated health status) are more likely to go on to WLS. QOL seems to be a particularly relevant index and may be able to help teams identify patients for which a low QOL domain prevents them from proceeding to surgery. Future research may examine the post-surgical outcomes in adolescents related to QOL.

38 Understanding the Preventability of our Pediatric Readmissions

William Cornwell, , Elizabeth Mack, Medicine, Pediatric Critical Care, MUSC.

Background: Readmissions for pediatric patients are stressful for patients and their parents and cost an average of $11,000 per readmission (1). In 2018 Our readmission rate increased to 3.796 remissions per 100 discharges (Figure 1), well above the SPS centerline (3.039). Objectives: Our aim is to identify modifiable factors that may contribute to readmission for pediatric patients and provide timely feedback to practitioners involved in patient care. Methods: We created surveys that were sent out to the members of the discharging and readmitting care teams for patients who returned to the hospital within seven days of a previous admission. We excluded scheduled readmissions for chemotherapy and EEG. Surveys were sent to Attending Physicians, Residents, Case Managers, and Social Workers. Results: We sent out 232 surveys between March 15th 2019 and June 15th 2019 and achieved a response rate of 50.6%. These surveys covered 77 unique patients with 44 patients having at least 1 survey that was completely answered. Respondents marked 9% of these readmissions as "preventable." Attending physicians completed the most survey out of any category of respondents accounting for 48.6 percent of completed surveys. Reason for readmission was marked as a medical condition related to the prior admission 50.8% of the time. For readmitted high risk patients, 17.4% of respondents indicated that there was no specialized care plan and 30.4% were unsure if there was a specialized care plan. Conclusions/Implications: Caregivers identified a variety of factors that played into readmissions including inadequate patient education, access to supplies, caregiver health literacy, delayed follow up, inability to schedule follow up appointments on weekends, failure to provide a contingency plan, and one instance of self sabotage. In the future, better engagement with Social Workers and Case Managers as well as more thorough discharge instructions and planning may prevent some readmissions.

39 Birthing Experience of Obese Parturients: Quality of Care During Pregnancy, Labor and Delivery

Matthew Turner, Zeiler Lydia, Joel Sirianni, Medicine, Anesthesiology, MUSC.

Obesity is an ever-increasing health concern. Obese patients often perceive weight stigma from their physicians, negating the trust necessary in the patient-physician relationship. The goal of the current study is to determine whether the perception of quality of anesthesia care differs between the obese and non-obese parturient at MUSC from labor to the immediate postpartum period. Postpartum participants were given a survey containing 22 questions pertaining to quality of care, with a majority of questions measured on a 5-point Likert scale. Demographic, obstetric, and neonatal data was collected from the patient's electronic medical record. Out of 981 total participants, 598 had a BMI equal to or greater than 30, while 373 had a BMI less than 30. A two-sample T test found that there was no significant difference ($p=0.1172$) between the mean overall pain reported by obese and non-obese postpartum women. When BMI was directly compared against reported pain, a linear regression model yielded a weak correlation coefficient of 0.682595 and a weak R-squared value of 0.465936, indicating that BMI and pain were not significantly related. A chi-square test of homogeneity between patient

satisfaction (ranked in five categories from Very Satisfied to Very Dissatisfied) of obese and non-obese patients was not statistically significant, indicating that there was no significant difference between the distribution of responses in the two groups. Although this study is over halfway to its stated goal of 1720 participants, the preliminary data suggests that there is not a significant relationship between patient BMI and reported pain. In addition, there was no significantly different distribution of responses in regard to patient satisfaction between obese and non-obese women. This suggests that, in terms of obstetric anesthesia, obese patients neither receive, nor believe that they have received, lower quality of care in comparison to non-obese patients. This work was supported by Anesthesiology Department of MUSC

40 Long-term Effects of Thyroid Procedures on Weight Change

Parker McDuffie, Reece Moore, Paige Broadley, Dr. Carneiro-Pla, Mahsa Javid, Medicine, Surgical Oncology, MUSC.

Background: Patients undergoing thyroid procedures are often concerned about the potential to gain weight postoperatively. Research on whether patients gain weight or not following lobectomy or total thyroidectomy procedures is somewhat inconclusive, though. Some studies have found statistically significant short-term weight changes within 1 year post-surgery for patients. However, another study investigating long term weight changes found that patients undergoing thyroidectomy for thyroid cancer had no significant weight gain. Most studies focus on a specific procedure, usually total thyroidectomies for a single pathology with a short-term follow-up. The aim of our study was to investigate patients undergoing a variety of procedures for several different pathologies, and to achieve a longer follow-up time. Patients with a baseline preoperative weight and at least 6 month follow-up weight data were included. Methods: Using a retrospective analysis of prospective data, we grouped patients based on pathology and procedure from 2007-2012 and compared their weight changes to patients undergoing parathyroidectomies (control). We included labs when available both preoperatively and 1, 6 and 12 months postoperatively. Results: With a median follow-up time of 61 months, the longest follow-up for any study covering multiple pathologies and procedures, patients receiving total thyroidectomies for any reason (benign or cancerous) significantly gained weight 12 months post-operation compared to parathyroid controls. Benign lobectomies also had a significant weight change compared to controls, although lobectomy procedures for cancer did not have a significant weight change 12 months post-operation. Weights were tracked up to 10 years post-operation, but due in part to incomplete follow-up, weight gain was not significant. It is worth noting that as long as 8 years post-operation, no groups had weight gains greater than 2 kg, and some even lost weight, which raises the question of whether the amount of weight gained long-term has any impact on quality of life.

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

Megan Sheridan, Dr. Nityananda Chowdhury, Dr. Ozlem Yilmaz, Dr. Besim Ogretmen, Besim Ogretmen, Graduate Studies, Biochemistry and Molecular Biology, MUSC.

Abstract Withheld from Publication

42 Fibroblast Derived STAT3 Promotes PDAC Tumorigenesis by Fostering an Immunosuppressive Tumor Microenvironment

Julia Lefler, Katie MarElia, Blake E. Hildreth III, Katie A. Thies, Maria C. Cuitino, Sudarshana Sharma, Samuvel Devadoss, Stacey Kneeshaw, Michael Ostrowski, Graduate Studies, Biochemistry and Molecular Biology, MUSC.

The tumor microenvironment (TME) is increasingly becoming a target for treatment of Pancreatic Adenocarcinoma (PDAC). Conventional therapies are largely ineffective due to the dense and immunosuppressive stroma associated with the disease. Within the stroma, cancer associated fibroblasts (CAFs) are one of the most abundant cell types and are involved in immunosuppressive signaling and fibrosis. Previous studies have shown both tumor promoting and tumor suppressive functions of the stroma, suggesting complex interactions between fibroblasts and tumor cells. IL-6 is a pleiotropic cytokine involved in several physiological functions and its increased expression is strongly associated with poor survival rates in PDAC patients. STAT3 is a major downstream target of IL-6, and its aberrant activation has been implicated in PDAC tumor progression and immune evasion. IL-6 expression and the IL-6/STAT3 signaling axis in PDAC has been characterized in epithelial tumor cells, however its stromal-specific function on 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 recently developed by our lab. Deletion of STAT3 in fibroblasts significantly increased the survival in a cohort of KPF mice compared to those with intact STAT3. In preliminary investigations, we found an increase in T cell infiltration and a decrease in immunosuppressive M2 macrophage population in the STAT3-deleted cohort. To elucidate the mechanisms by which STAT3 signaling alters the TME in PDAC, we will perform in vitro studies to look at different cytokine and chemokine levels in wild-type and STAT3-deleted pancreatic CAFs. These preliminary results demonstrate a previously unexplored role of IL-6/STAT3 signaling in fibroblasts during PDAC progression.

43 Novel non-canonical mechanisms by which ErbB3/HER3 contributes to MPNST tumorigenesis.

Laurel Black, , Steven Carroll, Graduate Studies, Pathology, MUSC.

Malignant Peripheral Nerve Sheath Tumors (MPNSTs) are highly metastatic and drug resistant neoplasms of Schwann cell origin. MPNSTs arise sporadically within the general population or occur in patients with neurofibromatosis type I (NF1) due to loss of the NF1 tumor suppressor gene. Currently, there are no effective treatments for this disease. These tumors have hyper-Ras activity and are frequently associated with overexpression of receptor tyrosine kinases (RTKs), like EGFR and ErbB4. We investigated whether aberrant activation of upstream RTKs can drive cellular proliferation, survival, differentiation and migration. Upon using a global shRNA screen to examine the role of all 58 RTKs and other signaling proteins, we discovered that ErbB3 and calcium ion (Ca2+) signaling is fundamental for cellular survival and proliferation in multiple MPNST cell lines. ErbB3, along with EGFR, HER2 and ErbB4, are members of the ErbB RTK family and each have differential involvement in Ca2+ signaling. ErbB3 is being actively investigated as a therapeutic target in several human cancers due to its potential role in drug resistance and the aggressive phenotype of EGFR and HER2-driven cancers. We previously demonstrated that MPNSTs are sensitive to Ca2+ signaling inhibitors and that NRG1β promotes MPNST mitogenesis and migration through ErbB3/ErbB4 enriched

invadopodia. Ca2+ is a major regulator of cytoskeletal reorganization processes including migration and pinocytosis. My hypothesis is that ErbB3 contributes to the aggressive nature of MPNSTs by promoting migration and/or macropinocytosis via modulation of calcium signaling. Utilizing a split-ubiquitin yeast two-hybrid assay we found that ErbB3 interacts with several Ca2+-involved proteins, HDAC6, S100A6 and REEP5. Furthermore, our microarray analyses of the NRG1β/ErbB3 cascade in rat Schwann cells showed enriched activation of proteins mediating Ca2+ signaling and cytoskeletal function. With these data, we are investigating possible non-canonical roles that ErbB3 may have in promoting tumorigenesis in hopes of uncovering novel therapies.

44 Development of Inhibitors of KDM4B as a Therapeutic Strategy for Periodontal Disease

Joy Kirkpatrick, Rachel Wilkinson, Jonathan Turner, Jessica Hathaway-Schrader, Chad Novince, Patrick Woster, Dental Medicine (DMD, PhD), Drug Discovery and Biomedical Sciences, MUSC.

Periodontal disease (PD) affects nearly half of the adult United States population and is characterized by bacterial-driven inflammatory bone loss. Traditional and emerging treatments for periodontitis management do not typically target the host immune response, which is the major source of tissue damage. The demethylation activity of lysine-specific demethylase 1 (KDM1A) at histone 3 lysine 4 leads to a decrease in pro-inflammatory cytokine transcription. By contrast, lysine specific demethylase 4B (KDM4B) is a histone demethylase that specifically demethylates histone 3 trimethyllysine 9 (H3K9me3). Interestingly, previous data has shown that cross talk between these two enzymes leads to a balanced system wherein lysine 9 methylation serves as a prerequisite to lysine 4 demethylation by KDM1A. The current study exploits this crosstalk for the design of new potential therapies for PD. The central hypothesis of this project is that promotion of KDM1A activity by introduction of a specific KDM4B inhibitor will alleviate PD by controlling the overactive immune system in diseased areas, enabling the host to better manage the disease and prevent its recurrence. KDM4B inhibition prevented the A.a-induced immune response. KDM4B inhibition also reduced osteoclast formation in vitro and caused a trend towards decreased bone loss in vivo. KDM4B activity is heightened in periodontal disease in clinical tissues as well as in murine calvarial tissue sections treated with A.a. KDM4B inhibition mediated immunosuppression relies on the concurrent overactivation of KDM1A. Computational chemical screens identified several hit scaffolds, one of which was optimized using phenotypic screen-guided binary QSAR. From an extensive in silico derivative library, 25 novel derivatives were synthesized, 8 of which caused significant immunosuppression. This work was supported by This project was supported by the South Carolina Clinical & Translational Research (SCTR) Institute with an academic home at the Medical University of South Carolina NIH - NCATS Grant Number UL1 TR001450 and NIH - NCATS Grant number TL1 TR001451, F30 DE027290 (JEK)

45 The role of paxillin in the pathogenesis of liver fibrosis

Nour Hijazi, Don Rockey, Graduate Studies (MSTP, PhD years), Chairman, MUSC.

Abstract Withheld from Publication

46 Alcohol cue-reactivity in treatment seeking individuals with Alcohol Use Disorder

Daniel McCalley, Ingrid E Contreras, Julia P Imperatore, Logan T Dowdle, Josh P Smith, Sarah W Book, Colleen Hanlon, Graduate Studies (MSTP, PhD years), Neuroscience, MUSC.

Introduction: Alcohol Use Disorders (AUDs) is a chronic, relapsing disorder that is often devastating and difficult to treat. One leading cause for relapse to alcohol is cue-induced craving. Among individuals who are not currently enrolled in treatment for AUD, alcohol cues reliably evoke activity in frontal and limbic brain regions. Few groups, however, have explicitly investigated whether alcohol cue-reactivity is elevated in a population of individuals currently seeking treatment for AUD. Objective: The primary objective of this study was to evaluate alcohol-cue reactivity in a sample of treatment seeking individuals with AUD. Subsequent analyses of these data will investigate the efficacy of transcranial magnetic stimulation (TMS) in reducing alcohol cue-reactivity. Methods: 41 individuals with AUD were recruited from MUSC's intensive outpatient program for AUD and completed a cue-reactivity task while undergoing functional magnetic resonance imaging. Whole brain reactivity to alcohol versus neutral beverage cues was assessed across all individuals. Region-of-interest (ROI) analysis was performed to assess cue-reactivity within 8 specific brain regions involved in salience and reward processing including the ventromedial prefrontal cortex, anterior cingulate cortex, insula, caudate, putamen, and ventral striatum. Results: Among treatment-engaged individuals with AUD, alcohol cues (vs. neutral beverage cues) evoked significant BOLD signal within the anterior cingulate cortex and medial prefrontal cortex ($p<0.0001$, FWE-corrected) and the superior frontal gyrus ($p<0.008$, FWE-corrected). ROI analysis revealed elevated cue-reactivity with the ventromedial prefrontal cortex, the right insula, and the bilateral anterior cingulate cortex. Conclusion: These data suggest that alcohol cues evoke similar patterns of activity within the salient reward processing network among treatment and non-treatment seeking individuals with AUD. Further, this study provides preliminary support that the medial prefrontal cortex may be a novel therapeutic target in treatment efforts to reduce alcohol cue-reactivity in individuals with AUD. This work was supported by NIDA: R01 (Hanlon), NIAAA: T32 (McCalley), GAANN Fellowship (McCalley)

47 Long-Term Treatment Strategy via AAV Delivery of an Inducible Vector Containing CR2-fH in a Murine Model of Choroidal Neovascularization

Nathaniel Parsons, Bärbel Rohrer, Graduate Studies, Ophthalmology, MUSC.

Age-related Macular Degeneration (AMD) is the leading cause of vision loss in the United States (US) for people over sixty. Eleven million people in the US have some form of AMD, wet or dry, and with a growing elderly population, numbers are predicted to double by 2050. Here we study wet AMD or neovascular AMD (nAMD), representing 10-20% of cases, that is a result of breaches in Bruch's membrane (BrM), new abnormal blood vessel growth, and fluid leakage from these newly formed vessels towards the center of the retina, the macula. The accumulating fluid causes detachment of the retina from the underlying retinal pigment epithelium (RPE). As a result, retinal photoreceptor cells die, and patients experience central vision loss. It has been shown that vascular endothelial growth factor (VEGF) and complement components accumulate in and drive nAMD pathology. Current treatments are intraocular injections of anti-VEGF therapeutics, which are provided monthly. Injections can lead to complications including retinal detachment, infection, cataracts, or drug resistance. We propose a one-time sub-retinal injection of adeno-associated virus serotype 5 (AAV5) that contains a regulatable, complement component 3 (C3)

promoter driven therapeutic that is composed of complement receptor 2 (CR2) fused to the inhibitory domain of factor H (fH) (CR2-fH). CR2 localizes fH to cells opsonized with complement activation product C3d via the CR2 domain. The expression of this mimetic construct is designed to mirror complement activation and increase or decrease accordingly. We have previously shown that systemic or intraocularly delivered CR2-fH protein alleviates pathogenicity via local inhibition of complement alternative pathway (AP). Furthermore, mouse eyes injected sub-retinally with AAV5 expressing CR2-fH under a constitutive promoter lessens AP activation in the eye, reducing pathology. We hypothesize that an inducible system, driving CR2-fH expression will control AP activation and mitigate AMD 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

48 Cellular Specificity of Matrix Metalloproteinase Activation on Accumbens Medium Spiny Neurons During Cued Heroin Seeking

Vivian Chioma, Peter Kalivas, Graduate Studies (MSTP, PhD years), Neuroscience, MUSC.

Heroin abuse is a leading cause of drug overdose-related deaths in the United States, highlighting a need for further research elucidating effects of maladaptive neuroadaptations following prolonged heroin use. Activation of the tetrapartite synapse in nucleus accumbens core (NAcore), which comprises of pre- and postsynapse, astrocytic processes, and surrounding extracellular matrix (ECM), has been linked to increased relapse vulnerability. Specifically, degradation of the ECM by activated matrix metalloproteinases (MMPs) is involved in extracellular synaptic remodeling both constitutively and transiently. Following chronic heroin self-administration and extinction training, transient increases in MMP-9 activity in NAcore were elicited after 15 mins of cued heroin seeking compared to heroin-extinguished and saline control rats. Although increases in MMP-2,9 fluorescence can be localized to the soma and dendritic processes of medium spiny neurons (MSNs) in accumbens, it is unknown which specific cell types harbor changes in MMP activity under heroin-extinguished and cued reinstatement conditions. We hypothesized that D1-receptor expressing MSNs express increased pericellular localization with MMPs during transient cued heroin seeking, while D2-receptor expressing MSNs express increased localization following extinction. We used an AAV cre-dependent mCherry virus to transfect accumbens MSNs in D1 and D2 cre-dependent rats and measured the localization of activated MMP-2,9 after FITC-gelatin microinjection under extinguished and reinstated conditions. For D1 MSNs, we observed increased MMP-2,9 localization with dendritic surfaces in reinstated animals compared to both yoked saline controls and heroin-extinguished animals. While D2 MSNs showed increased MMP-2,9 localization only in heroin-extinguished animals, but MMP-2,9 localization after 15 min reinstatement was reduced to yoked saline levels. Next, we used pharmacological MMP-2,9 inhibitors to determine which were contributing to increased localization, specifically around D1 MSNs during reinstatement and D2 MSNs after extinction. These findings reveal how NAcore extracellular matrix signaling underlying constitutive and transient synaptic plasticity relies in part on specific cell-types. This work was supported by F30 DA046143 (VCC), R01 DA003906 (PWK)

49 Feasibility of an Animated Video Combined with Standard Radiation Therapy Education for Patients with Breast Cancer: Breast RAdiotherapy Video Education, BRAVE

Michelle Pembroke, Julie Bradley, Marina Mueller, Michelle Mollica, Lynne Nemeth, Lynne Nemeth, Nursing, College of Nursing, MUSC.

Introduction: Previous studies have demonstrated a high prevalence of anxiety for patients with breast cancer prior to undergoing radiotherapy. Contributing to this anxiety includes a lack of knowledge or understanding of the benefits and side effects of radiotherapy, fear of the radiation treatment planning process, and delivery of radiation. Methods: This study was a single arm, prospective, interventional, pre- and post-test feasibility study. The aims were to determine the feasibility and preliminary outcome measures of incorporating an animated, oncology nurse developed educational video shown during the radiation treatment consultation. Twenty participants diagnosed with breast cancer were recruited from an outpatient radiation oncology facility in the southeast US. Feasibility was measured by Acceptability of Intervention Measure, Intervention Appropriateness Measure, Feasibility of Intervention Measure, patients' responses to open ended post intervention questions, and a PI logbook to document technical issues. Secondary outcomes included assessment of patient reported anxiety, distress, and radiation concerns using the RT Concerns Needs Scale (score range 0-81), PROMIS Emotional Distress-Anxiety (score range 6-30), and Distress Thermometer (score range 0-10). Results: Both radiation oncologists reported the highest possible score of 20 on each feasibility measure. Analysis of patient reported qualitative data signified a high level of satisfaction, clarity of content, and likeability of the video. The difference in means of total scores comparing post to pre intervention decreased for the RT Concerns Needs Scale by 36.2 (SD ± 23.5; 95% CI 25.2; 47), for The Distress Thermometer by 3.3 (SD ± 3.3, 95% CI 1.7; 4.8) and for the PROMIS Emotional Distress-Anxiety by 4.8 (SD ± 5.8, 95% CI 2; 7.5). Conclusion: Feasibility of implementing the video during the consult visit was successfully achieved. The decrease in total mean scores of all instruments suggests the video may have a positive effect on reducing patient distress, anxiety, and radiation concerns.

50 Transcription is Suppressed by Replication-Coupled Histone De-Acetylation

Colleen E. Quaas, John K. Barrows, David Long, Graduate Studies, Biochemistry and Molecular Biology, MUSC.

Histone octamers interact with DNA to form a nucleosome, the basic building block of chromatin structure. Histone "tails" that extend from the N- and C-termini of each protein subunit are subject to a wide variety of post-translational modifications (PTMs), including acetylation, phosphorylation, ubiquitylation, and methylation. Collectively, the location, type, and number of histone PTMs (referred to as the histone code) regulate nearly all aspects of chromatin activity within the cell. Utilizing Xenopus laevis egg extract, we have developed a system to investigate how histones regulate transcription of chromatinized plasmid substrates. With this system, we found that replication of plasmid DNA abrogated transcription from an otherwise active promoter. Interestingly, transcription of the plasmid did not recover after replication had completed, suggesting that replicated chromatin was modified to suppress subsequent transcription. A major mechanism of transcriptional suppression involves acetylation and deacetylation of histones. Using different histone deacetylase (HDAC) inhibitors, we found that histone deacetylases 1 and 2 (HDAC1/2) were required to maintain transcription suppression after replication. Based on these data, we aim to answer several key questions about how the activities of HDAC1/2 are regulated to maintain genome integrity during DNA replication. This work was supported by R35GM119512

51 Diabetic Rats are More Susceptible to Infarction and Cognitive Decline in a Microemboli Based Model of Vascular Cognitive Impairment and Dementia (VCID)

Raghavendar Chandran, Weiguo Li, Lianying He, Yasir Abdul, Sarah Jamil, Maria de Fatima Falangola, Adviye Ergul, Medicine, Pathology and Laboratory Medicine, MUSC.

Diabetes doubles the risk of vascular cognitive impairment and dementia (VCID) but underlying reasons are not known. Given that diabetes mediates early cerebrovascular dysfunction and increases the risk of microemboli that can penetrate into the brain parenchymal arterioles we tested the hypothesis that entrapment of microemboli in dysfunctional vessel walls accelerates the development of SVD ultimately leading to VCID. Diabetes was induced by a high fat (HF) diet and low dose streptozotocin (35 mg/kg; STZ) injection in male Wistar rats. 8 weeks after HF-STZ treatment, control and diabetic rats received cholesterol crystal microemboli (40-70 µm) injection (Group A - 3000 or Group B - 6000 crystals) through internal carotid artery. Cognitive function was assessed by novel object recognition (NOR) test. White matter injury was assessed by Luxol fast blue (LFB) and hematoxylin/eosin (HE) staining in Group A. Diffusion MRI was used in Group B to monitor the structural changes longitudinally. At baseline, diabetic animals had lower discrimination index scores (-0.02±0.09), a measure for working memory as compared to control rats (0.39±0.03). Six weeks after microemboli injection, there was a further decline in working memory in the diabetic animals (-0.05±0.05) compared to the controls (0.23±0.11). Histopathology indicated greater white matter degeneration in diabetic animals which was worsened by microemboli. In Group B, preliminary MRI data before microemboli injection showed a decreasing trend in diffusivity in the cortex and dorsal hippocampus suggesting neurodegeneration (particularly axonal degeneration) in diabetic rats. MRI analysis showed that 50% of diabetic animals developed infarction (2/4) while there was none in controls. These results suggest that white matter degeneration starts in the early stages of diabetes and that microemboli exacerbate these pathological changes. Future studies will test whether treatment of diabetic animals with vasculoprotective drug combination of isosorbide mononitrate and cilostazol before microemboli injection improves cerebrovascular function. 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

52 Treatment with FK506 promotes noise-induced hearing loss through inhibition of calcineurin and activation of autophagy

Zuhong He, Song Pan, Hongwei Zheng, Shan Xu, Qiaojun Fang, Suhua Sha, Medicine, Pathology and Lab Medicine Research, MUSC.

The contribution of calcium influx into sensory hair cells following noise exposure to the pathogenesis of hair cell loss and hearing loss has been well documented. Treatment with FK506, an inhibitor of calcineurin (CaN) attenuates noise-induced hearing loss (NIHL), supporting the notion that calcium influx activates CaN. Although FK506 is a CaN antagonist that is used clinically in humans as immunosuppressor, the detailed mechanisms of prevention of NIHL by FK506 remain unknown. In this study, adult CBA/J mice were used by treatment with FK506. In agreement with the previous report, we found that noise-induced expression of CaN and NFAT are significantly increased in OHCs. Such increases are significantly suppressed by treatment with FK506. Consequently, treatment with FK506 significantly reduces noise-induced losses of hair cells and synapses and NIHL. Furthermore, treatment with FK506 activates autophagy signaling, as assessed by autophagy marker microtubule-associated protein light chain 3B (LC3B) in GFP-LC3 mice. Importantly, the prevention of NIHL by treatment with FK506 was abolished by pretreatment with siLC3B. These results indicate that treatment with FK506 attenuates noise-induced OHC loss and hearing loss via inhibition of CaN and activates of autophagy. This work was supported by grant R01 DC009222 from the National Institute on Deafness and Other Communication Disorders, National Institutes of Health.

53 Coronary Artery Calcification on Computed Tomography in Patients with ST-elevation Myocardial Infarction

Mohamed Faher Almahmoud, Umair, Malik., Jasjeet, Khural., Katrina, Bidwell., Sandra, Coons. , Valerian Fernandes, Medicine, Cardiology, MUSC.

Background: Coronary artery calcification (CAC) is a strong predictor of future cardiovascular (CV) events. It improves risk reclassification of intermediate risk individuals who may benefit from intensive statin therapy. We studied the prevalence of CAC in patients with ST-elevation myocardial infarction (STEMI) and evaluated history of statin use in the presence of CAC. Methods: We retrospectively included consecutive patients who presented with STEMI activation between 2014 and 2019. We qualitatively reported the presence of coronary calcification seen on previous CT scans that included the heart. We collected data on demographics, risk factors, and prior medications. Patients were classified based on culprit vessel into acute vessel thrombosis (angiographic STEMI) and no culprit vessel (no angiographic STEMI). We evaluated LDL control in patients with angiographic STEMI and CAC. Student t test was used for continuous variables and Chi square test was used for categorical variables. Results: We included 186 patients (mean age=61±12, 76% males), of them 131 with angiographic STEMI. 62 (33%) patients had prior CT. CAC was present in 85% in those with angiographic STEMI vs 46% in the second group. Patients with CAC were older (63 vs 54 years), had longer fluoroscopy time (12 vs 8 minutes), and had more contrast (89 vs 70 mL). Of those with angiographic STEMI and CAC on a prior CT, 17% were not on lipid lowering therapy, 21% were on statin but had elevated LDL levels, and only 62% were optimally treated. Interestingly, men with angiographic STEMI were more likely to have CAC (96% vs 67%, $p<0.001$). Conclusion: Majority of patients with angiographic STEMI had CAC on prior CT. The presence of CAC on regular chest CT represents an important opportunity to modify risk factors especially hyperlipidemia.

54 Screening of non-electrophilic Bach1 inhibitors in in vitro and in vivo model of neuroprotection

Manuj Ahuja, Navneet Ammal Kaidery, Irina Gaisina, Kazuhiko Igarashi, Otis C. Attucks, Sudurshana Sharma, Thomas Bobby, Medicine, Pediatrics, Neuroscience, Drug Discovery, MUSC.

Abstract Withheld from Publication

55 miR-145a regulates pericyte function and outcomes of a murine model of sepsis

Yan Wu, Pengfei Li, Andrew J. Goodwin, James A. Cook, Perry V. Halushka, Hongkuan Fan, Medicine, Department of pathology and lab medicine research, MUSC.

Introduction: Sepsis, triggered by microbial infection, is a common and life-threatening systemic disease. Microvascular dysfunction and vascular leakage are recognized as important features of severe sepsis. Pericytes are essential for vessel maturation and endothelial barrier function. Our previous studies demonstrated that Fli-1 regulates pericytes loss and contributes to the vascular dysfunction of sepsis. Thus Fli-1 may become a therapeutic target for sepsis. MicroRNA (miRNA) are non-coding endogenous RNAs that target mRNA and regulate gene expression at the post-transcriptional level. Using predicted software we found Fli-1 have complementarity with miR-145a. miR-145a regulates many cellular functions, but its role in pericyte biology during sepsis remains unexplored. We investigated the functional interaction of miR-145a and Fli-1 control of vascular leakage and inflammation, and consequently impact on sepsis outcomes. Methods and Results: Mice were rendered septic by cecal ligation and puncture (CLP). CLP led to decreased miR-145a expression in lung pericytes. Cultured lung pericytes transfected with miR-145a mimic inhibited LPS-induced increases in inflammatory cytokines and chemokines. To assess the functions of miR-145a in vivo, we constructed knock-out mice that deleted miR-145a in pericytes (miR-145a-/-). Pericytes lacking miR-145a lead to increased vascular leak, and reduced survival rate during sepsis. Sepsis induced both liver and renal injury as evidenced by the increased alanine aminotransferase (ALT), blood urea nitrogen (BUN) and creatinine levels in the plasma of septic versus control mice. However, miR-145a-/- mice significantly aggravated these organ injuries. In addition, we found miR-145a targets Fli-1 with the predicted binding site at nucleotide positions 97 to 103. Western-blot showed overexpression of miR-145a caused a reduction of Fli-1 in lung pericytes. Conclusuion: This study demonstrated the critical role of miR-145a in pericyte function in sepsis, and identifies miR-145a as a potential therapeutic target in sepsis. This work was supported by National Institute of Health1R01GM113995 (HF), 1R01GM130653 (HF), 1K23HL135263-01A1 (AG), UL1TR001450 (PVH)

56 Normalizing altered finger force direction post stroke: randomized controlled study protocol

Changki Kim, Corey Morrow, Christian Finetto, Parker Rhoden, Jillian Harvey, Viswanathan Ramakrishnan, Derek Kamper, Na Jin Seo, Health Professions, Ralph H. Johnson VA Medical Center, Department of Health Professions, MUSC.

Both finger force control and finger movement control are impaired post stroke. Both are functionally important because they directly relate to dexterous task execution in daily activities. Independent neural strategies are used for controlling finger force versus movement. Therefore, both neural strategies must be rehabilitated for restoring hand function post stroke. However, current treatment focuses on movement; force control is rarely addressed in therapy. This is due, in part, to a lack of tools to provide explicit feedback to patients about finger force control. This project aims to determine whether finger force control training with explicit feedback is an effective tool in restoring hand function post stroke. Methods: Sixty adults 3-9 months post stroke with moderate to severe hand impairment will be randomly assigned to either an experimental or a control group. Both groups will undergo 3 1-hr training sessions per week for 6 weeks in which they practice finger force control in various directions. The experimental group will receive explicit feedback in 3D force, while the control group will receive feedback in 1D force only (i.e., no feedback in directional force control). Evaluation will occur at baseline, every 2 weeks during a 6-week intervention, post-intervention, and at 1-month follow-up. Outcome measures: Action Research Arm Test (primary), Box and Block Test (secondary), Stroke Impact Scale, perceived meaningfulness of the intervention, and finger force control, muscle activation pattern, and postural control during reach/grasp/transport/release. Conclusions: This study is a randomized controlled trial determining the effect of finger force training in restoring hand motor function after stroke. The results of this study will serve as the basis for developing an innovative therapeutic tool to improve force control in stroke survivors. This tool is expected to augment current movement-focused treatment, thereby enhancing treatment outcomes for stroke survivors with hand impairment. Trial Registration Number: NCT03995069. This work was supported by VA Merit I01 RX003066 from the Rehabilitation Research and Development Service Program.

57 Analytical methods for characterization of transplantable collagenous soft tissue

Glenn Hepfer, Peng Chen, Kelvin Brockbank, Alyce Jones, Zhen Chen, Elizabeth Greene, Lia Campbell, Gregory Wright, Amanda Burnette, Hai Yao, Dental Medicine (DMD, PhD), Oral Health Sciences, Clemson Bioengineering, MUSC.

Introduction/rationale: Tissue preservation and engineering techniques strive to produce tissues that are readily available for transplantation. Tissues such as heart valve, tendon, 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 AATB, NIH DE021134, NIH DE018741, and NIH AR055775

58 Investigating the role of EPHB2 in autism and autism-associated behaviors

Ahlem Assali, Chris Cowan, Graduate Studies, Neuroscience, MUSC.

Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder characterized by impairments in social interaction/communication along with restricted and repetitive interests/behaviors. ASD is caused by a complex interaction between genetic and environmental factors. Current mechanistic hypotheses based on converging findings from clinical neuroimaging and human post-mortem brain analyses attribute

the pathophysiology of ASD to widespread disruptions in brain connectivity. A de novo nonsense (Q857X) and a de novo missense (G900S) mutations were discovered in autistic individuals in EPHB2, a gene coding for a transmembrane receptor with an intracellular tyrosine kinase signaling domain. By mining whole-exome sequencing of ASD patients and controls from the Simons Simplex Collection, we identified ~30 inherited, rare variant missense additional mutations in EPHB2. We found so far that de novo mutation, Q857X, produces truncated EPHB2 proteins and causes a loss of EPHB2 intrinsic tyrosine kinase activity. Since EPHB2 is involved in axon guidance/pruning, synapse formation/plasticity, we investigated whether heterozygous genetic disruption of EphB2 in mice could produce behaviors relevant to autism. Global EphB2 heterozygous mice show normal social interaction and normal anxiety levels. However, EphB2 heterozygous females, but not males, display repetitive behaviors, a hindering core symptom of autism, as well as common autism-associated behaviors including hyperactivity, learning and memory deficits and enhanced acoustic startle response, suggesting an altered sensitivity to sounds. Together with the fact that the de novo mutation (Q857X) has been found in a female with ASD, our results suggest a sex-specific function of EphB2 in autism and autism-related behaviors. To better understand how EPHB2 mutations increase autism risk in genetically affected individuals, future studies are required to identify the tissue, cell type and developmental processi in which EPHB2 is involved to induce behavioral deficits.

59 GATA6 is required for chromatin reorganization and modification during human definitive endoderm formation and specification

James Heslop, Stephen Duncan, Medicine, Regenerative Medicine and Cell Biology, MUSC.

The GATA family of transcriptional regulators are essential for the development, homeostasis and regeneration of numerous tissues. Of these factors, GATA6 is essential for definitive endoderm formation. The mechanisms which underlie this developmental importance are incompletely understood. GATA factors have been associated with pioneer function - the capacity to bind and alter the accessibility of chromatin, making previously refractive regions of DNA permissive to non-pioneer transcription factors. We hypothesize that GATA6 is essential for proper epigenetic patterning during the development of endoderm-derived tissues. Using pluripotent stem cells as a model of human development, in combination with CRISPR/Cas9 and next-generation sequencing technologies, we have investigated the pioneer role of GATA6. Our results demonstrate that GATA6 is required for chromatin reorganization and histone modifications at sites of developmental significance during endoderm formation and specification. Further investigation of GATA6-dependent pioneer activity will elucidate the mechanisms and co-factors required to facilitate the epigenetic modifications identified.

60 Motor protein MYO1C participates in retinal function by regulating STRA6 trafficking

Ashish Solanki, Glenn Lobo, Ehtasham Arif, Pankaj Shrivastava, Bushra Rahman, Deepak Nihalani, Medicine, Medicine, MUSC.

Introduction-Understanding the mechanisms that participate in photoreceptor(PR) cell death and loss of eye function has been the major focus of our research. Human retina is a multilayered structure, where the PR cellular layer relies heavily on RPE(retinal pigment epithelium) layer containing STRA6, whose basolateral localization is critical for retinol uptake and thus maintaining retinal function. While STRA6 is known to play an essential role in retinal cell development and function, the cellular trafficking events that regulate its basolateral localization remain unknown. Rationale-Association of the identified genetic mutations in Myo7a with retinal degeneration in Usher syndrome suggested that unconventional myosin's may play a critical role in eye development and function. Since MYO1C has an established role in cellular trafficking along with a tethering function that associates its cargo proteins with membranes and actin, we hypothesized that MYO1C-mediated mechanism, that regulates STRA6 localization at the basolateral membrane, is a key component of retinal function. Methods-Myo1c knockout mice were generated and performed electroretinogram(ERG), mRNA-profiling from isolated retina, retinal sections analyis by immunofluorescence and histologic analysis. Results-ERG analysis showed significantly impaired visual response in Myo1c-KO mice. Histological examination revealed significant retinal degeneration of photoreceptor outer segments where they were fewer in number and shorter in length. Interestingly, STRA6 staining pattern was significantly changed, where increased cytoplasmic distribution of STRA6 was noted in the RPE of Myo1c-KO mice; in comparison, typical basolateral localization of STRA6 was present in the RPE of wild type mice. Binding and localization studies further revealed that MYO1C interacted and partially co-localized with STRA6. mRNA-profiling analysis showed upregulation of GNAI3, whose human mutations lead to ocular albinism and is involved in vesicle trafficking, as one of the distinct proteins in the retina of Myo1c-KO mice. Conclusions: Genetic deletion of Myo1c resulted in severe eye dysfunction possibly due to defective STRA6 trafficking. This work was supported by NIH RO1

61 Workflow for Immune Monitoring during Clinical Trials by using unsupervised high dimensional augmented intelligence assisted analysis

Alessandra Metelli, Silvia Guglietta, Luis Cardenas, John Wrangle, Mark Rubinstein, Mark Robinson, Zvi Fridlender, Carsten Krieg, Medicine, Immunology an Microbiology, MUSC.

Recent advances in the field reveal that each cancer and each individual patient develops anti-cancer immunity in his own context. Given the growing portfolio of immune targeted therapeutics, precision medicine tools are necessary to stratify patients to the correct therapeutic. High throughput multi-omic approaches are necessary to identify all features of possible immune responses during treatment. We present a portfolio of multi-omic approaches including high-dimensional mass cytometry (CyTOF) and single cell sequencing in combination with unsupervised machine-learning bioinformatics to perform in depth characterization of immune responses during clinical (immuno)therapy. The analysis is data driven, can be adapted to high throughput approaches and can model arbitrary trial designs. Here we show three proof of concept projects using biobanked peripheral blood mononuclear cells (PBMCs). In the first study, pre and post-dose samples after 12 weeks of anti-PD-1 therapy were analyzed. The most evident difference in responders before therapy was an enhanced frequency of CD14+ CD16+HLA-DRhi classical monocytes. We found a clear correlation of enhanced monocyte frequencies before therapy initiation with clinical response such as lower hazard and extended progression-free and overall survival. In a second study, we used CyTOF and our unbiased artificial intelligence-driven immune workflow to monitor immune responses in 21 patients receiving a novel combination of anti-PD-1 and IL-15 super- agonist (ALT-803) after initially failing on anti-PD-1 therapy. Unexpectedly, our high dimensional unbiased analysis was able to detect and characterize a strong expansion of innate tumor-reactive effector NK cells. In our third and unpublished study we were able to identify neutrophils as predictors of outcome in lung cancer patients. In conclusion, our unbiased artificial intelligence-driven immune workflow is a powerful tool to monitor immune responses during (immuno)therapy and serves as a novel approach for identifying

therapeutic targets, providing further opportunity to integrate our approach to the bedside. This work was supported by recruitment package

62 Towards a Model of Methylmalonic Acidemia using Human Induced Pluripotent Stem Cells

Behshad Pournasr, Stephen Duncan, Medicine, Regenerative Medicine and Cell Biology, MUSC.

Methylmalonic Acidemia (MMA) is an inherited metabolic disorder detected by a defect(s) in the enzyme methylmalonyl CoA mutase (MCM). MCM is one of the enzymes required for the metabolism of branched chain amino acids including Leucine, Isoleucine, and Valine. Mutations in the MUT gene, which encodes MCM, leads to the accumulation of organic acids and other toxic metabolites. MMA patients suffer from a wide range of symptoms including vomiting, dehydration, hypotonia, developmental delay, lethargy, and hepatomegaly. Long-term complications can include feeding problems, intellectual disability, chronic kidney disease, and inflammation of the pancreas. The study of MMA would benefit from a cell model that could potentially provide a platform for drug discovery and to understand the unknown molecular pathology of the disorder. We used CRISPR/Cas9 to introduce indels into the MUT gene in human induced pluripotent stem cells (hiPSC) with the goal of generating null alleles. We then generated MUT-17/+2 cells containing a wild-type MUT cDNA whose expression was doxycycline (Dox) dependent (MUT -17/+2;indMUT). These cell lines and wild-type induce to differentiated to hepatocyte and evaluated for MUT expression, MUT activity, mitochondrial membrane potential, ROS production, and oxygen consumption rate. We have successfully generated hepatocytes from MUT-/- hiPSCs. These cells will provide an in vitro cell model for the study of Methylmalonic Acidemia and provide a platform for future drugs screens. In our experiments TMRE, DCFDA staining, and seahorse assay showed that exogenous MCM protein could not rescue the KO-cell line. It may be the result of a non-reversal effect(s) of toxic product accumulation in the cells regarding malfunctioning of MCM enzyme during the branched chain amino acid metabolism which need to be considered.

63 Suboptimal ER stress Induced Autophagy Regulates Anti-Tumor T Cell Response

Paramita Chakraborty, Shilpak Chatterjee, Danh T. Tran, Dosung Kim, Satish N. Nadig, Carl Atkinson, Hongjun Wang, J. Alan Diehl. , Shikhar Mehrotra, Health Professions, Surgery, MUSC.

Endoplasmic reticulum (ER) stress, induced by external or internal stimuli activates a number of well-orchestrated cellular signaling processes aimed to promote either cell apoptosis or to restore cellular function and resolve the stress. In the tumor microenvironment, induction of ER stress is known to dampen the antitumor activity of T cells by reducing their mitochondrial function. However, if the magnitude of ER stress governs the T cell fate and function is unknown. Using melanoma antigen gp100 reactive T cells, we found that a low level of ER stress enhances T cell stemness and promotes mitochondrial biogenesis, whereas a high level of ER stress triggers T cell death. Moreover, upon adoptive transfer, T cells treated with low dose ER stress inducer are able to form long-lived memory in vivo, express the reduced level of the co-inhibitory molecule, and demonstrate superior anti-tumor immunity by increasing overall survival of B16 murine melanoma bearing mouse. Mechanistically, we discovered that, upon ER insult at a suboptimal level, a protective autophagy pathway is induced to promote cell survival and maintain stemness through the protein kinase R-like endoplasmic reticulum kinase (PERK)/ activating transcription factor-4 (ATF4)-dependent manner. Conversely, knockdown of PERK abrogates autophagy activation, hampers mitochondrial biogenesis in response to suboptimal ER stress, which in turn compromises the antitumor function of melanoma antigen-specific T cells. Furthermore, we demonstrated that blocking autophagy in T cells hampers T cell anti-tumor activity. Lastly, T cells that initiate the autophagic process due to suboptimal ER stress show better potential to control tumor compared to those, that do not enter into the process. Overall, these preclinical data highlights that a low level of the ER stress response is important for healthy cellular function and therapeutically, ER stress pathways can be manipulated in T cells in order to regulate their antitumor potential. This work was supported by Department of Surgery, MUSC, NIH R21 CA198646, NIH PO1 CA 154778, NIH PO1 CA203628 AAI Careers in Immunology Fellowship.

64 An iPSC derived Hepatocyte Platform to Investigate the Mechanism and Treatment of Mitochondrial DNA Depletion Syndromes

James Corbett, Stephen Duncan, Graduate Studies, Regenerative Medicine and Cell Biology, MUSC.

Mitochondrial DNA Depletion Syndromes (MTDPS) are a group of genetic disorders characterized by a severe loss of mitochondrial DNA (mtDNA). mtDNA establishes the efficiency of cellular respiration by controlling the overall level of electron transport chain proteins and subsequently the overall ATP output in a cell. Reduction in cellular mtDNA lowers the available energy and can lead to disfunction in vulnerable cells populations. Disruption to deoxyguanosine kinase (DGUOK) and the Ribonucleotide Reductase Regulatory TP53 Inducible Subunit M2B (RRM2B) are two common causes of congenital MTDPS. There is currently no cure for MTDPS and available treatments rely on symptom management, with most patients dying during early infancy. Our group has developed a robust, high throughput drug screening system consisting of CRISPR engineered induced pluripotent stem cells differentiated to hepatocytes to investigate how allelic variation in DGUOK effects disease severity and to explore candidate drugs for treatment of MTDPS. Using our screening system, we found we were able to recapitulate the variable severity of DGUOK mutants in vitro as well as identify 4 drugs that significantly restored ATP production in RRM2B knockout cells. Furthermore, we found that combinations of the drugs were able to increase the degree of ATP production over that of wild type cells. Identifying the molecular mechanisms by which the drugs restore ATP, as well as further investigation of the MTDPS phenotype in hepatocytes will aid us in developing novel disease treatments and help to advance our finding for future clinical research.

65 Dose Dependent Effects of tDCS on Post-operative Pain

Georgia Mappin, Jeffery Borckardt, Medicine, Psychiatry, MUSC.

Introduction: Opioid narcotics are a commonly used pharmacotherapy for post-operative pain management. Post-operative pain management contributes to perioperative factors such as length of hospital stay and recovery time. Total knee arthroplasty (TKA) is an increasingly prevalent orthopedic procedure. Despite the deleterious side effects of opioid medication, few advances have been made in the pain management alternatives, and narcotics remain the predominant treatment. Transcranial direct current stimulation (tDCS) is a noninvasive brain stimulation technique that may reduce the need for patient-controlled analgesics. Objective: The purpose of this study was to examine the effects tDCS on reducing post-operative pain, as determined by morphine equivalent doses post-surgery. We

hypothesize that tDCS will be associated with decreased morphine equivalency dose compared to sham. Furthermore, we hypothesize there will be a dose dependent effect of tDCS providing a larger analgesic effect with more real stimulation. Methods: This study implemented a double-blind sham-controlled trial of tDCS in veterans undergoing unilateral total knee or hip replacement at Ralph H Johnson VA Medical Center. tDCS was delivered bilaterally over the left and right dorsolateral prefrontal cortex (DLPFC), with the anode placed over the left DLPFC. Stimulation was delivered at 2mA for 20 minutes over four sessions during routine post-operative hospital stay. Participants were assigned to one of four groups that received either real or sham stimulation at each timepoint. Morphine equivalency dose of medication during hospital stay was measured. Results: There were no adverse events. There was a strong trend in tDCS and morphine equivalency dose during hospital stay. Participants that received all four real tDCS sessions had a 27.73% reduction in morphine equivalent medication compared to all sham. Conclusions: tDCS may offer an alternative or adjunct to opioid analgesics for post-operative pain management, without concerns of drug interactions. This work was supported by Ralph H Johnson VA Medical Center

66 Therapeutic Concentrations of Statins Hyperpolarize Mitochondria and Inhibit Cell Proliferation Without Promoting Cell Death in Human Hepatocarcinoma Cells

Elizabeth Hunt, Diana Fang, Amandine Rovini, Charleston Christie, Kareem Heslop, Eduardo Maldonado, Graduate Studies, Department of Drug Discovery & Biomedical Sciences, MUSC.

BACKGROUND: Statins, inhibitors of HMG-CoA reductase, are widely used cholesterol-lowering drugs. Statins may also decrease the risk of developing liver, breast and lung cancer. The high concentration of statins (10-100 μM) used in most in vitro studies is 1,000- to 10,000-fold higher than plasmatic therapeutic concentrations (10-100 nM), making it difficult to determine a potential clinical relevance. In preliminary work, we showed that simvastatin (SIM) and lovastatin (LOV) at 10 μM increased mitochondrial membrane potential (ΔΨ) and decreased respiration and ATP production in HepG2, Huh7 and HCC4006 cells. We also showed that the bcl-XL inhibitor ABT-737 prevents mitochondrial hyperpolarization induced by the ATP synthase inhibitor, oligomycin. Here, we hypothesize that SIM at nanomolar concentrations increases ΔΨ contributing to decrease cell proliferation and that both mitochondrial hyperpolarization and inhibition of cell proliferation are influenced by bcl-XL. METHODS: Confocal fluorescence microscopy of tetramethylrhodamine methyl ester assessed ΔΨ. CHOL levels were determined after lipid extraction from whole HepG2 cells and isolated mitochondria using an Amplex Red Cholesterol Fluorometric Assay Kit. Respiration was assessed using a Seahorse XFe96 Analyzer and cell proliferation by direct cell counting of live/dead cells. RESULTS: SIM increased mitochondrial ΔΨ in a dose-dependent fashion (20<100 nM) in HepG2 cells at 24 h. SIM (100 nM for 24 h and 10 μM for 6 h) increased ΔΨ by ~120 % and 160 % respectively. High ΔΨ promoted by SIM (100 nM and 10 μM) was sustained for at least 72 h. ABT-737 (1 μM) blocked mitochondrial hyperpolarization induced by SIM. SIM both at 100 nM and 10 μM decreased cell proliferation without promoting cell killing. The inhibition on cell proliferation was partially blocked by pretreatment with ABT-737. CONCLUSION: Therapeutic concentrations of statins decreased cell proliferation without promoting cell killing possibly by modulation of mitochondrial metabolism mediated by bcl-XL. This work was supported by NIH R01CA184456, GM103542

67 Characteristics and Behavior of Primary Mouse Cardiac Fibroblasts on Tissue Culture Plates of Varying Stiffness

Tiffany Dean, Yuhua Zhang, Amy Bradshaw, Graduate Studies, Division of Cardiology, MUSC.

Fibroblasts are specialized cells that are found throughout the human body. These cells produce extracellular matrix (ECM) and participate in processes such as wound repair. When a tissue such as the heart is damaged, for example in heart failure, fibroblasts participate in the repair of the heart by secreting collagen and other ECM proteins. Fibroblasts respond to their environment and therefore, their behavior is dependent on environmental factors. One factor that is known to influence fibroblast activity is tension. Collagen and ECM tend to accumulate contributing to increased stiffness in the myocardium. To better understand how fibroblast behaves within the human body, especially the heart, improved models that more closely mimic tissue environments are needed. To this end, we seek to investigate the characteristics and behavior of primary cardiac fibroblasts when plated onto tissue culture plates of increasing stiffness. We hypothesize that utilizing culture plates with increasing stiffness will affect cardiac fibroblasts behavior. Primary cardiac fibroblasts were cultured from age-matched sham-treated mice and mice with transverse aortic constriction (TAC) for approximately 4 weeks. Fibroblasts were plated onto substrates with increasing stiffness values of 8kPa (Cytosoft, Advanced Biomatrix), indicative of healthy hearts, 16kPa, representative of fibrotic HFpEF hearts, and plastic. Initially, we observed, by cell density and pellet size, that fibroblasts tend to adhere more strongly to plastic culture plates versus softer elastic modulus Cytosoft plates. Furthermore, fibroblasts plated on Cytosoft plates demonstrate a more round, elongated morphology in comparison to those on plastic. Future experiments will measure changes in ECM production. Ultimately, this study will help to optimize culture conditions for primary cardiac fibroblasts. This work was supported by National Institute of Health 5-R25-GM113278, VA Merit

68 Discrete populations of enteric progenitor cells revealed by cell lineage analysis in mice.

Meagan Branch, Takako Makita, Graduate Studies, Pediatrics, MUSC.

Hirschsprung disease (HSCR) is a congenital gut motility disorder characterized by defective caudal migration of neural crest cells into the bowel that results in loss of the enteric nervous system (ENS). Affected individuals suffer from impaired colonic peristalsis. In humans, several genetic loci associated with HSCR have been identified, including glial-cell derived neurotrophic factor signaling (GDNF and RET) and endothelin signaling (EDN3 and EDNRB). The genetic and molecular intersections of GDNF and endothelin pathways in genesis of HSCR is not well understood. Previous studies have demonstrated that global mutation of Ret in mice results in the total loss of the ENS along the gut. Thus, Gdnf-Ret signaling is required for enteric progenitor (EP) migration into the gut. To demonstrate roles of Ret within the endothelin responsive population of EP cells in mice, we crossed an Ednrb-Cre allele with a conditional Ret allele, and combined this with the conditional cell lineage tracer R26RlacZ. Further, embryos were isolated at embryonic day E10.5, stained in whole-mount with Xgal, followed by microscopy evaluation of Xgal staining pattern in the gut. In control embryos, Ednrb-Cre+ lineage-labeled cells populated the foregut and reached the midgut by E10.5. We observed a significant reduction of labeled cells in the foregut through midgut region of Ednrb-Cre/Ret mutant embryos. However, this population was not completely eliminated. Our results reveal a heterogeneity in EP cells. First, of the progenitors that express Ednrb, some require Ret for their migration. Second, a separate population expresses Ednrb, but does not require Ret for foregut entry and migration; this population is still able to populate the gut in Ednrb-Cre/Ret mutants. Because global absence of Ret eliminates both populations from the developing gut, these observations suggest that the second population (Ret independent) requires the

preceding entry of other Ret-dependent enteric progenitors in order to properly migrate. This work was supported by NIH Grant R25 GM113278 awarded to Dr. L. Kasman & Dr. C. Wright

69 Inventing and testing a new, open-source 3D-printed transcranial magnetic stimulation coil tracker holder for MRI-guided neuronavigation studies

James Lopez, Kevin A. Caulfield, Claire E. Cox, Donna R. Roberts, Lisa McTeague, Graduate Studies, Brain Stimulation Laboratory, Department of Psychiatry, Medical University of South Carolina, Charleston, SC USA, MUSC.

Background: Transcranial magnetic stimulation (TMS) is an effective, noninvasive brain stimulation method that is FDA-approved for the treatment of multiple neurological and psychiatric conditions. A recent advance is to use each individual's magnetic resonance imaging (MRI) scan to more accurately target specific brain regions, a technique that is called "neuronavigation." However, commercially available neuronavigation equipment is expensive and cannot easily be adapted to critical prospective double-blind, sham-controlled TMS studies. Objective: Here we invented and tested the utility of a new 3D-printed TMS coil tracker holder for use in MRI-guided neuronavigation studies. We hypothesized that our 3D-printed TMS coil tracker holder would have non-inferior accuracy as commercially available models but would be significantly faster and easier to use. Methods: We first designed and 3D-printed multiple prototypes for the TMS coil tracker holder. After settling on a design, we tested how long it took 10 trained TMS providers to switch between the active and sham sides of a double-blind TMS coil. We additionally tested the accuracy with which the TMS providers could target a location marked on a participant's MRI scan. We compared these data to the timing and accuracy of using a commercially available TMS coil tracker holder using a within-subjects, counterbalanced design. Results: Preliminary data suggest that our 3D-printed TMS coil tracker holder is easier and faster to use than a commercially available model, with non-inferior accuracy. Conclusions: Our 3D-printed TMS coil tracker holder can be implemented in prospective double-blind, sham-controlled studies. It is easier and faster to use than commercially available products while retaining a similar level of accuracy for targeting different brain regions. We have made the .stl files for 3D-printing open-source and freely available online.

70 Activity-regulated cytoskeleton-associated protein (arc/arg3.1) regulates addiction-related behavior via action in the nucleus accumbens.

Dalia Martinez, Sarah Barry, Rachel Penrod, Christopher Cowan, Christopher Cowan, Graduate Studies, Neuroscience, MUSC.

Substance use disorder is a chronic, relapsing condition, characterized by cycles of intoxication, withdrawal, and drug-seeking. Previous work has identified glutamatergic plasticity in the nucleus accumbens (NAc) as a key regulator of addiction-related plasticity, but the molecular mediator(s) of this plasticity remain unclear. The immediate early gene, activity-regulated cytoskeleton-associated protein (Arc, also known as Arg3.1), is a known regulator of glutamatergic synaptic strength, and its expression is upregulated in the NAc following cocaine exposure. In our initial observations of Arc-deficient mice (Arc KO), we found behavioral phenotypes consistent with enhanced sensitivity to cocaine. We next used a viral-mediated shRNA approach to knockdown Arc expression specifically in the NAc. In our preliminary studies in mice, we find that Arc knockdown in the NAc decreases sensitivity to cocaine. Interestingly, this effect appears restricted to or more robust in males than females. Current work is focused on identifying the cell-type(s) mediating Arc's effects on cocaine sensitivity using cre-dependent shRNA in mice expressing cell-type specific cre recombinase. Other work is focused on identifying the cellular consequence of Arc knockdown, with a focus on changes in glutamatergic synaptic strength and plasticity. Finally, while it is clear that the cocaine hypersensitivity observed in Arc KO mice is not mediated by the NAc, it remains unclear whether this effect is derived from loss of Arc in other brain regions or a more complex developmental consequence of total Arc knockout. Our current findings indicate that Arc usually functions in the NAc to increase the effects of cocaine. Understanding the cell-types and mechanisms through which Arc mediates this effect may identify novel therapeutic targets and help us to understand the underlying neurobiology that drives substance use disorder. This work was supported by NIDA F32 DA036319, NIDA R01 DA027664, NIDA R01 DA032078

71 Impact of Industry, Age, and Gender on Incidence, Rate, and Days Lost from Work for Workplace Foot and Ankle Injuries

Alexander Caughman, Christopher Gross, Medicine, Orthopaedics, MUSC.

Introduction According to the Bureau of Labor Statistics (BLS) in 2017 over 92,000 foot and ankle injuries resulted in lost work days. The average ankle injury claimed $17,028 with $12,861 in indemnity. The average foot injury claimed $15,140 with $11,428 in indemnity. This study compares the incidence, rate, and days lost from work due to foot and ankle injuries compared to other musculoskeletal injuries. This study's findings will help us better understand which industries are greater impacted by these injuries. Methods Patient data from the BLS Workplace Injuries and Illnesses Nonfatal Cases Involving Days Away From Work: Selected Characteristics database was analyzed with SPSS statistics software to identify the industries, gender, and ages associated with the highest rates and days off work for each type of injury (ankle sprain, ankle fracture, foot fracture, amputation). The Incidence and rate were obtained for a ten-year period (2007-2017) and days lost from work was obtained for a seven year period (2011-2017). Additionally, data from the private and public sectors was compared to determine if these differ in days missed and incidence rate. Results Incidence rates, as well as days missed from work, were highest for both foot and ankle injuries in industries involving manual labor such as construction, mining, and manufacturing. However, the incidence rates and days missed from work for of both types of injuries were statistically significant from each other for corresponding industries. Data analysis involving gender and age is ongoing. Conclusions This study's findings will help us better understand how factors such as age, gender, and industry influence the occurrence of foot and ankle injuries within the workforce. This information could potentially be used to identify industries in need of additional safeguards to protect workers from injury and provide companies with estimates of costs incurred from injured employees.

72 Motor-Activated Auricular Vagus Nerve Stimulation (MAAVNS) to Restore Upper Limb Function in Chronic Stroke Patients

Andrew Fortune, Scott Hutchison, Sean L. Thompson, Steve Kautz, Mark S. George, Bashar Badran, Health Professions, Psychiatry, MUSC.

Introduction: The temporal pairing of vagus nerve stimulation (VNS) with motor rehabilitation can restore pathologically insufficient neural activity and correct maladaptive activity. This pairing of VNS and restorative behavioral intervention is known as "targeted plasticity" and is a

promising approach that may potentially transform current rehabilitation approaches. Recently, a noninvasive alternative known as transcutaneous auricular vagus nerve stimulation (taVNS) has emerged as a promising alternative to conventionally implanted cervical VNS. taVNS targets the auricular branch of the vagus nerve, which innervates the human ear and activates the afferent and efferent vagal networks, theoretically allowing for a noninvasive, simple, and rapid translation of cervically implanted VNS findings. We hypothesize that using taVNS combined with task specific training (TST) may boost the effects of the current gold-standard TST rehabilitation therapy. This study explores the development of a novel taVNS system and its subsequent test in a clinical population. Methods: We developed a motor-activated auricular vagus nerve stimulation (MAAVNS) system using electromyography (EMG) sensors placed on four different target muscles (anterior/mid deltoid, biceps, triceps, flexor carpi radialis/ulnaris). Unilateral motor activity measured by EMG will be recorded in 5 adults and analyzed for spatial and temporal resolution of upper extremity kinematics. We then will enroll 20 adult stroke survivors with unilateral hemiparesis into an open-label pilot trial using MAAVNS to deliver taVNS concurrently with TST to improve upper extremity motor outcomes. Results: So far, our MAAVNS system reliably administers stimulation paired with upper extremity movement which is initiated during therapist-guided task specific training. This system appears safe, portable, and the preliminary findings from our open-label pilot trial will be reported. Conclusions: MAAVNS is a promising new tool in neurorehabilitation that automates and simplifies the delivery of pairing noninvasive vagus nerve stimulation with motor rehabilitation training. This trial will test whether MAAVNS is feasible in a chronic This work was supported by COBRE (Center for Biomedical Research Excellence)

73 Epigenetic Therapy for Sickle Cell Disease

Steven Holshouser, Joy Kirkpatrick, Hyacinth Hyacinth, Patrick Woster, Graduate Studies (MSTP, PhD years), Drug Discovery, MUSC.

The symptoms of sickle cell disease (SCD) often begin in the first year of life and worsen over time, or in some cases do not present until later in life. Symptoms vary from person to person, but can include swelling of the hands, widespread acute pain, acute chest syndrome, splenic sequestration, and a host of others. There is currently no cure for SCD; the current clinical standard of therapy, the myelosuppressive agent hydroxyurea (HU) increases g-globin and fetal hemoglobin (HbF) content in sickle cells. Unfortunately, HU is highly underutilized due to concern for adverse effects and major complications. SCD is caused by a single nucleotide polymorphism on chromosome 11 in the b-globin gene that results in a mutant form of hemoglobin known as hemoglobin S (HbS). At birth, humans produce fetal hemoglobin (HbF, 2 a- and 2 g-subunits). By 6 months of age, the DRED epigenetic complex silences the g-globin gene, and HbF is replaced by adult HbA (a2b2), or HbS (a2bs2) in SCD patients. We seek to overcome current therapeutic barriers by developing novel and effective small molecule therapies for the treatment of SCD. The DRED complex contains the epigenetic eraser LSD1, deoxynucleotide-N-methyltransferase 1 (DNMT1) and the nuclear receptor proteins TR2/TR4, and interacts with the co-repressors NuRD and CoREST. The rationale for our approach is the finding that LSD1 inhibitors can disrupt the DRED epigenetic complex, leading to re-expression of g-globin and formation of HbF. HbF is a potent inhibitor of sickle cell polymerization, thus alleviating the symptoms of SCD. Our recently discovered 1,2,4-triazole derivatives inhibit LSD1 and promote chromatin remodeling in vitro without significant toxicity while simultaneously promote an extended up-regulation of g-globin production. Using the approach outlined above, we aim to identify a novel clinical candidate for use as an innovative and effective treatment for SCD. This work was supported by NIH

74 Combination of tumor localized PD1 blockade and IL-12 (p70) results in potent systemic antitumor efficacy

Carrie Fisher, Cody Gowan, Mee Bartee, Eric Bartee, Graduate Studies, Microbiology and Immunology, MUSC.

Combination therapies employing checkpoint inhibitors and oncolytic virotherapy (OV) are drastically changing the cancer immunotherapy landscape. We have previously reported that a recombinant myxoma virus engineered to express a soluble PD1 transgene effectively eliminates directly treated tumors in multiple preclinical models. Unfortunately, subsequent studies demonstrated that this virus is not effective against already metastasized disease. Therefore, to generate a more effective agent we constructed a series of additional recombinant myxomas which expressed both soluble PD1 and one of a series of proinflammatory cytokines including: IL2, IL12, IL15, IL17, and IL18. Of these constructs, we observed that only the virus expressing both PD1 and IL12 (vPD1/IL12) was effective at eradicating both injected and non-injected lesions. This construct, however, displayed synergistic efficacy not seen following treatment with control viruses expressing either soluble PD1 or IL12 alone and was highly effective in multiple preclinical models. Despite its systemic efficacy, biodistribution studies indicated that neither virus nor therapeutic transgenes could be detected in non-treated tumors following localized injection. Additionally, despite the fact that both PD1 and IL12 are predominantly known as adaptive immune-modulators and localized treatment with vPD1/IL12 induced strong lymphocyte infiltration into tumors, the efficacy of therapy was totally independent of both CD4 and CD8 T cells. Further experiments have also suggested that efficacy is not entirely interferon gamma mediated. These data suggest that localized treatment with oncolytic myxoma virus secreting both PD1 and IL12 creates a promising immune therapy for multiple forms of metastatic cancer. This work was supported by 8C780, 8D084, 87455

75 Analysis of statin use for modulation of cardiovascular disease risk in HIV patients in a southern academic medical center

Miranda McGee, Anupha Mathew, Richard Lueking, Eric G. Meissner, James New, Stephanie Kirk, Emily Ware, Pharmacy, MUSC Pharmacy Ambulatory Care, MUSC.

Patients living with Human Immunodeficiency Virus (PLWH) are at a higher risk for developing atherosclerotic cardiovascular disease (ASCVD), even when virologically suppressed. Increased risk for ASCVD in PLWH may be due to changes in body composition, antiretroviral therapy (ART), comorbid conditions, and chronic inflammation that persists even when HIV is well controlled. A baseline fasting lipid profile should be measured in all PLWH according to U.S. Department of Health and Human Services guidelines. Frequency of lipid monitoring thereafter is dependent on age and risk factors. According to 2017 American Association of Clinical Endocrinologists and American College of Endocrinology guidelines, initiation of statin therapy can be based on lipid values, risk factors, and calculated risk for ASCVD. The Framingham risk equation allows for calculation of a 10-year risk cardiovascular score and is a composite of patient age, sex, blood pressure, LDL, HDL, diabetes and smoking status. The objective of this study is to evaluate the frequency with which patients at our HIV clinic, housed in a Southern academic medical center, received annual lipid panel monitoring, received statin therapy, and the overall percentage of PLWH who have met a goal LDL based on their risk category. Our primary outcome is to define an overall frequency of statin prescribing in an academic medical center. The secondary outcome is to distinguish the differences in statin prescribing among multiple parameters including age, prescribers, and HIV regimens. We conducted a retrospective chart review on all patients actively prescribed ART and followed in the

MUSC Infectious Disease clinic between July 1, 2017 and June 30, 2018 (n=1200). We determined patient age, sex, race, BMI, medication list, hemoglobin A1c, average systolic blood pressure, smoking status, and lipid panel. This data was utilized to identify areas for improvement in the prescribing of statins per AACE guidelines for PLWH.

76 Sex-specific auditory functional deficits in a mouse model of autism

Josef Blaszkiewicz, Junying Tan, Kenyaria Noble, Ahlem Assali, Christopher Cowen, Hainan Lang, Medicine (MSTP, MD years), Department of Pathology and Laboratory Medicine, MUSC.

In individuals with autism spectrum disorder (ASD), auditory functional deficits may contribute to impaired communication and atypical sensory processing. To test this hypothesis, peripheral auditory function was examined in a mouse model of ASD. Ephrin type-B receptor 2 (EphB2) is a receptor tyrosine kinase that has multiple functions in axon guidance, cell proliferation and differentiation, and localization of other membrane receptors. Mutations in the EphB2 gene have been linked to ASD in humans. Mice that are heterozygous for EphB2 exhibit several behavioral phenotypes relevant to ASD. To determine if hearing loss is present in this model, we performed auditory brainstem response (ABR) recordings on EphB2 heterozygous mice and examined their ABR thresholds across a range of frequencies. Wild-type littermates were used as controls. While there was no significant difference in observed ABR thresholds between wild-type and heterozygous female animals, male heterozygotes showed significantly increased thresholds compared to the wild-type controls for low to mid-range frequencies. Cochlea were collected from the animals and analyzed by electron microscopy to determine if any pathology was evident. Heterozygous EphB2 males showed evidence of degeneration in the auditory nerve in the apical region of the cochlea. Pathological alterations were also observed in the intermediate cells of the stria vascularis, which are critical for maintaining endocochlear potential. Overall, these findings indicate that auditory function is impaired in a sex-specific manner in the EphB2 deficient model, and will inform future studies that examine other models of ASD by establishing sex as an important variable in assessing their peripheral auditory function. This work was supported by NIH Grant P50 DC000422 NIH Grant R56 DC012058

77 Characterization of the Angiogenic Factor SFRP2 in Papillary Thyroid Cancer

Wyatt Wofford, Julie Siegel, Rupak Mukherjee, Denise Garcia, Eleanor Hilliard, Patrick Nasarre, Nancy Klauber-DeMore, Mahsa Javid, Medicine, Department of Surgery, MUSC.

Each year, over the last ten years, there has been an average increase of 3.1% in thyroid cancer diagnosis rates. However, few molecular markers exist to identify clinically aggressive phenotypes. The angiogenic factor, secreted frizzled-related protein 2 (SFRP2), is known to be involved in several other malignancies, such as breast cancer and melanoma. The role of SFRP2 in thyroid cancer has yet to be investigated. Immunohistochemistry (IHC) was performed to (1) determine the differential expression of SFRP2 in human papillary thyroid carcinoma (PTC), benign thyroid adenomas, and normal thyroid using tissue protein microarrays; (2) compare the expression of SFRP2 in normal thyroid tissue (from patients without cancer) versus normal adjacent tissue (NAT) (non-cancerous tissue from patients with PTC) using tissue protein microarrays; and in-vitro studies were performed to (3) explore the response of two PTC cell lines, PTC classical (PTC-CV) and PTC follicular variant (PTC-FV), when treated with an anti-SFRP2 mAb, control IgG, and vehicle control in an apoptosis/necrosis assay and a proliferation assay. IHC was scored on a scale from 0 - 12.0. IHC on 226 PTC samples, 79 benign thyroid adenomas, and 30 normal thyroid samples had median expression scores of 9.0, 6.0, and 0 ($p<0.05$), respectively. IHC on 112 NAT samples and 30 normal thyroid samples scored 4.0 and 0 ($p<0.05$), respectively. Proliferation assays on the PTC-C and PTC-FV cell lines showed no difference across the groups. The apoptosis/necrosis assay on the PTC-C and PTC-FV cell lines showed an increase in apoptosis for the treatment group against the controls by 126% and 40%, respectively. In this work, we have investigated the differential expression of the angiogenic factor, SFRP2, in PTC and tested the response of PTC cell lines against an anti-SFRP2 mAb to suggest a dependence on SFRP2 in PTC. This work was supported by HCC Clinical Scholars Award

78 DCHS1 Regulated miRNA Processing and Its Effects on Valve Endocardium Stabilization

Mary Rumph, Kelsey Moore, Rebecca Stairley, Diana Fulmer, Reece Moore, Janiece Glover, Joyce Nair-Menon, Amanda Daulagala, Courtney Gensemer, Lilong Guo, Christina Wang, Antonis Kourtidis, and Russell Norris, Russell Norris, Graduate Studies, Cell Biology and Regenerative Medicine, MUSC.

Mitral valve prolapse (MVP) is one of the most common forms of cardiac valve disease and affects 1 in 40individuals worldwide. MVP can lead to arrhythmias, heart failure, and sudden cardiac death and 1 in 10 patients will require valve surgery. Surgery for MVP is now the fastest growing cardiovascular intervention in the Western world. As such, MVP carries a significant burden of morbidity and mortality. Our lab was the first to identify the cause of non-syndromic MVP using a combination of linkage analyses, as well as exome and capture sequencing to identify loss of function mutations in the cadherin gene, DCHS1. Two-hybrid screens were undertaken to further understand Dchs1 function and the RNA binding protein, LIX1L was identified as the only interacting protein. LIX1L binds and promotes miRNA processing through interactions with the microprocessor which is made up of the proteins DROSHA and DGCR8. Expression studies have corroborated this theory as DCHS1, LIX1L, and the microprocessor proteins are expressed in endothelial cells in the mitral valve. Cell culture data shows that a loss of DCHS1 compromises processing of target miRNAs through the microprocessor leading to a significant decrease in pre-miRNA expression. Expression studies have also shown that loss of Dchs1 reduces valve endocardial stability, which may be caused by the loss of miRNAs. These studies illustrate the importance of DCHS1 effects on valve endocardium stabilization in MVP. Uncovering how these changes lead to clinically significant pathology later in life is crucial to the characterization of MVP.

79 Prospective surveillance of infectious disease with application to SC seasonal influenza data

Joanne Kim, Andrew Lawson, Graduate Studies (MSTP, PhD years), Public Health Sciences , MUSC.

Timely detection of possible infectious disease outbreak has been the important issue in the public health domain since United States still has the wide spread infectious disease threat such as measles outbreak in 2019. In order to detect the change of disease outbreak status, prospective surveillance of the disease of interest is required and it is essential to have the accurate and prompt measure of surveillance, to decide added new data support a change in public health risk. To address this issue, we investigated the performance of several detection

methods such as Surveillance conditional predictive ordinate (SCPO) and other residual and posterior functionals based on the Bayesian hierarchical modeling framework. During the modeling stage, we proposed the Bayesian spatial-temporal models which accommodate the spatial dependency and lagged dependency of time. Our models consist of two components and consider both endemic and epidemic periods to detect the changes in risk over time. Different surveillance measures are applied to publicly available influenza outbreak data of SC from the acute influenza data archive of the South Carolina Department of Health and Environment Control (SCDHEC). Future research is planned for the new combination of surveillance measures and the consideration of directionality of infectious disease outbreak. This work was supported by This work was funded through a contract from Johns Hopkins University.

80 Big Gaps for Little People: A Scoping Review of Access to Rehabilitation Services for Children with Down Syndrome

Jacquelyn Ross, Morgan Callahan, OTS; Caroline Walsh, OTS; Grace Grantland, OTS; Emily Patten, OTS; Cristina Reyes Smith, OTD, OTR/L; Addie Middleton, PhD, DPT; Elizabeth A. Brown, PhD, MPA; Joni Nelson, PhD, MS; Heather Shaw Bonilha, PhD, CCC-SLP, Cristina Smith, Health Professions, MUSC CHP Division of Occupational Therapy, MUSC.

Background: The literature shows us that individuals in under-represented minority and socioeconomic groups are often less likely to have access to healthcare services resulting in health disparities. Children with disabilities are especially vulnerable to poor access for essential health services. This scoping review aimed to assess the current literature pertaining to healthcare disparities among children with disabilities. More specifically, the goal was to determine if previous research exists regarding children with Down syndrome and their utilization of rehabilitative services. Method: A review of the literature was conducted, based on the Aday and Anderson "Access to Care" framework from 1974, examining articles pertaining to healthcare for children with Down syndrome. Literature published from 2001 to 2019 was examined from multiple databases. During the article search process, keywords were used related to "Health professions" in general and specifically "Occupational therapy" such as: "disparities," "Down syndrome," and "Medicaid," "pediatric," and "social determinants of health." A scoping review protocol was applied to identify articles within the given inclusion criteria. Findings: The information gathered from the scoping review indicates that disparities appear to exist in healthcare services and access to care for pediatric populations related to race, ethnicity, geographical location, and socioeconomic status (SES). Unmet healthcare related needs due to gaps in health insurance coverage, health literacy, specialty referrals, provider availability, and geographic barriers were found to adversely impact utilization of services. However, limited data existed related specifically to pediatric health disparities within rehabilitation sciences. Implications: Trends in the literature indicate that healthcare disparities may exist regarding access to care and utilization of healthcare services and rehabilitative services among children with disabilities such as Down syndrome. More research is needed to determine the depth and breadth of these disparities and their impact on utilization of rehabilitative services for pediatric populations. This work was supported by Sponsored by the MUSC Division of Occupational Therapy

81 Influence of hospital encounters for falls on potentially inappropriate medication use among older patients

Yara Salem, Maha Assadoon, Matthew Hebbard, Erin Weeda, Pharmacy, MUSC- Department of Clinical Pharmacy & Outcomes Sciences, MUSC.

Introduction: Older age places people at increased risk of experiencing a fall as well as poor outcomes following these falls. Potentially inappropriate medication (PIM) use may further contribute to falls in these individuals. The objective of this study is to describe PIM use among older patients presenting to our hospital after a fall. Methods: This is a retrospective cohort study conducted at the Medical University of South Carolina (MUSC). We identified all patients ≥65 years old who presented to our hospital due to a fall (ICD-10-CM code W00-W19 in the primary diagnostic position and confirmed via chart review) between January 2019 and March 2019. PIM use (including the number of PIMs and PIM class) was ascertained from admission and discharge medication lists. PIMs were defined as 2019 Beers criteria medications that have been associated with falls. Results: A total of 292 patients presenting to our institution after a fall were included. The median age of patients was 74 (interquartile range=69-82) and 58.2% (n=170) were female. Upon admission, 70.9% (n=207) of patients were on PIMs and this increased to 78.8% (n=230) at discharge ($p<0.001$). The most commonly prescribed PIMs at discharge included antidepressants (n=123), opioids (n=111), anticonvulsants (n=88) and benzodiazepines (n=50). Conclusion: More than two thirds of patients in our study were on PIMs upon admission and this number increased upon discharge, suggesting that PIM use in older patients experiencing falls is frequent. Future studies should evaluate if PIM use increases the risk of hospital encounters for recurrent falls.

82 Program Evaluation of CARES Therapy Clinic: Barriers and Facilitators for Using Standardized Outcome Measures

Shelly Law, Hattie Johnson, Megan Lebov, Emily Lievsay, Meghan Martin, Maddi Wever, Tambra Marik, Craig Velozo, Health Professions, Department of Health Professions/Division of Occupational Therapy, MUSC.

Background: Use of outcome measures to monitor improvement in patients is considered good clinical practice. Unfortunately, routine outcome measurement has largely failed to become embedded in rehabilitation therapy clinics. Purpose: To investigate the barriers and facilitators to collecting, managing and applying outcome measures in the Community Aid Relief Education Support (CARES) Therapy Clinic Methods: We applied structured interviews of occupational therapy, physical therapy and Masters of Health Administration student clinicians and CARES board members. Students were randomly chosen and anonymously interviewed. Narratives were initially coded by data collectors and final coding was arrived by team consensus. Statements were either "positively coded" - supportive of the use of outcomes or "negatively coded" - unsupportive of using outcomes. Results: Codes including, "meaning", "knowledge/experience", "utilization", "confidence", "culture" and "time" appeared in the respondent narratives. An example of a positively coded statements is, "The COPM [Canadian Occupational Performance Measure] tells me what is important to the patient..." and an example of a negatively coded statements is, "I have little knowledge of that [reliability and validity]." In general, the narratives included more positively than negatively coded outcomes. Conclusion: Overall, CARES student therapists demonstrated support for using outcomes in their student-run clinic. The qualitative information from this program evaluation provides direction for developing supports to improve outcomes collection and applications in our CARES student run therapy clinic.

83 The Effect of TheraBracelet and In-Home Therapy on Neural Plasticity and Hand Function

Emma McCarthy, Nicole Bradford, Julia Campbell, Amanda Vatinno, Will DeVries, Andrew Fortune, Michelle Woodbury, Viswanathan Ramakrishnan, Leonardo Bonilha, Na Jin Seo, Health Professions, Department of Health Professions, MUSC.

Background- The majority of stroke survivors live with sensorimotor impairments that affect their ability to complete functional daily tasks. Sensory input is an essential part of executing movement. Thus, when therapy is augmented with sensory stimulation, it enhances motor recovery, as supported by meta-analysis. Previous research showed that TheraBracelet, a subsensory vibration to the affected wrist, is safe and feasible to use during therapy and at home, and that use of TheraBracelet during in-lab therapy increased motor recovery more than therapy alone. The important question is whether in-home use of TheraBracelet can increase the treatment dose substantially beyond typical clinic visits, thereby contributing to increased motor recovery. TheraBracelet may be Incorporated in in-home therapy to increase carryover into everyday life. Objective- The purpose of this study is to determine the effect of in-home use of TheraBracelet and self-directed therapy on neural plasticity and hand function. Method- In a double-blind randomized control trial, chronic stroke survivors are randomly assigned to a control or treatment group. Both groups wear a wristband device for at least 8 hours a day every day for a month, and also complete self-directed home therapy 5 days a week under the consultation of an occupational therapist. Only the treatment group receives subsensory TheraBracelet stimulation from the wristband device. Outcome measures are obtained at baseline, weekly during the month of intervention, and at 3-month follow-up. Results- The study is ongoing. Four participants are in follow-up. Three participants' clinical data have been analyzed. Researchers remain blinded. On average, participants increased their upper extremity motor capacity as measured by the Action Research Arm Test. Additionally, participants' perceived performance and satisfaction of meaningful activities of daily living improved, based on the Canadian Occupational Performance Measure. Conclusion- The study may result in a cost-effective treatment program for post-stroke upper extremity rehabilitation. This work was supported by NIH/NIGMS 2P20GM109040-06

84 Medication Adherence to Rivaroxaban and Dabigatran in Patients with Non-valvularAtrial Fibrillation: a Meta-analysis

Irene Ruiz, Ashley Prentice, Erin Weeda, Pharmacy, MUSC College of Pharmacy, MUSC.

Background: Adherence to direct oral anticoagulants (DOACs) is necessary to maximize the benefits of these agents. Several real-world studies have evaluated DOAC adherence in patients with non-valvular atrial fibrillation (NVAF); however these studies have not been systematically summarized. We performed a meta-analysis to compare adherence to rivaroxaban versus dabigatran therapy in United States (US) patients with NVAF in a real-world setting. Methods: Medline and Scopus were searched from January 2010 to August 2018 using keywords and MeSH terms related to adherence and oral anticoagulants. We included real-world studies of US adults with NVAF comparing adherence to dabigatran and rivaroxaban. Studies evaluating adherence by a measure other than proportion of days covered (PDC) were excluded. The proportion of patients with a PDC≥80 (a commonly utilized definition of adherence) served as the primary outcome of interest. We conducted a meta-analysis of included studies using the Hartung-Knapp random-effects model to estimate risk ratios (RRs) with corresponding 95% confidence intervals (CIs). The I2 statistic was used to assess the percentage of variability in the treatment estimate that is attributable to heterogeneity. Results: We included 5 studies evaluating 80,230 patients (range: 2,667-22,571). Median follow-up across studies was 6 months (range: 3-12 months). The proportion of patients with a PDC≥80 ranged from 59.5% to 83.5% for rivaroxaban users and 57.3% to 78.3% for dabigatran users. Upon meta-analysis, rivaroxaban use was associated with increased adherence compared with dabigatran use (RR= 1.08 95% CI=1.03-1.12; I2=88%). Discussion: Rivaroxaban was associated with increased adherence. Possible explanations for this include dosing frequency or patient tolerance. A limitation of our analysis is that we were unable to assess the impact of adherence on outcomes for these agents. Nonetheless, the inclusion of real-world studies increases applicability.

85 Instillation of povidone-iodine ophthalmic solution onto the eye surface causes a decrease in respiratory rate in spontaneously breathing children under general anesthesia undergoing strabismus surger

Melanie Rubin, Bethany Jacobs Wolf, PhD , Alexandra Ritter, BS , Christopher L. Heine, MD , Tracy E. Wester, MD , Cory M. Furse, MD, MPH, FAAP, Michelle Rovner, Medicine, Department of Anesthesia & Perioperative Medicine, Medical University of South Carolina, MUSC.

Abstract Withheld from Publication

86 Observational Study of Patients Demographics in Those Presenting with Acute ST-Elevated Myocardial Infarction: a 5-Year Review at a High-Volume Institution

Alexander Canova, Katrina Bidwell, Billy Joe Mullinax, Valerian Fernandes, Medicine, Cardiology, MUSC.

INTRODUCTION: The Framingham Heart Study was the gold standard for the determination of epidemiologic risk factors in myocardial infarction. Although it identified cigarette smoking as an independent predictor of future MI, it also recognized certain other risk factors such as age and gender. Recent work has shown an increased prevalence of MI in younger adults and our study aims to evaluate this trend while identifying any gender disparities. METHODS: We evaluated records of 397 consecutive patients between 2014 and 2019 that triggered a STEMI alert on presentation to our center. Chart review included age at catheterization, gender and 30-day mortality following percutaneous coronary intervention (PCI). Angiography videos were individually reviewed to corroborate evidence of coronary artery disease-induced MI. T-tests were run to compare PCI outcomes between genders, as well as mean age of presentation. RESULTS: A total of 268 patients (188M, 80F) who underwent left heart catheterization at our institution between 2014 and 2019 were found to have angiographic evidence of coronary artery disease consistent with area of infarcted myocardium. The average age of these patients was 61.13 ± 11.97 with a statistically significant younger age of male events versus female events ($M = 59.97$, $F = 63.91$; $p < 0.05$). There was no significant 30-day survival difference between genders ($M = 94.15\%$, $F = 92.50\%$; $p > 0.5$). The average BMI was 29.45 ± 6.69 (N=215). CONCLUSIONS: Multiple large volume studies including the Atherosclerotic Risk in Communities study and Cardiovascular Health Study found significant difference in average age at first MI in 2012 (M=64.5yrs, F=70.3yrs). A recent study in Boston has shown an increasing incidence of MI in adults <50, and it appears that the average age of first heart attack may be declining according to our findings.

87 Correlating pre-operative Mini-Cog screening scores with post-operative delirium

Brenton Davis, Benjamin Kalivas, Medicine, Department of Medicine, MUSC.

Introduction: Delirium is a well-known post-operative neuropsychiatric complication that has been shown to increase mortality, length of stay (LOS), post-op complications, nosocomial infections and can lead to long term cognitive sequelae. In our hospital we screen all non-ICU adults admitted to our hospital twice daily using a Confusion Assessment Measurement (CAM) to monitor for delirium. We hypothesized that patients seen in pre-operative clinic with a high-risk Mini-Cog would correlate with an increased incidence of positive CAM postoperatively while admitted. Methods: We reviewed the pre- and post-operative course of 221 patients scheduled to receive an elective surgery. We evaluated patients for demographic information, Mini-Cog score, CAM results while in the hospital, psychiatric/neurologic diagnoses and discharge destination. Thirty-three patients were excluded, there were 5 duplicate patients and 28 patients whose surgeries were cancelled or scheduled on a future date. CAM results were recorded for 108 patients. Results: The average age of patients enrolled was 73.7± 6.8 (mean± SD) years. Of the 221 patients initially enrolled, 188 patients had both a completed pre-admission screen with Mini-Cog score and were discharged after their completed procedure. 46 (24.46%) patients had a Mini-Cog score ≤2, which has been shown to indicate probable cognitive impairment. 108 of the 188 (57.44%) patients with completed procedures had CAM scores recorded in EPIC irrespective of their admission floor. Of the 108 recorded CAM scores, 3 (2.78%) were positive. The average LOS of all patients was 2.17±3.62 days. The average LOS for the three CAM positive patients was 12.67 days. Conclusion: Identifying at risk patients for delirium and associated comorbidities is challenging. Despite using validated screening tools like the Mini-Cog, we did not find that low mini-cog scores correlated with delirium.

88 Role of T cell Subsets in Glaucoma

Alexa DeMaio, Singh Sudha, Mehrotra Shikhar, Shahid Husain, Medicine, Ophthalmology, MUSC.

Glaucoma, a leading cause of blindness worldwide, is characterized by progressive loss of retinal ganglion cells (RCGs), an excavated appearance of the optic nerve, and vision loss. The pathophysiology of glaucoma is multifactorial involving biomechanical stress, neuroinflammation, oxidative stress, and the immune system. While the eye is an immune privileged organ it is also subject to autoimmune destruction. No study has yet explored the differences in T cell subsets (i.e., activated immunogenic T cell effectors vs. suppressive/tolerogenic regulatory T cells) influence on the RGC death process in glaucoma. We hypothesize that under pathologic conditions certain activated effector T cells can infiltrate the retina, reduce suppressive Treg cells, and enhance the production of proinflammatory cytokines. The precise role of the immune system, particularly effector T cell induced RGC death, and the neuroprotective role of suppressive Treg cells remains undefined. To determine a pathological role of activated effector T cells in glaucoma, we used a Brown Norway Rat Glaucoma model, which was develop using 2.0 M hypertonic saline injected into the limbal veins to raise intraocular pressure. Using Western blotting and immunohistochemistry, we analyzed the changes in the expression of CD3 in retinas and observed a significantly increased in CD3 expression in glaucomatous eyes. FoxP3+ (a Treg marker) expression was also reduced in glaucomatous eyes when compared to the normal eyes. This data forms a strong rationale that T cell/Treg cell imbalance exists during glaucomatous injury and may be a key player to determine the fate of RGCs. Further study of the mechanisms of T cell induced RGC death and neuroprotection and by suppressive T effector and enhancing Treg cells population may provide novel immunologic therapy for glaucoma. This work was supported by National Institutes of Health grants (EY-027355)

89 Diagnostic Efficacy of Computed Tomography in detecting Radiographic Extranodal Nodal Extension (rENE) in Head and Neck Squamous Cell Carcinoma (HNSCC): A Systemic Review & Meta-Analysis

Flora Yan, Young Jae Byun, Shaun Nguyen, Medicine, Otolaryngology, MUSC.

Abstract Withheld from Publication

90 Evaluation of the Accuracy of Multiple Digital Impression Systems on a Fully Edentulous Maxilla

Madison Hoover, Walter Renne, Zachary Evans, Mark Ludlow, Griffin Revell, Anthony Mennito, Dental Medicine, College of Dental Medicine - Department of Oral Rehabilitation, MUSC.

This study aimed to compare six different intraoral scanning systems for accuracy when completing a full arch scan on an edentulous cadaver maxilla. Six digital intraoral impression systems were used to scan a fully edentulous cadaver maxilla. A master scan using an industrial grade scanner was also taken to provide a point of comparison. The digital intraoral scans were compared to the master scan using a comparison program that allows for three dimensional images to overlay one another and interpret the deviations. Our results concluded that the scanner type does affect accuracy. From most to least true scanner: Element (p value=0.0003) > Trios 4 (p value=<0.0001) > Primescan (p value = 0.0017) > Trios 3 (p value=0.0023). From most to least precise scanner: Trios 3 (p value=0.007) > Trios 4 (p value=<0.0001). The area being scanned also affects the accuracy of the scan. From most to least true region: palate> maxilla >ridge. From most to least precise region: maxilla >ridge>palate. With the limitations of this in vitro study, it was found that the six different intraoral scanners show differences when completing a full arch scan on an edentulous cadaver maxilla. The scanner type does affect accuracy. The area being scanned also affects the accuracy of the scan. This work was supported by Medical University of South Carolina College of Dental Medicine - Department of Oral Rehabilitation

91 Predictive Value of Hormones in Sperm Retrieval Surgery

Nicholas Major, Kent Edwards, Kit Simpson, Marc Rogers, Medicine, Assistant Professor, Urology, MUSC.

Non-obstructive azoospermia (NOA) causes male factor infertility in about 10% of cases. Multiple techniques have been described to obtain sperm from the testicle for use with assisted reproductive technologies. Conventional testicular sperm extraction (cTESE) is the most common but some argue that microdissection testicular sperm extraction (mTESE) is preferred for its superior sperm retrieval rates (SRR) and decreased microvascular damage to the testicle. However, mTESE is generally more expensive, time consuming, and requires more equipment. Previous work has attempted to identify variables that predict positive SRR with mTESE versus cTESE. The objective of this

review was to create a model comparing the commonly evaluated variables; follicle stimulation hormone (FSH), testicular volume (TV), and testosterone (T), to better predict SRR. Based upon pooled available datam, mTESE is more successful than cTESE for sperm retrievals in NOA patients. No predictive model was able to be created at this time incorporating T, TV, and FSH levels. FSH alone can be predictive of retrieval success and used to counsel patients. More standardized data collection and publication will be useful for future modeling to allow improved outcomes and counseling for patients.

92 A comparison of a new fast brain MRI protocol to CT scans in pediatric trauma

Chelsea Shope, Mohammed Alshareef, Vittoria Spampinato, Tyler Vasas, Ramin Eskandari, Medicine, Neurosurgery, MUSC.

Introduction: Traumatic brain injury (TBI) is a frequent injury that brings pediatric populations to the emergency department. Computed tomography (CT), an imaging modality that can result in cumulatively high radiation exposure in pediatric patients, is often utilized in the evaluation of TBI. Recently, the fast brain magnetic resonance imaging (fbMRI) protocol has been employed for rapid and targeted acquisition of sequential imaging of hydrocephalus in the pediatric population. We investigate the role of a modified, trauma-focused fbMRI protocol with additional sequences in non-hydrocephalus indications, including TBI. Methods: A retrospective review was performed in our institution for all pediatric patients who underwent a trauma fbMRI within 72 hours of a CT scan using a 1.5 or 3T MR scanner. Patients with hydrocephalus, procedures performed between the CT and fbMRI scan, presence of documented change in neurologic exam between the scans, and imaging done outside of the 72-hour window were excluded. Forty patients met the inclusion criteria. We performed a comparison of findings on the reads of CT and fbMRI and the time to final reports. Results: All patients included in the study had fbMRI with CT comparison. Imaging reports revealed a higher rate of detection for intraparenchymal hemorrhages (IPH), subdural and epidural hematoma, and stroke in fbMRI as compared to CT. Skull fractures without underlying hematoma were missed on more fbMRI scans as compared to CT and had a higher false negative rate. Conclusion: In pediatric populations the trauma fbMRI protocol provides a valid alternative to CT in the detection of intracranial hemorrhages and stroke. Although not as sensitive in detection of isolated skull fractures, the trauma fbMRI protocol can detect most pathologies implicated in the acute decline of TBI patients while minimizing radiation exposure from repeat CT imaging.

93 Effect of Malnutrition on Hearing Loss in Children

Joshua Van Swol, Michaela Close, Charmee Mehta, Josh Van Swol, James Dornhoffer, Yuan Liu, Shaun Nguyen, Teddy McRackan, Ted Meyer, Ted Meyer, Medicine, Otoloaryngology, MUSC.

Worldwide, protein-calorie malnutrition (PCM) is detrimental to pediatric longevity and quality of life due to many different factors. Most consider childhood malnutrition as solely a problem in developing countries; however, it undeniably exists in the United States while still being poorly understood. This project explores the association between PCM and hearing loss (HL) in children using the Audiological and Genetic Database (AudGenDB). AudGenDB is an exclusively pediatric hearing database containing medical and audiological data exceeding 175,000 patients. Children under 18 years of age with malnutrition were identified within this database using ICD9 and ICD10 diagnostic codes. Children with a diagnosis of PCM, including kwashiorkor or marasmus, and an audiogram one month before or any time after the diagnosis of malnutrition were included. A comparison group was created using a sample of all children from the database without PCM. Of 770 children with PCM, 57.8% had HL, compared to 45.5% of children without PCM ($p<0.001$) Severely malnourished children had significantly higher odds of moderate-profound HL (aOR 2.27, 95% CI 1.47-3.43), high-frequency HL (aOR 1.82, 95% CI 1.21-2.75), and sensorineural or mixed HL (aOR 1.60, 95% CI 1.05-2.41) compared to children without PCM. In addition, HL in children with moderate to severe malnourishment were significantly less likely to improve (aOR 0.47, 95% CI 0.25-0.82 and aOR 0.4, 95% CI 0.2-0.9) compared to those without PCM. In light of these findings, children with PCM should be considered an at-risk group for poor audiological outcomes due to the increased likelihood and severity of hearing loss. Clinicians should focus on early prevention and intervention for this population and should perform regular audiological evaluations in children who have been malnourished.

94 Two Cases in Pediatric Neurology

Matthew Roberts, Kerry Roberts, Dan Williams, Medicine, Pediatrics, MUSC.

Here we describe two cases in pediatric neurology. First, we report a case of idiopathic seventh nerve palsy in a six-week-old infant. While congenital and birth-trauma-related cranial nerve (CN) VII palsy are common in the neonatal period, cases of idiopathic facial palsy are scarcely reported in young infants. Within this age group, less than five cases have been documented worldwide, and this case represents the first instance of complete (grade 6/6) Bell's palsy without a prodromal illness as well as the shortest successful duration of steroid therapy to achieve remission in such a severe case. We also describe the case of remarkable cognitive improvement in response to a gluten- and casein-free (GFCF) diet in a patient with Mowat-Wilson syndrome, a rare genetic disease associated with significant mental impairment and developmental delays. By age five, the patient had a vocabulary of 20 words and was not toilet-trained. Within two weeks of implementing a GFCF diet, he was using hundreds of words in short sentences, learned to use a toilet, and graduated from diapers. Testing for celiac disease and other diet-related inflammatory conditions were all negative, suggesting a possible interaction between the pathogenesis of the disease itself and these dietary compounds that has previously been undescribed in the literature.

95 Rib-based anchors can induce proximal translational deformity in Early Onset Spinal Deformity patients undergoing growth-friendly surgical treatment

Connor Burke, Brett Goodloe, John Hughes, William Barfield, James Mooney, Robert Murphy, Medicine, Pediatric Orthopaedics, MUSC.

Growth friendly surgery for Early Onset Spinal Deformity (EOSD) utilizing rib-based distraction techniques can induce/potentiate proximal sagittal plane kyphotic deformity in some patients. However, any effect of rib-based anchors on translation of the proximal spine relative to the ribs is unknown. All patients with EOSD from a single center treated with implantation of proximal rib-based anchors in the setting of distraction- based, growth friendly techniques with minimum 2-year follow up were queried. Radiographic parameters were assessed pre-operatively, immediately post-operatively, and at 1- and 2-year follow up. Twenty-seven patients qualified for inclusion (13 female) with an average age at initial implantation of 5 years (range 1-9). Twenty-one (78%) patients demonstrated an increase in the distance from the rib

anchors to the anterior vertebral body. Although minimal increase occurred at 1 year postoperatively (26±1 mm; p=0.24), there was a significant increase in mean translation at two years (29±1 mm, p=0.001). Patients with early onset scoliosis treated with rib-based anchors demonstrate an increase in the translational deformity of the spine relative to the anchors during growth friendly treatment. These findings highlight a previously unreported sequela of rib- based anchors. This work was supported by MUSC Department of Orthopaedics

96 Sphingosine Kinase 1 Inhibition Attenuates Hypertension-Induced Left Ventricular Hypertrophy

Matthew Bridges, Katherine A. Robinson, Rupak Mukherjee, Hesham El-Shewy, Medicine, Medicine, MUSC.

Background: The sphingosine kinase 1 (SK1) signaling pathway has been identified as a potential therapeutic target for several pathological conditions, including cardiovascular diseases. We have recently reported that inhibition or genetic deletion of SK1 significantly decreased elevated blood pressure in acute and chronic angiotensin (AngII)-induced hypertension mouse models. However, the effect of SK1 inhibition on left ventricular (LV) geometry and function with AngII-induced hypertension remains unexplored. Methods/Results: Hypertension was induced in wild-type mice (C57BL/6, 12 week old male; n=26). Mice were assigned to saline control (n=7), AngII (n=11), and AngII and treated with SK1 inhibitor (SK1I; n=8) by implantation of osmotic minipumps (ALZET 1007D) to deliver either saline or AngII at a rate of 600 ng/kg/min. Hypertension was confirmed at one week after pump implantation in the mice infused AngII. Baseline and terminal echocardiograms were analyzed to determine LV end-diastolic diameter (LVIDd), LV wall thickness (LVWth), LV mass (LVmass), and fractional shortening (FS). Body weights at baseline and terminal were similar in the 3 groups. LVIDd was increased from baseline in the AngII mice (3.52±0.09 vs. 3.86±0.11 mm, p<0.05), but was attenuated with AngII+Inh (3.61±0.10 mm, p<0.05). LVmass was increased from baseline in the AngII mice (96±7 vs. 136±4 mg, p<0.05 vs. AngII), but was attenuated with AngII+Inh (122±8 mg, p<0.05vs. AngII), with concomitant changes in LVWth. FS was decreased in the AngII group compared to baseline (39±2 vs. 30±3%, p<0.05), but remained similar to baseline values in the AngII+Inh group (36±3%, p<0.05 vs. AngII). Conclusions: These findings suggest that activation of the SK1 pathway contributes to LV hypertrophy with AngII-mediated hypertension and inhibition of this pathway may represent a novel means to attenuate deleterious changes in left ventricular geometry with hypertension. This work was supported by The American Heart Association 17GRNT33700223 and NIH/COBRE in Lipidomics and Pathobiology at MUSC

97 Assessment of Impairment Following Oral and Vaporized Cannabis Administration in Infrequent Users

Erin Martin, Tory Spindle, Megan Grabenauer, Michael Milburn4, Ryan Vandrey, Graduate Studies, Johns Hopkins University School of Medicine, Department of Psychiatry, MUSC.

Background: Cannabis has become more accessible following recent policy changes. Increasingly, cannabis is ingested orally or inhaled via vaporizer. There is a need to characterize cannabis doses that are likely to cause impairment, and to identify measures that reliably detect this impairment. Methods: Twenty infrequent cannabis users (≥ 30 days since last use) completed six, double-blind outpatient sessions (separated by 1 week) in which they consumed cannabis brownies (0, 10, or 25mg THC) or inhaled vaporized cannabis (0, 5, or 20mg THC). Blood was sampled and subjective, cognitive, and psychomotor effects were assessed before cannabis administration and for 8hrs thereafter. The Digit Symbol Substitution Task (DSST), Paced Serial Addition Task (PASAT), Divided Attention Task (DAT), field sobriety tests (FSTs), and DRUID Application measured cognitive/psychomotor performance. Results: For oral and vaporized cannabis, ratings of "Drug Effect" increased significantly in a dose-dependent manner. For oral cannabis, 10mg qualitatively impaired performance on the DAT and PASAT, while 25mg significantly impaired performance on the DSST, DAT, PASAT, and DRUID compared with placebo. For vaporized cannabis, 20mg significantly impaired performance on the DAT, PASAT, and DRUID compared with placebo, but 5mg did not. Mean peak DRUID scores for the 20mg vaporized dose and the 25mg oral dose were similar to alcohol exposure at a .08 BAC in a prior study. Drug effects/impairment on these tasks often persisted after blood THC concentrations returned to zero. FSTs did not reliably discriminate between impaired and unimpaired participants. Conclusions: 10 and 25mg oral and 20mg vaporized doses increased subjective drug effects and impaired cognitive/psychomotor performance on most tasks compared to placebo; 5mg vaporized cannabis produced discriminative drug effects without significant impairment. The DAT and DRUID appeared to be the most robust measures for identification of impairment. Reliable markers of cannabis intoxication/impairment are needed given the expanding legal cannabis market. This work was supported by National Institute of Justice

98 A Novel Method of Individualizing Transcranial Direct Current Stimulation Dosage Using Reverse-Calculation Electric Field Modeling

Kevin Caulfield, Bashar W. Badran, William H. DeVries, Philipp M. Summers, Emma Kofmehl, Xingbao Li, Jeffrey J. Borckardt, Marom Bikson, Mark George, Graduate Studies, Psychiatry, MUSC.

BACKGROUND: Unique amongst brain stimulation tools, transcranial direct current stimulation (tDCS) currently lacks a method of individualizing dosage. This shortcoming may cause many individuals to receive subtherapeutic amounts of tDCS and could be the underlying reason for mixed findings in the tDCS literature. OBJECTIVE/HYPOTHESIS: Is it possible to individualize dosage? We developed a novel method of reverse-calculating electric-field (E-field) models based on Magnetic Resonance Imaging (MRI) scans that can be used to determine individualized tDCS dose. A further step assessed the validity of this measure by measuring transcranial magnetic stimulation (TMS) motor threshold (MT) and single pulse, suprathreshold transcranial electrical stimulation (TES) MT against electric-field (E-field) modeling. METHODS: In 29 healthy adults, we acquired TMS MT, TES MT, and structural MRI scans with a fiducial marking the motor hotspot. We then used custom "Realistic vOlumetric-Approach to Simulate Transcranial Electric Stimulation" (ROAST) E-field modeling scripting codes and reverse-calculated the required tDCS dose at the fiducial needed to cause a 1.00V/m E-field at the cortex. Finally, we examined whether the predicted E-field values correlated with each participant's measured TMS MT or TES MT. RESULTS: We successfully developed a novel reverse-calculation method that can predict individualized tDCS dose using 5 reverse-calculated ROAST E-field models. TES MT significantly regressed with the required tDCS dose determined by E-field modeling ($R2 = 0.509$, $p < 0.001$). The mean required tDCS dose to produce a 1.00V/m E-field change at the cortex was 6.38 mA (SD = 1.34mA), with a range of 3.86 to 10.21 mA. CONCLUSIONS: ROAST E-field modeling, alone or in combination with TES MT, can be used to individualize tDCS dose. The large range of the required tDCS doses underscores the likely need to individualize tDCS dose, and TES MT combined with E-field modeling may be the solution. This work was supported by NC NM4R

99 E2F8 tumor suppressive role in nonalcoholic Steatohepatitis

Shaaron Ochoa-Rios, Lindsey Kent, Julian M Clouse, Yannis Hadjiyannis, Gustavo Leone , Graduate Studies, Department of Biochemistry and Molecular Biology, MUSC.

Non-Alcoholic Steatohepatitis (NASH) is the aggressive form of Non-alcoholic Fatty Liver Disease (NAFLD). Some of the main conditions that distinguish NAFLD from NASH are severe liver inflammation, increase lipid accumulation and fibrosis. NASH is caused by an excess of fat in the liver which is linked to obesity and diet. Diets high in fats and sugars, typical of a Western diet, have been shown to induce NASH. Approximately 25% of NASH cases progress to Hepatocellular Carcinoma (HCC). Currently, there is no approved therapy for NASH and complication due to NASH is estimated to be the number one reason for liver transplant. E2F8, a member of a family of transcription factors that are well known for regulating the cell cycle, has been shown to promote hepatic steatosis in a zebrafish model. Previous research from our lab has demonstrated that E2F8 has a tumor-suppressive role and loss of E2F8 leads to HCC in a DEN-induced model. Here, we use an mouse model to conditionally delete E2f8 in hepatocytes to sensitize to liver cancer and evaluate the effects of E2F8 on NASH development. Mice were fed with a low-fat diet (LFD), high-fat diet (HFD), choline-deficient high-fat diet (CDHFD) or Western diet (WD). Our results show that control mice in a LFD maintained a normal liver and E2F8 had a tumor-suppressive role for all diets including LF. However, a HFD induced NAFLD while a CDHFD and WD caused NASH by inflammation and fibrosis, respectively. We demonstrate that E2f8 ablation influences collagen deposition, lipid accumulation, and E-cadherin expression. We hypothesize, that E2F8 has a role in the regulation of liver metabolism. Collectively, our study demonstrates that a WD and E2F8 hepatocyte deletion leads to an increase in lipid and collagen accumulation and HCC occurrence. This work was supported by National Institutes of Health/R01CA121275, Hollings Cancer Center/P30 CA1138313

100 Generation and Validation of a Novel Model for Mitral Valve Prolapse Based on Human Familial Mutations

Cortney Gensemer, Christina Wang, Diana Fulmer, Lilong Guo, Kelsey Moore, Tyler Beck, Mary Kate Rumph, Janiece Glover, Annette Krzyzanski, Reece Moore, Rebecca Stairley, Michael Borger, Robert Levine, Russell Norris, Graduate Studies, Regenerative Medicine and Cell Biology, MUSC.

Mitral valve prolapse (MVP) is the most common cardiac valve disease affecting 1 in 40 individuals with poorly understood etiology. Surgical intervention is currently the only available treatment option. Despite surgical repair/replacement of the valve, roughly 20% of patients still develop left ventricular remodeling, significant myocardial fibrosis and associated arrhythmias and heart failure. This underscores the importance for developing genetically accurate murine models to study the natural history of MVP and decipher the molecular origins of the left ventricular fibrosis. Through a combination of linkage and exome sequencing, we identified a mutation in the cilia gene, DZIP1 in multiple families with inherited non-syndromic MVP. CRISPR-Cas9 genome editing was used to generate a mouse model with the same human variant. Histology and immunohistochemistry (IHC) were performed to validate phenotype as well as determine whether fibrosis is evident in the left ventricle as observed in some patients. Myxomatous degeneration of the mitral valves was confirmed by histology and IHC and MVP was observed by echocardiography in 100% of adult animals analyzed. Pronounced papillary fibrosis coincident with MVP was observed in all affected animals and excess collagen deposition was detected in the inferobasal myocardium. These data demonstrate the first generation of a genetically accurate murine model for non-syndromic MVP can be used to identify pathways that contribute to collagen deposition and left ventricular fibrosis in MVP.

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

Aunay Miller, Raghavendar Chandran, Adviye Ergul, Graduate Studies, Pathology and Lab Science, MUSC.

Diabetes increases the risk and severity of poststroke cognitive impairment. Females suffer more from post-stroke cognitive impairment, but underlying reasons are poorly understood. Potential explanations include 1) use of healthy animals without common comorbid diseases like diabetes into research study design, and 2) Inadequate use of female rat models in stroke research. The long-term goal of this study is to gain better understanding of the long-term cognitive and psychological outcomes of stroke in diabetes in both sexes. Our global hypothesis is that post-stroke outcomes are sex and comorbid disease dependent. To assess cognition in male and female rats before and after stroke, we used the passive avoidance behavioral paradigm, which is based on the rat's instinct to prefer darkness. Animals were trained and tested with a multi-trial method in which animals were first habituated to the dark and light chambers without a foot shock (Test 1). Then trained in three trials in which they received a footshock upon transferring to the dark chamber (Test 2). Following Test 2, animals were subjected to stroke induced by middle cerebral artery occlusion and their retention of the memory of foot shock 2 weeks prior to stroke will be measured in Test 3 (Retention). The amount of time it takes for them to enter the dark chamber is recorded and given as average of 3 trials. Baseline results showed that there wasn't a significant difference in the latency to enter the dark room between male and female rats. The average latency time for males and female rats in Test 1 was approximately 20.04 seconds and 18.64 seconds, respectively. In Test 2, the corresponding average latencies were 17.12 seconds and 18.35 seconds. These results suggest that there was no difference between the groups in their learning ability to associate the dark chamber with the shock. This work was supported by NIH, NIDDK, VA

102 Glutamatergic modulation recovers multiple behavioral deficits in a model of AUD/PTSD comorbidity

Heyam Saleh, Cora E. Smiley, Justin T. McGonigal, Samantha Melton, Thomas Valvano, Justin Gass, Graduate Studies, Neuroscience, MUSC.

Post-Traumatic Stress Disorder (PTSD) and Alcohol Use Disorder (AUD) are often comorbid disorders that result in dysregulation in various shared neuronal pathways. In the overall population, the chances of this comorbidity represent rates of 41-79%. Patients with PTSD/AUD exhibit behavioral deficits such as stress induced alcohol consumption and cognitive inflexibility, both of which are associated with learning and memory. These studies aim to ameliorate the deficits of comorbid PTSD/AUD using the glutamatergic modulator, N-acetylcysteine (NAC). The role of NAC in preventing stress-induced alcohol consumption using a cue-induced alcohol self-administration protocol was observed, resulting in stress-induced changes in alcohol consumption. Following restraint stress paired with a scent cue, rats were trained to self-administer ethanol by pressing a lever. NAC treatment was administered for five days before and after the stressor. Rats then underwent extinction training. Following extinction, the stress-related scent was presented to reinstate alcohol-seeking behavior.

Interestingly, animals treated with NAC demonstrated attenuated relapse-like behavior. We then sought to analyze the effectiveness of NAC treatment in the potential restoration of impaired cognitive flexibility shown in clinical populations of PTSD patients. Animals were exposed to restraint stress and put through a set-shifting paradigm to measure cognitive flexibility. Rats were treated with NAC five days prior to acute restraint stress and in the subsequent five days. Cognitive deficits were rescued in animals treated with NAC, providing evidence that NAC can attenuate relapse, prevent alcohol consumption induced by stress, and enhance cognitive flexibility in models of PTSD. Future studies are needed to elucidate the mechanism of NAC treatment that occurs to repair these deficits. This work was supported by NIH RO1AA024526

103 Placental cardiovascular gene expression in preeclampsia and diabetes: Defining subpopulations of a prevalent disease of pregnancy

Kelsey Tjen, Kelsey Tjen, Kymbreana Coley, Clare Kelley, Misti Leyva, Mary Starrett, Eugene Y. Chang, Timothy J. Lyons and Kyu-Ho Lee, Kyu-Ho Lee, Medicine (MSTP, MD years), Pediatrics (Cardiology), MUSC.

Preeclampsia (PE) affects ~5% of pregnancies worldwide and is a significant source of maternal and neonatal morbidity and mortality, yet the mechanisms underlying PE remain unknown. While diabetes in pregnancy greatly enhances the risk of PE (~20% vs ~5% in the general population), the cause of this increased risk has also not been determined. Previous studies in this lab have associated differential placental expression of the cardiovascular developmental transcription factor Nkx2-5 and its target genes with early onset and severe preeclampsia. The objective of this project was to determine whether the expression of Nkx2-5, its target genes, and several markers previously associated with preeclampsia exhibit differential expression in the setting of diabetes mellitus (DM). Using qPCR, we examined the expression of eight gene markers (Nkx2-5, Sam68, sFlt1, VEGFR1, PlGF, Endoglin, VEGF and Ccdc117) in placental tissue from 40 pregnancies in the presence or absence of PE or DM. As in our previous studies, placental expression levels of the genes constituting an "Nkx2-5 axis" showed highly significant cross-correlation (Spearman's Rank Correlations, $p << 0.05$) in the population as a whole and varied significantly among the disease categories. Further significant trends were identified among individual markers, both independent and dependent of DM status, using Mann Whitney U Tests. Although Nkx2-5 and sFlt1 expression levels were predictive for PE risk in diabetic and non-diabetic women in the study population taken as a whole, some of Nkx2-5's target genes did not consistently correlate with PE risk in the setting of diabetes. This suggests a modifier effect of diabetes on PE and possibly on Nkx2-5-regulated placental development. Statistical analyses were limited by small group sizes, so we hope to further this study through the collection and analysis of additional placental samples, as well as through the study of an Nkx2-5 driven mouse model of PE. This work was supported by National Center for Advancing Translational Sciences of the National Institutes of Health under Grant Number UL1 TR001450

104 Development of Wearable Stimulation App to Increase Hand Functional Recovery in Patients with Neurological Movement

Corey Morrow, Andrew Fortune, Changki Kim, Viswanathan Ramakrishnan, Na Jin Seo, Health Professions, Department of Health Professions, MUSC.

Introduction: More than 4 million stroke survivors in the U.S. suffer from post-stroke hand disability. Hands are our primary means of interacting with the world. Post-stroke hand impairment diminishes abilities for activities of daily living including self-care and leisure and lowers independence. One way to augment hand function recovery is peripheral sensory stimulation. Afferent input is a powerful driver of change in the motor cortex. Vibratory sensory stimulation from the TheraBracelet standalone watch device has been shown to improve motor recovery. However, 16% of adults in the US already have a commercial smartwatch. It may be easier for mass implementation of the vibration technology if stroke survivors can use a commercial smartwatch with TheraBracelet app. The objective of this study is to determine if vibration from a commercial smartwatch via custom-developed app improves post-stroke hand function as much as vibration from the TheraBracelet standalone watch device. Methods: A total of 40 subjects will be recruited in this study. Enrollment is ongoing with 12 subjects currently enrolled. The study design is a double-blind randomized controlled design. The smartwatch app will deliver the TheraBracelet stimulation for the treatment group and no stimulation for the control group. Hand function will be assessed using standardized clinical assessments at baseline, while the stimulation is turned on, and after the stimulation is turned off. Analysis: We will perform a repeated measures analysis and use contrasts to test the difference between the two groups during the stimulation. The current study is powered to detect a difference at least as big as 80% of the effect (following FDA guidelines) observed in the TheraBracelet standalone device in a previous study. Results/Conclusion: If the vibration from a commercial smartwatch app is as effective as the standalone device already tested, then availability of the stimulation technology to patients would increase. This work was supported by SCTR Technology Development Award

105 Refining hotspot identification methods in the lower extremities using a double-cone TMS coil post stroke: MEP amplitude vs. latency

Jessica Ergle, John H Kindred, Charalambos C Charalambous, Elizabeth C Wonsetler, Mark Bowden, Health Professions, College of Health Professions, MUSC.

Introduction - Transcranial magnetic stimulation (TMS) is used to probe the nervous system and make assessments regarding available neuromotor control. Finding the "hotspot" of the motor cortex is critical as it represents the location from which we get the most robust response to stimulation. Hotspot location is usually assessed by examining motor evoked potential (MEP) amplitude (peak-to-peak EMG signal) but MEP-latency (time to MEP-onset) could also be used. The purpose of this study was to determine the best mechanism to locate hotspots of the lesioned hemisphere of individuals post-stroke. We hypothesized that using MEP-latency will be a more consistent way to find the hotspot for the tibialis anterior and soleus. Methods - A 3x5 grid, 1 cm spacing, was overlaid on an MRI of the brain. Participants were calibrated to the MRI and surface EMG electrodes were placed on paretic tibialis anterior and soleus. We delivered a single suprathreshold TMS pulse to each grid point and the MEPs were recorded. Hotspots were identified using MEP-amplitude and MEP-latency. We used Fisher's Exact Tests and a RMANOVA to compare the results using MEP-amplitude and MEP-latency. Results - We recorded 2 grids on 2 separate days on 14 participants. Within a single grid, only 17 of hotspots identified with MEP-amplitude were the same as the hotspots identified with MEP latency (N=56). Between the grids, 10.9% of amplitude identified hotspots were the same compared to 5.7% for latency hotspots ($p=0.489$). Distances between the two selected hotspots were significantly closer when using MEP-amplitude compared to MEP-latency for both muscles when analyzed together ($p=0.035$). Discussion - Based on the results, there is less distance between

hotspots when using MEP-amplitude. Therefore, we will continue to use MEP-amplitude to determine the hotspot, but continued investigation in finding the best method to identify hotspots is required.

106 Donor Lung Beta 2 microglobulin deficiency delays the onset of acute rejection

Dorian Frazier, Changhai Li, Zhenxiao Tu,Jerec Ricci, Dianna Nord, Carl Atkinson, Graduate Studies, Microbiology and Immunology, MUSC.

Abstract Withheld from Publication

107 Targeted Kappa Opioid Receptor Antagonist Treatment in the CeA or BNST Attenuates Stress-Potentiated Alcohol Consumption.

Harold Haun, Logan Manusky, William Griffin, Marcelo Lopez, Howard Becker, Graduate Studies, Psychiatry and Behavioral Sciences, Neuroscience, and VAMC, MUSC.

Stress is widely known to promote excessive alcohol consumption which contributes to Alcohol Use Disorder (AUD) and dependence. Increased activity at the kappa opioid receptor (KOR) is thought to mediate negative affective states associated with stress and withdrawal which potentiate excessive drinking and relapse. In a preclinical model of stress-potentiated alcohol drinking, we have previously demonstrated that systemic KOR antagonist treatment blocks the ability of repeated forced swim stress (FSS) to escalate dependence-related alcohol (ethanol) intake in mice with a history of dependence achieved through chronic intermittent ethanol (CIE) exposure. The present studies seek to determine the exact site of KOR-mediated excessive drinking by targeting two discrete regions of the extended amygdala known to be responsive to stress and ethanol: the central amygdala (CeA) and bed nucleus of the stria terminalis (BNST). Male C57BL/6J mice received bilateral guide cannulae above either the CeA or BNST and were introduced to CIE and FSS exposure. Mice with a history of CIE exposure consumed more alcohol than non-dependent controls, and mice with a combined history of CIE+FSS drank significantly more alcohol than CIE alone. Compared to microinjection of vehicle (1xPBS), the KOR antagonist, nor-binalorphimine (nor-BNI; 0.25 ug/side) reversed both CIE and CIE+FSS-enhanced drinking when microinjected into the CeA. Similarly, nor-BNI infusion into the BNST significantly reduced alcohol intake in mice with a history of CIE and CIE+FSS. Non-dependent control drinking was not affected by nor-BNI administration into either the CeA or BNST suggesting that the suppressive effect of nor-BNI on alcohol intake is specific to drinking in mice with a history of dependence. Together, these data suggest that KOR within the extended amygdala mediate stress-potentiated drinking and point to this peptide system as a potential therapeutic intervention for AUD and stress-related drinking. This work was supported by Supported by NIAAA grants (P50-AA1076, R01-AA02653, U01-AA014095, U01-AA020929, F31-AA027420-02, T32-AA007474) and VA Medical Research (BX000813).

108 Improving identification of hub genes and gene sub-networks through data integration with the stochastic block model

Carter Allen, Dongjun Chung, Graduate Studies, Public Health Sciences, MUSC.

The study of gene networks associated with a given disease area often involves analysis of multiple sources of network data that feature weak and widespread signal and low signal-to-noise ratio. In this setting, interest commonly lies in detection of possible latent community structure, such as unknown hub genes and sub-networks within a given gene network. The stochastic block model (SBM) is a flexible statistical model with the ability to perform community detection. However, the standard SBM still suffers from poor performance in the case of weak and widespread signal. With improvement of genomic profiling technologies, multiple relevant experiments for a given disease area have become more abundant providing unprecedented opportunity for integrative analyses. Examples of such complimentary data sources are gene expression, DNA methylation, and more recently, literature mining data, each of which are concerned with measuring associations among a similar sets of genes and often feature low signal to noise ratio. To address the issue of weak and widespread signal in network data, we propose a data integration framework for the SBM, whereby multiple available data sources are combined into a unified network model. We show through simulation studies that our proposed method offers improved detection of hub genes and gene sub-networks for a variety of settings when compared to SBMs fit to single data sources or under alternative data integration approaches. In future work, we plan to extend our data integration method to the Bayesian setting to allow for inclusion of prior biological knowledge to guide detection of hub genes and gene sub-networks, and further improve SBM performance in the case of weak and widespread signal. In addition, we also plan to apply the proposed framework to the genomic studies of twins with systemic sclerosis (SSc) to help investigation of the genetic causes of SSc. This work was supported by SCTR TL1 Training Program

109 Improved survival with immune checkpoint inhibitors in the SEER-Medicare population

Ashley Howell, Kelly Hunt, Mulugeta Gebgregziabher, Bruce Thiers, Chrystal Paulos, John Wrangle, Kristin Wallace, Graduate Studies (MSTP, PhD years), Public Health Sciences, MUSC.

Introduction: Immune checkpoint inhibitors (ICIs) have dramatically changed the treatment landscape for advanced melanoma, but their use in elderly patients remains understudied. Outcomes following treatment with immunotherapy can be influenced by the host's immune system, so the decline in immune function that occurs naturally with age is of theoretical concern when considering ICI treatment for older patients. We aimed to evaluate the effectiveness of ICIs in patients aged ≥65 years. Methods: We conducted a retrospective cohort study using data from the SEER-Medicare linked database. Our cohort was comprised of patients aged 65 and older who were diagnosed with unresectable stage III or stage IV cutaneous melanoma between 2012 and 2015. Kaplan-Meier methods, chi square, and Wilcoxon tests were used for bivariate analyses, and Cox proportional hazards regression was employed for a multivariate landmark analysis. Results: A total of 592 patients were included in this study. Half of the patients (49.5%) were not treated with a systemic therapy. Forty-four patients (7.4%) received chemotherapy, 56 (9.5%) targeted therapy, and 199 (33.6%) ICIs as their first systemic treatment. Median survival differed significantly between groups and was highest in patients treated with ICIs (627.0 days, 95%CI: 429-854), followed by targeted therapy (294 days, 95%CI: 208-363), chemotherapy (214.5 days, 95%CI: 128.0-333) and no systemic therapy (112.0 days, 95%CI: 96.0-154.0, p<0.0001). The ICI survival benefit persisted after adjusting for demographics, cancer characteristics, comorbidity burden, SES status, and hospital factors (aHR for ICI vs no treatment=0.65, 95%CI: 0.50-0.86). In a separate model of patients aged 75 and older, the ICI treatment effect was even stronger (aHR=0.51, 95%CI: 0.34-0.74). Conclusions: In a national 'real world' setting, we show that ICI therapy significantly improved

survival in patients aged 65 and older with advanced melanoma. Further research is needed to clarify age-related differences in response to ICI therapy. This work was supported by HCC Graduate Fellowship, NIH/NCATS Grant Number UL1TR001450

110 Difluoromethylornithine and Checkpoint Blockade/Oncolytic Virotherapy Combination Treatment in a Murine Melanoma Model

Parker Dryja, Thomas Benton, Patrick Woster, Eric Bartee, Graduate Studies, Microbiology & Immunology, MUSC.

Polyamines are polycationic organic molecules that are ubiquitously found in living cells, and in humans, are present as putrescine, spermidine, and spermine in increasing amination steps. Polyamines have been demonstrated to be directly and indirectly involved in proliferation, migration, and DNA/RNA stabilization, and are downstream targets of several common and clinically-relevant oncogenic families such as Myc, Ras, and Raf. Importantly, polyamine metabolism has been increasingly demonstrated to also play a critical role in branches of the immune system, particularly the biological activity of myeloid-derived suppressor cells (MDSCs) and M2 macrophages that are recruited by several types of immunosuppressive cancers. With the anti-cancer and anti-immunosuppressive characteristics combined, the negative modulation of polyamine metabolism serves as an attractive target that may potentiate the therapeutic efficacy of existing immunotherapies that are typically hindered by tumoral MDSC/M2 macrophage immunosuppression. Oncolytic virotherapy and checkpoint blockade immunotherapies were hypothesized to potentially benefit from combinatory treatment with a polyamine biosynthesis inhibitor; while viral oncolytics directly potentiates immunogenicity of tumors through virally mediated cell lysis, and checkpoint blockade can prevent direct tumor-mediated immunosuppression, we proposed that the therapy may benefit from the anti-immunosuppressive effects of difluoromethylornithine (DFMO, an inhibitor of the first committed step in polyamine biosynthesis) treatment. In this study, the therapeutic value of combining DFMO treatment with PD-1/IL-12 recombinant myxoma virus and systemically delivered αPD-1 was determined in vivo in a murine melanoma model. This work was supported by NIH-NCI (R01-CA194090)

111 Interaction of the Extracellular Matrix with the Cell-cell Junction Associated RNAi Machinery in Colon Cancer

Amanda Daulagla, Mary C. Bridges, John Yost, Lauren Rutledge, Joyce Nair-Menon, Michael Yost, Antonis Kourtidis, Antonis Kourtidis, Graduate Studies, Regenerative Medicine and Cell Biology, MUSC.

Colon cancer is the third most common and second deadliest type of cancer in the United States. Loss of epithelial tissue integrity is widely observed in colon tumors. Cell-cell junctions are essential for the maintenance of epithelial tissue integrity. The Adherens Junction (AJ) is an adhesion complex composed of E-cadherin and the catenin family of proteins. We have shown the E-cadherin-p120 catenin partner, PLEKHA7 is critical for epithelial integrity. Importantly, we showed PLEKHA7 recruits the core components of the RNAi machinery AGO2, DGCR8 and DROSHA, at mature apical AJs, to regulate miRNA levels and activity. Loss of PLEKHA7 disrupts the function of the associated RNAi machinery and promotes pro-tumorigenic cell behavior. We hypothesize that PLEKHA7 acts as a sensor of epithelial homeostasis by regulating a junction-associated RNAi machinery. Prolonged wound and fibrosis are key precursors to colon cancer by extensive deposition of extracellular matrix (ECM). Investigation of colon epithelial cells grown on different ECM substrates, namely collagen, laminin and fibronectin, showed differences in the localization of PLEKHA7 and the junction-associated RNAi machinery. In addition, investigation of biomechanical effects using stiffness assays and 2D stretch assays resulted in disturbances in the proposed localization model of the RNAi machinery at high stiffness conditions, which are a feature of fibrotic and tumor tissues. Interestingly, PLEKHA7 depletion also resulted in increased levels of a series of ECM-related proteins, revealing an extensive, bi-directional cross-talk between PLEKHA7 and the ECM. Examination of normal human colon tissues confirmed co-localization of PLEKHA7 and of the core RNAi components at the apical surface of fully differentiated colon crypts. However, this localization is disrupted or lost in colon tumor samples from patients. Together, our data point towards a novel putative tumor suppressor mechanism tethering tissue mechanosensing with cell behavior, of which we are currently investigating its modes of regulation. This work was supported by 1) College of Medicine Digestive Diseases Pilot & Feasibility Studies Award, MUSC 2) P20 GM103444 South Carolina Bioengineering Center for Regeneration and Formation of Tissues (SC BioCRAFT) Pilot Award 3) Conquer Cancer Now Award, Concern Foundation 4) Start-up funding, Department of Regenerative Medicine and Cell Biology, MUSC 5) NIH National Center for Advancing Translational Sciences (NCATS) through Grant Number UL1 TR001450.

112 Speech Pathology and Occupational Therapy Feeding Interventions Impact Health Outcomes and Health Care Costs for Preterm Infants with Feeding Problems: A Retrospective Analysis

Brooke Mulrenin, Megan Richmond, Cindy Dodds, Annie Simpson, Health Professions, Healthcare Leadership and Management, MUSC.

Introduction: Preterm birth often leads to a range of developmental sequelae, including feeding problems. Prospective studies have shown that early feeding interventions improve outcomes for preterm infants. However, prospective studies tend to examine the effects of specific feeding intervention protocols, while in clinical practice, a much wider array of feeding interventions are utilized. Retrospective data analysis provides an opportunity to examine the effects of the much broader scope of feeding interventions used in practice. Additionally, it allows for comparison of long term health care costs for infants who receive feeding interventions versus infants who do not. Methods: In this retrospective analysis, we examined a cohort of 8990 infants who were born preterm (<37 weeks gestation) and diagnosed with feeding problems during their birth hospitalization. We aimed to determine whether receiving feeding interventions (SLP or OT) improved health outcomes. We used propensity score matching to control for baseline characteristics that were likely to influence whether infants received feeding interventions (i.e. illness severity). We created a matched sample with two groups: 1) infants who received feeding interventions during the first six months after hospital discharge and 2) infants who did not receive feeding interventions despite having similar baseline characteristics. We compared adjusted and unadjusted outcomes for these two groups of infants. Results: In the unadjusted comparison, infants who received feeding interventions after hospital discharge had health care costs that were two times as high as those who did not. However, our adjusted comparison showed that when the groups were matched to control for illness severity, health care costs were the same for each group. These findings underscore the need to match in order to accurately estimate the effects of feeding interventions. Further examinations of clinical outcomes including rates of re-hospitalization for feeding problems and poor weight gain will also be presented. This work was supported by predoctoral training grant (T32 DC0014435)

113 Complement Driven Auto-Reactive Antibodies in Lung Transplantation

Alexander McQuiston, Kunal Patel, Changhai Li, Zhenxiao Tu, Carl Atkinson, Graduate Studies, Department of Microbiology and Immunology, MUSC.

Abstract Withheld from Publication

114 Kynurenine, an Endogenous AhR Agonist, Upregulates CXCL12- and Hdac3-Targeting miRNAs Inhibiting Osteogenesis

Ahmed Elmansi, Nada Eisa, Dmitry Kondrikov, Galina Kondrikova, Sadanand Fulzele, Meghan mcGee-Lawrence, Mark Hamrick, Carlos Isales, William Hill, Graduate Studies, Department of Pathology and Laboratory Medicine, MUSC.

Abstract Withheld from Publication

115 Analysis of High-Dimensional Neuroimaging Data in Characterizing Alzheimer's Disease Progression

Daniel Baer, Brandon Vaughn, Jane Joseph, Andrew Lawson, Graduate Studies, Public Health Sciences , MUSC.

There is an ongoing need to characterize the progression of Alzheimer's disease (AD) in order to delay or prevent its onset in patients. Characterization of AD risk progression can be accomplished by the longitudinal study of mild cognitive impairment (MCI) patients via neuroimaging. In particular, a graph-theory based (GTB) network analysis of neuroimaging data is appealing; it is hypothesized that degradation in network communications as captured by GTB neuroimaging measures could characterize AD risk progression in patients. Furthermore, in order to validate the clinical relevance of the GTB AD network model, we can associate longitudinal measures of patient cognition with GTB neuroimaging measures via statistical models. However, these GTB neuroimaging measures are often high-dimensional, and these longitudinal measures of patient cognition are correlated over time. Our research hypotheses are that patient resting state functional MRI (rsfMRI) GTB neuroimaging measures can identify regions of the brain most associated with patient cognitive status over time, and that these identified regions vary based on the type of GTB neuroimaging measure considered. To this end, we examined high-dimensional GTB neuroimaging covariate data and longitudinal Mini-Mental State Examination (MMSE) questionnaire outcome data from the Alzheimer's Disease Neuroimaging Initiative (ADNI) (including data from patients with MCI). To address our research hypotheses, we performed a novel application of a fully-Bayesian variable selection model to these high-dimensional and longitudinal data. We were able to identify a parsimonious subset of brain regions which were persistently associated with patient cognitive status over time, and that these identified brain regions differed on the basis of the GTB neuroimaging measure considered for the analysis. These findings suggest that the GTB network analysis framework is promising in terms of gleaning the neurodegenerative process underlying AD and thus providing researchers a means to better characterize AD risk progression. This work was supported by TL1 TR001451, UL1 TR001450, U01 AG024904, W81XWH–12–2–0012

116 Reverse Phase Protein Array Reveals Differential Basal and Adaptive Protein Expression Profiles in BMSCs Cultured in Normoxic vs. Chronic Physiologically Relevant Bone Marrow Low Oxygen Conditions

Nada Eisa, Ahmed Elmansi, Dmitry Kondrikov, Brian Volkman, Louis Luttrell, Carlos Isales, Mark Hamrick, Meghan McGee-Lawrence, Sudanand Fulzele, Jie Chen, William Hill, William Hill, Medicine, Pathology and Laboratory Medicine, MUSC.

Abstract Withheld from Publication

117 Identification and targeting of novel vulnerability in RAS for tumor inhibition

Imran Khan, Akiko Koide, Eric Denbaum, Mariyam Zuberi, Matthew Rhett, Kai Wen Teng, Russell Spencer-Smith, Shohei Koide, John O'Bryan, Medicine, Department of Cell and Molecular Pharmacology & Experimental Therapeutics, MUSC.

RAS is one of the most commonly mutated oncogenes in cancer and about 30% of all cancers have mutations in one of the three RAS genes (H,K and N-RAS). RAS mutations are early triggers for carcinogenesis, however potent RAS selective inhibitors remain elusive. Previously, our lab devised an innovative approach using Monobody (Mb) technology to screen for biologics that inhibit RAS function and were successful in isolating a H/K-RAS specific Mb called NS1. NS1 inhibited RAS driven oncogenesis both in vitro and in vivo. Building on this platform and our prior discovery of the existence of RAS in nucleotide free state (apoRAS), we aimed to isolate Mbs that bind to apo-RAS. We identified several such Mbs and extensively characterized one of them called R15. In vitro, R15 binds exclusively to the apo state of all three RAS isoforms. Surprisingly however, when co-expressed intracellularly, R15 inhibited the signaling and oncogenic activity of RAS mutants that have high spontaneous release of nucleotides (e.g. G13D, Q61L, and A146T) but not slow cycling mutants like RAS(G12V). The inhibitory effects of R15 are RAS specific as it did not inhibit the signaling or biological activity of downstream oncogenic kinases. Further, R15 did not impair the signaling of RASless MEF's highlighting its lack of "off target effects". When genetically encoded as chemically regulated, intracellular reagent in oncogenic lines that endogenously harbor RAS mutations, R15 inhibited oncogenic RAS signaling and abrogated the anchorage independent growth of cell lines harboring fast cycling RAS mutants. Using xenograft tumor assays, we also demonstrate that inducible expression of R15 significantly decreased tumor growth highlighting the efficacy of R15 at inhibiting selected RAS mutants in vivo models. Thus, contrary to conventional wisdom, our approach offers a new avenue to inhibit certain RAS mutants by targeting them in an apo-state with drug-like molecules. This work was supported by NIHR01, VA merit Award

118 Circulating exosomes contribute to acute respiratory distress syndrome development in patients with sepsis

Pengfei Li, Andrew J. Goodwin, James A. Cook, Perry V. Halushka, Hongkuan Fan, Medicine, Department of Pathology and Laboratory Medicine, MUSC.

Abstract Withheld from Publication

119 Evaluation of aspirin platelet inhibition assay in LVAD population

Eva Morgan, Dr. Jaclyn Hawn, Dr. Holly Meadows, Dr. Brian Houston, Johana Fajardo, Caroline Perez, Pharmacy, Pharmacy, MUSC.

Following implantation of a left ventricular assist device (LVAD), patients require antiplatelet therapy to prevent pump thrombosis, stroke, and mortality. Within post-operative days 1 through 3, patients are started on aspirin 81 mg (Heartmate III) or 325 mg daily (Heartware). Post LVAD, patients are monitored for coagulopathy and bleeding, which can increase the risk for right-heart failure and infection. It has been assumed patients may acquire uninhibited aspirin assays 3 months postoperatively. It is possible to test for aspirin platelet inhibition by evaluating Aspirin Reactive Units (ARU). Previous research has concluded an ARU <550 is therapeutic, while an ARU >550 implies resistance. This study was a retrospective, observational, single center, academic medical center assessing patients who underwent placement of Heartware or Heartmate III. Patients were followed from June 30, 2018 until July 31, 2019. Descriptive statistics were used to analyze the results. The primary objective was to evaluate how patients are managed with antiplatelets post LVAD in relation to aspirin platelet assay results. The secondary objective was to assess how aspirin assays correlate with morbidity and mortality. A total of 28 patients underwent Heartware (10) and Heartmate III (18) placement during the study period. At month 3, 7 (28%) patients who tested therapeutic with aspirin platelet function assay on initiation were found to be un-inhibited. By 6 months, 4 (19%) patients who were initially therapeutic, were found to have un-inhibited assays. Of the patients who reported un-inhibited assays, 4 patients (4% at 3 months, 14.3% at 6 months) were managed with an aspirin dose increase. Pump thrombosis (17.9%), bleeding (25%), and stroke (14.3%) were identified among patient outcomes. Mortality was determined among 3 (10.7%) patients. In this study involving implantation with Heartmate III or Heartware, patients were found to lose aspirin inhibition by 3 months with worsening morbidity and mortality.

120 SARM1 Mediates Dopaminergic Neurodegeneration in a Mouse Model of Parkinson's Desease

Navneet Ammal Kaidery, Rebecca Banerjee., Lichuan Yang, Noel Y Calingasan, Aihao Ding, Carl F Nathan, Flint Beal, Anatoli Starkov, Bobby Thomas, Medicine, Pediatrics, Neuroscience and Drug Discovery, MUSC.

Introduction: Activation of stress signaling pathways in conjunction with mitochondrial dysfunction play a key role in selective degeneration of dopaminergic neurons in Parkinson's disease (PD). Here we show that Sarm1 (sterile alpha and Toll interleukin 1 receptor (TIR) motif), a neuronally expressed mitochondria associated adaptor protein mediates nigrostriatal dopaminergic neurodegeneration by modulating stress activated protein kinase signaling and mitochondrial calcium capacity. Methods: Dopaminergic neurotoxicity in wild type and SARM1 knockout (KO) mice using the acute and sub-acute regimens of parkinsonian neurotoxin 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) was determined by tyrosine hydroxylase-positive (TH+) cell counts. Wild type (WT) and Sarm1 siRNA knockdown (KD) N2A cells were assessed for mitochondrial activity and calcium measurements. Immunobloting and realtime PCR were used for gene expression analysis. Results: KO mice were resistant to both acute and sub-acute MPTP-neurotoxicity than wild type analyzed by stereological counts of TH+ neurons of substantia nigra pars compacta (SNpc). SARM1 mediated MPTP-neurotocixicity was associated with co-immunoprecipitation of SARM1 with stress activated protein kinase JNK3 on the mitochondria. Assessment of JNK3 mediated signaling pathways by immunoblot and confocal microscopy showed that phosphorylation of c-jun in SNpc dopamine neurons were significantly reduced in MPTP treated KO and MPP+-treated KD cells compared to wild types. SARM1 deletion caused inhibition of MAPK/JNK3 signaling both in vivo and in vitro and reduced translocation of JNK3 to mitochondria during MPTP/MPP+ toxicity compared to wild types. Mitochondrial functional analysis showed significantly higher oxygen consumption rates, increased mitochondrial calcium capacity and reduced caspase-3 activity in the presence of MPP+ in brain mitochondria from SARM1 null mice and in KD cells when compared to WT controls. Conclusion: Our findings suggest SARM1 mediates dopaminergic neurodegeneration by serving as a mitochondrial adaptor to recruit cytosolic JNK3 and modulating mitochondrial calcium capacity. This work was supported by NIH grant NS060885, NS062165, Par fore Parkinson, National Parkinson Foundation (CSRA) Chapter.

121 S-Nitrosoglutathione invokes beneficial eNOS activity in a mouse model of experimental stroke

Pavan Kumar, Qiao Fei, Avtar K. Singh, Inderjit Singh, Mushfiquddin Khan, Medicine, Pediatrics, MUSC.

Background: Stroke causes loss or deterioration of brain function due to the disruption in blood supply to the brain. In stroke settings, the nitric oxide (NO)-producing activity of endothelial nitric oxide synthase (eNOS) plays a significant role in maintaining endothelial function and protecting against the stroke injury. However, the activity of the eNOS enzyme and the metabolism of major NO metabolite S-nitrosoglutathione (GSNO) are dysregulated after stroke, causing endothelial dysfunction. We investigated whether an administration of exogenous of GSNO or enhancing the level of endogenous GSNO protects against neurovascular injury in wild-type (WT) and eNOS-null (endothelial dysfunction) mouse models of transient cerebral ischemia-reperfusion (IR). Methods: Transient cerebral ischemic injury was induced by middle cerebral artery occlusion (MCAO) for 60 minutes in male adult WT and eNOS null mice. GSNO (0.1 mg/kg body weight, intravenously) or N6022 (GSNOR inhibitor, 5.0 mg/kg body weight, intravenously) was administered 30 minutes before MCAO in pre-injury and at the reperfusion in post-injury studies. Brain infarctions, edema, and neurobehavioral functions were evaluated at 24 h after the reperfusion. Results: eNOS-null mice had a higher degree ($p<0.05$) of injury than wild-type. Pre- or post-injury treatment with either GSNO or N6022 significantly reduced infarct volume, improved neurological and sensorimotor function in both wild-type and eNOS-null mice. Conclusion: Reduced brain infarctions and edema, and improved neurobehavioral functions by pre- or post-injury GSNO treatment of eNOS knock out mice indicate that GSNO can attenuate IR injury, likely by mimicking the eNOS-derived NO-dependent anti-ischemic and anti-inflammatory functions. Neurovascular protection by GSNO/N6022 in both pre- and post-ischemic injury groups support GSNO as a promising drug candidate for the prevention and treatment of stroke injury. This work was supported, in part, by Ralph H. Johnson VA Medical Center Charleston, SC. This work was supported by This work was supported by grants from the U.S. Department of Veterans Affairs (RX002090 and BX003401).

122 Differential effects of iron chelation with deferoxamine on post-stroke neurovascular inflammation: Disease and sex interactions

Victoria Wolf, Weiguo Li, Yasir Abdul, Guangkuo Dong, Rebecca Ward, Sarah Jamil, Lianying He, Susan C Fagan, Adviye Ergul, Graduate Studies, Pathology & Laboratory Medicine, MUSC.

We have shown that 1) poor recovery in diabetes is associated with greater hemorrhagic transformation and significant loss of the cerebrovasculature, and 2) iron chelation therapy with deferoxamine (DFX) improves sensorimotor and cognitive outcomes while preventing vasoregression in male diabetic animals after stroke. This study tested the hypotheses that 1) diabetes mediates pathological post-stroke neovascularization in females and 2) DFX attenuates microglial activation and pathological neurovascular remodeling in both sexes. Control and diabetic animals were subjected to embolic middle cerebral artery occlusion (MCAO). DFX (100 mg/kg) or vehicle was given 1hour after MCAO and repeated every 12h for 7 days after stroke. Functional outcomes were assessed over time. Vascular indices, microglial morphology (activation), and neurovascular integrity (IgG and unpolarized Aquaporin-4) were measured at Day 14. Male and female microvascular endothelial cells (BMVECs) treated with iron and/or DFX were tested for viability and endothelial mesenchymal transition (EndMT) markers. DFX preserved vascular volume post-stroke in diabetic males. Stroke did not cause vasoregression in diabetic female animals; however, DFX reduced vascular indices while improving sensorimotor but not cognitive outcomes in both control and diabetic females. Ischemic injury amplified microglial activation and neurovascular remodeling in diabetes while DFX treatment restored these changes to control levels in male diabetic animals but not in females. Microglial protrusions (5.28±0.30 vs 4.14±0.16), endpoints (37.15±2.35 vs 24.50±2.79), and branch length (1036.32±50.31 vs 613. 28±66.95) were increased (n=5, $p<0.05$) post-stroke in diabetic males with DFX treatment compared to vehicle treatment. Female BMVECs grown under diabetic conditions expressed α-SMA and N-cadherin while VE-cadherin was decreased, indicative of EndMT ($p<0.05$ vs normal glucose). Data suggest that DFX treatment has sex- and disease-dependent effects on post-stroke neovascularization. Additional studies will aim to address the mechanisms by which DFX exerts these differential effects on functional outcomes and neurovascular remodeling. 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).

123 Voltage Dependent Anion Channels Regulate Proliferation of Cancer Stem Cells

Amandine Rovini, Elizabeth Hunt, Kareem Heslop, Monika Gooz,Sheghuin Qin, Gavin Wang, Eduardo Maldonado, Pharmacy, Drug discovery and Biomedical Sciences, MUSC.

BACKGROUND: Cancer stem-like cells (CSCs) are associated with tumor progression and resistance to chemotherapy. The relative contribution of oxidative phosphorylation (OXPHOS) and aerobic glycolysis in CSCs is dynamically regulated. Increased glycolysis favors proliferation. Mitochondrial metabolism and membrane potential (ΔΨ) are contributed by the ingress of respiratory substrates, ADP and Pi into mitochondria through voltage-dependent anion channels 1/2/3 (VDAC). We previously demonstrated that free tubulin closes VDAC and erastin antagonizes the tubulin inhibition of only VDAC1/2. VDAC closing decreases OXPHOS favoring glycolysis. Here, we hypothesized that different VDAC isoforms, by controlling oxidative metabolism, regulate proliferation of CSCs. METHODS: CSCs from HepG2 and Huh7 human hepatocarcinoma and HCC4006 lung adenocarcinoma cells (spheres >50 µm diameter) were generated using ultra-low attachment plates (DMEM-F12 medium supplemented with B-27, EGF and bFGF). Pluripotent markers were assessed by qRT-PCR, western blotting and immunostaining. Spheres were counted using 50 µm side grid units. Tetramethylrhodamine methyl ester fluorescence was determined both using a microplate reader and confocal fluorescence microscopy to assess ΔΨ. RESULTS: The relative abundance of each VDAC isoform was similar for all CSCs and bulk cancer cells (CCs). By contrast, VDAC 1/2/3 mRNA levels in CSCs were higher compared to bulk HepG2 and Huh7. In HCC4006 CSCs mRNA levels of VDAC2/3 but not VDAC1 were higher compared to bulk CCs. VDAC1 single knockdown decreased sphere formation by ~30%. VDAC2 and VDAC3 single knockdown increased both the amount (by ~18% and 102%, respectively) and the size of spheroids. VDAC1/2/3 single knockdown decreased ΔΨ. Erastin decreased sphere formation and promoted intra-sphere cell death in HepG2 and Huh7 CSCs. CONCLUSION: VDAC1/2 but not VDAC3 contribute to the maintenance and proliferation of CSCs. VDAC1/2 opening by erastin may decrease sphere formation and promote cell death by enhancing oxidative metabolism and decreasing glycolysis. This work was supported by NIH NCI RO1 CA184456, COBRE P20GM103542

124 Insulin-like Growth Factor (IGF)-II- Mediated Fibrosis in Pathogenic Lung Conditions

SM Garrett, Eileen Hsu, Justin Thomas, Joseph Pilewski, Carol Feghali-Bostwick, Medicine, Medicine, MUSC.

Type 2 insulin-like growth factor (IGF-II) levels are increased in fibrosing lung diseases such as idiopathic pulmonary fibrosis (IPF) and scleroderma/systemic sclerosis-associated pulmonary fibrosis (SSc). Our goal was to investigate the contribution of IGF receptors to IGF-II-mediated fibrosis in these diseases and identify other potential mechanisms key to the fibrotic process. Cognate receptor gene and protein expression were analyzed with qRT-PCR and immunoblot in primary fibroblasts derived from lung tissues of normal donors (NL) and patients with IPF or SSc. Compared to NL, steady-state receptor gene expression was decreased in SSc but not in IPF. IGF-II stimulation differentially decreased receptor mRNA and protein levels in NL, IPF, and SSc fibroblasts. Neutralizing antibody, siRNA, and receptor inhibition targeting endogenous IGF-II and its primary receptors, type 1 IGF receptor (IGF1R), IGF2R, and insulin receptor (IR) resulted in loss of the IGF-II response. IGF-II tipped the TIMP:MMP balance, promoting a fibrotic environment both intracellularly and extracellularly. Differentiation of fibroblasts into myofibroblasts by IGF-II was blocked with a TGFβ1 receptor inhibitor. IGF-II also increased TGFβ2 and TGFβ3 expression. Therefore, IGF-II promoted fibrosis through IGF1R, IR, and IGF1R/IR, differentiated fibroblasts into myofibroblasts, decreased protease production and extracellular matrix degradation, and stimulated expression of two TGFβ isoforms, suggesting that IGF-II exerts pro-fibrotic effects via multiple mechanisms. This work was supported by SmartState® and Kitty Trask Holt Endowment (CFB), NIH 5T32AR050958 (SMG), K24 AR060297 (CFB).

125 Age-related hearing loss and the potential role of disinhibition and neural synchrony in the recovery of auditory-evoked cortical responses

Carolyn McClaskey, James W. Dias, Kelly Harris, Medicine, Otolaryngology - Head & Neck Surgery, MUSC.

Age-related hearing loss (ARHL) is thought to contribute to widespread changes throughout the auditory system, including decreased neural inhibition and poorer neural synchrony. Despite increased hearing thresholds, older adults often exhibit larger than expected cortical response amplitudes that are similar to those of younger adults. Older adults' enhanced cortical responses are thought to arise from either the recruitment of additional cortical neurons, which occurs with changes in inhibition, or from a recovery of neural synchrony at the cortex. To investigate the contribution of these two mechanisms, we examined the extent to which increasing cortical responses with increasing stimulus level were associated with increases in neural synchrony. We hypothesized that ARHL would lead to neural disinhibition and subsequent recoveries in cortical response amplitudes, despite diminished neural synchrony. Cortical auditory-evoked responses were measured from younger (18-30 years) and older (55+ years) adults in response to brief tone bursts presented at 80, 90, and 100 dB SPL. Tones had stimulus frequencies of 1 and 4 kHz, corresponding to frequency regions in which older listeners had lesser and greater levels of hearing impairment, respectively. Consistent with previous reports of recovered cortical responses, response amplitudes increased with increasing stimulus level and did not differ between groups. Neural synchrony showed frequency-specific effects and was significantly lower in older adults compared to younger adults only for frequency regions in which older adults exhibit age-related hearing loss. The frequency-specific effects observed in the current study suggest that potential differential effects of disinhibition versus neural synchrony may contribute to enhanced cortical responses in cortical regions with and without hearing loss. This work was supported by NIH/NIDCD R01 DC017619, NIH/NIDCD R01 DC014467, NIH/NIDCD P50 DC00422, NIH/NIDCD T32 DC014435. The project also received support from the South Carolina Clinical and Translational Research (SCTR) Institute with an academic home at the Medical University of South Carolina, NIH/NCRR Grant number UL1RR029882.

126 Mechanical Activation of the Angiotensin II Type I Receptor (AT1R) Promotes Abdominal Aortic Aneurysm Formation in Spontaneously Hypertensive Mice

Nicholas Ward, Armaan Amin-Javaheri, Hayes Lanford, R. Tyler Grespin, Christine Couch, Rupak Mukherjee, Jeffrey A. Jones, Jean Ruddy, Medicine, Department of Surgery, MUSC.

Introduction: In addition to ligand-specific activation, the Angiotensin II Type 1 receptor (AT1R) can activate under conditions of mechanical stretch. However, whether this activity contributes to abdominal aortic aneurysm (AAA) development is unknown. This study evaluated the hypothesis that mechanical AT1R activation occurs under conditions of hypertension and promotes AAA formation. Methods: BPH/2 mice, which demonstrate neurogenic hypertension not mediated by AngII, and normotensive BPN/3 mice underwent AAA induction via CaCl2 model, with or without osmotic mini-pump delivering 30mg/kg/d of losartan. Systolic blood pressure (SBP) was measured at baseline and weekly after surgery. Aortic diameter (AoD) was measured at baseline and terminal surgery at 21 days. Aortic tissue was harvested for immunoblot (pERK/ERK ratio) and expressed as fold-change from BPN/3. Data was analyzed by ANOVA. Results: At baseline, all BPH/2 mice demonstrated elevated SBP relative to BPN/3 (178.42±4.02mmHg vs. 135.69±4.38mmHg, $p<0.05$). Losartan treatment caused a similar decrease in SBP in both BPH/2 and BPN/3 mice (181.17±2.4mmHg vs. 152.94±2.77mmHg and 127.65±4.20 vs. 113.37±6.30, respectively; $p<0.05$). AAA induction did not affect SBP. Percent increase in AoD was significantly larger in BPH/2 mice relative to BPN/3 (101.28±4.19% vs. 75.59±1.67%, $p<0.05$). Losartan treatment significantly attenuated AAA growth in both BPH/2 and BPN/3 mice (33.88±2.97% and 43.96±3.05%, respectively; $p<0.05$). Baseline ERK1/2 activity was increased 3.70±0.75 fold ($p<0.05$) in BPH/2 mice relative to BPN/3. In BPH/2 and BPN/3 mice with AAA, ERK1/2 activity was increased (3.03±0.66 and 3.66±1.02 fold, respectively; $p<0.05$). However, losartan decreased ERK1/2 activity in both BPH/2 and BPN/3 mice (1.57±0.37 and 1.27±0.65 fold, respectively; $p<0.05$). Conclusion: Aneurysm growth is amplified in BPH/2 mice, but losartan attenuated growth in each strain. ERK1/2 activity was significantly elevated in BPH/2 mice and with aneurysm induction, but attenuated with losartan treatment. These data suggest mechanical activation of AT1R promotes AAA development and may be an effective therapeutic target. This work was supported by T32 Institutional Training Grant: Training to Improve Cardiovascular Drug Therapies (NIH/NHLBI)

127 Heparin Administration in the Emergency Department for ST-Elevation Myocardial Infarction and Culprit Vessel Patency

Katrina BIdwell, Katrina Bidwell, MD, Jasjeet Khural, MD, Umair Malik, MD, Mohammed Almamoud, MD, Sandra Coons, RN BSN, Valerian Fernandes, Medicine, Cardiology, MUSC.

Intravenous unfractionated heparin is a familiar and well-tested strategy for anticoagulant therapy at the time of percutaneous coronary intervention (PCI) for ST-elevation myocardial infarction (STEMI); its use at the time of intervention is a Class I recommendation in the most recent ACC/AHA guidelines on the management of STEMI. Use of intravenous heparin has been shown to decrease early thrombin activity, improve culprit artery patency and reduce reocclusion1,2,3. It is notoriously difficult to achieve and maintain the aPTT within this target range, and under-treatment is a significant problem. Aspirin and a second oral antiplatelet agent are conventionally administered to a patient at the time of arrival in the emergency department. This is occasionally administered in conjunction with a bolus of intravenous heparin prior to transfer to the cardiac catheterization lab although not universally. We sought to investigate the frequency with which heparin was administered to patients presenting with STEMI and whether or not its early administration has a significant relationship with culprit vessel patency at the time of initial angiogram (defined as a TIMI flow of 1 or more), fluoroscopy time during the procedure, or total dose of administered contrast during the procedure. Retrospective data was collected on patients who were a STEMI activation at the Medical University of South Carolina from 1/1/2018-6/16/2019 (121 patients) regarding whether or not patients received unfractionated heparin in the emergency department prior to transfer to the cardiac catheterization lab based on emergency medicine documentation. This was compared with culprit vessel patency based on review of catheterization films (as determined by TIMI flow of 0 vs 1-3) using a chi squared test and the length of fluoroscopy time and contrast dose using the student's t-test. There was no significant relationship between heparin administration in the emergency department and vessel patency, fluoroscopy time or contrast dose.

128 Modified cochlear surface preparation in the adult mouse

Shan Xu, Qiao-Jun Fang, Fan Wu, Suhua Sha, Graduate Studies, Pathology and Laboratory Medicine, MUSC.

Auditory processing in the cochlea depends on the integrity of the mechanosensory hair cells. Over a lifetime, hearing loss can be acquired from numerous etiologies such as exposure to excessive noise, the use of ototoxic medications, bacterial or viral ear infections, head injuries, and the aging process. Loss of sensory hair cells is a common pathological feature of the varieties of acquired hearing loss. Additionally, the inner hair cell synapse can be damaged by mild insults. Therefore, cochlear surface preparations in combination with immunolabeling techniques and confocal imagery, are a very useful tool for the investigation of cochlear pathologies, including losses of ribbon synapses and sensory hair cells, changes in protein levels in hair cells and supporting cells, hair cell regeneration, and determination of report gene expression (i.e., GFP) for verification of successful transduction and identification of transduced cell types. With the availability of molecular and genetic information and the ability to manipulate genes by knockout and knock-in techniques, mice have been widely used in biological research, including in hearing science. However, the adult mouse cochlea is miniscule, and the cochlear epithelium is encapsulated in a bony labyrinth, making microdissection difficult, although dissection techniques have been developed and used in many laboratories. Here, we modified microdissection method using cell and tissue adhesive. The main advantage of this technique is that adherence of pieces of cochlear epithelium to a 10-millimeter round coverslips facilitates immunolabeling procedure while avoiding tissue loss during the multiple washing steps. It can be used in all types of adult mouse cochleae following decalcification. This work was supported by R01 DC009222

129 Elevated LVEDP in STEMI presentation does not guide use of temporary mechanical circular support systems.

Jasjeet Khural, Mohamed Almahmoud, Umair Malik, Katrina Bidwell, Valerian Fernandes, Medicine, Internal Medicine, MUSC.

Abstract Withheld from Publication

130 A screen using human iPSC-derived hepatocytes to identify novel drugs for the treatment for hypercholesterolemia

Jui Tung Liu, Mary Paige Lamprecht, Yuri K. Peterson, Steven L. Holshouser, Patrick M Woster, Duncan Stephen, Medicine, Regenerative Medicine and Cell Biology, MUSC.

Abstract Withheld from Publication

131 Structural basis of cephalosporins resistance in N. gonorrhoeae Penicillin-Binding protein 2

Avinash Singh, Robert A Nicholas, Christopher Davies, Medicine, Biochemistry and Molecular Biology, MUSC.

Neisseria gonorrhoeae, the causative agent of gonorrhea, has become a major threat to human health worldwide due to its reduced susceptibility against extended-spectrum cephalosporins (ESCs). A better understanding of its resistance mechanisms is needed in order to develop countermeasures against resistant strains. Mutations in penA gene, which encodes penicillin-binding protein 2 (PBP2), is a major cause of cephalosporin resistance in Neisseria gonorrhoeae. In order to understand the molecular mechanism underpinning cephalosporin resistance, we have investigated PBP2 from the cephalosporin-sensitive strain FA19 (wild type) and resistant strain H041 (CephR). The decrease in the rate of acylation confers resistance against ESCs, and in PBP2 derived from the CephR strain H041, rate decreases by >12,000 fold for cefixime compared to PBP2 from FA19. We have solved the crystal structures of apo and acylated forms of PBP2 from FA19 and H041 strains. Comparison of apo and complex structures of PBP2FA19 suggests acylation proceeds through twisting and rolling of a β strand in the active site region. The structure also reveals that recognition of the β-lactam carboxylate by a Thr498 triggers these conformational changes. Mutations in PBP2H041, when compared to PBP2FA19, causes significant structural differences, especially in the functionally important beta3-beta4 loop region. The mutations appear to increase the rigidity of the structure. Acylated structures comparison reveals that ligand binding in resistant strain PBP2 is constrained, as a G545S mutation traps the β-lactam carboxylate and prevent its interaction with Thr498, thus restricting the conformational changes. It also leads to sub-optimal binding of the ligand in the active site. Hence, the G545S mutation, along with other mutations, restricts the conformational changes required for efficient acylation. Overall, our data suggest that mutations in PBP2 increase rigidity in the protein structure, leading to restriction of protein dynamics and sub-optimal binding of the ligand in the active site. This work was supported by NIH award GM066861

132 Can We Noninvasively Stimulate Deep Brain Structures? An Initial Study Using Low Intensity Focused Ultrasound Pulsation (LIFUP) of the Anterior Thalamus To Modulate Pain

Sasha Stomberg-Firestein, Kevin A. Caulfield, Philipp M. Summers, Matthew T. Savoca, Scott Henderson, Xingbao Li, Logan T. Dowdle, Christopher Austelle, Baron Short, Mark S. George, Bashar Badran, Medicine, Brain Stimulation Laboratory, MUSC.

Abstract Withheld from Publication

133 Cancer immunotherapy findings of T cell behavior in responsive or non-responsive melanoma models

Amalia Rivera Reyes, Amalia M. Rivera Reyes, Megan M. Wyatt, Connor J. Dwyer, Hannah M. Knochelmann, Aubrey S. Smith, Guillermo O. Rangel Rivera, Dimitrios C. Arhontoulis, Nicholas P. Restifo, Chrystal Paulos, Graduate Studies (MSTP, PhD years), Department of Microbiology and Immunology, MUSC.

Patients that respond to immunotherapy with malignancies have high mutation burden although it is unclear how tumor mutations impact T cells behavior, persistence and phenotype. To address this question, in collaboration with the NIH, we generated two models where mice bearing melanoma with either a responsive or non-responsive to tumor when exposed to the same therapy [adoptively transferred CD8+ T cells]. Analogous to the clinic, this treatment eradicated solid tumors with high but not low mutations. Herein, we discovered that infused donor T cells persisted with a central memory phenotype in mice bearing tumors with high mutations. Conversely, compared to the responsive model, few donor T cells were detected in subjects with low mutations. Future studies will focus on using this information to re-

wire either T cells or the tumor microenvironment to increase patient responsiveness to immunotherapy. This work was supported by 5R01CA208514-04

134 Females have decreased CD8 T-cell survival and exosome release after activation

Sarah Pippin, Miguel Troncoso, Kristine DeLeon-Pennell, Medicine, Cardiology, MUSC.

Cardiovascular diseases including myocardial infarction (MI) are the leading cause of death in the US. Elevated CD8 T-cell counts (>1065 cells/mm3) have been linked with increased mortality rate (2-fold) in post-MI patients. In a previous study conducted by our lab, it was concluded that CD8 T-cells regulate macrophage recruitment and impair collagen deposition during the early phase post-MI leading to adverse cardiac remodeling and decreased survival. Interestingly, survival was improved in male but not female mice lacking activated CD8 T-cells ($p<0.05$). As a result of this study, new questions arose concerning sex differences in CD8 T-cell regulation of the post-MI remodeling process. We hypothesized that CD8 T-cells from males are detrimental in regulation of the post-MI remodeling process. CD8 T-cells isolated from the spleens of male and female mice were cultured in RPMI supplemented with 10% FBS and 1% antibiotics as a positive controls and 0.1% FBS (serum starved) as a negative control. Stimulation groups were divided into: 1) IL4 (1.5 ng/mL), 2) IL12 (1 ng/mL), 3) IL4 (1.5 ng/mL) +MMP9 (1ng/mL), and 4) IL12 (1 ng/mL) +MMP9 (1 ng/mL). CD8 T-cells isolated from females after 4 hours of interleukin-4 and -12 stimulation showed a decrease by 2-fold in tetraspanin-14, a marker of exosome release, compared to CD8 T-cells isolated from males ($p<0.05$ for all). By 24 hours, this decrease is no longer present. After 24 hours, serum starvation and IL12 stimulation decreased cell survival of CD8 T-cells from females compared to males ($p<0.05$ for all) indicating that females may have an adverse response to metabolic and inflammatory stressors. No differences between groups were observed at the 4 hour time point ($p=0.207$). In conclusion, CD8 T-cells influence the inflammatory responses differently in males and females. This work was supported by VA, NIH, APS

135 Investigating the Interaction between Vimentin and DZIP1 in Mitral Valve Prolapse

Christina Wang, Janiece Glover, Russell Norris, Graduate Studies, Regenerative Medicine, MUSC.

Mitral valve prolapse (MVP) is the most common valvular heart disease in the developed world, affecting millions with an increasing incidence. If left untreated, MVP can lead to a variety of secondary complications, including mitral regurgitation, left ventricular (LV) remodeling, congestive heart failure, and cardiac death. Currently, the etiology of MVP remains poorly understood. However, our lab previously identified the primary cilia gene DZIP1 as critical in the development of MVP. We recently performed a two-hybrid screen using the DZIP1 protein as bait and identified the intermediate filament protein, Vimentin, as a novel binding partner. Thus, we hypothesize that DZIP1 tethers primary cilia to the intermediate filaments of the cytoskeleton through its interactions with Vimentin. Immunohistochemistry (IHC) was performed on murine valve tissue throughout development and revealed similar expression patterns between Vimentin and primary cilia. Biochemical techniques will also be used to further examine the DZIP1/Vimentin interaction on a molecular level. By understanding the molecular and developmental mechanisms underlying the inception of disease based on genetic insights from MVP patients, these findings aim to contribute to the development of alternative therapies for minimizing the impact of MVP on a clinical level. This work was supported by R25 GM1132778

136 Alterations in Posterior Cingulate Cortex Resting-State Connectivity Specific to PTSD Patients with Comorbid Substance Use Disorder

Madeline Hohmeister, Jane Joseph, Graduate Studies, Neuroscience, MUSC.

Background: Posttraumatic Stress Disorder (PTSD) and Substance Use Disorder (SUD) comorbidity can have devastating psychiatric, medical, and social consequences. The co-occurrence of these disorders is extremely frequent and often exacerbates symptoms. Although neural mechanisms underlying PTSD and SUD have been investigated separately, little is known about how the brain is affected when the two disorders co-occur. Studies have shown communication between and within neural networks becomes dysregulated in patients diagnosed with PTSD or SUD alone. The present study aimed to determine whether comorbid PTSD/SUD causes specific variations in resting-state functional connectivity patterns formed by the posterior cingulate cortex (PCC), a critical hub for communication between neural networks. Method: Subjects exposed to trauma and subsequently developed either comorbid PTSD/SUD (n=21), PTSD alone (n=8), or neither (n=10) and non-trauma exposed subjects (n=42) completed a resting-state fMRI scan. fMRI time series were extracted from a dorsal and ventral region of the PCC and submitted to seed-based connectivity analysis in order to create a connectivity map of the PCC for each subject group. Results: PTSD/SUD subjects showed significantly stronger connectivity between the dorsal PCC and hippocampus and between the ventral PCC and cerebellar regions than both PTSD-only and trauma control subjects. Further analysis showed comorbid subjects had significantly stronger connectivity between the left hippocampus and both dorsal and ventral regions of the PCC when compared to non-trauma exposed subjects. Conclusion: These findings show that PTSD/SUD comorbidity is associated with alterations in functional brain connectivity that are unique from alterations associated with PTSD alone. These atypical connectivity patterns lend insight into neural correlates of comorbid PTSD/SUD. Future studies should investigate the clinical significance of these connectivity patterns.

137 taVNS for Oromotor Infant Feeding III. Does doubling the dose matter?

Sarah Huffman, Daniel Cook, Morgan Dancy, William H. DeVries, Georgia Mappin, Sean Thompson, Philipp Summers, Marom Bikson, Mark S. George, Bashar W. Badran, Dorothea Jenkins, Medicine, Department of Pediatrics, MUSC, MUSC.

Infants who are born premature or who suffer hypoxic ischemic encephalopathy (HIE) are at high risk for motor problems, which primarily manifest as oromotor dyscoordination. This dyscoordination may result in the failure to achieve full oral feeds and gastrostomy tube (G-tube) placement. Pairing vagus nerve stimulation (VNS) with a physical activity improves motor function in adults after stroke. In this first use of transcutaneous auricular VNS (taVNS) in neonates, we investigated whether taVNS paired with oromotor rehabilitation would show a dose response in motor learning in infants who failed oral feeding and were clinically determined to need a G-tube. Infants enrolled in the unblinded, taVNS-paired feeding phase-0 trial received once daily (n=14) or twice daily (n=10) taVNS-paired bottle feeds for 2-4 weeks or until full oral feeds with adequate weight gain (>20 grams/day) were attained. Pulses were delivered via left ear electrode at 0.1mA less than perceptual threshold, frequency 25Hz, pulse width 500μs, 30min oral feed. Total daily volume of oral feeds were averaged over one

week prior to taVNS, and compared to average volumes after the start of taVNS. Diffusion MRI data was performed pre- and post-treatment. Overall, 14 of 24 (58%) infants achieved full oral feeds with weight gain; 10 did not and received a G-tube as planned. All responders showed significant improvement in mean oral feeding volumes in the two weeks during taVNS compared to the week prior ($p=0.023$, paired t-test). Among responders, twice daily treatments resulted in shorter mean time to full feeds (7.7±3.8 days, n=6) versus once daily taVNS (15.5±7.8 days, n=8, $p=0.044$, t-test). There were no differences in mean oral volumes or incidence of responders by daily dosing (57% vs 60%, respectively). With this positive dose response data and an automated electromyographically-triggered taVNS system, we may confidently proceed to a phase I/II randomized trial. This work was supported by The National Center of Neuromodulation for Rehabilitation (NC NM4R) NICHD, NIH P2CHD086844; SC Center for Stroke Recovery, COBRE, P20 GM109040.

138 Sex differences in posterior cingulate cortex connectivity in amnestic Mild Cognitive Impairment

Shaquanda Ross-Simmons, Madeline Hohmeister, Andreana Benitez, Ph.D, Jane Joseph, Medicine, Neuroscience, MUSC.

Amnestic Mild Cognitive Impairment (aMCI) is a syndrome characterized by a decline in memory that presents a risk for the development of probable Alzheimer's disease (AD). More women have probable AD than men. Therefore, understanding sex differences in aMCI may expand knowledge of AD etiology and inform prevention and treatment. The posterior cingulate cortex (PCC) is a key structure that is connected to the default mode network and hippocampal regions and is thought to be involved in memory retrieval processes, which are compromised in aMCI. Resting-state fMRI (rsfMRI) is a promising approach that can be used to examine PCC connectivity. Objective: To examine sex differences in functional connectivity of the PCC to hippocampal and other memory-related brain regions in aMCI. To better understand sex differences, modulation of PCC connectivity by age, and cognitive performance was also examined. Methods: Nineteen participants were included in the analysis (11 Males, 8 Females; 60 to 85 years of age). Each subject completed one 6-minute rsfMRI scan as well as the Montreal Cognitive Assessment (MoCA). Seed-based functional connectivity analyses with the left and right ventral PCC as seed regions were conducted to examine the effect of sex, age and MoCA scores as well as Sex x Age and Sex x MoCA score interactions for PCC connectivity. Results: Although there were no sex differences or interactions involving sex in ventral PCC-hippocampal connectivity there was a significant Sex x MoCA interaction for left PCC- right insula/opercular connectivity.This interaction showed that weaker connectivity was associated with poorer cognitive performance in women. Conclusion: Connectivity of the PCC with insula/opercular regions was modulated by cognitive performance differently in aMCI men and women. This region, which has been implicated in switching from the default mode network to the central executive network, showed decreased connectivity in those with aMCI and AD.

139 Unique Inflammatory Signatures in Response to Viral Dosage of Myxoma

Erica Flores, Mee Bartee, Eric Bartee, Graduate Studies, Microbiology & Immunology, MUSC.

Members of the family Poxviridae are currently under investigation as candidates for oncolytic therapy due to their cancer cell tropism, ease of genetic modification, and generation of an anti-tumor response. In particular, our research focuses on using Myxoma, a lagomorph poxvirus, as an oncolytic agent. Our purpose for this study was to investigate the effects on tumor burden and host immune response with a range of viral doses of our standard Myxoma virus that expresses GFP (MYXV-GFP). It was expected that more virus would lead to higher viral replication within the tumor and elicit a greater immune response for a more efficacious treatment. For our study, mice bearing B16/F10 tumors were treated with a logarithmic titration series of MYXV-GFP ranging from 1 x107 FFU/mL to 1 x 104 FFU/mL. We found that with viral treatment alone, there was no significant difference between tumor growth or survival. However, an unexpected finding was the recovery of similar amounts of infectious virus from these tumors, despite the log differences in viral input. Interestingly, we do see increased survival and reduced tumor burden in high viral dose groups compared to low dose groups when mice are treated in combination with PD-1 blocking antibody. We hypothesized that differences in transcript expression within the tumor may explain the sensitivity of these tumors to respond to PD-1 therapy. Further investigation reveals unique inflammatory signatures in the transcriptomes, Tumor Infiltrating Lymphocyte (TIL) populations, and cytokine secretion between the two treatment groups, despite near identical levels of viral replication. These differences in host immune response may account for the susceptibility of these tumors to respond to the addition of PD-1 blockade therapy. It is critical to understand how viral dosage affects viral replication and the host immune response within the tumor microenvironment in order to better target oncolytic therapy. This work was supported by NIH, ACS, RSG, Systems Oncology Sponsored Research, MUSC and Hollings Cancer Center Internal Funding

140 Preliminary results of 60-min vs 90-min Prolonged Exposure sessions with active duty personnel.

Gabrielle Frook, Stephanie Hart MPH, Ron Acierno PhD, Wendy Muzzy, Nursing, College of Nursing, MUSC.

Symptoms associated with Posttraumatic Stress Disorder, such as depression, anxiety, problems concentrating, sleep difficulties, flashbacks, and irritability, have detrimental effects on a person's ability to function, especially for active duty military personnel. Research has shown that 11-20% of OIF/OEF veterans develop PTSD. Prolonged Exposure is for the foremost evidence based treatment for PTSD. However, the protocol prescribes 90-minute therapy sessions, making it difficult for military providers to adopt it as a standard treatment as they schedule by 60 minute blocks. This randomized, controlled, non-inferiority trial examined the effectiveness of using 60-minute PE sessions compared to 90-minute sessions. If found to be non-inferior, it would remove a significant barrier to treatment for active duty personnel experiencing PTSD symptoms. This RCT was funded by the DoD. Participants were active duty personnel in the Charleston and Savannah area. The CAPS-5 and PCL-5 were administered and psychophysiological data were collected. For the preliminary results, the PCL-5 scores from pre- and post-treatment will be analyzed. Data are still being collected. This work was supported by subcontract through the University of Pennsylvania with funding from the Department of Defense

141 The effects of low dose sacubitril and/or valsartan on renal disease progression in salt-sensitive hypertension

Mark Domondon, Iuliia Polina, Rebecca Fox, Mikhail Fomin, Daria Ilatovskaya, Medicine, Medicine/Nephrology, MUSC.

Introduction. Atrial Natriuretic Peptide (ANP) is known to promote salt excretion, vasodilation and BP reduction. The goal of this project was to test if increasing the circulating ANP level using a low dose of sacubitril in combination with a RAS blocker valsartan is beneficial for the mitigation of salt-sensitive (SS) hypertension renal damage. Methods. Dahl SS rats were fed a 0.4% NaCl (normal salt, NS) diet until 8 weeks

of age, when they were switched to a 4% NaCl (high salt, HS) diet for 21 days. Vehicle (veh), sacubitril (sac), valsartan (val) or a 1:1 mix of both drugs (sac/val) were administered at 75 ug/day via subcutaneous osmotic pump immediately before the diet change. Metabolic cage studies and GFR measurements were performed before the diet switch, and at the end of the protocol. Kidneys, blood plasma and urine were collected at the end of the protocol to examine electrolyte levels, glomeruli health, proteinuria, protein cast formation, and fibrotic damage. Results. Upon the HS challenge, GFR was lowered in the control group, but elevated in the sac/val sac and val groups. Urinary flow, as well as urinary Na+ and Cl- levels, were significantly increased across all groups. Proteinuria was less pronounced in sac/val and val groups after the HS challenge (vs the control). Lower urinary KIM-1 was found in sac/val and val animals compared to the control. Less protein cast formation was found in sac/val and val groups compared to veh and sac groups. Conclusion. A combination of sacubitril and valsartan, or valsartan by itself, attenuated proteinuric renal damage and KIM-1 excretion caused by salt sensitive hypertension. Further studies are warranted in order to determine if the use of sacubitril is a feasible treatment for the progression of SS hypertension. This work was supported by NIDDK R00 DK105160, Dialysis Clinic Inc Reserve Fund, the MUSC SCTR support program via NIH/NCATS UL1TR001450, and the American Physiological Society awards (all to DVI)

142 Attenuation of thoracic aortic aneurysm development by inhibition of membrane type-1 matrix metalloproteinase activity

Isis Thomas, Xiong, Y., Stroud, R.E., Nadeau, E.K., Mukherjee, R., Jeffery Jones, Graduate Studies, Surgery, MUSC.

Abstract Withheld from Publication

143 Blood vessel atrophy and macrophage dysfunction in age-related hearing loss

Tyreek Jenkins, Kenyaria Noble, Hainan Lang, Graduate Studies, Pathology and Laboratory Medicine, MUSC.

Introduction: Age-related hearing loss (ARHL) affects about one in three adults between the ages of 65 and 74 and almost half who are 75 years or older in the United States. ARHL is generally defined as a progressive sensorineural hearing loss due to the degeneration/loss of cells in multiple cochlear components. It has been shown in pathogenic conditions that laminin expression alters the biological activity of immune cells; however, the relationship between laminin expression, activated macrophage activity, and strial microvessel atrophy in ARHL has yet to be determined. Our study tested the hypothesis that age-related cochlear cellular degeneration is associated with an increase in macrophage number and changes in laminin expressing microvessels in the strial vascularis and spiral ligament of the cochlear lateral wall. Materials and methods: Auditory brainstem response measurement, confocal microscopy, and quantitative immunohistochemistry analysis were performed in young adult and aged CBA/CaJ mice. Results: We found that macrophage number decreased and laminin expressing microvessels increased with age in the apical and middle turns of the stria vascularis. Contrarily, the inverse relationship between macrophage presence and laminin accumulation was shown in the basal turn. For the spiral ligament in all three turns, laminin expression within microvessels increased with age, while macrophage presence decreased. Moreover, microvessels in the cochlear lateral wall do not appear to have a significant loss with aging in some cochlear regions but demonstrate morphological changes associated with laminin increase. Discussion: Our study revealed a correlative relationship between age-related changes in macrophage activity and laminin expression within the cochlear lateral wall. Further investigation is needed to identify the regulatory roles of laminins in age-related macrophage dysfunction, strial microvessel atrophy, and hearing loss. The research was supported in part by NIH grants P50 DC000422 and R56DC012058.

144 Effects of maternal supplementation and vitamin D binding protein polymorphisms on vitamin D status in breastfed infants

Simran Paintlia, Danforth A. Newton, Manjeet K. Paintlia, John E. Baatz, Renee Washington, Judy R. Shary, Carol Wagner, Medicine, Pediatrics, MUSC.

Background: Vitamin D binding protein (VDBP) is an abundant protein that transports 85-90% of circulating vitamin D (vitD) metabolites in the blood. Common polymorphic alleles of VDBP impact the circulating levels of 25-hydroxyvitamin D (25-D). Recently, we documented that vitD status is affected by VDBP genetic variability in children following the prescribed recommended daily allowance (RDA) of vitD intake. In the current study, we hypothesize that VDBP alleles may also affect vitD status in breastfed infants whose mothers are part of a vitD supplementation trial. Methods: 70 mothers and breastfed infants were enrolled in an ongoing lactation pilot study at MUSC. In this blinded study, mothers were supplemented with either 600 or 6600 IU/day vitD3, while breastfed babies received 400 IU/d or placebo, respectively. Plasma 25-D concentrations at V1 and 4 (1 and 4 months after birth) were measured by radioimmunoassay. VDBP alleles (Gc1S, Gc1F, Gc2) in infants and mothers were determined by RFLP analysis, and plasma VDBP protein concentrations were determined by ELISA. Results: Mean vitD sufficiency was achieved in infants during this 4-month study. There was a significant linear correlation between mother and baby 25-D when maternal 25-D increased >10 ng/ml from V1 to V4. There was a lower, but still significant linear correlation between mother and baby 25-D when maternal 25-D increased <10 ng/ml or decreased from V1 to V4. No significant associations between circulating 25-D to VDBP concentrations were observed in mothers or infants. VDBP genotypes for 20 mother/infant pairs were determined so far. Conclusions: In this ongoing study, mean vitD sufficiency in breastfed infants could be achieved by direct vitD supplementation or by increasing maternal vitD status through supplementation. We will continue to collect enough numbers of genetic variants by VDBP genotyping.

145 Post-hoc Analysis of NICHD Vitamin D Pregnancy Cohort and The Role of Functional Vitamin D Deficiency in Pregnancy

Elliott Lyles, Shelly Davis, Judy R. Shary, Myla Ebeling, Bruce W. Hollis, Carol Wagner, Medicine, Neonatology, MUSC.

Objective: Write a Post-hoc analysis using data from the NICHD vitamin D pregnancy study by Hollis et al., which reported on the effect of vitamin D supplementation in pregnant women; and determining the potential interaction between parathyroid hormone (PTH) concentrations, vitamin D status, and comorbidities associated with pregnancy. It is hypothesized that women with low 25(OH)D and high PTH concentrations during pregnancy, known as functional vitamin D deficiency (FVDD), are more likely to acquire complications also affecting their neonates. Design: Data collected from a diverse group of pregnant women participating in the NICHD study, was applied to investigate the applicability of FVDD in pregnancy (Hemmingway et al.) in identifying potential risks for comorbidities of pregnancy. This

analysis defines FVDD as maternal serum 25(OH)D concentrations below 20 ng/mL and PTH concentrations above 65 pg/mL creating a definitive ratio number, 0.308, to classify mothers as having FVDD one month prior to delivery (PTD). Results: There were 269 women, 75 black, 113 Hispanic, and 81 white, who participated in the study and had 25(OH)D and PTH concentrations measured one month PTD. No statistically significant association was found between mothers who were classified as having FVDD, one month PTD, and their likelihood of acquiring hypertensive disorders of pregnancy (which included gestational hypertension, preeclampsia, hemolysis/elevated liver enzymes/low platelet count (HELLP)), infection, or admittance to the NICU. Participants in the NICHD trial, however, who met the criteria for FVDD, one month PTD, were 7.4 times more likely to have preterm birth (<37 weeks) than those who did not. Conclusions: Participants from the NICHD vitamin D pregnancy study were more likely to have preterm birth if they had FVDD. This study extends prior FVDD knowledge by discovering associations between FVDD and pregnancy outcomes, which support the importance of a functional definition of vitamin D deficiency during pregnancy.

146 Frequency and severity of medication side effects and causes of noncompliance in Kidney transplant patients

Anushka Fernandes, David Taber, Pharmacy, Department of Transplant Surgery, MUSC.

Abstract Withheld from Publication

147 Th17 Cells Uniquely Induce IL-6 and Possess Potent Antitumor Activity

Reilley Chamness, Hannah M Knochelmann, Chrystal Paulos, Graduate Studies, Microbiology and Immunology, MUSC.

Introduction: CD4+ T cells have shown promise for adoptive cell transfer therapy (ACT) for aggressive, metastatic malignancies. Given the heterogeneity of the CD4 subset, understanding their relative antitumor properties is important for improving long-term responses in patients. Th17 cells have stem-like properties that have been deemed advantageous for immunotherapy in contrast to other helper subsets. Our previous work demonstrates that Th17 cells induce high levels of IL-6 post ACT; however, it remains unknown whether T helper subsets produce IL-6 or differentially induce IL-6 in hosts receiving immunotherapy. Materials and Methods: Cytokine production by polarized T helper cells was assessed by flow cytometry. ACT therapy was conducted using the TRP-1 transgenic mouse model where CD4+ T cells express a T cell receptor specific for TRP-1 expressed by melanoma. T cells were polarized to Th0, Th1, Th9 and Th17 phenotypes. ELISA was performed on supernatant post peptide-specific activation to assess cytokine levels of these helper subsets. Results: T helper cells were successfully polarized into predefined subsets. These subsets have distinct memory phenotypes after four days of ex vivo expansion. Post adoptive transfer, Th17 cells were the only subset to promote antitumor responses while Th0, Th1, and Th9 cells were not therapeutic in equal doses. Th17 cells had the highest engraftment and persistence suggesting they could elicit long term immunity. Cytokine analysis in mouse serum one week post ACT revealed that Th17 cells induce significantly higher levels of IL-6 and other cytokines including IL-17, MCP-1, KC, and G-CSF. Conclusions and Further Directions: Th17 cells induce high levels of cytokines in the serum post adoptive transfer and elicit long term immunity, which appears specific to this CD4+ subset. Future studies will investigate how IL-6 specifically promotes a memory phenotype in Th17 cells compared to other helper subsets and if this phenotype further enhances therapy. This work was supported by R01s--NCI R01 CA175061, NCI R01 CA208514, SURP

148 Chronic Consumption of Dietary Advanced Stage Glycation End-Products (AGE)s Activates Mammary Fibroblasts in vivo

Reid Schuster, David Turner, Lourdes Nogueira, Bradley Krisanits, Victoria Findlay, Graduate Studies, Pathology, MUSC.

Many studies have indicated that Advanced Stage Glycation End Products, or AGEs and their corresponding receptor, the Receptor of AGE (RAGE) have roles in several chronic diseases such as diabetes, and heart disease due to their pro-inflammatory properties. Recently AGE: RAGE signaling has been shown to have potential roles in a number of cancers including prostate and breast cancer, however how AGE: RAGE signaling effects these cancers has not been elucidated. Our lab has previously observed that the consumption of a high AGE diet results in increased stromal recruitment to ductal structures and hyperproliferation within developing mouse mammary glands. Considering the well documented and diverse roles of carcinoma associated fibroblasts (CAFs) in breast cancers we wanted to determine whether AGE: RAGE signaling in the mammary stroma contributed to a CAF-like phenotype in mammary fibroblasts. If AGEs could cause an 'activation' fibroblast profile that culminates in increased epithelial migration/invasion, then there may be a higher likelihood of metastasis should a mammary carcinoma develop. We used a dietary-AGE mouse model to examine the impact of consumption of a high AGE diet on the stromal microenvironment during pubertal growth. This study shows that fibroblasts isolated from mammary glands exhibit an upregulation in a panel of fibroblast activation markers when fed a high AGE diet. Furthermore, we observe that both in vivo- and ex vivo- treated fibroblasts with AGE results in increased HC11 epithelial cell migration. However, treatment of epithelial cells directly with AGE has no effect. Finally, we show that RAGE is required for AGE-mediated activation of fibroblasts and subsequent epithelial cell migration. These results provide insights into the AGE: RAGE signaling axis in normal mammary development and highlight the importance of the pubertal window of susceptibility and future breast cancer risk. This work was supported by Funding: MUSC College of Medicine - Institutional Bridge Funding (Findlay)

149 Non-peptidic Galectin-1 Inhibitor OTX008 Suppresses Glioblastoma Growth

Wayne Glore, David Cachia, William A. Vandergrift III , Scott M. Lindhorst, Abhay K. Varma, Sunil J. Patel, Arabinda Das, Graduate Studies, Department of Neurosurgery, MUSC.

Galectin 1 (Gal-1) is a carbohydrate binding protein that has been noted for having influence in tumor growth, proliferation, and angiogenesis. Gal-1 promotes tumor growth and survival in the face of immunotherapy such as Anti- VEGF treatment with glioblastoma (GB). Gal-1 induces cell death in T-cells, and other immune response cells to suspend the immune response of the body to fight off the cancerous cells. Gal-1 has a direct influence with CXCR4 expression. CXCR4 expression alters the microenvironment to promote tumor growth and generate drug resistance to treatment. High levels of Gal-1 expression have been shown in GB cells. Inhibiting Gal-1 would potentially have the impact to restore sensitivity to GB treatment. For this experiment the Gal-1 inhibitor OTX008 is used to analyze and validate if altering Gal- 1 expression has a direct response to tumor growth. The functionality and efficacy of OTX008 on GB is tested through Western Plotting. Alzet osmotic pumps with OTX008 were treated by In- vitro cell culture and in vivo GL261 murine models of GB. Magnetic

Resonance Imaging (MRI) was incorporated to measure tumor size and growth. Results show that inhibiting Gal-1 led to a decrease in expression of CXCR4. In vivo,100ng/kg OTX008 treatment via Alzet osmotic pumps over 14 days reduced tumor growth of GL261 murine model after 3 weeks of implantation. In conclusion, inhibiting Gal-1 might be an effective method to lower tumor drug resistance and slow down the potential for tumor growth or relapse after treatment. This work was supported by Department of Neurosurgery, MUSC

150 Noise-induced loss of sensory hair cells is triggered by ROS/p-AMPK-alpha pathway

Fan Wu, Hao Xiong, Suhua Sha, Medicine (MSTP, MD years), Pathology and Laboratory, MUSC.

Accumulation of reactive oxygen species (ROS) has been well-documented in noise-induced hearing loss (NIHL). Our previous study showed that activation of AMPK-alpha (formation of p-AMPK-alpha) is one of the key factors triggering noise-induced outer hair cell (OHC) death. However, the relationship between ROS and activation of AMPK-alpha remains unknown. In this study, we use forskolin and N-acetyl cysteine (NAC) to explore the link between ROS and activation of AMPK-alpha in OHCs since both NAC and forskolin are well-known antioxidants. We first established conditions for NIHL with CBA/J mice at the age of 8 weeks. Then we found that treatment with forskolin attenuates noise-induced losses of OHCs and synaptic ribbons as well as NIHL. Furthermore, treatment with forskolin significantly increases cAMP in OHCs. Finally, treatment with forskolin or NAC attenuates noise-induced ROS formation in OHCs, assessed by the relative levels of 4-hydroxynonenal (4-HNE) and 3-nitrotyrosine (3-NT), and decreases noise-induced activation of AMPK-alpha. Additionally, hydrogen peroxide (H2O2)-induced HEI-OC1 cell death is prevented by administration of forskolin. HEI-OC1 cells treated with H2O2 confirmed that activation of AMPK-alpha is triggered by ROS accumulation. Our data indicate that noise induces activation of AMPK-alpha in OHCs through accumulation of ROS, at least in part. These results indicate that noise-exposure-induced OHC death is triggered by a ROS/p-AMPK-alpha-dependent pathway. Forskolin may serve as a powerful compound for prevention of NIHL. This work was supported by R01 DC009222

151 Associations Between Parent Psychopathology and Youth Mental Health and Early Alcohol Use Behaviors

Alexis Garcia M.S., Michaela Hoffman, Ph.D., Rachel Tomko, Ph.D., Lindsay Squeglia Ph.D, Graduate Studies (MSTP, PhD years), Psychiatry and Behavioral Sciences, MUSC.

Background: Early substance use has gained substantial attention in the last decade. Identifying early predictors of precursory drinking behaviors are important for informing prevention and intervention approaches. Given mental health conditions are highly genetic, it is crucial to examine how symptoms of parent psychopathology (PP) play a role in child mental health and risk-related behaviors. Thus, the goal of the current study is to examine how PP is associated with youth internalizing and externalizing problems, familial conflict, and alcohol sipping behaviors. Methods: The current sample consisted of 11,879 youth (mean age = 9.91 years, range = 9-10 years) and their parents participating in the multi-site Adolescent Brain Cognitive Development (ABCD) study. The Total Problems composite on the Adult Self Report Questionnaire was used to measure PP. Youth psychopathology was measured by parent report on the Child Behavior Checklist. Parents and youth completed ratings of familial conflict, and youth self-reported non-religious sipping behavior. Results: All analyses controlled for age, sex, ethnicity, race, parent income, marital status, and highest education. PP predicted higher levels of externalizing ($b = .47$, $p < .001$) and internalizing problems ($b = .55$, $p < .001$). PP was also associated with youth ($b = .02$, $p < .01$) and parent ($b = .07$, $p < .001$) reported conflict. PP was not related to youth alcohol sipping. Conclusion: Understanding the role of PP is crucial in identifying risk factors associated with poor mental health outcomes in youth. These findings suggest that PP is related to youth mental health and family conflict, but not alcohol sipping behaviors by age 10. Targeting PP in family-based psycho-social interventions may lead to enhanced treatment outcomes for youth, especially those at-risk for future substance use. This work was supported by NIH

152 Histamine receptors and sodium reabsorption in the Cortical Collecting Ducts

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

Histamine is an important homeostatic regulator produced in mast cells and histaminergic neurons. Histamine receptors, H1R-H4R, are G-protein coupled receptors we found to be expressed in renal rat collecting duct (CD) cells and tubular epithelial cells. HRs can be differentially expressed in inflammatory disease states; however, their potential role in renal pathophysiology is unclear. Our goal was to determine if HRs affect the activity of Epithelial Na+ Channels (ENaC), and thus sodium reabsorption, in the CD cells. HRs expression and localization were tested via immunocytofluorescence (ICF) staining in polarized mpkCCDc14 cells grown on permeable supports. All 4 receptors were observed to be expressed in these cells, further verified with Western Blotting. H1R and H4R were localized apically, while H3R and H4R were diffusely distributed in the cytoplasm. H1R and H4R expression was significantly increased upon stimulation with histamine (200 uM for 4 h). We further showed with immunohistochemical staining that all four receptors are expressed in renal collecting ducts of rats. In short-circuit current aimed at measuring ENaC activity, mpkCCDc14 cells were apically exposed to vehicle, histamine only, AVP (a known ENaC activator, control), and AVP with histamine (concentration range 10 nM-1.5 mM). Current measurements were taken for 8 hours, ENaC current was confirmed with amiloride. We report here an inhibition of the AVP-stimulated ENaC-mediated by histamine (most pronounced decrease observed at 6 hours post histamine exposure). In conclusion, we demonstrated that HRs are expressed in the CDs in cultured cells and renal tissues. We showed that histamine has a dose-dependent effect on ENaC-mediated currents and ENaC expression. This will provide insight into the role of histamine receptors in sodium reabsorption as well as the implications of histamine in renal disease. This work was supported by NIDDK R00 DK105160, Dialysis Clinic Inc Reserve Fund, the MUSC SCTR support program via NIH/NCATS UL1TR001450, and the American Physiological Society awards (all to DVI)

153 Mitochondrial respiration and biogenesis in the glomeruli of Dahl SS rats

Regina Sultanova, Mark Domondon, Anna Nikiforova, Iuliia Polina, Mikhail Fomin, Krisztian Stadler, Daria Ilatovskaya, Medicine, Department of Medicine/Nephrology, MUSC.

The mechanisms of salt-sensitive (SS) hypertension are complex and far from clear. SS hypertension is accompanied with an early onset of proteinuria, which results from the loss of podocytes. Many reports highlight that in this disease ultrastructural abnormalities and deficient metabolism in the renal mitochondria may precede histological injury. We hypothesized that podocyte damage occurs in part due to

mitochondria dysfunction. Dahl SS rats were used here as an established animal model of SS hypertension. 8 weeks old rats were challenged with a high salt (HS) 4% NaCl diet for 21 days. At the end of the protocol BP was measured, kidneys were cleared from blood, tissues were collected, and cortical glomeruli were isolated and subjected to other applications. Systolic BP was elevated in the HS diet fed rats (171±9 vs 148±6 mmHg in HS vs NS diet fed rats). HS diet fed rats exhibited renal lesions, kidney hypertrophy, decreased GFR and exacerbated glomeruli damage compared to the NS group. We did not observe changes in the mitochondrial biogenesis. Seahorse assay performed on freshly isolated glomeruli revealed that mitochondria respiration were lower in the HS group (28 ± 14%, 47 ± 15% and 37 ± 9% lower, respectively, vs NS group). Using confocal imaging and mitoPY1 staining we detected higher baseline H2O2 level and lower antioxidant capacity. EM analysis showed that HS mitochondria have structural abnormalities (swelling, enlargement, less defined cristae, and reduced number). We conclude that glomerular mitochondria in SS hypertension are functionally and structurally impaired. This work was supported by NIDDK R00 DK105160, Dialysis Clinic Inc Reserve Fund, the MUSC SCTR support program via NIH/NCATS UL1TR001450, and the American Physiological Society awards (all to DVI)

154 Oral Antibiotic Therapy Critically Regulates Osteoimmune Response Effects and Skeletal Homeostasis in the Alveolar Bone Complex

Brooks Swanson, Jessica Hathaway-Schrader, Amy Warner, Matthew Carson, Joy Kirkpatrick, Alex Alexseyenko, Sakamuri Reddy, Chad Novince, Graduate Studies, Department of Oral Health Sciences, MUSC.

Abstract Withheld from Publication

155 Analyzing Safety in a Phase I trial on Boswellia, an extract from Frankincense, for breast cancer primary tumors

Ingrid Bonilla, Abbott, Andrea, MD, Garcia, Denise, MD, Spruill, Laura, MD, Cole, David, MD, Hill, Elizabeth, PhD, Lockett, Mark, MD, Nancy DeMore, Medicine, Surgery, MUSC.

Abstract Withheld from Publication

156 Dchs1 and the septin cytoskeleton: a molecular and developmental etiology underlying mitral valve prolapse

Reece Moore, Kelsey Moore, Rebecca Stairley, Diana Fulmer, Lilong Guo, Russel Norris, Medicine, Department of Regenerative Medicine and Cell Biology, MUSC.

Introduction: Mitral valve prolapse (MVP) is a major source of morbidity and mortality and is becoming one of the most common indications for cardiac surgery. Our group has previously reported that MVP is associated with missense mutations in DCHS1, a gene widely implicated in tissue development and organization. Dchs1 is predicted to interact with the septin cytoskeleton via Lix1L in order to mediate proper mitral valve morphogenesis. Methods: Dchs1 protein interactions were determined using two-hybrid screen. H&Es of P0 mouse mitral valves were done for valve 3D reconstructions. IHC of mouse mitral valves at time points E13.5-P30 was completed to visualize expression levels of Dchs1, Lix1L, and Septin9 throughout development. ICC, G/F actin pellet assays, and contraction assays aimed to elucidate the effects of Dchs1/Septin9 reduction on septin and actin cytoskeleton function. Results: Two-hybrid screen and IHC indicate the presence of a Dchs1-Lix1L-Septin9 (DLS) interaction in human and mouse MVP valve cells. Both Lix1L KO and Lix1L/Dchs1 compound heterozygote mouse models show increased geometric dimensions in the mitral valve consistent with MVP pathology. These mice also show a marked decrease in Septin9 expression. Furthermore, loss of Dchs1 resulted in impaired actin polymerization and stability in valve interstitial cells (VICs). A 70% decrease in F-actin was observed in the diseased model. Inactivation of cofilin, a mediator of actin depolymerization, was decreased by 80% in association with loss of Septin9. In addition, loss of the DLS interaction impaired VIC-mediated contraction of collagen gels. Conclusion: These studies illustrate the importance of the Dchs1-Lix1L-Septin9 pathway and its role in mitral valve disease. Dchs1, through its interaction with the septin cytoskeleton, must regulate and stabilize actin dynamics in mitral VICs leading to proper valve development. Non-surgical interventions for MVP may be identified through establishing the downstream effects of Dchs1 mutations in our model.

157 Mechanism of action and antibacterial activity of alkynyl bisbenzimidazoles

Jordan Chamberlin, Sandra Story, Nihar Ranjan, Geoffrey Chesser, Dev Arya, Medicine, Chemistry, MUSC.

Novel antimicrobial agents are desperately needed to combat antibiotic resistance. Benzimidazoles with terminal alkynyl linkers have been shown to be selective inhibitors of bacterial topoisomerase I with potent Gram-positive activity but their antibacterial mechanism has not been ascertained in a live cell model. Utilizing Bacterial Cytological Profiling (BCP) we show a dual mechanism of action of DNA synthesis and cell membrane permeation contributing to the antibacterial action of these compounds. Fluorescence microscopy analysis revealed changes in cellular ultrastructure including induction of spheroplasts and membrane lysis consistent with a novel mechanism of action distinct from topoisomerase II inhibition. Coverage was extended to Gram-negative multidrug resistant Acinetobacter baumanii and Escherichia coli using the cytoskeleton recruitment enzyme inhibitor A22 in conjunction with alkynyl-bisbenzimidazole 154 at 4 micromolar each. Further synergy studies with efflux pump inhibitors and membrane permeation assays suggest outer membrane permeabilization to be the major barrier for efficacy. Time-kill curves with 154 and A22 combination demonstrate kinetics comparable to Norfloxacin alone. Alkynyl bisbenzimidazoles likely inhibit both DNA synthesis in a novel way and induce membrane permeability against many Gram-positive bacteria and in synergy with A22 against multidrug resistant E. coli and A. baumanii. This work was supported by NIH

158 Commensal Microbiota Regulates Skeletal Development through C3aR/C5aR-Mediated Complement Signaling

Megan Kuhn, Amy J. Warner, Brooks A. Swanson, Matthew D. Carson, Andrew Reynolds, Jessica D. Hathaway-Schrader, Chad Novince, Dental Medicine, Oral Health Sciences, MUSC.

Abstract Withheld from Publication

159 Accuracy of Intraoral Scanning Systems in an Edentulous Maxilla with Implants and Scan Bodies

Griffin Revell, Walter Renne, Dental Medicine, College of Dental Medicine, MUSC.

Increasing utilization of endosseous dental implants as a restorative solution coupled with digital dental design software have led to the need for better understanding of how accurately these distinct yet related areas interface. This study has two primary goals: measuring the accuracy of 5 intraoral scanning systems in replicating implant scan bodies and gingival tissues in an edentulous maxilla with 5 implants and scan bodies, and understanding the effect of operator experience on scan accuracy. A fresh cadaver specimen was acquired, and the maxilla was immediately resected. A digital scan of the maxilla was made with an ATOS Capsule scanner to generate a 3D model. This reference standard scan was used in Geomagic Control X 3D inspection and metrology software to compare against the 5 intraoral scanners. 16 scans were made with each of the 5 intraoral scanners, 8 by an experienced clinician and 8 by an inexperienced clinician. These scans were compared using iterative closest point algorithm used in Geomagic Control X. Average differences between the experimental scans and reference standard scan were recorded. Additional analyses were performed to compare variations in the implant platform surface between the various scans. Deviation in implant platform scans between experienced and inexperienced scanners from greatest to least was iTero Element 2 > Medit i500 > Primescan > Trios 3 > Trios 4. Experience with intraoral scanning devices should be considered by clinicians when implementing these systems. Additional research should be performed to better understand the clinical relevance of these discrepancies. This work was supported by SCTR

160 taVNS for Oromotor Infant Feeding II: Overall Clinical Outcomes in the First 14 Subjects

Daniel Cook, Sean Thompson, Morgan Dancy, William DeVries, Georgia Mappin, Sarah Huffman, Philip Summers, Marom Bikson, Mark S. George, Bashar W. Badran, Dorothea Jenkins, Medicine, Pediatrics, MUSC.

Introduction/Rationale: Neonates born premature or who suffer brain injury at birth often have oral feeding disfunction and do not meet intake requirements needed for discharge. Low oral intake volumes result in extended stays in the hospital (>2 months) and can lead to surgical implant and explant of a gastrostomy tube (G-tube). Transcutaneous auricular vagus nerve stimulation (taVNS), a novel form of noninvasive vagus nerve stimulation, has emerged as a potential facilitator of neuroplasticity. Pairing taVNS with bottle feeding rehabilitation may improve oromotor coordination and lead to improved oral intake volumes, ultimately avoiding the need for G-tube placement. Methods: We enrolled 14 neonates who were recommended for G-tube placement in a prospective, open-label clinical trial to determine the safety and efficacy of taVNS-paired feeding rehabilitation. Oromotor activation associated with a nutritive suck during a bottle feed was used to initiate paired taVNS stimulation. taVNS stimulation was administered via custom neonatal electrodes which attach to the left ear and deliver electrical stimulation (500us pw, 25Hz, up to 30 minutes) during one feed per day. Daily oral intake volumes were recorded prior to enrollment and over the course of the treatment (16±6 days). The primary outcome was whether or not G-tube placement was required for discharge. Results: 57% (8 of 14) of the subjects enrolled achieved oral intake volumes necessary for discharge without G-tube. A significant increase in feeding volume trajectory was observed in subjects who responded to treatment ($p<0.05$). No adverse events were observed related to taVNS treatment. Conclusions: taVNS-paired feeding rehabilitation is safe, well tolerated and may improve oral feeding outcomes compared to the current standard of care. These promising findings support the need for a definitive, large scale, randomized controlled trial. This work was supported by The National Center of Neuromodulation for Rehabilitation (NC NM4R) NICHD, NIH P2CHD086844; SC Center for Stroke Recovery, COBRE, P20 GM109040

161 The Need for ED Based Primary Care: A Study of the Socioeconomic Factors Leading Patients to Consider the ED to be their Medical Home

Cameron Weekley, Berlene Shipes, Ryan Wolf, Dr. Renee Martin, Steven Saef, Medicine, Department of Emergency Medicine, MUSC.

Previous data from our group has shown that many patients who have ambulatory care sensitive conditions (ACSCs) consider the ED to be their Medical Home (MH) over Primary Care (PC). Previously identified factors leading to this preference include convenience of the ED, the ability to be seen regardless of financial status and the trust these patients put into Emergency Physicians (EP) over other physicians. In this study, we added measures of socioeconomic status (SES) to our survey. Adult patients (>18 years old) presenting to our urban, academic ED who were willing and able to participate were eligible. Our dependent variable was the survey item: "Do you consider the ED to be the first place you turn to when you need a doctor?" Those responding "yes" were assumed to consider the ED to be their MH. We used backward selection to create a parsimonious logistic regression model which explained perception of the ED as a MH. We enrolled 337 patients who considered themselves local to the area: 46.9% Caucasian, 54.0% women, 32.7% with Medicaid or no insurance, 49.9% lived within 20 minutes of the study site. Average age was 47.5 (18.23 SD). Patients more likely to consider the ED to be their MH were Non-Caucasian (OR 4.0; 95% CI: 2.3-7.0), had not seen a Primary Care Physician in the last year (OR 4.0; 95% CI: 2.2-7.5), were seeking treatment for an ACSC (OR 2.2; 95% CI: 1.2-4.0), preferred the EP over other physicians (OR 2.8; 95% CI: 1.2-6.2), or were seeking preventive care for heart attacks or strokes (OR 5.1; 95% CI: 2.8-9.2). In our data, patients from all walks of life considered the ED to be their MH. Emergency Medicine as a specialty should assume responsibility for offering rudimentary PC to their patients.

162 The Need for Emergency Department Based Primary Care: A Descriptive Study of Patients Who Seek Preventive Care in the Emergency Department

Ryan Wolf, Virginia Shipes, Cameron Weekley, Renee Martin, Steven Saef, Medicine, Emergency Department, MUSC.

Objectives: Many patients seem to prefer the Emergency Department (ED) over a Primary Care Clinic (PCC) clinic to obtain preventive care for heart attacks or strokes. We sought to explain that preference using descriptive data. Methods: We surveyed adults (>18yrs old) presenting to a southeastern, urban, academic ED regarding their use of the ED for preventive care. Our outcome of interest was whether patients perceived the ED over a PCC for the care they needed to prevent a heart attack or stroke. Backward selection was used to create a parsimonious model which always included the descriptive statistics: age, race, sex, and insurance type. Only patients local to the study site were included. Results: Our sample included 339 adults: 46.9% Caucasian, 54% women, 32.7% with Medicaid or no insurance, average age 47.54 (18.23 SD), and 49.9% lived within 20 minutes of the study site. Those who preferred the ED for preventive care had Medicaid or no insurance (OR 2.3; 95%CI: 1.2-4.2) and reported the ED to be their Medical Home (MH) (OR 6.0; 95% CI: 3.2-11.4). Except for those living 31-45 minutes away, patients living <60 minutes away preferred the ED. Patients with Sickle Cell crises (OR 7.7; 95% CI: 1.2-47.8) and UTI (OR

4.5; 95% CI: 1.5-13.5) were more likely and patients with CKD (OR 0.25; 95% CI: 0.07-0.85) were less likely to come to the ED for preventive care. Patients whose families always came to the ED for healthcare showed a strong trend toward preferring the ED (OR 2.5; 95% CI: 1.0-6.0). Age, race and sex were not associated with choosing the ED for preventive care (Table 1). Conclusions: Many patients, regardless of age, race and sex, prefer the ED for preventive care. Future research directed at delivery of preventive care from the ED is justified.

163 Determining specific chemical modification dependence on nanocarrier characteristics of a 599 peptide carrier-siRNA complex

Chance Wagner, Travis Hedrick, Charles Holjencin, Yanping Liu, Jeremy Gilbert, Andrew Jakymiw, Dental Medicine, Department of Oral Health Science, MUSC.

Abstract Withheld from Publication

164 The effects of sexual dimorphisms and temporomandibular disorder on mandibular morphometrics

Linda Thomas, Dr. Matthew Coombs, Shuchun Sun, James Grant, Hai Yao, Dental Medicine, Clemson-MUSC Bioengineering Program, MUSC.

Temporomandibular disorder, or TMD, is a musculoskeletal condition that affects the temporomandibular joint (TMJ) and the muscles of mastication; females are more likely to seek treatment for this condition than males. The purpose of this study was to investigate the effects of sex and TMD on mandibular morphometrics in order to better understand the factors related to the development of TMD. Different mandibular morphometrics can affect the biomechanics of the jaw and therefore the mechanobiology of the TMJ, which could result in the development and progression of TMD. It was hypothesized that females and patients with TMD would have smaller mandibular and condylar measurements than males and patients without TMD. The measurements were taken on three-dimensional models developed from CBCT scans of 7 females with unilateral TMD, 3 females without TMD, and 8 males without TMD. The results from t-tests and one-way ANOVA tests showed no statistically significant differences in any of the measurements between males and females or unilateral TMD patients and healthy controls with the exception of the intercondylar width and condylar major axis length in males vs female and the intercondylar width in unilateral TMD vs healthy controls. As a result, the original hypothesis was generally not supported, likely due to the small sample size. This work was supported by MUSC SHP Program

165 Investigating the role of LINE-1 retrotransposons in genomic instability of autophagy deficient ovarian cancer

Christian Jones, Joe Delaney, Graduate Studies, Biochemistry, MUSC.

Ovarian cancer is the fifth leading cause of cancer death among women. The most common type, serous ovarian cancer, has 94% of cases diagnosed at stage III or IV (ACS). Unlike most cancers, serous ovarian cancer typically only has a mutation in one tumor suppressor: p53, occurring in 95% of samples. However, ovarian cancer is abundant in copy number alterations1. Although individual autophagy genes may only be affected one third of the time, autophagy, as a pathway, is downregulated in most serous ovarian cancers. Additionally, increased LINE-1 activity is seen in ovarian cancer when compared to normal ovarian epithelial cells2. LINE-1 mRNA has been shown to be regulated via autophagy in the cytoplasm3. A decrease in autophagy promotes chromosomal instability4, but the link between autophagy, LINE-1, and genomic instability in ovarian cancer has not been established. We used SKOV3 and IGROV1 cell lines with knockdowns in autophagy genes, LC3B and BECN1, to model serous ovarian cancer. LINE-1 activity was decreased genetically, through shRNA, and pharmacologically. We hypothesize that autophagy downregulation causes increased activity of LINE-1 elements, as seen in serous ovarian cancer. This LINE-1 retrotransposition causes aneuploidy due to an increase in double strand DNA breaks, via Orf2p endonuclease activity during the LINE-1 life cycle. We utilized a LINE-1 GFP reporter and anaphase bridge formation to determine a relationship between autophagy, LINE-1 retrotransposon activity, and genomic instability. To find the role of LINE-1 activity in terms of genomic instability, DNA repair mechanisms were examined through DNA repair reporter plasmids and probing for DNA repair markers in immunofluorescence and western blot. These results confirmed the autophagic regulation of LINE-1 while determining the influence of LINE-1 activity on genomic instability. The role of DNA repair pathways mending LINE-1 induced DNA breaks could be one influence on the development of copy number alterations.

166 Characterizing hnRNP E1's function in genome stability and DNA transactions at cancer gene promoters

Joseph Karam, Bidyut Mohanty, Breege Howley, Simon Grelet, Philip Howe, Graduate Studies, Biochemistry and Molecular Biology, MUSC.

Abstract Withheld from Publication

167 IL-6 fuels durable memory for Th17-mediated responses to tumors

Hannah Knochelmann, Connor Dwyer, Aubrey Smith, Jacob Bowers, Megan Wyatt, Michelle Nelson, Guillermo Rangel Rivera, Joshua Horton, Carsten Krieg, Gregory Lesinski, Zihai Li, Mark Rubinstein, Kent Armeson, Chrystal Paulos, Graduate Studies (MSTP, PhD years), Microbiology & Immunology, Dermatology & Dermatologic Surgery, MUSC.

Abstract Withheld from Publication

168 Protein-based targeted complement inhibition ameliorates experimental autoimmune encephalomyelitis, a mouse model of multiple sclerosis

Davis Borucki, M Mahdi Sleiman, Bärbel Rohrer, Stephen Tomlinson, Graduate Studies (MSTP, PhD years), Microbiology & Immunology, MUSC.

Abstract Withheld from Publication

169 Specific Commensal Gut Bacterium Critically Regulates Alveolar Bone Homeostasis

Matthew Carson, Jessica Hathaway-Schrader, Joy Kirkpatrick, Amy Warner, Brooks Swanson, Sakamuri Reddy, Caroline Westwater, Chad Novince, Graduate Studies, Oral Health Sciences, MUSC.

Abstract Withheld from Publication

170 Regular physical activity can prevent the oncogenic effects of lifestyle-associated advanced glycation end products

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

Advanced glycation end-products (AGEs), are reactive metabolites produced endogenously as result of glucose metabolism. AGEs accumulate in tissues as we grow older promoting multiple chronic diseases. AGE pathogenic effects are mediated through modification of protein function, genetic fidelity, stress responses and cellular signaling pathways. Critically, disparity factors such as; sedentary lifestyle, obesity and an unhealthy diet have been shown to contribute to the accumulation of AGEs. We've examined circulating and tumor AGE levels in clinical specimens of prostate cancer (PCa) and identified a race-specific, tumor-dependent pattern of accumulation. AGE levels were highest in aggressive tumors, especially those with African ancestry. AGE levels correlated with an up-regulation in the receptor for advanced glycation end-products (RAGE) and activated NfkB. In a syngeneic sub-cutaneous PCa mouse model, chronic consumption of AGEs resulted in a 3-fold increase in tumor growth. Increases in tumor growth were accompanied by a mis-localization of AR, elevation in MYC, RAGE, AGE and cell proliferation. Given the links between lifestyle and AGEs we examined the effects of regular physical activity (PA) on AGE induced tumor growth in our syngeneic sub-cutaneous dietary-AGE PCa model. Mice exposed to PA for 1 hour, 5 days/week showed a significant decrease in AGE induced tumor growth. We also examined the effects of dietary-AGEs on prostate intraepithelial neoplasia (PIN) progression using the FVB-Tg(C3-1-TAg)cJeg/JegJ transgenic spontaneous PCa mouse model. This model progresses to low grade PIN at 24 weeks. However, chronic consumption of AGEs resulted in progression towards moderate to high grade PIN. When exposed to regular PA, we observed delayed progression of PIN in both dietary groups, but most significantly in the high AGE fed mice. These studies support the concept that AGEs represent a biological consequence of socioeconomic and environmental factors that promote cancer disparities, which may be at least in part reversed via PA. This work was supported by U54CA210962, HCC Incentive Funds, HCC Pre-Doctoral Fellowship

171 Feasibility of and Adherence to a Home-Based Duck Duck Punch Protocol

Emerson Hart, Austen Hayes, Larry Hodges, Kevin Jett, Christian Finetto, Scott Hutchison, Michelle Woodbury, Health Professions, CHP Occupational Therapy, CHP Health Science and Research, MUSC.

Stroke is a leading cause of chronic disability which often leaves survivors with a loss of functional movements. Research has shown that high repetitions of specific movements are required for motor recovery, and frequently, therapists provide patients with home-based exercises to fulfill this high repetition demand. Studies have shown that patients do not always adhere with these programs for various reasons. Duck Duck Punch (DDP) is a Kinect-based post-stroke rehabilitation game designed to promote high repetitions of specific movements through a game scenario. The purpose of this study is to evaluate the feasibility and adherence of a home-based DDP protocol. We hypothesized that it would be feasible and that participants would adhere to this protocol. 66 community-dwelling participants were randomized to play DDP or a commercially available computer game (Microsoft Kinect Target Shoot, KTS) in their homes 60 minutes a day, 3 times per week, for 6 weeks. Adherence data were collected on numbers of days played, minutes played, and the average minutes per session. Adherence data were compared between games (DDP or KTS), as well as to the instructed dose. A focus group was also held to assess feasibility of set-up and home use with participants or caregivers. DDP is feasible for patients to use in the home setting. Patients demonstrated statistically significant higher adherence to DDP home program compared to KTS, shown by more days played (15.55 vs. 9.83), more minutes played per session (37.33 vs. 20.26), and more total minutes played (906.79 vs. 420.33). The data suggest that DDP is feasible as a self-directed in-home therapy program, and that patients were able to adhere to dose instructions. This may have implications for the use of DDP in a variety of settings (e.g. home, hospital) as an option for self-directed therapy outside of traditional therapy hours. This work was supported by NIH/NINDS Direct to Phase II Small Business Initiated Research (SBIR) Award, #R44NS097061, NCT03053492, mPIs: ML. Woodbury and A. Hayes. NIH/NIGMS Institutional Development Award (IDeA), P20GM109040, PI: S. Kautz.

172 EEG as a Predictor of Post-Stroke Recovery: A Systematic Review and Meta-Analysis

Amanda Vatinno, Viswanathan Ramakrishnan, PhD, Annie Simpson, PhD, Heather Bonilha, PhD, CCC-SLP, Na Jin Seo, Health Professions, Occupational Therapy, MUSC.

Post-stroke recovery outcomes are heterogeneous despite similar initial clinical presentations. Uncertain prognosis makes it difficult for therapists to develop personalized treatment plans for patients. Improved prognosis for recovery may guide clinical management for stroke survivors by helping therapists set realistic therapy goals and determine the maximally efficient course of treatment. Currently, prognosis is largely based on initial behavioral impairment level which has high variability in recovery outcomes. Prognostic accuracy may be enhanced by measures of initial neural function, such as electroencephalography (EEG). The objective of this study is to perform a systematic review and meta-analysis on the prognostic utility of EEG in stroke recovery. A literature search was conducted using three electronic databases, including PubMed, Scopus, and CINAHL. Key search terms were "EEG," "stroke," and "rehabilitation". Only peer-reviewed journal articles published in English that examined the relationship between EEG and a standardized clinical outcome measure(s) at a later time in stroke patients were included. Two independent raters completed data extraction and assessed methodological quality of the studies with the Downs and Black form. A linear meta-regression was performed across a subset of individual studies that utilized a common clinical outcome measure to determine the association between EEG and clinical outcome while adjusting for sample size and study quality. Fifty-six papers met the inclusion criteria and were included in the systematic review. The prognostic value of EEG was evidenced at both the acute and chronic stages of stroke. The addition of EEG enhanced prognostic accuracy more than initial clinical assessment scores and/or lesion volume alone. Nine papers were included in the meta-analysis, resulting in an overall correlation estimate of 0.6. EEG has demonstrated prognostic utility in stroke recovery and is correlated with clinical outcomes. Future research may investigate an optimal protocol that maximizes prognostic accuracy and is feasible for clinical adoption.

173 READ-TV - Open Source, Interactive, Visualization Software of Surgical Work Flow Disruptions. A tool to Improve Patient Safety in OR Settings

John Del Gaizo, Kenneth Catchpole, Alexander Alekseyenko, Graduate Studies, Biomedical Informatics Center, MUSC.

Surgical technology continues to improve patient outcomes, but also introduces novel challenges and risks. These include increased costs, increased load on operating room (OR) team members, communication complexities, and intraoperative equipment troubleshooting. The OR team experiences work flow disruptions (FD) when they address and respond to these challenges. FDs are deviations from the expected operation progression, and have the potential to negatively impact patient safety. Specifically, the following adverse outcomes are correlated with high FD rates: increased patient mortality, procedure duration, OR member stress, perceived workload, and surgical errors. Evidence suggests that specific FD patterns may precede serious disruptions. One hypothesis is a snowballing effect where a series of small FDs leads to a higher rate of subsequent disruptions. Similarly, "bottleneck" FDs may have a disproportionately large impact on subsequent work flow. However, these analyses are mathematically advanced, while the research in minimizing surgical risk entails interdisciplinary collaboration between medical personnel, human factors experts, systems engineers, and statisticians/informaticians. Visualization software of the FD data with intuitive time markers of important change points, bottle neck candidates, and snowball patterns can facilitate interpretation of the analyses and act as a communication bridge between subject matter experts and quantitive researchers. Therefore, we have developed a prototype of an open-source visualization software application, Research and Exploratory Analysis Driven Time-data Visualization (READ-TV). READ-TV is interactive software to visualize time-stamped data, such as flow disruptions. It allows for visualization of individual surgeries, as well as aggregate comparisons between groups of surgeries categorized by user-specified criterion. Preliminary prototype demonstrations have received positive reviews and feedback from several human factor practitioners in the field of FD modeling. At the research day, we will present READ-TV and demonstrate current features. This work was supported by TL1 TR001451, UL1 TR001450

174 Bayesian Latent Pattern Models

Jonathan Beall, Dr. Elizabeth Hill, Dr. Hong Li, Dr. Bonnie Martin-Harris, Elizabeth Hill, Graduate Studies (MSTP, PhD years), Department of Public Health Sciences, MUSC.

Latent class analysis is a statistical modeling strategy that facilitates the discovery of an unmeasured classification system, such as latent disease severity classes, given a set of observed (manifest) variables. These latent classes are characterized by their probabilities of observing a response for each of the manifest variables, where these probabilities are called item response probabilities. Latent class analyses often involve determining the number of latent classes best supported by the data through the comparison of goodness of fit measures of models constructed with differing numbers of assumed latent classes. We propose an adaptation of the traditional latent class model, which we call the Bayesian Latent Pattern (BLP) Model. For a set of manifest variables, the BLP Model allows for the discovery of unobserved patterns in item response probabilities and allows for the estimation of the optimal number of latent classes. We define a latent pattern class as a set of individuals who are identified by their set of item response probabilities and we propose the use of a Dirichlet Process Mixture Model (DPMM) to learn these latent pattern classes. The DPMM is a modeling strategy which allows for both the estimation of the number of classes and their respective latent patterns, forgoing the tedious process of determining the optimal number of latent classes utilized in traditional latent class analyses. We demonstrate through simulation studies that the model is a reliable approach of re-capturing an imposed underlying latent pattern structure, where model performance improves with increasing sample size and number of manifest variables, which avoids complexities associated with standard analyses.

175 Comparison of minimal sufficient balance and minimization for subject randomization in clinical trials with a binary endpoint

Steven Lauzon, Viswanathan Ramakrishnan, Paul J. Nietert, Jody D. Ciolino, Michael Hill, Wenle Zhao, Viswanathan Ramakrishnan, Graduate Studies, Public Health Sciences, MUSC.

When the number of baseline covariates that need to be balanced is large, minimization is the most commonly used method for treatment assignment in randomized controlled trials. The lack of allocation randomness associated with the minimization method has been the source of controversy, and the zero tolerance for imbalance inherent to the minimization algorithm has been challenged. The minimal sufficient balance method is a better alternative to the minimization method. It prevents serious imbalance from large number of covariates while maintaining a high level of allocation randomness. In this study, we compare the two treatment allocation methods with regards to the effectiveness of balancing covariates across treatment groups in equal allocation clinical trials with a binary endpoint. In addition, we consider allocation randomness and we verify preservation of type I error rate in analyses for both randomization algorithms. This work was supported by National Institutes of Health (National Center for Advancing Translational Sciences grant number UL1TR001450)

176 How to account for transplant when examining survival in acute liver failure research

Sherry Livingston, Bethany Wolf, Valerie Durkalski, Graduate Studies, Public Health Sciences, MUSC.

Background: Acute liver failure (ALF) is a rare but serious disease, and clinical decision-making in the setting of adult ALF is challenging for several reasons, including the possibility of liver transplantation. Because new therapies are not on the near horizon, researchers conduct prognostic modeling to determine the predicted probability of good outcome for patients being treated in the acute setting. Prognostic indices have been developed and validated in this population including the King's Criteria, the MELD score, and most recently the ALF Prognostic Index, which predicts the probability of spontaneous survival. Although these are good bedside resources for the treating physician, the question arises on the best method for inclusion of transplanted patients in the model-building process when the outcome of interest is survival without transplant. The ALF Prognostic index models death or transplant as a composite outcome, making the assumption that transplanted patients would have otherwise died. We aim to compare this approach to alternative analytic methods for this specific setting to provide guidance to the clinical research community. Methods: The registry data of close to 3000 ALF patients in the US and Canada maintained by the Acute Liver Failure Study Group (ALFSG) is used to compare analysis approaches. Different models are constructed using known predictor variables, and these models are then compared based on accuracy of predictions and on the

concordance statistic (C-statistic) which measures goodness of fit for binary outcomes. Results: The analyses demonstrate that logistic regression, inverse probability weighting, and multiple imputation can all be used to model transplant-free survival in ALF patients, and these methods exhibit comparable model-fit and prediction accuracy. Conclusions: There are alternative frameworks for modeling survival with a native liver in the ALF setting. Competing risk survival models, however, are not appropriate for this analysis and should not be used. This work was supported by Supported in part by a U-01 58369 from NIDDK to the Acute Liver Failure Study Group.

177 Common gamma chain cytokines modulate metabolism and tumor immunity of T cells in ACT

Guillermo Rangel Rivera, Connor J. Dwyer, Hannah M. Knochelmann, Aubrey Smith, Megan M. Wyatt, Chrystal Paulos, Medicine (MSTP, MD years), Microbiology & Immunology, MUSC.

Introduction/Rationale: Adoptive T cell Therapy (ACT) is effective in ~40% of patients with melanoma unresponsive to other therapies. ACT protocols expand T cells from tumor biopsies with interleukin-2 (IL-2). The expanded T cells are highly differentiated, show impaired bioenergetics and fail to prevent relapse. IL-2 belongs to the common gamma chain cytokine family. In particular, IL-7, IL-15 and IL-21 are important for T cell memory, however systematic analysis of all other members is lacking. We hypothesized that IL-21 would improve T cell bioenergetics and tumor control as it prevents T cell differentiation and improves bioenergetics. Methods: Melanoma specific T cells from the transgenic pmel-1 mouse were conditioned with 1uM hgp100 peptide and 10ug/mL of each common gamma chain cytokine or no cytokine. Cells were expanded for 7 days and T cell phenotype, mitochondrial mass, and glucose uptake were assessed. Mitochondrial function was assessed by seahorse analyzer. We tested tumor immunity in vivo with ACT. For in vivo experiments 500,000 B16F10 melanoma cells were implanted into B6 mice and grown to 20mm2. Tumor bearing mice were irradiated with 5Gy prior to T cell infusion. D7 T cells were re-stimulated and infused into mice. IL-2 complex was added on days 0, 3 and 6. Tumor area was measured with calipers. D7 post-ACT mice were bled (N=5). In vivo and in vitro, ANOVA with Bonferroni correction were performed for tumor area, and Kaplan-Meier survival analysis was performed (N=8-10). Results: IL-7 and IL-15 promoted the formation of T cell memory compared to all other cytokines. IL-7 and IL-15 also showed an enhanced mitochondrial spare respiratory capacity. IL-15 showed enhanced T cell survival compared to IL-7, and other conditions which showed poor tumor control and survival. Conclusions: IL-7 or IL-15 improves T cell bioenergetic capacity, but IL-15 enhances T cell bioenergetics and survival. This work was supported by NIH Training grant T32 5T32GM008716-19 and MUSC CGS Provost to GR. NIH T32 AI132164-01 to CD. HCCGF to AS. NIH R50 CA233186 to MW. NIH R01 CA175061, R01 CA208514, KL2 SCCTR grant UL1 TR000062, ACS-IRG grant 016623-004 and MUSC Start-up funds to CP.

178 CD8+ T cells break tolerance to tumors in a B cell-dependent manner

Aubrey Smith, Hannah Knochelmann, Connor Dwyer, Megan Wyatt, Guillermo Rangel Rivera, Dimitrios Arhontoulis, Amalia Rivera-Reyes, Mark Rubinstein, Eric Bartee, Jessica Thaxton, Bei Liu, Chrystal Paulos, Graduate Studies, Microbiology and Immunology, MUSC.

Toll-like receptor (TLR) agonists augment T cell-mediated tumor immunity. However, TLR agonist therapy can be toxic when administered to patients, particularly when combined with other therapies. Thus, we hypothesized that using TLR agonists ex vivo, during the expansion protocol, would generate a T cell product with improved anti-tumor properties and circumvent potential toxicities associated with combination therapy. To test this hypothesis, we used the Pmel-1 CD8+ T cells' bearing a TCR that recognizes the gp100 epitope on melanoma. Pmel splenocytes were expanded in the presence of the TLR9 agonist CpG (ODN-1668) for one week and then infused into tumor-bearing mice. T cells expanded with CpG gained a unique phenotype (IL-2Ralpha high, ICOS high, CD39 low) and had superior anti-melanoma ability over traditionally expanded T cells. These outcomes were B cell dependent as the signature T cell phenotype and anti-tumor activity was lost when B cells were depleted from the cultures. T and B cell interactions were key for tumor immunity as efficacy was lost when this relationship was disrupted. B cells upregulated several surface proteins post-CpG treatment which might be responsible for augmenting this communication and thus T cell function. Thus, we discovered that the TLR9 agonist CpG can be repurposed to expand T cell products with enhanced anti-tumor capacity. B cells, rather than other professional antigen-presenting cells, were responsible for generating T cells with improved persistence and immunity in the context of CpG. Results from this work will bolster the design of next generation cell therapies. This work was supported by HCC Graduate Fellowship, RO1 CA208514

179 Elucidating components of novel MyoD co-repressor complex on stemness genes

Alexander Oles, Denis Guttridge, Graduate Studies (MSTP, PhD years), Pediatrics, MUSC.

Abstract Withheld from Publication

180 Antibody Panel Based N-glycan Imaging of Patient Serum for Discovery of Hepatocellular Carcinoma Biomarkers

Alyson Black, Peggi Angel, Richard Drake, Anand Mehta, Graduate Studies, Cell and Molecular Pharmacology, MUSC.

The majority of biomarkers used in the detection of cancer are glycoproteins, and numerous studies indicate that changes in N-glycans found on serum glycoproteins occur with the development of hepatocellular carcinoma (HCC). However, accurate glycoprotein biomarker assays are lacking, and there is a need for higher throughput biomarker discovery. We have developed a new platform for multiplexed N-glycoprotein biomarker analysis from patient serum that can be used in the context of disease detection. This platform combines matrix-assisted laser desorption/ionization mass spectrometry imaging (MALDI MSI) workflows with slide-based antibody panels. Antibody Panel Based N-glycan imaging allows for specific capture of serum N-glycoproteins by antibodies and N-glycan analysis in a multiplexed manner without additional sample clean-up. Serum glycoproteins were captured in a concentration-dependent manner while maintaining specificity of capture. As a proof of concept, cirrhotic patient serum samples were compared to healthy serum, and a previously characterized increase in an IgG N-glycan was observed. A small cohort of HCC patient samples were also analyzed and showed decreased sialylation of A1AT N-glycans. This novel approach to N-glycoprotein analysis can be further expanded to include any glycoprotein for which a validated antibody exists. This platform can be increasingly multiplexed for the analysis of potentially 100s of individual glycoproteins from patient samples in just one imaging run. Additionally, this platform can be adapted for any biofluid or biological sample that can be analyzed by antibody arrays. This technique has exciting potential to be applied in the clinic as both a biomarker discovery tool as well as a screening tool for liver

diseases in readily available clinical samples with minimal consumption. This work was supported by TL1 TR001451, UL1 TR001450, R21 CA225474, U01CA242096, U01CA226052

181 Localized regulation of RNAi-lncRNA interactions by epithelial adherens junctions

Mary Bridges, Joyce Nair-Menon, Antonis Kourtidis, Antonis Kourtidis, Graduate Studies, Reg Medicine and Cell Biology, MUSC.

The adherens junctions (AJs) are essential architectural elements of epithelial tissues. Compromised junctional integrity is a common precursor to colon cancer. Recently, we identified a novel mechanism whereby the AJs of non-transformed colon cells recruit the microprocessor and RISC, core elements of the RNAi machinery, as well as miRNAs, to suppress oncogenic mRNAs. Knockdown of the AJ component PLEKHA7, disrupts this RNAi-mediated signaling program, leading to pro-tumorigenic cell transformation. Interestingly, PLEKHA7 RNA-CLIP and subsequent RNA-Seq analysis identified association with numerous long non-coding RNAs (lncRNAs). While a number of lncRNAs have been associated with tumorigenesis, the underlying mechanisms of their regulation during tumor progression are still unclear. As lncRNAs can interact with the RNAi machinery, we hypothesize that the AJs regulate lncRNAs via this localized RNAi mechanism. Examination of PLEKHA7-depleted cells by RNA-seq revealed differential expression of 49 junction-associated lncRNAs. The top upregulated lncRNA is MIR17HG, a recognized oncogenic lncRNA. Junctional localization of MIR17HG was confirmed by RNA-FISH. Adherens junctions destabilization by E-cadherin knockdown also led to the upregulation of MIR17HG, demonstrating the role of junctional integrity in MIR17HG suppression. Data from AGO2 knockdown, antago-miR, and miRNA mimetic experiments show that PLEKHA7 suppresses the levels of the MIR17HG transcript through the junction-associated RISC and miRNAs. We observe extensive mis-localization or loss of PLEKHA7, co-existent with mis-localization of junctional RNAi machinery, in colon cancer tissues and cell lines. Ectopic expression of PLEKHA7 in aggressive colon cancer cells that lack endogenous PLEKHA7 expression, suppressed MIR17HG levels, as well as anchorage independent growth. We are currently examining the role of MIR17HG as a functional intermediate of PLEKHA7's loss on colon cell transformation. In summary, our data point towards a novel mechanism of lncRNA regulation that tethers epithelial architecture with cell behavior. This work was supported by SCTR Institute: TL1 TR001451, UL1 TR001450; Dept of Reg Med and Cell Biology; ACS: IRG-16-185-17; Conquer Cancer Now Award, Concern Foundation

182 Human Cardiac Organoids for Cardio-Oncology

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

Advances in oncolytic therapeutics have led to substantial increases in cancer survival. However, numerous FDA approved oncolytics show severe cardiotoxicity. Current in vivo and in vitro cardiotoxic screening platforms inadequately recapitulate human heart pathophysiology following oncolytic treatment. This study aims to demonstrate the potential of a high throughput cardiotoxic screening platform using 3D cardiac organoids composed of human induce pluripotent stem cell-derived cardiomyocytes. Doxorubicin, a widely used chemotherapeutic known for its acute and chronic cardiotoxicity, was used to examine oncolytic-induced pathophysiology in cardiac organoids. Doxorubicin-induced toxicity was assessed by observing morphological, functional and metabolic changes in cardiac organoids. Doxorubicin impaired mitochondrial function, reduced contractility and led to higher disorganization of alpha-sarcomeric actinin in cardiac organoids, consistent with clinical observations. This study showcases the potential for human cardiac organoid for assessing oncolytic cardiotoxicity. This work was supported by T32 HL007260, R01 HL133308, NIH/NIGMS P20 GM103542

183 DCHS1 based cell adhesions direct the septin cytoskeleton during critical stages of mitral valve disease inception

Kelsey Moore, Reece Moore, Diana Fulmer, Lilong Guo, Cortney Gensemer, Rebecca Stairley, Mary Kate Rumph, Janiece Glover, Tyler Beck, Christina Wang, Russell Norris, Graduate Studies, Regenerative Medicine and Cell Biology, MUSC.

Mitral valve prolapse (MVP) affects 1 in 40 individuals worldwide and is the most common reason for mitral valve surgery in the Western world. MVP is defined by enlarged, myxomatous and biomechanically incompetent mitral valve leaflets that fail to properly close during ventricular systole. Currently, there are no effective nonsurgical treatments for MVP and therapeutic efforts have been hindered by an incomplete understanding of its fundamental causes.However, we now have compelling genetic and functional evidence that significantly advances our understanding of MVP disease pathogenesis. Our group was the first to identify mutations in the atypical cadherin gene, DCHS1, in multiple families with non-syndromic MVP and have traced the origin of disease back to defects in fetal valve morphogenesis. In an effort to define the functional and molecular consequences of DCHS1-based cell adhesions, we recently performed a series of two-hybrid screens and co-immunoprecipitation experiments that identified novel interactions between DCHS1, Lix-1 like (LIX1L), and septin-9 (SEPT9). In vivo epistasis experiments supported a genetic interaction between Dchs1 and Lix1L as compound heterozygosity had a synergistic effect on murine valve leaflet enlargement. Since SEPT9 is able to crosslink and bundle the actin cytoskeleton, we measured septin-actin filament organization and F-actin content and observed significant reduction of both in cardiac fibroblasts (CFs) lacking DCHS1 and/or LIX1L. As a result, intracellular tension was decreased as indicated by increased cell and nuclei volume. Through application of a novel 3D culture system that recapitulates the mechanical tension of the native mitral valve, we found that DCHS1-LIX1L-SEPT9 interactions were necessary for actin filament, cell and extracellular matrix (ECM) alignment. Together, these data support a mechanism in which DCHS1 based cell adhesions regulate actin stability through LIX1L-SEPT9 interactions during critical stages of valve development and MVP disease inception. This work was supported by NIH T32 HL007260

184 Identification of penicillin-binding protein 2 (PBP2) inhibitors as agents against penicillin- and cephalosporin-resistant strains of Neisseria gonorrhoeae

Jonathan Turner, Samantha Zygmont, Patrick M Woster, Christopher Davies, Graduate Studies (MSTP, PhD years), Biochemistry & Molecular Biology, MUSC.

Abstract Withheld from Publication

185 Dissociating drug reward from contextual cues: The cell type-specific role of nucleus accumbens NPAS4

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

Substance use disorder is a chronic, relapsing behavioral disorder that is characterized by compulsive drug seeking and use despite negative consequences to the individual. During the course of drug use, persistent neuroadaptations develop in the nucleus accumbens (NAc), a brain region predominately composed of dopamine D1 receptor- and D2 receptor-expressing medium spiny neurons (MSNs) and whose activity is associated with reward and motivation. The progression from casual drug use to abuse is mediated in part by the strong association between the rewarding 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 in abstinent addicts. However, the molecular and cellular mechanisms underlying these drug-context memories are not well understood. One possible regulator of neuroadaptations in the NAc 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. Here, we show that following exposure to a novel drug-paired environment, a small population of NAc neurons induce NPAS4 and, of those, ~50% are D1R- or D2R-expressing MSNs. Cell type-specific reduction of NPAS4 in the adult NAc, using a cre-dependent shRNA virus in D1- or D2-cre mice, revealed a critical role for NPAS4 in D2-MSNs for cocaine reward-context learning and memory without altering sensitivity to cocaine-induced locomotor responses and sensitization. In addition, ongoing studies may reveal important roles for NPAS4 in MSN synaptic transmission. Together, our current findings suggest an important cell type-specific role for NPAS4 in the NAc for regulating the development of drug reward-context associations. This work was supported by F31 DA048557 (BWH), T32 DA07288 (JFM), R01 DA027664 (CWC), R01 DA032708 (CWC)

186 Neuroimmine Dysfunction in a Mouse Model of MEF2C Haploinsufficiency Syndrome

Catherine Bridges, Adam J. Harrington, Stefano Berto, Ahlem Assali, Yongjoo Jennifer Cho, Christopher Cowan, Graduate Studies (MSTP, PhD years), Psychiatry and Neuroscience, MUSC.

Abstract Withheld from Publication

187 Inhibition of insulin signaling in the brain adversely impacts cognition in mice.

Crystal Smith, Catrina Robinson, Graduate Studies (MSTP, PhD years), Neurology, MUSC.

Brian insulin promotes neuroplasticity, synaptogenesis, has anti-inflammatory, anti-thrombotic, vasodilatory, anti-apoptotic properties, and is involved in cognition. Given these properties of brain insulin, it may play a therapeutic role in recovering stroke and improving cognition. Our previous studies demonstrated that increasing brain insulin, using intranasal insulin, improved functional stroke recovery in high-fat diet mice, a model of hyperinsulinemia. Hyperinsulinemia, characterized as elevated levels of insulin circulating in the blood and brain insulin deficiency and impaired insulin signaling. In order to develop other therapeutic strategies to improve outcomes after stroke and enhance cognitive impairment, there is a need to understand the impact of reducing brain insulin signaling in the brain. We hypothesize that inhibiting brain insulin signaling through the use of intranasal insulin affibody will lead to impaired cognition. The insulin affibody binds to the insulin resulting in reduced insulin signaling downstream. This reduction is evident by a decrease in the ratio of phosphorylated protein Kinase B (pAkt) to protein kinase B (Akt), which is activated by insulin. To explore our current hypothesis, 16 week old C57BL6J mice on a standard diet were administered the intranasal affibody for 5 days. Cognition was assessed through the novel object (NOR) and novel tactile (NTR) recognition behavioral tests. The animals participated in NOR and NTR, 8 weeks before receiving the intranasal treatment to establish baseline and 3 days after receiving either 1 L, 5 L, or 10 L of the intranasal insulin affibody treatment. Preliminary results indicate animals receiving increased amounts of the insulin affibody perform worse on the NOR and NTR behavioral test, as well as having decreased pAkt/Akt expression observed through western immunoblotting. Our preliminary studies indicate the importance of insulin in cognition. This work was supported by This work was supported by the National Institute of Health (NINDS 1R01NS099595, and IMSD NIGMS #R25GM072643)

188 taVNS for Oromotor Infant Feeding IV: Microstructural diffusion MRI changes before and after Treatment in Neonates with Feeding Failure

Hunter Moss, Jens H. Jensen, Bashar W. Badran, Daniel Cook, Morgan Dancy, William H. DeVries, Georgia Mappin, Sean Thompson, Philipp Summers, Marom Bikson, Mark S. George, Dorothea Jenkins, Graduate Studies, Neonatalogy, MUSC.

Premature or hypoxic ischemic (HIE) birth is associated with impairment of motor skills, failure to achieve full oral feeding, and requirement for a gastrostomy tube (G-tube). Transcutaneous auricular vagus nerve stimulation (taVNS), paired with oromotor feeding, is being tested as a novel therapy that may lead to remodeling of motor cortex and improved feeding skills. We investigated whether diffusional kurtosis imaging (DKI) of white matter (WM) tract integrity would show a response to treatment. We performed DKI (3T Siemens Skyra) on unsedated preterm or HIE infants (n=12), enrolled in the taVNS-paired feeding trial, at a mean 44±5 weeks gestational age (GA) before and after the 2-3-week taVNS-paired feeding treatment. Diffusion and kurtosis tensors were calculated using Diffusional Kurtosis Estimator (DKE) resulting in mean diffusivity (MD), fractional anisotropy (FA), and mean kurtosis (MK) parametric maps. Bilateral regions of interest delineated from a neonatal WM brain atlas were used for voxel-wise averaging. Paired t-test compared pre- to post-treatment FA, MD and MK within individuals, normalized by week of development. Parameters for infants who attained full oral feeds (responders) were compared to those who required G-tube placement (non-responders) in a general linear model (GLM) with GA at birth and scan as covariates. DKI identified significant differences in maturational changes before and after taVNS treatment in specific WM tracts between responders and non-responders: Responders showed greater changes in FA per week in right external capsule and corpus callosum ($p< 0.05$), and lower axial kurtosis per week in right inferior frontal-occipital fasciculus (IFOF) and left posterior thalamic radiations (PTR, $p< 0.025$), consistent with more robust axonal integrity. FA changes in both groups were greater than that expected with normal development. 2-3 weeks of taVNS-paired feeding likely stimulates microstructural maturation in sensorimotor integration WM tracts that may be important in response to taVNS treatment. This study was funded by the National Center of Neuromodulation for Rehabilitation (NC NM4R), supported by the Eunice Kennedy Shriver National Institute of Child Health & Human Development, and the Pilot project program of the Center of Biomedical Research Excellence (COBRE) in Stroke Recovery supported by the National Institutes of Health under P2CHD086844 and P20GM109040, which were awarded to the Medical University of South Carolina. Further funding was provided by NINDS F31NS108623 to Hunter Moss.

189 Hyperinsulinemia induced brain microvessel insulin resistance correlates with reduced insulin transport

Luke Watson, Crystal Smith, Alexus Williams, Catrina Sims-Robinson, Graduate Studies, Neurology, MUSC.

During Alzheimer's disease and stroke, two of the most common age related neurodegenerative disorders, patients present with systemic hyperinsulinemia. Systemic hyperinsulinemia is associated with reduced CNS insulin levels, however the mechanisms underlying this are not well understood. Insulin is fundamental in the brain for neuroplasticity, and has anti-apoptotic, -inflammatory, -thrombotic, and -vasodilatory properties. Insulin must be transported across the blood brain barrier (BBB). Some have suggested this occurs via insulin receptor-mediated transcytosis. Thus, the purpose of the following studies are to determine the impact of hyperinsulinemia on insulin transport across the BBB. In the current study, at four weeks of age, B6 mice were placed on either a standard diet (STD) or a high-fat diet (HFD) for 6 and 24 weeks. Hippocampal microvessels were extracted and the levels of serine-phosphorylated insulin receptor substrate, a docking protein that can inhibit insulin receptor function, were measured. Furthermore, these microvessels were stimulated with insulin to determine the ability to activate downstream insulin signaling. We observed evidence of insulin resistance in HFD microvessels and impaired insulin signaling. To explore whether these alterations impacts insulin transport, we utilized primary brain endothelial cells, a key component of the BBB, and exposed the cells to hyperinsulinemic conditions to evaluate insulin resistance, signaling, and transport. Our data demonstrates that insulin resistance and impaired insulin signaling correlates with reduced transport. Future studies will seek to validate these findings in more complex BBB systems. This work was supported by NIHNHLBI HL007260, NINDS NS099595, NINDS 1R01NS099595-01A1, NINDS 5K01NS079461, AARGD-16-440893

190 Host ectonucleotidase-CD73 and the opportunistic pathogen Porphyromonas gingivalis cross-modulation underlies a new homeostatic mechanism for chronic bacterial infection in human epithelial cells

Jaden Lee, Nityananda Chowdhury, JoAnn Roberts, Ozlem Yilmaz, Dental Medicine (DMD, PhD), Oral Health Sciences, MUSC.

Abstract Withheld from Publication

191 Alpha-conotoxin activity on nicotinic acetylcholine receptor subtypes

Meghan Grandal, Clare Stokes, Roger Papke, Frank Mari, Graduate Studies, DDBS, MUSC.

Introduction: Nicotinic acetylcholine receptors (nAChRs) are ligand-gated ion channels involved in neuronal and neuromuscular signal transduction. Ligands of nAChRs are clinically important as treatments for addiction, cognitive disorders, neurodegenerative diseases, and pain. Alpha-conotoxins (alpha-Ctxs) are inhibitors of nAChRs and are the most ubiquitous venom components across the Conus genus. One alpha-Ctx, Vc1.1, made it to phase II clinical trial for neuropathic pain. To investigate novel alpha-Ctxs, transcripts from cone snail venom ducts were analyzed and three alpha-toxin sequences were chosen for peptide synthesis and functional characterization on nAChRs (PID, Nux1, and Ced1). Methods: RNA sequencing (NextSeq500, Illumina) and de novo transcriptome assembly (Trinity) was performed from venom ducts of 17 Conus species. Putative alpha-Ctx transcripts were extracted using a conserved signal sequence as a BLASTp search query. Three were chosen for peptide synthesis (BIOMATIK, Ontario, Canada). Seven human nAChR subtypes were heterologously expressed in Xenopus laevis oocytes. Alpha-Ctx activity was tested using two-electrode voltage clamp recordings on an OpusXpress 6000A (Molecular Devices). Alpha-Ctx activity was measured as inhibition of acetylcholine-induced current (pA). T-tests were performed to determine significant current inhibition compared to acetylcholine controls ($p<0.05$). Results/Conclusions: Fifty-seven putative alpha-Ctx transcripts were extracted from transcriptomic data from 17 Conus species. PID, Ced1, and Nux1 were screened for inhibition of several different nAChR subtypes. Significant inhibition was measured by each alpha-Ctx on one or more subtypes. Ced1 showed selective inhibition for alpha-6 containing receptors ($p=0.002$) that are involved in nicotine-induced dopamine reward pathway in the midbrain. This work was supported by NIST

192 The Role of R-Ras Family Signaling in Malignant Peripheral Nerve Sheath Tumor Progression

Shannon Weber, Amanda Pretchl, Nicole Brossier, Stephanie Byers, Steven Carroll, Graduate Studies (MSTP, PhD years), Pathology, MUSC.

Abstract Withheld from Publication

193 Rib-hook Construct for Pediatric Hyperkyphosis and Kyphoscoliosis

Daniel Bonthius, Hai Yao, Graduate Studies (MSTP, PhD years), Oral Health, MUSC.

INTRODUCTION: The rib-hook construct is a novel method of treating childhood hyperkyphosis and kyphoscoliosis. The purpose of this study was to investigate the biomechanics, mechanism, and clinical outcomes of this novel technique. The overarching hypothesis was that the rib-hook construct is a safe and effective technique for correcting hyperkyphotic spinal deformity. METHODS: Biomechanical evaluation: An ex vivo biomechanical study compared traditional pedicle screw proximal fixation to the rib-hook construct in terms of fixation strength and construct stiffness. Porcine model hyperkyphosis correction with rib-hook construct: An in vivo hyperkyphotic porcine model was used to study the ability of the rib-hook construct to correct hyperkyphosis in the developing porcine spine. Human hyperkyphotic correction with rib-hook construct: A retrospective study was conducted to examine the radiographic outcomes and complication rates experienced by human patients that received rib construct implantation surgery. RESULTS: Biomechanical evaluation: The rib-hook construct was significantly less prone to proximal fixation failure and less stiff compared to pedicle screws. Porcine model hyperkyphosis correction with rib-hook construct: The average pre-op T6-T14 thoracic kyphosis was 18.9 ± 5.8°, which increased to 35.8 ± 3.2° at the time of initial hyperkyphosis creation surgery and remained unchanged prior to corrective surgery 4 weeks post-op. In response to corrective surgery with the rib-hook construct, T6-T14 thoracic hyperkyphosis decreased immediately post-op to 11.3 ± 7.8° ($p< 0.0001$) and continued to decrease to 10.4 ± 7.6° until final follow-up 8 weeks post-op. Human hyperkyphosis correction with rib-hook construct: Pre-op sagittal Cobb angle was 81 ± 31° and fell to 43 ± 24° post-op and to 38 ± 24° at final follow-up; indicating ~100% correction (normal thoracic kyphosis is 40°). Complication rate was 1.4 complications per patient. DISCUSSION: The results suggest that the rib-hook construct is a highly effective technique and superior to existing methods. This work was supported by Scoliosis Research Society (SRS), SCTR TL1 (T32)

194 Incidence and trends of head and neck rhabdomyosarcoma versus non-rhabdomyosarcoma in adult and pediatric patients

Vincent Desiato, Catherine Loftus, Eric Lentsch, Medicine, Department of Otolaryngology - Head and Neck Surgery, MUSC.

Introduction/Rationale: Rhabdomyosarcoma (RMS) is a soft-tissue sarcoma typically associated with childhood and adolescence. RMS has also been reported in adults, albeit far less frequently. The aim of this study was to assess incidence, and trends of RMS and non-RMS soft-tissue sarcoma in pediatric and adult patients using a nationwide database. Methods: Data pertaining to the incidence and frequency of RMS and non-RMS soft tissue tumors of the head and neck region were obtained using the Surveillance, Epidemiology and End Results (SEER) database from the National Cancer Institute (NCI). Results: A total of 1215 cases of RMS were reported in 656 (54.0%) males, and 559 (46.0%) females. The majority, 861 (70.9%), occurred in the pediatric population, while 354 (29.1%) occurred in adults. The most common morphological sub-type was embryonal, which was reported in 655 subjects (53.9%), and 328 (27.0%) tumors were of alveolar morphology. In the non-RMS group, a total of 8107 tumors were diagnosed in 6303 (77.7%) males, and 1804 (22.3%) females. A large proportion occurred in adult subjects, 7703 (95.0%), and only 404 (5.0%) occurred in pediatric subjects. In terms of age at diagnosis, RMS showed a clear preponderance for pediatric age groups, peaking around age five. Non-RMS shows a bimodal distribution. The first peak in diagnoses occurred between 25 and 50 years of age, and the second peak represented a large portion of patients over the age of 80 years at the time of diagnosis. Conclusions: RMS demonstrated a clear predilection for the pediatric group, peaking around five-years of age. Embryonal RMS almost exclusively affects those age 20 years or less, while diagnoses of alveolar RMS continue throughout the lifespan. Non-RMS demonstrated a bimodal distribution with an initial peak between age 25 and 50 years, and a second peak in those over 80 years of age.

195 Impact of post-LVAD Ventricular Arrhythmia & Heart Failure on Re-admissions and Overall Mortality: A Retrospective Review

Nagarajan Muthu, Jeffery A. Jones, Rupak Mukherjee, Steven Lauzon, Viswanathan Ramakrishnan, Lucian Lozonschi, Medicine, Cardiothoracic Surgery, MUSC.

BACKGROUND: Left ventricular assist devices (LVAD) have become important therapy for patients with advanced heart failure. The impact of post LVAD ventricular arrhythmias (VA) has not been thoroughly understood. This is partly due to the fact that LVAD flows and patient hemodynamics are not acutely compromised. However, patients who experience post implant VA seem to have higher rates of heart failure, readmission rates, and overall mortality rate. METHODS: A retrospective review of patients who received LVADs at MUSC between 8/1/2014 - 7/31/2018 was performed to characterize the impact of VA on readmission and overall mortality. RESULTS: We identified 79 patients who had complete follow up at our institution. All-cause 1-year mortality rate was 7.6% for all LVAD recipients. Patients with post implant VA and HF had a 1-year all-cause mortality rate of 10% compared with 6.1% for all other LVAD recipients. (RR: 1.63, OR 1.70). Patients with post implant VA represented 28% (29 off 103 readmissions) of all post LVAD readmissions within the first year of receiving LVAD. Combined with patients with post implant heart failure, they accounted for a staggering 38% (95% CI: 28.4 - 47.9%) of all LVAD readmissions within 1 year of discharge following LVAD placement. CONCLUSIONS: Patients who experience post implant VA have disproportionally higher readmission rates and 1-year mortality rate. These findings highlight the need for further studies utilizing larger national databases of LVAD recipients to further characterize these risks. The findings of this preliminary study highlight further investigations into adjuvant interventions targeted to reduce the incidence of post LVAD arrhythmia. This work was supported by Dept of Veterans Affairs under grant I07 BX000904-08A1 Dr. Muthu is supported by a NIH Trainee grant under T32 HL007260-42 National Center for Advancing Translational Sciences of the National Institutes of Health under UL1 TR001450.

196 Heated tumor volume decides effectiveness of drug delivery with thermosensitive liposomes

Krishna Ramajayam, Marissa Wolfe, Anjan Motamarry, John Yost, Mike Yost, Dieter Haemmerich, Graduate Studies, Pediatrics , MUSC.

Objective: Thermosensitive liposome (TSL) is a promising nanoparticle that releases encapsulated drug on exposure to hyperthermic temperatures (>40˚C). The goal of this study was to elucidate the impact of different hyperthermia (HT) methods on tumor drug uptake with TSL encapsulated doxorubicin (TSL-Dox). Methods: We developed a 3-D coupled computer model that simulated tissue heating and drug delivery. Three heating devices were simulated: (1) water bath (42ºC), (2) thermistor probe (50 ºC), and (3) infrared (IR) laser (42 ºC). We simulated TSL-Dox infusion of 5 mg/kg over 30 s. 15 min post infusion; HT was applied for 15 min, followed by 10 min of cooling. We report tumor temperature at HT conclusion and tumor drug concentration 10 min after HT cessation. We performed real time fluorescence imaging before and 3 min after HT treatment on nude mice carrying subcutaneous tumors (Lewis lung carcinoma). Results: Water bath hyperthermia achieved uniform heating (40.0-40.8ºC). The thermistor produced highly localized heating resulting in a smaller heated volume (37.6-42.7ºC). The IR laser produced localized heating with adequate tumor temperatures (39.3-40.7 ºC). Tumor drug concentrations for water bath, thermistor, and IR laser were: 10.9 µg/g, 11.5 µg/g and 15.2 µg/g. When compared to unheated tumors, the fluorescence of heated tumors increased by 1.7, 7.1, 6.3 fold with Water bath, Thermistor and Laser HT. The large-volumetric heating via water bath caused rapid depletion of encapsulated doxorubicin in the systemic circulation, which explains the lesser tumor drug uptake and marginal fold change in fluorescence. The thermistor caused higher tumor drug concentration than water bath, but likely underdosed some regions due to inadequate temperatures. The laser device focused the whole tumor to adequate temperature resulting in a drug concentration higher than the earlier methods. Conclusions: Overheating larger tissue volumes will decrease the drug available for TSL based delivery to tumors. This work was supported by NIH, Grant Number RO1CA181664.

197 Using a Site-Targeted Complement Inhibitor as a Therapeutic Approach for Cognitive Decline Post Chronic Traumatic Brain injury.

Khalil Mallah, Ali Alawieh, Reda Chalhoub, Farris Langley, Mikeala York, Henry Broome, Stephen Tomlinson, Graduate Studies, Microbiology and Immunology Department, MUSC.

Abstract Withheld from Publication

198 Fretting Mechanics in Modular Total Hip Arthroplasty: Si3N4 vs CoCrMo Femoral Head on Ti-6Al-4V Trunnion

Piyush Khullar, Jeremy Shealy Dongkai Zhu, Jeremy Gilbert, Medicine, Orthopaedics and Physical Medicine, MUSC.

Abstract Withheld from Publication

199 Role of the Glycolytic Enzyme Enolase-1 in Fibrosis

Shailza Sharma, Tomoya Watanabe, Carol Feghali Bostwick, Medicine, Medicine, MUSC.

Introduction-Fibrosis is a pathologic process characterized by excessive accumulation of extracellular matrix(ECM) components, such as collagen and fibronectin, and inflammatory cells in organs and tissues. It results from chronic inflammation which culminates in deregulated wound healing and remodeled and disrupted organ architecture, ultimately resulting in loss of function. Loss of organ function is the major cause of morbidity and mortality in individuals with progressive and fatal pulmonary fibrosis in diseases such as idiopathic pulmonary fibrosis and systemic sclerosis. Thus, there is an unmet clinical need for the development of effective therapies for lung fibrosis. Rationale-A hallmark of lung fibrosis is activation of pulmonary fibroblasts to produce excessive ECM and their transition to myofibroblasts. Glycolysis is required for myofibroblast differentiation, thereby is critical in the development of pulmonary fibrosis. Interestingly, Enolase, a glycolytic-metalloenzyme, is upregulated in cancer cells and its role in tumor cell invasion and metastasis is documented. Similar to its mechanism in cancer metastasis, we propose that Enolase engages the plasminogen system and promotes organ fibrosis. Methods- Primary human-fibroblasts were cultured from human lung tissues. Enolase-1 was cloned and expressed. Enolase-1 effects were assessed using qPCR and immunoblotting. Enolase was identified using mass-spectrometry. Results-Using immunoblotting and mass-spectrometry, we show that Enolase-1 dimerizes upon treatment of primary lung fibroblasts with TGFβ, a potent pro-fibrotic factor. Enolase dimers are also detected in primary lung fibroblasts from patients with SSc-associated pulmonary fibrosis. Further, transfection of Enolase (protein as well as enolase-expressing plasmid) in primary lung fibroblasts led to upregulation of pro-fibrotic proteins at both the mRNA and protein level, suggesting that Enolase regulates ECM components at the transcriptional level. Conclusions-Our findings identify a novel 'moonlighting' function for Enolase-1 as a pro-fibrotic protein that mediates the fibrotic effect of TGFβ. Targeting Enolase-1 in the glycolytic pathway may be effective for treating fibrotic diseases. This work was supported by RO1

200 ST Elevation Myocardial Infarction Presentation and Management Trends at the Medical University of South Carolina

Umair Malik, Mohamad Almahmoud, Jasjeet Khural, Katrina Bidwell, Alexander Conavo, Valerian Fernandes, Medicine, Medicine, MUSC.

Background: ST elevation myocardial infarction (STEMI) management has evolved considerably over the last five years. We studied the temporal trends in management of patients presenting with STEMI in 2014-15 compared to 2018-19 at our institution. Methods: We performed a retrospective chart review of all the patients presenting with STEMI to the Medical University of South Carolina (MUSC) during two time periods: Period 1 between June 2014 and March 2015, Period 2 between January 2018 and June 2019. We compared the use of radial artery access, mechanical circulatory support, aspiration thrombectomy, percutaneous transluminal coronary angioplasty (PTCA) prior to stenting, fluoroscopy time, and contrast volume in patients presenting with STEMI in 2014-15 compared to 2018-19. Results: During Period 1, there were a total of 67 STEMI activations, of these 41 (61%) were determined to be angiographic STEMI (acute thrombotic occlusion). During Period 2, there were 138 STEMI activations, of which 89 (64%) were determined to be angiographic STEMI. In the angiographic STEMI population, there was no statistically significant difference in the use of radial artery access (67% in Period 1 versus 75% in Period 2), or the use of mechanical circulatory support (14% versus 18%). Average fluoroscopy time decreased from 17.1 minutes to 14.7 minutes ($p<0.05$), and average contrast volume used decreased from 143 cc to 99 cc ($p<0.05$). Use of aspiration thrombectomy decreased from 52% to 36% ($p<0.05$) and use of PTCA increased from 50% to 84% ($p<0.05$). Conclusions: Over the last five years, there has been a statistically significant decrease in the average fluoroscopy time, contrast volume administered and aspiration thrombectomy performed in patients presenting with STEMI at our institution. The use of PTCA prior to stenting has increased over the same time period.

201 Predicting stroke recovery using neural networks

Barbara Marebwa, Julius Fridriksson, Chris Rorden, Leonardo Bonilha, Medicine, Neurology, MUSC.

Language difficulties is a common debilitating sequela of stroke which persists in up to 40% of chronic stroke survivors. We aimed to predict language recovery after anodal transcranial direct current stimulation (tDCS) coupled with speech therapy in chronic stroke patients 6-months after treatment using 3 different modalities: behavior, lesion volume, and white-matter connectivity. Sixty-seven participants (18 females, mean age 59.8 ± 10.1) with chronic aphasia were randomized into two groups and underwent 15 language therapy sessions in 3 weeks. One group (31 participants) received 1 mA anodal-tDCS while the other (36 participants) received sham-tDCS to the intact left temporoparietal region for the first 20 min of each session. The primary outcome was object naming (PNT) improvement. We reconstructed whole brain structural connectomes and quantified lesion volume for each subject. We then trained a pattern recognition neural net to dichotomize participants into two groups: responders and non-responders, and a and fitting neural network to determine a non-linear combination of behavioral or neuroanatomical factors that best predicted naming scores at 6 months. We employed a 70:15:15 cross-validation scheme. We were able to classify the subjects into two groups: those who maintained naming performance (at least a 15-point improvement from baseline) vs. those who performed worse 6 months after treatment with up to 80%accuracy for all models. We were further able to predict PNT scores with an R-squared of 0.78 (behavioral model), 0.93 (lesion model), 0.89 (right hemisphere connectivity), and 0.95 (left hemisphere connectivity). All models performed significantly better than random models. We present simple neural networks that can not only determine participant language recovery up to 6-months after treatment, but also offers useful insight into disentangling factors necessary for language recovery. This work was supported by NIDCD

202 Embryonic Mesenchymal Programs Persist in the Adult Pancreas during Physiology and Cancer

Lu Han, Gustavo Leone, Medicine, Biochemistry, MUSC.

Pancreatic ductal adenocarcinoma (PDAC) is one of most lethal cancers due to lack of effective treatments. While the tumor is of epithelial identity, the stromal fibroblasts also expand significantly during tumorigenesis. Such expansion is potentially from multiple cellular sources,

including recruitment from the bone marrow, epithelial to mesenchymal transition and proliferation of the tissue resident fibroblasts (TRFs). The TRF route is the least understood due to the lack of molecular markers and genetic tools. Those cancer associated fibroblasts (CAFs) have been evidenced to both restrain and enable PDAC. Such paradox is at least partly due to the existence of subtypes of CAFs, which is still poorly understood at the molecular and cellular levels. The interaction between the epithelium and mesenchyme is a recurring theme spanning fetal organogenesis and adult pathogenesis in the pancreas. Here in this study, we aimed to test the hypothesis that the persistence of fetal mesenchymal programs, including cellular descendants and molecular markers, defines a unique subtype of CAFs in the pancreas. Both genetically engineered mouse models and human patient samples were utilized in this work. Using mice carrying inducible creER and loxP reporter, we were able to genetically label fetal pancreatic mesenchyme with a single dose tamoxifen administration during mid-gestation. Lineage tracing of those progenitors revealed their cellular descendants as TRFs in the adult pancreas. Furthermore, we found that several gene signatures of the fetal pancreatic mesenchyme to be present in adult pancreatic TRFs. Importantly, these populations expand significantly during tumorigenesis, accounting for half of the overall CAFs. In summary, our study demonstrated the persistence of embryonic mesenchymal programs in the forms of either cellular descendants or molecular markers. This provided novel fibroblast stratification, allowing for further investigation of fibroblast subtype specific functions in PDAC. This work was supported by NIH/NCI P30 CA138313

203 The role of infralimbic cortical perineuronal nets in fear memory extinction after adolescent intermittent ethanol exposure

Kristin Marquardt, Lawrence Judson, Medicine (MSTP, MD years), Neuroscience, MUSC.

Alcohol use during adolescence alters cue conditioning and reward pathways, increasing later susceptibility to developing a pattern of uncontrolled drinking. Perineuronal nets (PNN) are specialized extracellular matrix that form around cortical neurons enhancing synaptic stability at the cost of flexibility. PNN are highly dynamic structures that can be altered by acute and chronic alcohol consumption. Here we tested the role of PNN in cue conditioning pathways in rats exposed to adolescent intermittent ethanol (AIE). In rats, a tone is paired with a mild foot shock, resulting in a learned fear response to the conditioned cue. Learning that the tone no longer predicts the shock during Extinction training, is a measure of an individual's ability to alter conditioned behaviors. When tested in adulthood, male rats exposed to AIE have slowed extinction learning and impaired extinction recall. Extinction learning and successful recall is mediated by an infralimbic (IfL) cortex and basolateral amygdala circuit. We have shown that disruption of perineuronal nets (PNN) in the IfL in adult rats, prior to extinction training, significantly improves extinction learning. These data suggest that impairment of fear extinction learning and recall in male AIE rats may be mediated by aberrant increases in PNN density in the IfL cortex. Seven, 26 and 56 days following the last cycle of ethanol exposure, AIE significantly increased PNN density in the mPFC. In a separate cohort male AIE rats, chondroitinase ABC (ChABC) was micro-infused bilaterally into the IfL to degrade PNN structures 24-hours prior to extinction training. AIE rats with degraded PNN in the IfL cortex learned extinction significantly faster than AIE rats receiving vehicle control. Current work utilizing fiber photometry is analyzing how alterations in PNN directly affects neural activity that is linked to impairments in extinction behavior. This work was supported by F32 AA027427-01

204 Visual Enhancement of Auditory Speech Identification is Predicted by Individual Differences in Frontal-Occipital Fasciculus Microstructure

James Dias, Carolyn McClaskey, Kelly Harris, Medicine, Otolaryngology, MUSC.

Frontal cortical structures involved in speech articulation, attention, and memory have been implicated in auditory, visual, and audiovisual speech perception. Passively watching and/or listening to visual and audiovisual speech is associated with correlated functional activity in the frontal and occipital cortices. This correlated frontal-occipital activity may be facilitated by their anatomical connectivity via the inferior frontal-occipital fasciculus (IFOF). We examined the extent to which individual differences in IFOF microstructure predicted auditory (AO), visual (lipreading) (VO), and audiovisual (AV) speech-in-noise identification. Sixteen younger adults with normal hearing and normal (or corrected-to-normal) sight participated. Following diffusion-weighted magnetic resonance imaging (DW-MRI), scalars for white-matter microstructure, including fractional anisotropy (FA), mean diffusivity (MD), radial diffusivity (RD), and axial diffusivity (AD), were extracted from each participant's whole-brain and IFOF tracts. Generally, robust white-matter microstructure is characterized as having higher FA and lower MD, RD, and AD. Individual differences in IFOF FA and diffusivity (MD, RD, and AD) failed to predict AO, VO, or AV speech identification on their own. However, lower IFOF diffusivity (left and right) did predict better AV speech identification after accounting for AO speech identification, suggesting the IFOF may facilitate AV speech identification by modulating visual speech input. To explore this possibility, psychometrics for the contributions of auditory and visual speech to the bimodal auditory-visual benefit when identifying AV speech, known as audiovisual gain, were computed. Lower IFOF diffusivity (left and right) accounted for more visual contribution, but not auditory contribution, to audiovisual gain. The results suggest that individual differences in IFOF microstructure may modulate the role of visual speech in audiovisual speech identification. The results also support theoretical accounts suggesting frontal cortical mechanisms modulate visual speech processing and the role of visual speech in audiovisual speech perception. This work was supported by NIH/NIDCD R01 DC014467, R01 DC017619, P50 DC00422, T32 DC014435

205 Single but not dual blockade of PI3K delta and PI3K gamma promotes robust CD8+ T cell responses to solid tumors

Connor Dwyer, Dimitrios C. Arhontoulis, Hannah M. Knochelmann, Aubrey S. Smith, Guillermo O. Rangel Rivera, Megan M. Wyatt, Amalia M. Rivera Reyes, Chrystal Paulos, Medicine, Microbiology and Immunology/Dermatology, MUSC.

Adoptive T cell transfer (ACT) therapy success in solid tumors is limited by cell survival and persistence of donor cells in the tumor microenvironment. Current expansion protocols rely on multiple reactivations and high dose interleukin-2 which drive cells to become heavily differentiated. Despite increased function, differentiation to an effector/effector memory phenotype attenuates antitumor efficacy compared to less differentiated stem/central memory T cells. PI3K/AKT inhibition expands less differentiated T cells with potent immunity when infused into mice bearing large tumors. However, immune cells use multiple forms of PI3K catalytic subunits, and the ideal therapeutic target remains to be elucidated. To identify the ideal PI3K catalytic subunit target, CD8+ T cells were expanded from the pmel-1 mouse model in the presence small molecule inhibitors against PI3K delta (CAL-101 or TGR-1202), PI3K gamma (IPI-549) or PI3K delta and gamma (IPI-145). Pharmaceutical inhibition produced less differentiated cell products, consisting of CD44hi CD62Lhi and CD44lo CD62Lhi T cells compared to a CD44hi CD62Llo phenotype with traditional expansion. Additionally, inhibitor treated cells were less apoptotic upon antigen

re-encounter, expressed more costimulatory markers with reduced expression of coinhibitory molecule Tim-3. Upon transfer into B16F10-bearing mice, inhibitor treated cells had improved antitumor immunity compared to untreated cells. Compared to sole inhibition of PI3K delta or PI3K gamma, dual inhibited T cells were less effective at clearing melanoma and persisted poorly. Similar results were obtained when inhibitors were used for expansion of human CAR T cells, generating a less differentiated cell product. However, PI3K delta inhibitor treated cultures were more effective at lysing human tumors. Taken together our data demonstrates that sole inhibition of PI3K delta or PI3K gamma provides a less differentiated and more therapeutic cell product. Our data also suggests that inhibition of PI3K delta is the best target in the PI3K/AKT pathway to improve ACT cell products. This work was supported by RO1CA208514, 1T32AI132164-01, 5T32DE01755

206 Neuronal dysfunction underlies autism-related behaviors in a mouse model of MEF2C haploinsufficiency syndrome

Adam Harrington, Kayla Blankenship, Ahlem Assali, Stefano Berto, Benjamin Siemsen, Yongjoo Jennifer Cho, Evgeny Tsvetkov, Acadia Thielking, Michael Scofield, Christopher Cowan, Christopher Cowan, Medicine, Neuroscience, MUSC.

Abstract Withheld from Publication

207 Residual brain white matter integrity predicts aphasia severity and recovery in patients with chronic left hemispheric stroke

Janina Wilmskoetter, Barbara Marebwa, Alexandra Basilakos, Julius Fridriksson, Chris Rorden, Brielle C. Stark, Lisa Johnson, Gregory Hickok, Argye E. Hillis, Graham Warner, Leonardo Bonilha, Medicine, Neurology, MUSC.

Rationale: Stroke lesion characteristics only partially explain patients' deficits and recovery after stroke. We sought to determine the impact of residual white matter integrity outside the lesion on post-stroke aphasia severity and recovery. We hypothesized that: 1) stroke-unrelated damage in residual white matter - quantified as age-related white matter hyperintensities (WMH) - is associated with aphasia severity, and 2) information spreading between crucial brain regions using residual white matter outside the stroke lesion is associated with aphasia severity and recovery. Methods: To assess hypothesis 1, we measured WMH severity and calculated percentages of short-, mid- and long-range white matter fibers of 48 individuals with chronic post-stroke aphasia. To assess hypothesis 2, we calculated the propagation speed using white matter connections outside the stroke lesion between language related grey matter regions of 69 individuals with chronic post-stroke aphasia. Aphasia severity was determined for all participants using validated, standardized tests. We performed multivariable linear regression modeling to assess the relationship between WMH, fiber-length, propagation speed and aphasia severity and recovery. Results: We found 1) a significant indirect effect of more severe WMH on worse aphasia severity mediated by a lower percentage of long-range and higher percentage of short-range fibers in the residual brain tissue outside the stroke lesion (effect=6.5078, Bootstrapping: SE=3.5797, lower limit 95-CI=-0.5672, upper limit 95%-CI=15.0571); and 2) a significant effect of propagation speed between the inferior frontal, middle temporal, posterior superior temporal and angular gyri on aphasia severity and recovery. Conclusions: We revealed that 1) age-related WMH affect aphasia severity through a change of the proportions of long- and short-range fibers, and 2) fast, alternative connections between crucial grey matter regions affect aphasia severity and recovery. These findings demonstrate that the integrity of white matter tissue outside the stroke lesion is a crucial determinant for post-stroke aphasia severity and recovery. This work was supported by NIH/NIDCD, AHA

208 GABAergic Neuronal Deficiency and Type 2 Potassium-Chloride Cotransporter Immaturity in Human Focal Cortical Dysplasia

Peng Cheng Han, Cynthia T Welsh, Michael T Smith, Robert E Schmidt, Steven Carroll, Medicine (MSTP, MD years), Pathology and Laboratory Medicine, MUSC.

Focal cortical dysplasia (FCD) is a common histopathologic finding in cortical specimens resected for refractory epilepsy. GABAergic neuronal abnormalities and K-Cl cotransporter type 2 (KCC2) immaturity may be contributing factors for FCD-related epilepsy. We examined surgical specimens from 12 cases diagnosed with FCD, and brain tissues without developmental abnormality obtained from 6 autopsy cases. We found that GABAergic neuronal density was abnormal in FCD with 2 distinct patterns. In 7 of 12 (58%) FCD subjects, the GABAergic neuron density in dysplastic regions and in neighboring nondysplastic regions was equally reduced, hence we call this a "broad pattern." In the remaining cases, GABAergic neuron density was decreased in dysplastic regions but not in the neighboring nondysplastic regions; we designate this "restricted pattern." The different patterns are not associated with pathologic subtypes of FCD. Intracytoplasmic retention of KCC2 is evident in dysmorphic neurons in the majority of FCD type II subjects (5/7) but not in FCD type I. Our study suggests that (1) "broad" GABAergic deficiency may reflect epileptic vulnerability outside the dysplastic area; and (2) abnormal distribution of KCC2 may contribute to seizure generation in patients with FCD type II but not in type I. This work was supported by Department of Pathology and Laboratory Medicine Resident and Fellow Research Grant

209 Comparative Enhancement of Motor Function and BDNF Expression Following Different Brain Stimulation Approaches in an Animal Model of Ischemic Stroke

Serena-Kaye K.C. Sims, Aitana Rizzo, Kern Howard, Ariana Farrand, Heather Boger, DeAnna Adkins, Graduate Studies, National Institute of Health- formally Neurosciences, MUSC.

Background: As a leading cause of disability in the United States, stroke can induce severe upper extremity motor impairments. Combinatory intervention such as high frequency (50-100Hz) excitatory cortical stimulation (ECS) given concurrently with motor rehabilitative training (RT) improves forelimb function, except in aged and severely impaired animals. Clinical studies suggest that low frequency (<1Hz) inhibitory (ICS) may provide an alternative approach to enhance recovery. Currently, the molecular mediators of CS-induced behavioral effects are unknown. Brain-derived neurotrophic factor (BDNF) has been associated with improved recovery and neural remodeling after stroke and thus may be involved in CS-induced behavioral recovery. Objective: To investigate whether inhibitory stimulation during RT improves functional recovery of severely impaired rats and aging rats, following focal cortical ischemia and if this recovery alters BDNF expression (Study 1) and is dependent upon BDNF binding to TrkB receptors (Study 2). Methods: Rats underwent ECS+RT, ICS+RT, or noCS+RT treatment daily for three weeks following a unilateral ischemic lesion to the motor cortex. After treatment, BDNF expression was measured

in cortical tissue samples (Study 1). In Study 2, the TrkB inhibitor, ANA-12, was injected prior to treatment daily for 21 days. Results: ICS+RT treatment significantly improved impaired forelimb recovery compared to ECS+RT and noCS+RT treatment. Inhibition of BDNF binding to the TrkB receptor significantly reduced forelimb recovery in groups that received ECS during RT. Conclusion: ICS given concurrently with rehabilitation improves motor recovery in severely impaired animals (both severely impaired 4 month animals and animals that are aged), and alters cortical BDNF expression; nevertheless ICS mediated improvements are not dependent upon BDNF binding to TrkB. However, inhibition of TrkB receptors does disrupt motor recovery in ECS+RT treated animals. This work was supported by NIH BluePrint D-SPAN Award (F99/K00) (SK). The Delaware-CTR ACCEL Institutional Development Award (IDeA) from the (NIGMS/NIH U54-GM104941) NC NM4R (P2CHD086844) COBRE in Stroke Recovery (P20 GM109040) MUSC's NIH training grants (R25 GM072643, TL1 TR001451 and TL1 TR000061) (DLA)

210 Commensal Oral Microbiota has Distinct Osteoimmunomodulatory Effects Driven by Induction of MHC-II Antigen Presentation and Toll-Like Receptor Mediated Immunity

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

Abstract Withheld from Publication

211 Outcomes of Inter-facility Helicopter Transportation in Acute Stroke Care

Eyad Almallouhi, Christine Holmstedt, Medicine, Neurology, MUSC.

Abstract Withheld from Publication

212 Dendritic Cells Regulate the Immunological Landscape of Breast Tumors

Stephen Iwanowycz, Yingqi Li, Christopher Koivisto, Soo Ngoi, Bei Liu, Medicine, Microbiology and Immunology, MUSC.

The recent success of tumor immunotherapies has revealed the potential of the immune system to identify and eliminate tumors; however, lasting responses are only achieved in a minority patients. The strongly suppressive tumor microenvironment (TME) presents a major obstacle for generating effective immune responses. Dendritic cells bridge the gap between the innate and adaptive immune systems. They can adopt stimulatory or regulatory phenotypes depending on their environment and critically regulate the type, magnitude, and duration of immune response. Conventional dendritic cells (cDC) are classified into two main subsets, cDC1 or cDC2 which preferentially present antigens to CD8 or CD4 T cells respectively. Stimulatory cDC1s are critical for generating effective immune responses against melanoma; however, their role in the microenvironment of breast cancer is less clear. Therefore, we implanted Breast cancer cells into the mammary gland of cDC1 deficient BATF3 KO mice. We found that tumor growth was significantly inhibited due to increased tumor infiltration and activation of CD4 T cells and M1 macrophages. Recently we have discovered that inhibition of the immunological chaperone gp96 specifically within DCs results in an intrinsic loss of regulatory potential and an increased immune response in an environment rich with foreign antigens. We used this model to reprogram DCs within the TME of breast cancer and investigate their contribution to its development. Genetic deletion of DC specific gp96 resulted in significantly decreased tumor development in a model of spontaneous breast cancer. Histological analysis revealed that tumor initiation occurred at similar rates, but tumors progressed significantly slower in KO mice. Increased T cell and NK cell responses were detected in KO mice in both early and advanced tumors. These surprising results identify the unique suppressive ability of cDC1 in breast cancer and reveal the ability of DCs to regulate the immune surveillance of breast tumors. This work was supported by NIH/NCI (CA193939) , NIH/NIAID (AI125859), NIH/NCI (T32 CA193201), NIH/NIAID (T32 AI132164)

213 CD26 enzymatic activity modulates efficient migration of adoptively transferred cancer-specific T cells to solid tumors

Megan Wyatt, Stefanie Bailey, Michelle Nelson, Hannah Knochelmann, Aubrey Smith, Connor Dwyer, Dimitrios Arhontoulis, Guillermo Rangel Rivera, Amalia Rivera Reyes, Chrystal Paulos, Medicine, Microbiology and Immunology, MUSC.

The inadequate ability of adoptively transferred T cells to eradicate solid tumors limits their use in treatments for patients afflicted with those cancers. Efforts to improve ACT for solid tumors aim to identify strategies that poise T cells for optimal response. We have previously identified a specific subset of CD4 T cells that produce a tremendous response in humanized solid tumor models. These cells express high levels of the ubiquitous ectoenzyme dipeptidyl peptidase-4 (DPP-4), also known as CD26. We sought to investigate the importance of CD26 on T cells using in vitro and in vivo strategies. We adoptively transferred tumor specific CD26+ T cells into melanoma tumor-bearing CD26 knockout mice, and continuously blocked the CD26 enzymatic activity of the donor cells in vivo with sitagliptin (75 mg kg-1), an established competitive inhibitor of this enzyme. Persistence of adoptively transferred cells in the peripheral blood was diminished with sitagliptin treatment, as was tumor infiltration of donor cells and host CD8 and CD4 cells. Tumors in sitagliptin-treated mice eventually reached size endpoint (> 400mm2) while tumors untreated mice were regressed for 130+ days. A 32-plex cytokine array of blood plasma collected 10 days post-treatment revealed a diminished profile of cytokines and chemokines, indicating that the inflammatory response of the T cells was dampened with sitagliptin treatment. Further experiments characterized the ability of CD26+ T cells to respond to tumor trafficking signals with a transwell migration assay and found that sitagliptin treatment significantly impaired their migratory capacity. However, sitagliptin did not impair the ability of T cells to functionally respond to antigen. These data suggest that the enzymatic activity of CD26 is important for the ability of T cells to migrate to the tumor site in order to mount an effective antitumor response. This work was supported by R01 CA208514, R50 CA233168

214 The Rising Incidence of Pediatric Head and Neck Cancers in the United States

Catherine Loftus, Avigeet Gupta BS; Clarice Clemmens MD; Shaun A. Nguyen MD, Eric Lentsch, Medicine, Otolaryngology, MUSC.

Abstract Withheld from Publication

215 Exosome-mediated long-range communication in stressed retinal pigment epithelial cell mono layers - focus up-take mechanisms.

Crystal Nicholson, Navjot Shah, Masakii Ishii, Bala Annamalai, Carlene Brandon, Tamara Nowling, Baerbel Rohrer, Graduate Studies, Department of Ophthalmology, MUSC.

Abstract Withheld from Publication

216 Minocycline-Induced Dysbiosis of Gut Microbiota Alters Normal Osteoimmune Processes in Post-Pubertal Skeletal Development

Amy Warner, Matthew Carson, Jessica Hathaway-Schrader, Joy Kirkpatrick, Brooks Swanson, Alex Alekseyenko, Jose Aguirre, Chad Novince, Dental Medicine, Oral Health Sciences, MUSC.

Abstract Withheld from Publication

217 MicroRNA-204 as a driver of the neuroendocrine phenotype through direct negative regulation of the Androgen Receptor

Lourdes Nogueira, Arabia Satterwhite, Sean Cosh, Michael Lilly, David P Turner, Ashley-Knowell and Victoria Findlay, Victoria Findlay, Graduate Studies, Pathology and Lab Medicine, MUSC.

Prostate cancer affects African American (AA) men disproportionately in the US, but even more so in the state of South Carolina, with 3 times higher mortality rates for AA men when compared to European American (EA) men. Neuroendocrine prostate cancer (NEPC) is a subtype of castrate resistant prostate cancer with aggressive clinical features and poor overall survival. NEPC is associated with androgen independence and a lack of therapeutic options. Although de novo NEPC is rare, recent studies support the idea that transformation of prostate adenocarcinoma cells through a process of neuroendocrine differentiation (NED) into NEPC as a mechanism of resistance to androgen receptor-directed therapies (ADT). This study examines a lifestyle factor known as advanced glycation end-products (AGEs) that promotes a more aggressive prostate cancer phenotype through the induction of a specific microRNA (miR-204) and MYC (a known driver of NEPC). Recent studies show that miR-204 plays an oncogenic role in Androgen Receptor (AR) negative cells representing NEPC and a tumor suppressor role in AR positive cells representing prostate adenocarcinoma. We previously showed that AGEs upregulate miR-204, MYC and drive NED in vitro and drive aggressive tumor growth in vivo. Relevant as both AGEs and miR-204 are elevated in AA men, when compared to EA men, with prostate cancer. This study examines the impact of miR-204 on the Androgen Receptor as a direct target and the impact on driving the neuroendocrine phenotype. This innovative study is the first to link a lifestyle factor (AGE) and a plasma biomarker (miR-204) together as drivers of racial disparities in prostate cancer aggression, and as drivers that can be clinically targeted and may be informative for novel therapeutic interventions to delay or prevent the emergence of NEPC during ADT. This work was supported by NIH/NCI 1U54CA210962

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