Sigma Xi, The Charleston Chapter

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

Please consider joining the Charleston Chapter of Sigma Xi. 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 one of the few that is not affiliated with a single University, with members from the Medical University of South Carolina, The College of Charleston, The Citadel, Trident Tech, Bayer Corporation, NOAA, and SCDNR. 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 the broad range of scientific disciplines in which they are engaged.

- **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” – a week-long seminar series in February to celebrate Darwin’s birthday.

- **Annual Banquet.** Once a year, each spring, we recognize the outstanding accomplishments of scientists and teachers in our Chapter and we have a keynote address of particular scientific or policy interest to the members of our Chapter.

- **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, complete the nomination form available at: [http://www.sigmaxi.org/member/join/nom.html](http://www.sigmaxi.org/member/join/nom.html). We can provide nomination signatures if you do not know other Sigma Xi members.

New member dues: $90 (students $25) + one time $20 initiation fee (chapter dues waived).

Transitional dues for recent graduates (e.g. postdocs): $45.00 + $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. Holly Bevsek, President
Charleston Chapter of Sigma Xi
Department of Chemistry
171 Moultrie Street
Charleston, SC, 29409
Phone: 843-953-7790; E-mail:  bevsekh1@citadel.edu
Eric James, PhD

“PfSPZ Vaccine*: Translating a concept into a vaccine for eliminating malaria”

[*live attenuated sporozoite (SPZ) vaccine against Plasmodium falciparum (Pf)]

Dr. Eric James is Senior Managing Director, Vaccine Stabilization and Logistics at Sanaria in Rockville, MD. Sanaria is a biotechnology company developing vaccines protective against malaria. Vaccines developed by Sanaria have proven highly protective in humans. Dr. James has dedicated himself to the continued work on the development of these vaccines.
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

MUSC Sponsors:
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The MUSC Research Day Committee

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Danielle Scott College of Graduate Studies, Student Representative
Kate Williams College of Graduate Studies, Student Representative
Diana Fulmer College of Graduate Studies, Student Representative
Bradley Krisanits College of Graduate Studies, Student Representative
INFORMATION FOR PARTICIPANTS

Poster Presentation Sessions:

Poster sessions will be held in the Harper Student Center Gym. You 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 between 8:00 and 8:30 AM:** Session time: 8:30 – 10:00 AM
- **Group B between 10:00 and 10:30 AM** Session time 10:30 – 12:00 PM

with numbers corresponding to the abstract numbers in this program.

Group A should take their posters down at 10:00 AM so Group be can put their posters up. Judging begins at 8:30 for Group A and at 10:30 for Group B. Group B can take their posters down at 12:00 noon. Presentations should be 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 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 memory stick (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 3rd. Oral presentation time slots are 15 minutes. An oral presentation should last **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 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, there will also be judges selecting presentations for prizes in the following categories: Sigma Xi, Interprofessional Research, Ralph H Johnson VA Research, and an Innovation Award - these judges will be operating as separate teams, and if your presentation qualifies for one of these categories 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 11:00 am.

Awards Ceremony:

The Awards Ceremony will begin at 4:30 pm in the Drug Discover Auditorium (Rm 110) on Friday, November 3rd. 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 PRESENTATIONS - Harper Wellness Center Gym

Group A - 8:30 am - 10:00 am

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Group B - 10:30 am - 12:00 noon

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ORAL PRESENTATIONS - Colbert Education Center and Library

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EL = Colbert Education Library
POSTER PRESENTATIONS - Harper Center Gym

Poster Group A 8:30 am – 10:00 am

Session 1: Undergraduate I

001-A BMP-Notch Interaction in the Endocardial Lineage Plays an Essential Role for AV Endocardial Cushion Maturation and Remodeling, Miriam M Atteya¹, Patrick Smith¹, Thomas Trusk², Yukiko Sugii²; ¹College of Charleston, Honors College, ²Regenerative Medicine and Cell Biology, MUSC.

002-A The Relationship Between Quadriceps Strength and Size Following Anterior Cruciate Ligament Reconstruction, Kelli B Adams¹, Jennifer L Hunnicutt³, Chris M Gregory², Michelle M McLeod¹, Harris S Sline³; ¹Health and Human Performance, CofC, ²Health Science and Research, MUSC, ³Orthopedics, MUSC.

003-A Microgravity Induction of Syncytin-A Enhances Osteoclast Formation, James M Sinkway IV, Purushoth Ethiraj, Reddy V Sakamuri; Pediatrics/DCRI - MUSC.

004-A Mechanism of TGFβ-induced Cancer Stem Cell Formation Through ILEI and LIFR, Sean M Bloos¹, Annamarie C Dalton², Alec N Woosley², Philip Howe²; ¹Biochemistry, USC, ²MUSC.

005-A Tuning Micelle Composition to Improve Targeted Delivery of Chemotherapy to Brain Tumors, Stephen C Frederico, Suraj Dixit, Yu Lin Jiang, Ann-Marie Broome; Pharmacology, MUSC.

006-A Factors That Predict Likelihood of Breastfeeding Among Women with Lupus, Priyanka K Fernandes, Jim C Oates, Gary S Gilkeson, Diane L Kamen; Medicine, MUSC.

007-A Varenicline and N-acetylcysteine: A Better Treatment for Nicotine Addiction?, Jade D Doolittle¹, Lauren N. Beloate², Peter W. Kalivas²; ¹CofC, ²Neurosciences, MUSC.

Session 2: Clinical / Professional / Masters I

008-A Relationship Between Frequency of Keratinocyte Carcinoma Lesions and Strength of the Association Between History of Keratinocyte Carcinoma and Risk for Another Type of Cancer: A Case-control Study, Ashley Wilson¹, James Small², Catherine Flanagan³, David Perry⁴, Richard Marchell⁵, Bruce Thiers⁶, Anthony Alberg²; ¹College of Medicine, MUSC, ²Public Health Sciences, MUSC, ³Hollings Cancer Center, MUSC, ⁴Dermatology and Dermatologic Surgery, MUSC.

009-A Developing Rehabilitation Treatment Plans By Capitalizing on the Relationship Between Metabolic Equivalents and Activities of Daily Living, Alexandra Gross, Meredith Kenyon, Julianne Laura, Anna McGovern, Ashton Wagner, Brittany N Hand, Craig A Velozo; Occupational Therapy, MUSC.

010-A Examining the Validity and Reliability of the Recovr Rehabilitation System, Alanna Herman¹, Jamie Toto¹, Allison Blackburn¹, Stephanie Hand¹, Larry Hodges², Michelle Woodbury¹, Scott Hutchison¹, Christian Finetto³; ¹Health Professions, MUSC, ²Clemson University, ³Health Science and Research, MUSC.
011-A  Radiology Perspective on Long-Term Monitoring of Colonic Interposition As a Treatment for Esophageal Atresia: A Case Report, Dani C Inglesby1, Meryle J Eklund2, 1College of Medicine, MUSC, 2Radiology, MUSC.

012-A  Effects of Resveratrol on Endothelial and Glioblastoma Cells, Cameron E Callahan1, Kendall Cole2, Yu-Lin Jiang3, Ann-Marie Broome3, 1MUSC, 2South Carolina Governor’s School of Science and Mathematics, 3Cell and Molecular Pharmacology, MUSC.

013-A  Generation of T-Cells Expressing a Chimeric Antigen Receptor Targeting Stress Protein Gp96, Christopher Duckworth, Xingjun Wu, Zihai Li; Microbiology and Immunology, MUSC.

014-A  PGE2 Treatment of Bone Marrow Derived Macrophages Induces PD-1 Surface Expression, Alexander Oles, Dingzhi Wang, Raymond Dubois; Biochemistry, MUSC.

015-A  HDAC1 and PKA Combination Therapy for Targeted Chemotherapy Resistant FLT3-IDT+ Acute Myeloid Leukemia, Guillermo O Rangel Rivera1, Besim Ogretmen2, Natalia Oleinik2, Shanmugan Panneer Selvam2, Rose Waridi Ndeto2, Kyla Baron2; 1College of Graduate Studies, MUSC, 2Biochemistry and Molecular Biology, MUSC.

016-A  Effect of Alcohol Septal Ablation on Renal Function of Patients with Hypertrophic Obstructive Cardiomyopathy. Does Relief of Obstruction Ameliorate Acute Contrast-Induced Nephropathy?, Alex Canova1, Mira Patel1, Billy Mullinax1, Ashley MD Waring1, Chris MD Capps1, Christopher MD Nielson1, Valerian MD Fernandes2; 1MUSC, 2Ralph H. Johnson VAMC.

017-A  Primary Cilia, Ka’la D Drayton1, Russell Norris2, Katelynn Toomer2, Diana Fulmer2; 1College of Medicine, MUSC, 2Regenerative Medicine and Cell Biology, MUSC.

018-A  The FPR1 and Activation of Fibroblasts, Aariel L Dees, Titus A Reaves; Regenerative Medicine and Cell Biology, MUSC.

019-A  A Novel PGlcNAc Nanofiber Scaffold Used to Augment Bone Healing: A Histological Analysis, Brayden Oakes1, R Nicole Howie2, Emily Durham2, Zachary Grey2, R Amanda LaRue3, Martin Steed4, Robin Musie-Helmericks5, James Cray1, 1College of Dental Medicine, MUSC, 2Oral Health Sciences, MUSC, 3Pathology and Laboratory Medicine, MUSC, 4Oral and Maxillofacial Surgery, MUSC, 5Regenerative Medicine, MUSC.

Session 3: Clinical / Professional / Masters II

020-A  The Relationship Between Posttraumatic Stress Disorder, Executive Function, and the Dopamine Receptor D4 Exon 3 Variable Number of Tandem Repeat Polymorphism, Allen Green, Zhewu Wang; Psychiatry, MUSC.

021-A  Is Burning Odor Sensitivity a Biomarker of Fear and Anxiety?, Samuel L Howard, Caitlin Paquet, Thomas W Uhde, Bernadette M Cortese; DART, MUSC.

022-A  Attitudes of Emergency Medicine Providers About Prescribing Buprenorphine in Emergency Department Settings, Bennie L Padgett1, Lillian Christon2, Marc Bartman3, Kelly Barth2; 1College of Medicine, MUSC, 2Psychiatry, MUSC, 3Emergency Medicine, MUSC.


025-A The Development and Utilization of an Online Professional Medical Series Addressing the Knowledge Gaps in the Management of Hypertension. Allyson Hill, Vanessa Diaz, Donald DiPette, Robert Malcolm, Jennifer Voeks, Daniel Lackland; 1College of Medicine, MUSC, 2Family Medicine, MUSC, 3Internal Medicine, USC, 4Psychiatry and Behavioral Sciences, MUSC, 5Neurology, MUSC.

026-A Do Patients, Visitors and Staff Perceive a Safety Benefit From the Use of Metal Detectors At an Urban, Academic Emergency Department? Patricia Jokl, Russell Allinder, Steven H Sae, Diann M Krywko; 1College of Medicine, MUSC, 2Emergency Medicine, MUSC.

027-A Qualitative Review of Publications Regarding Quadriceps Tendon Autograft Use in ACL Reconstruction. Walker M Heffron, John W Xerogeanes, Jennifer L Hunnicutt, Shane K Woolf, Harris S Stone; 1Orthopaedics, MUSC, 2Orthopaedics, Emory, 3Health Science and Research, MUSC CHP.

028-A Evaluation of Machine Learning Algorithm to Convert Unstructured to Structured Radiological Reports in Patients with Pulmonary Embolism. Adam J Spandorfer, Cody Branch, Puneet Sharma, Pooyan Sahbaee, Taylor Duguay, U Joseph Schoepf, James Ravenel, John Nance; 1Medicine, MUSC, 2Radiology, MUSC.

029-A Open Versus Minimally Invasive Decompression and Stabilization for the Treatment of Thoracolumbar Traumatic Spine Fractures. Gibson AE Klapthor, Mohammed Alshareef; 1COM, MUSC, 2Neurosurgery, MUSC.

030-A A Novel Approach for Creating and Maintaining Ankle Joint Effusions in a Cadaver Model. David Wynn, Graeme Ross, Nick Ashenburg, Alex Clendening, Jordan McCarthy, Brad Presley, Steven Kubalak, Ryan Barnes; 1Medicine, MUSC, 2Emergency Medicine, MUSC, 3Regenerative Medicine and Cell Biology, MUSC.

031-A Opioid Prescribing Habits of Different Specialties for Non-surgical Low Back Pain. Matthew T DeMarco, Elizabeth C Durante, Christopher E Gross; 1College of Medicine, MUSC, 2Orthopaedics, MUSC.


Session 4: Clinical / Professional / Masters III

033-A Does a Patient’s Use of a Primary Care Physician Impact Their Use of the Emergency Department? James W Infanzon, Sarah Katchen, Warren Harvey, Steven Sae; 1College of Medicine, MUSC, 2Emergency Medicine, MUSC.

034-A PD71-04 An Independent, Multi-Institutional, Prospective Study in the Veterans Affairs Health System Confirms the 4KScore Accurately Predicts Aggressive Prostate Cancer. Edward L Held, Sanoj Punnen, Stephen Freeland, Thomas Polascik, Stacy Loeb, Edward Uchio, Sharad Mathur, Stephen Savage; 1MUSC, 2University of Miami, 3Cedars-Sinai, 4Duke Cancer Center, 5New York University, 6University of California Urvine, 7Kansas City Veterans Center, 8Urology, MUSC.
035-A Defining the Prevalence of Hypophosphatasia in MUSC’s Pediatric Population: A Retrospective EMR Analysis, Lauren E Gabriel1, Amanda Blue2, Remberto Paulo3, Katherine Lewis4, Deborah Bowby5; 1College of Medicine, MUSC, 2Pediatric Endocrinology, MUSC, 3Endocrinology, MUSC.

036-A An Assessment of Clinical Investigators and ‘Team Science’, Brenda A Alvarado1, Daniel T Lackland2, 1Medicine, MUSC, 2Neurology, MUSC.

037-A Alterations in Phosphorylated Substrates in Nucleus Accumbens Tissue of Rats in a Self-Administration Model of Alcohol Addiction, Helen L Martin1, Clemence Obellianne2, Joachim D Uys2; 1College of Medicine, MUSC, 2Cell and Molecular Pharmacology, MUSC.

038-A Diffusion Kurtosis Parameters in Pediatric Diffuse Intrinsic Pontine Gliomas, Kristen Herring1, Vittoria Spampinato2, Milad Yazdani2; 1College of Medicine, MUSC, 2Neuroradiology, MUSC.

039-A Association Between Magnesium Intake, Serum Magnesium Levels, and Depression in an At-Risk Population, Emily A Young1, Kristen B Johnson2, Bernadette P Marriott3; 1COM, MUSC, 2University of Tennessee, 3Gastroenterology and Hepatology, MUSC.

040-A Characterizing Macrophage Polarization in Bone Wounds Following Administration of RhBMP2 and PGlcNAc, Zachary J Grey1, R Nicole Howie1, Emily Durham1, Sarah Rose Hall1, Martin Steed2, Robin Muise-Helmericks3, James Cray1; 1Oral Health Sciences, MUSC, 2Oral & Maxillofacial Surgery, MUSC, 3Regenerative Medicine, MUSC.

041-A Radiographic Presentation of Adamantinoma, a Rare Primary Bone Tumor of the Tibial Diaphysis, Ashley S Williams1, Meryle Eklund2; 1Medicine, MUSC, 2Radiology, MUSC.

042-A AGE Ingestion During Puberty Alters the Breast Microenvironment to Create Potential Pre-Neoplastic Lesions Via Metabolic Imprinting, Jaime F Randise1, Bradley A Krisanits1, Lourdes M Nogueira1, Kristi Helke1, Taaliah Campbell1, Victoria J Findlay1, David P Turner1; 1Pathology, MUSC, 2Biology, Claflin University.

043-A Impact of Rotavirus Vaccine Introduction on Diarrheal Hospitalizations in Children Under 5 Years Old in Haiti, 2009 - 2016, Emily A Cloessner1, Stanley Juin2, Eleanor Burnett3, Dante Bugli3, Eyal Leshem3, Negar Aliabadi3; 1MUSC, 2Centers for Disease Control and Prevention, Haiti, 3Centers for Disease Control and Prevention.

044-A Impact of Sensory Stimulation on Improving Post-stroke Upper Extremity Therapy Outcomes, Caroline M Roark1, Lauren E Landers1, Sarah K Phillips1, Ryan J Downey2, Leonardo Bonilha3, V Ramakrishnan4, Na Jin Seo1; 1Occupational Therapy, MUSC, 2Health Professions, MUSC, 3Neurology, MUSC, 4Public Health Sciences, MUSC.

045-A The Relationship Between Neglect and Real-World Paretic Arm Use in Stroke Survivors, Kristin B Housholder1, Nicole T Bertolino1, Roblin F Lynch1, Myra L Nicks1, Michelle L Woodbury2, Sara Kraft3, Emily S. Grattan4; 1Occupational Therapy, MUSC, 2Health Science and Research, MUSC, 3Physical Therapy, MUSC.

046-A Alcohol Use During a Cannabis Cessation Trial: Evaluating N-acetylcysteine Treatment, George A Book1, Nathaniel L Baker1, Jason A Tran2, Rachel L Tomko1, Erin A McClure1, Kervin M Gray1, Lindsay M Squeglia1; 1Psychiatry and Behavioral Sciences, MUSC, 2University of California Riverside.
Session 5: PhD I: Years 1-2

047-A Module-based Analyses of Lower Extremity Muscle Coordination During Walking in Individuals Post-Stroke: A Systematic Review, Bryant A Seamon¹, Richard R Neptune², Steven K Kautz¹; ¹Health and Research, MUSC, ²Mechanical Engineering, The University of Texas at Austin.

048-A Invasive and Non-invasive Subpopulations in MPNSTs Differ in Multiple Aspects of Their Biologic Behavior and Responsiveness to Drugs Targeting Key Signaling Cascades., Laurel Black, Amanda Prechtl, Jody Longo, Steven Carroll; Pathology, MUSC.


050-A The Effect of Vibratory Sensory Stimulation on Cortical Activity During Grip in Stroke Survivors: an FMRI Study, Amanda A Vatinno¹, Leonardo Bonilha², Na Jin Seo¹; ¹Health Sciences and Research, MUSC, ²Neurology, MUSC.

051-A The Role of Histone H4 in Regulated Repair of DNA Crosslinks, Colleen E Quaas, David T Long; Biochemistry and Molecular Biology, MUSC.

052-A Functional Characterization of Mutant BRCA1, John Barrows, David Long; Biochemistry and Molecular Biology, MUSC.

053-A High-Throughput Glycoprotein Biomarker Discovery By MALDI Mass Spectrometry Imaging of Antibody Arrays, Alyson P Black, Richard R Drake, Peggi M Angel, Anand S Mehta; Pharmacology, MUSC.

054-A Akt3 Links Mitochondrial Homeostasis and Mitosis Via the Regulation of WDR12 and Aurora B Kinase, Zachary J Hough, Robin C Muise-Helmericks; Regenerative Medicine and Cell Biology, MUSC.

Session 6: PhD II: Years 3+

055-A Effects of Modified Lipoproteins in First Trimester Trophoblast Cells: a Role in Pre-eclampsia in Pregnancies Complicated By Diabetes?, Rebecca H McLeese¹, Jiawu Zhao², Jeremy Y Yu¹, Derek P Brazil², Timothy J Lyons¹; ¹Endocrinology, MUSC, ²Experimental Medicine, Queen's University Belfast.

056-A Direct Conversion and Detection of Reactive Oxygen Species on a Cathodically-biased Metallic Surface, Michael J Wiegand, Jeremy L Gilbert; Bioengineering, Clemson.

057-A Targeting Fli-1 in T Cells Prevents Chronic Graft-versus-Host Disease, Steven D Schutt¹, Anusara Daenthalasanmak¹, Wu Yongxia¹, Hung Nguyen¹, M. Hanief Sofi¹, David Bastien¹, Supinya Iamsawat¹, Carole Wilson², Lynn M Schnapp², Zhang K Xian², Xue-Zhong Yu²; ¹Microbiology and Immunology, MUSC, ²Medicine, MUSC.

058-A Defining the Tissue N-Glycome of Genomic Subtypes of Breast Cancer, Danielle A Scott¹, Rita Casadonte², Laura Spruill³, Anand Mehta⁴, Nicole Simone⁵, Mark Kriegsmann⁶, Joerg Kriegsmann⁶, Richard Drake⁷, ¹Pharmacology, MUSC, ²Proteopath GmbH, ³Radiation Oncology, Thomas Jefferson University, ⁴Pathology, University of Heidelberg, ⁵Pathology, MUSC.
059-A DZIP1-KIAA2026 Interactions Are Required for Normal Mitral Valve Development, Lilong Guo, Diana Fulmer, Katelynn Toomer, Joshua Lipschutz, Russell Norris; Regenerative Medicine and Cell Biology, MUSC.

060-A Proteomic Imaging Analysis of Injured Cochlear Tissues, Kenyaria V Noble¹, Michelle Reyzer², Jeremy Barth³, Kevin Schey⁴, Edward Krug⁵, Hainan Lang¹; ¹Pathology, MUSC, ²Tissue Core, VU, ³Regenerative Medicine, MUSC.

061-A Modeling Regulatory T Cell (Treg) Immunosuppression, Ravyn M Thompson, Cara Coleman, Dolloff G Nathan; Cellular and Molecular Pharmacology and Experimental Therapeutics, MUSC.

062-A Physical and Self-Reported Function Following Anterior Cruciate Ligament Reconstruction with Quadriceps Tendon Autografts, Jennifer L Hunnicutt¹, Kelli B Adams², Michelle M McLeod², Chris M Gregory¹, Harris S Slone³; ¹Health Science and Research, MUSC, ²Health and Human Performance, CofC, ³Orthopedics, MUSC.

Session 7: PhD III: Years 3+

063-A The Role of the BAF/VRK1 Signaling Axis on the DDR in Nestor-Guillermo Progeria Syndrome (NGPS), Maya F El-Sabban, Aye Mon, Paula Traktman; Biochemistry and Molecular Biology, MUSC.

064-A Mitral Valve Prolapse: A Congenitally-based Disease of Primary Cilia, Katelynn Toomer, Diana Fulmer, Guo Lilong, Hughes Michaela, Brooks Brittany, Norris Russell; Regenerative Medicine and Cell Biology, MUSC.

065-A Heroin Self-administration and Extinction in Rats Alter Prefrontal Cortical Astroglial Synaptic Contacts Which is Normalized By Chronic N-acetylcycteine Treatment During Extinction, Ben M Siemsen¹, Michael D Scofield², Jacqueline F McGinty¹; ¹Neuroscience, MUSC, ²Anesthesiology, MUSC.

066-A Effect of Oxytocin on Stress-Induced Reinstatement of Alcohol-Seeking Behavior in Male and Female Mice, Courtney E King¹, Howard C Becker²; ¹Charleston Alcohol Research Center, MUSC ²VA Medical Research Center.

067-A Noise-induced Dysregulation of Quaking RNA Binding Proteins Contributes to Auditory Nerve Demyelination and Hearing Loss, Clarisse H Panganiban¹, Jeremy L Barth², Lama Darbelli³, Yazhi Xing¹, Jianning Zhang¹, Hui Li¹, Stephane Richard³, Hainan Lang¹; ¹Pathology, MUSC, ²Regenerative Medicine, MUSC, ³McGill University.

068-A Withdrawn

069-A Role of NAD+ Availability and Sirt6 Expression in the Regulation of Antioxidant Defenses in Astrocytes, Benjamin Harlan, Kelby Killoy, Mariana Pehar, Marcelo Vargas; Pharmacology, MUSC.

070-A Differential AKT Signaling in PTEN Null Triple Negative Breast Cancer Cells, Ericka L Smith, Christiana S Kappler, Stephen P Ethier; Pathology, MUSC.
071-A Adolescent Binge-like Ethanol Exposure Differentially Affects Probabilistic Reversal Learning in Long-Evans Versus Sprague-Dawley Rats, S C Garr¹, J T Gass¹, S B Floresco², L J Chandler¹; ¹Neurosciences, MUSC, ²Psychology, University of British Columbia Vancouver.

Session 9: Postdoc / Resident / Fellow / Staff Scientist I

072-A Stromal Platelet Derived Growth Factor Receptor-Beta (PDGFRB) Promotes Breast Brain Metastasis, Katie A Thies¹, Anisha M Hammer², Blake E Hildreth III¹, Luke O Russell², Steven T Sizemore², Anthony J Trimboli³, Gina M Sizemore³, Michael C Ostrowski¹; ¹Biochemistry & Molecular Biology, MUSC, ²The Comprehensive Cancer Center, The Ohio State University, ³The Hollings Cancer Center, MUSC.

073-A Progressive Decrease in Left Atrial Volume Over 8 Years Following Alcohol Septal Ablation for Hypertrophic Obstructive Cardiomyopathy, Ashley A Waring, John Lecluyse, Amy Wahlquist, Alexander Canova, Mira Patel, Valerian Fernandes, Christopher Neilson, Sheldon E Litwin; MUSC.

074-A Changes in Left Hemisphere Perilesional Grey and White Matter Predict the Evolution of Language Abilities in Chronic Stroke Aphasia, Alexandra Basilakos¹, Lisa Johnson¹, Grigori Yourganov², Leonardo Bonilha³, Chris Rorden², Julius Fridriksson¹; ¹Communication Sciences, USC, ²Psychology, USC, ³Neuroscience, MUSC.

075-A MiRNA Expression Shifts As an Initiator Event in Carcinogenesis Induced By Bisphenol A in Human Prostate Cells., Willian A da Silveira¹, Ludivine Renaud², Jonathan Simpson³, Matthew Huff³, W Bailey Glen Jr¹, Hazard E Starr³, Dongjun Chung⁴, Gary Hardiman¹; ¹Bioinformatics, MUSC, ²Medicine, MUSC, ³Library Science and Informatics, MUSC, ⁴Public Health Sciences, MUSC.

076-A Modeling Metabolic Acidosis Disorders Using Human Induced Pluripotent Stem Cells, Behshad - Pournasr, Stephen A Duncan; Regenerative Medicine And Cell Biology, MUSC.

077-A The Modulation EphA2-induced Cytoskeleton Re-organization: a New Insight Into the Role of Extracellular Hsp90, Abdelkader Daoud¹, Udhayakumar Gopai², Jasmine Kaur¹, Jennifer S Isaacs³; ¹Pharmacology, MUSC, ²Pathology, DUSM, ³Pharmacology, MUSC.

078-A Perturbation of Hedgehog Signaling in The Mesothelial Cell Lineage Results in Severe Congenital Heart Defects, Emilye Hiriart, Tara Burns, Ray Deepe, Turner Rainwater, Andy Wessels; Regenerative Medicine and Cell Biology, MUSC.

079-A Ultrasound Capability and Patient Volume in Two Urgent Care Clinics in Nicaragua, Kyle Emberton, Lacey MenkinSmith; Emergency Medicine, MUSC.

080-A Long-Term Outcomes Outcomes of Alcohol Septal Ablation for Hypertrophic Obstructive Cardiomyopathy: A 16 Year Study, Christopher D Capps, Jeremy Rier, Ashley Waring, Justin Heizer, Barbara Griffin, Shaji Shawn, Billy Mullinax, Valerian Fernandes; Cardiology, MUSC.

081-A Role of EphB1 in Axon Guidance and Learning and Memory, Ahlem Assali¹, Benjamin Zirlin¹, George Chenaux², Michael Robichaux², Mark Henkemeyer³, Christopher Cowan¹; ¹Neuroscience, MUSC, ²UC Davis, ³Baylor College of Medicine, ⁴UT SouthWestern Medical Center.
082-A The Neurodevelopmental Disorder-linked Gene, MEF2C, Regulates PCDH17 to Control Cortical Synapse Density, Adam J Harrington, Aram Raissi, Carly Hale, Kayla Blankenship, Alexandra Bowen, Jennifer Darnell, Kimberly Huber, Christopher Cowan; Adam Harrington.

083-A Age-related Differences in Time-compressed Sentence Identification Are Predicted By Cognitive Processing Speed and Cortical Oscillatory Activity, James W Dias, Carolyn M McClaskey, Kelly C Harris; Otolaryngology, MUSC.

**Poster Group B**

10:30 am – 12:00 pm

**Session 1: Undergraduate I**

001-B Assessing Cognitive Changes Due to Microgravity Using Windows Spaceflight Cognitive Assessment Tool (WinSCAT), Kaylen B Bradley¹, Donna R Roberts², Davud Asemani³; ¹Biology, Clemson University, ²Radiology, MUSC.

002-B The Impact of Denomination on Participation in Faith Based Blood Pressure Measurement, Ciara Wilson¹, Daniel Lackland²; ¹Public Health, CSU, ²Neurology, MUSC.

003-B Feasibility of Including Women of Childbearing Age in a Faith-based Study, Alondra DeSantiago¹, Daniel T Lackland²; ¹Public Health Sciences, Clemson University, ²Neurology, MUSC.

004-B Molecular Basis Underlying Calcium-dependent Regulation of Cardiac and Skeletal Muscle Calcium Release Channels (ryanodine Receptors), Hannah G Addis¹, Jordan S Carter², Naohiro Yamaguchi³; ¹Biology, CofC, ²Regenetic Medicine and Cell Biology, MUSC ³Regenetic Medicine and Cell Biology, MUSC.

005-B Neonatal Abstinence Syndrome: A Look At The Maternal-Infant Dyads At The Medical University of South Carolina, Susan Fields¹, Olivia Kapera², Price Ward³, Dorothea Jenkins³; ¹Washington and Lee University, ²CofC, ³Neonatology, MUSC.

006-B Neural Circuit Disruptions in Emotional Processing Across Psychiatric Disorders, James W Lopez¹, Benjamin M Rosenberg⁵, David M Carreon⁵, Julia M Huemer⁴, Ying Jiang⁵, Simon Eckhoff⁵, Amit Etkin⁶, Lisa M McTeague⁷; ¹College of Charleston, ²University of California-Los Angeles, ³Stanford University School of Medicine, ⁴Medical University of Vienna, ⁵Washington University in St. Louis ⁶Heinrich-Heine University Dusseldorf, ⁷MUSC.

**Session 2: Clinical / Professional / Masters I**

007-B A Regional Analysis of Healing in Large Cranial Defects Augmented with BMP2 and an Osteoconductive Matrix, Reed A Houck¹, Nicole Howie², Emily Durham³, Zachary Gray², Amanda LaRue⁸, Martin Steed⁹, Robin Muise-Helmericks⁸, James Cray¹; ¹College of Dental Medicine, MUSC, ²Oral Health Sciences, MUSC.

008-B Too Fat for Joint Replacement: The Fate of the Morbidly Obese Patient with Joint Pain, Glenn D Heftet¹, Russell A Reeves², Richard D Williams³, Sarah M Guess³, Jacob C Balmer³, Bennett L Haskins³, Vincent D Pellegrini Jr², Harry A Demos²; ¹Bioengineering, MUSC, ²Orthopaedics, MUSC, ³College of Medicine, MUSC.
009-B Adoption of the ACMG-AMP Standards and Guidelines for the Interpretation of Sequence Variants, Annie Niehaus¹, Danielle Azzariti², Harrison Steven², DiStefano Marina², Hemphill Sarah², Senol-Cosar Ozlem², Rehm Heidi³; ¹Medicine, MUSC, ²Partners Healthcare Personalized Medicine, ³Brigham & Women’s Hospital and Harvard Medical School.

010-B Effects of Interprofessional Education on Dental Students’ Ergonomics, Payton A Donley¹, Rachel E Crossland¹, Madison L Farrell¹, Madison E Smith¹, Joe Vuthiganon², Peter J Bowman¹; ¹Occupational Therapy, MUSC, ²Dental Medicine, MUSC.

011-B E-learning Innovation: An Interprofessional Mobile Application for Teaching Ambulatory Assistive Devices, Hannah L Boyce, Addison Bensch, Hannah Cassilly, Autumn Jones, Sara Kraft, Amanda Giles; Health Professions, MUSC.

012-B Cultural Caring: An Educational Initiative to Promote Client-Centered Care with Diverse Communities, Sandra Hoyt, Caroline Emanuel, Eliza Gunner, Alexandra Skousen, Cristina R Smith; College of Health Professions, MUSC.

013-B Empowering Women in Haiti: Perceptions of the Days for Girls International Program, Emma L Hanmer¹, Rachel L Baez¹, Patricia Coker-Bolt¹, Janet O’Flynn¹, Leslee Jaeger³, Marie Laurent³; ¹Occupational Therapy, MUSC, ²Rehabilitation, Episcopal University of Haiti, ³Medicine, Helping Haiti Work, ⁴Nursing, Episcopal University of Haiti.

014-B Characterization of Metabolic Fitness of T Cells in Tumors, Matthew Essman¹, Kiley Lawrence², Katie Hurst², Thomas Valente³, Lee R Leddy¹, Jessica E Thaxton¹; ¹College of Medicine, MUSC, ²Orthopaedics, MUSC, ³Medicine, MUSC, ⁴ Hollings Cancer Center.

015-B The Impact of Mitochondrial Permeability Transition Pore Opening on Endothelial Cell Immunogenicity in Transplantation, Scott Esckilsen¹, Danh T Tran², Carl Atkinson², Satish N Nadig³; ¹College of Medicine, MUSC, ²Microbiology & Immunology, MUSC, ³Surgery, MUSC.

016-B Inhibiting Donor Complement Receptor 3 Signaling Mitigates Brain Death-Induced Immunologic Injury Post Lung Transplantation, Sylvia J Jang¹, Qi Cheng¹, Kunal Patel¹, Biao Lei¹, Lindsay Rucker¹, Patterson Allen¹, Satish Nadig¹, Carl Atkinson², ¹Surgery, Transplant, MUSC, ²Microbiology and Immunology, MUSC.

017-B Chemotherapeutic Combinations to Improve Therapeutic Efficacy in Glioblastoma Cells, Molly C Shields¹, Adriannah Drolapas₂, Jamie Harrell³, Ann-Marie Broome¹; ¹MUSC, ²Wofford.

018-B Extended Post-Exposure Effects on Human Neurons and Preliminary Astrocyte Migration Studies Using a Novel Ex-Vivo Hydrocephalus Model, Ryan Gedney, Ramin Eskandari, Michael Smith; MUSC.

019-B Radiologic Evaluation of Cardiac Sarcoidosis: Prognostic Value of FDG-PET/CT in Clinical Management, Paul H Hargrave, Philip Burchett, Carlo De Cecco; Radiology, MUSC.

Session 3: Clinical / Professional / Masters II

020-B Neonates Who Get G-tubes At MUSC, Katherine A George¹, Kristen Morella², Anbesaw W Selassie², Aaron P Lesher³, Alison Chapman⁴, Rita M Ryan⁴; ¹College of Medicine, MUSC, ²Public Health Sciences, MUSC, ³Surgery, MUSC, ⁴Pediatrics, MUSC.
021-B Observational Analysis of Near Vision in Monofocal Pseudophakic Children, Hallie R Hahn¹, Rupal Trivedi², Marion E Wilson²; ¹College of Medicine, MUSC, ²Ophthalmology, MUSC.

022-B Geographic Variation in Total Hip and Knee Arthroplasty Utilization is Influenced By the Presence of Orthopaedic Residency Programs, James J Gregory¹, Russell Reeves², Alexander Chiaramonti², Keith Orland², William Barfield², Jacob Drew², Vincent Pellegrini²; ¹Medicine, MUSC, ²Orthpaedics, MUSC.

023-B The Correlation Between Pre-Operative Cochlear Implant Patients’ Quality of Life and Speech Perception Ability, Nicholas B Aizcorbe, Jonathan Hatch, Shaun A Nguyen, Theodore R McRackan; Otolaryngology.

024-B Piece It Together: Testing Balance of Youth with Autism Spectrum Disorder and Other Neurodevelopmental Disorders in a Novel Wellness Program, Conner McDonald¹, Eve Spratt², Carrie Papa², Jessa Norton³, Janis Newton⁴, Alicia O'Connor⁴; ¹College of Medicine, MUSC, ²Developmental Pediatrics, MUSC, ³College of Charleston, ⁴Wellness Center, MUSC.

025-B Do Patients Who Come to an Urban, Academic ED Consider the Emergency Physician to Be the Doctor They Trust the Most?, Elizabeth Dawley¹, Sarah Katchen¹, Warren Harvey¹, Steven Saef²; ¹Medicine, MUSC, ²Emergency Medicine, MUSC.

026-B The Effect of Socioeconomic Status on Patient-Reported Outcomes After Renal Transplantation, Andrew J Cole, David J Taber, Prabhakar K Baliga; Surgery, MUSC.

027-B Gastrointestinal Complaints in Williams Beuren Syndrome and Supravalvular Aortic Stenosis Suggest a Vascular Contribution, Alexandra O Hamberis¹, Phoebe CR Parrish², Michael Lugo¹, Mark D Levin², Beth A Kozel³; ¹College of Medicine, MUSC, ²NHLBI, NIH.

028-B Utilization and Efficacy of Staged US/CT Algorithm in Suspected Appendicitis in MUSC Pediatric Patients, Caroline E Hubbard¹, William S Russell², Robert A Cina³, Jeanne G Hill⁴; ¹College of Medicine, MUSC, ²Pediatric Emergency Medicine, MUSC, ³Surgery, MUSC, ⁴Radiology and Radiological Science, MUSC.

029-B Self-reported Pain Vs Discomfort Levels in Emergency Room Patients with Chest or Abdominal Pain, Joshua Shaffer¹, Shilpa Sreedharan¹, Trinh Chu¹, Steven Saef²; ¹Medicine, MUSC, ²Emergency Medicine, MUSC.

030-B Case Study of a Small Bowel Angiodysplasia Via Computer Tomography, Ian C Miller¹, Meryle Eklund²; ¹College of Medicine, MUSC, ²Radiology, MUSC.

031-B The Esophageal Sweep: Inter-observer Variability, Accuracy, and Utility of Inclusion of Limited Upright Single Contrast Esophagram As Part of Modified Barium Swallow Studies, Brenton G Davis¹, Douglas H Sheafor²; ¹Medicine, MUSC, ²Radiology, MUSC.

032-B Surgical Skills in Video Recordings of ENT Procedures, Ryan Metts¹, Ted Meyer², Heather Schopper²; ¹College of Medicine, MUSC, ²Otolaryngology, MUSC.

Session 4: Clinical / Professional / Masters III

033-B A Fatal Case of Necrotizing Pancreatitis in Sickle Beta Thalassemia Zero, Taylor L Turnbull¹, Peter Houston², Nicholas Batalis²; ¹College of Medicine, MUSC, ²Pathology, MUSC.
034-B Alcohol Septal Ablation (ASA) Produces Similar Changes to CBC As Atherosclerotic Myocardial Infarction (MI) But Platelet Counts Are Not Elevated. Is There Less Inflammation With ASA?, Billy J Mullinax¹, Patel Mira¹, Canova Alex², Waring Ashley³, Nielsen Christopher⁴, Fernandes Valerian⁵; ¹Medicine, MUSC, ²MUSC, ³Ralph H. Johnson VA Medical Center.

035-B Infantile Scimitar Syndrome Leading to Surgical Repair, Michael N Melson¹, Merle Eklund²; ¹COM, MUSC, ²Pediatric Radiology, MUSC.

036-B Superiority of Remnant Clostridium Difficile Diarrhea Specimens in Detecting Carbapenem-Resistant Enterobacteriaceae (CRE) Colonization in a Tertiary Care Hospital with Low Endemicity, Fadyah Albalawi, Lisa L Steed, Michael G Schmidt; Microbiology & Immunology, MUSC.

037-B Determining the Role of Dicer1e Regulation of MiR-548k Levels in Oral Cancer Pathogenesis, Austin A Hughes, Lourdes Andino, Tessa Streeter, Andrew Jakymiw; Oral Health Sciences, MUSC.

038-B High Frequency RTMS in Adults with Autism Spectrum Disorder and Depression: A Pilot Study, Hussam Alsarraf¹, Melanie G Wiley², Danielle Lowe³, Erin A Henneberry³, Philipp Summers³, Gregory Sahlem³, Mark George³, McLeod F Gwynette³; ¹COM, MUSC, ²Radiology, MUSC, ³Orthopaedics, Stanford University, ⁴Orthopaedics, MUSC.

039-B MRI Utilization By Orthopaedic and Non-orthopaedic Providers for Acute or Chronic Ankle Pain, Elizabeth C Durante¹, Russel Chapin², Ariel Palanca³, David Hocking¹, Julia Hermann¹, Christopher Gross⁴; ¹College of Medicine, MUSC, ²Radiology, MUSC, ³Orthopaedics, Stanford University, ⁴Orthopaedics, MUSC.

040-B Examining The Relationship Between Upper Extremity Movement Impairment, Functional Ability, and Perceived Difficulty Of Everyday Activities In Stroke Survivors, Kathryn M McCarty¹, Rebecca J Baltenberger¹, Michaela J Cornforth¹, Laura M Winters¹, Michelle L Woodbury²; ¹Occupational Therapy, MUSC, ²Health Sciences and Research, MUSC.

041-B When Worlds Collide: Th17 Cells in Cancer Immunotherapy and Autoimmunity, Sierra Amaya¹, Stefanie Bailey¹, Hannah Knochelmann², Dirk Elston¹, Joni Mazza-McCrann¹, Chrystal Paulos¹; ¹Microbiology and Immunology, MUSC, ²Medicine, MUSC.

042-B The Impact of Early Neuroimaging and Developmental Assessment in a Preterm Infant Diagnosed with Cerebral Palsy, Lily Gullion¹, Jennifer Stansell¹, Katy Hallman², Hunter Moss², Patty Coker-Bolt¹, Dorothea Jenkins²; ¹Occupational Therapy, MUSC, ²Medicine, MUSC.

043-B Perturbing Emotion Neurocircuits: A Concurrent TMS-fMRI Investigation, Oliver J Mithoefer¹, James W Lopez², Logan T Dowdle¹, Bashar W Badran¹, Philipp M Summers¹, Mark S George¹, Lisa M McTeague¹; ¹Psychiatry & Behavioral Sciences, MUSC, ²Psychology, CoF.C.

044-B Monte Carlo Analysis of Aztreonam-avibactam and Ceftazidime-avibactam Against Wild-type and Carbapenem-resistant Gram-negative Pathogens, Aaron T Smith, Roger L White; MUSC College of Pharmacy.

045-B Monte Carlo Analysis of Plazomicin in a Representative Tertiary Care Inpatient Population, Sahand Askarian¹, Roger L White²; ¹SCCP, MUSC, ²Clinical Pharmacy and Outcome Sciences, MUSC.
Session 5: PhD I: Years 1-2

047-B The Rational Design of Peptidomimetic Inhibitors of PD-1, Thomas Z Benton, Pieter Burger; Drug Discovery, MUSC, Pharmacy, MUSC.

048-B Chemogenetic Inhibition of Prelimbic Cortical Pyramidal Neurons Blocks BDNF-mediated Attenuation of Cocaine-seeking, Giuseppe Giannotti, Sarah M Barry, Ben M Siemsen, Jacqueline F McGinty; Neuroscience, MUSC.

049-B N-Linked Glycan Imaging By MALDI FT-ICR for Early Biomarker Detection in Hepatocellular Carcinoma, Connor A West, Harmin Herrera, Yuko Kono, Peggi M Angel, Richard R Drake; Pharmacology, MUSC, Medicine, University of California San Diego.

050-B The Role of a Host Adenosine-generating Ectoenzyme CD73 in Modulating Porphyromonas Gingivalis Survival and Growth in the Oral Epithelium, Jaden S Lee, Nityananda Chowdhury, JoAnn S Roberts, Zachary Messick, Ozlem Yilmaz; Oral Health Sciences, MUSC.

051-B Behavioral Testing in a Murine Maternal Immune Activation Model of Neurodevelopmental Disorders, Catherine Svetcharnik, Adam Harrington; MSTP, MUSC, Neuroscience, MUSC.

052-B Understanding Hospice Family Preferences and Needs Related to Time of Death Visits, Kathy S Katzenberger, Michelle Nichols; Nursing, MUSC.

053-B Regulation of Cue-induced THC Seeking in the Nucleus Accumbens, Vivian C Chioma, Peter W Kalivas; Neurosciences, MUSC.

Session 6: PhD II: Years 3+

055-B The Role of Transcription Factors in Sinoatrial Node Differentiation, Yunkal Dai, Kemar Brown; Bioengineering, Clemson, Mount Sinai College of Medicine, Columbia University.

056-B The Role of ADAMTS5-mediated Aggrecan Turnover in the Development of the Mandibular Condyle in the Temporomandibular Joint, Alexandra W Rogers, Sarah E Cisewski, David L Billings, Christine B Kern; Regenerative Medicine and Cell Biology, MUSC.

057-B Delivery of Therapeutic Doxorubicin Dose Across the Canine Blood-brain Barrier with Hyperthermia and Temperature-sensitive Liposomes, Anjan Motamarry, Amy-Lee Bredlau, Chao Chen, Ann M McCracken, Kris Helke, Ann-Marie Broome, Dieter Haemmerich; Pediatrics, MUSC, Regeneron Pharmaceuticals, Pharmacology, MUSC, Comparative Medicine, MUSC.

058-B Relationship Power Imbalance and History of Partner HIV Testing Among Pregnant Women in Uganda, Caroline J Vrana, Jeffrey Korte, Angela Malek, Esther Buregyeya, Joseph Matovu, Harriet Chemusto, William Musoke, Rhoda Wanyenze; Public Health Sciences, MUSC, School of Public Health, Makerere University, Mildmay Uganda.

059-B Maternal Cardiometabolic Determinants of Breastfeeding Noninitiation in South Carolina By Maternal Race and Ethnicity, Danielle R Stevens, Kelly Hunt; Public Health Sciences, MUSC.
Inhibition of the Central Amygdala Selectively Decreases Alcohol Consumption in Mice with a History of Stress and Alcohol Dependence, Harold L Haun\textsuperscript{1}, William C Griffin\textsuperscript{2}, Marcelo F Lopez\textsuperscript{2}, Howard C Becker\textsuperscript{3}; \textsuperscript{1}Neuroscience, MUSC, \textsuperscript{2}Psychiatry, MUSC, \textsuperscript{3}Ralph H. Johnson VA Medical Center.

A Theory of Mental Imagery, Jesse Breedlove\textsuperscript{1}, Ghislain St-Yves\textsuperscript{1}, Cheryl Olman\textsuperscript{2}, Thomas Naselaris\textsuperscript{1}; \textsuperscript{1}Neurosciences, MUSC, \textsuperscript{2}Psychology, Univ. Minnesota.
063-B Intracellular Calcium Stores in the Prelimbic Cortex Regulate Drug Related Behaviors, Paul Culver, Carrie Bailes, Bethany Pavlinchak, Jeffrey Parrilla-Carrero, William Butcha, Arthur Riegel; Neuroscience, MUSC.

064-B Inhibition of Protein Synthesis in Adoptively Transferred T Cells Promotes Complete Tumor Response, Katie E Hurst, Kiley A Lawrence, Lee R Leddy, Jessica E Thaxton; Orthopaedics, MUSC.

065-B Patient-derived Xenograft Model to Advance Rectal Cancer Personalized Therapy, Scott A Becker¹, Yun Zhu¹, Cindy Wang², Katie E Hurst¹, Brenda J Hoffman², Elizabeth G Hill³, Victoria J Findlay⁴, Ramsey Camp¹; ¹Surgery, MUSC, ²Medicine, MUSC, ³Public Health Sciences, MUSC, ⁴Pathology, MUSC.

066-B Hypovitaminosis D and Risk Factors in Pregnant Women and Their Newborns in the Middle East: a Systematic Review, Shayesteh Hajizadeh, Judy R Shary, Susan Reed, Carol L Wagner; Children’s Hospital, MUSC.

067-B IL-15 Superagonist and Anti-PD-1 Monoclonal Antibody Combination Therapy Leads to Enhanced CD8+ T Cell Functionality, Luis E Cardenas¹, Marzena Swiderska-syn¹, Samantha Suriano¹, Kristina Andrijauskaite¹, Caroline Martin¹, John Wrangle², Mark Rubinstein¹; ¹Surgery, MUSC, ²Medicine, MUSC.

068-B S1P Secretion By Hematopoietic Stem Cell-Derived Osteoblasts Enhances Osteosarcoma Progression, Uday K Baliga¹, Inhong Kang¹, Shikar Mehrotra², Ogretmen Besim³, Meenal Mehrotra¹; ¹Pathology, MUSC, ²Surgery, MUSC, ³Biochemistry, MUSC.

069-B Determining the Role of CD26 in T Cell-Based Cancer Immunotherapy, Megan M Wyatt, Stefanie R Bailey, Michelle H Nelson, Chrystal M Paulos; Microbiology and Immunology, MUSC.

070-B Lifestyle Associated Metabolites Drive Neuroendocrine Differentiation in Prostate Cancer, Lourdes M Nogueira⁵, Sean Cosh⁶, Michael B Lilly³, David P Turner¹, Victoria J Findlay¹; ¹Pathology, MUSC, ²Biology, Clemson, ³Medicine, MUSC.
## Oral Presentations:

### Session 11: Undergraduate II  
**EL 113**

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<tr>
<td>12:30 – 12:45</td>
<td><strong>084</strong> Investigation Into Serotonylation of Extracellular Matrix Proteins in Periodontal Disease</td>
<td>Nicolas G Shealy¹, Amy D Bradshaw²; ¹Biology, CofC, ²Gazes Cardiac Research Institute, MUSC.</td>
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<td>12:45 – 1:00</td>
<td><strong>085</strong> CD8+ T Cells Mediate Immune Response to Combination Therapy with IL-15/IL-15Ralpha Complexes and Anti-PD-1 MAb</td>
<td>Caroline S Mart, Marzena Swiderska-syn, Samantha Suriano, Luis Cardenas, Kristina Andrijauskaite, John Wrangle, Mark Rubinstein; Surgery, MUSC.</td>
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<td>1:00 – 1:15</td>
<td><strong>086</strong> Effect of Scent-Paired Restraint Stress on Heroin Reinstatement and Corticosterone Levels</td>
<td>Jordan S Carter¹, Rachel A Weber², Carmela M Reichel²; ¹Biology, CofC, ²Neuroscience, MUSC.</td>
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### Session 12: Clinical / Professional / Masters IV  
**EL 109**

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<tr>
<td>12:00 – 12:15</td>
<td><strong>090</strong> Identifying the Role of Complement in Triggering Neuroinflammation After Traumatic Brain Injury</td>
<td>Farris Langley¹, Ali Alawieh¹, Shannon Weber¹, DeAnna Adkins², Stephen Tomlinson³; ¹Medical Scientist Training Program, MUSC ²Neurosciences, MUSC ³Microbiology and Immunology, MUSC.</td>
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<tr>
<td>12:15 – 12:30</td>
<td><strong>091</strong> Gut Flora Metabolites Modulate Autoimmune Inflammation in the Central Nervous System</td>
<td>Davis M Borucki¹, Veit J Rothhammer², Isabel M Garcia Sanchez³, Guillermo Izquierdo⁴, Howard L Weiner⁵, Francisco J</td>
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12:30 - 12:45
092 The Impact of Advanced Glycation End Products (AGES) to Prostate Cancer Disparity, Narges Anbardar, Danzell Smith, Dion Foster, Lourdes Nogueira, Laura Spruill, Thomas Keane, Steve Savage, Victoria J Findlay, David P Turne
MUSC.

12:45 - 1:00
093 The Role of Ccdc117 in Modulating the Formation of Exosomes Via Hsp40, Timothy Jiang, Kyu-Ho Lee, Pamela Riggs-Gelasco; Pediatrics, MUSC.

1:00 - 1:15
094 Exploring the Role of MiRNA-204 in Low Milk Supply, Clare E Burton, Jerrica Walden, Martina Mueller, David P Turner, Sarah N Taylor, Victoria J Findlay; Pathology, MUSC, Biology, USC, Nursing, MUSC, Pediatrics, MUSC.

1:15 - 1:30
095 The Identification of Leukocyte Populations in the Synovial Fluid of Patients with Osteoarthritis, Thomas A Valente, Kiley Lawrence, Matthew Essman, Katie Hurst, Vincent Pellegrini Jr, Jessica Thaxton; COM, MUSC, Orthopedics, MUSC, Microbiology & Immunology, MUSC.

1:30 – 1:45 BREAK

1:45 - 2:00
096 Roles of an Nkx2-5 Target Gene in the Developing Placenta, Balakrishnan Pillai, Kyu-Ho Lee; Pediatrics, MUSC.

2:00 - 2:15
097 Regulation of the TGF-Beta Pathway During Thoracic Aortic Aneurysm (TAA) Development, Megan G Gross, Robert E Stroud, Elizabeth K Nadeau, Mukherjee Rupak, Jeffrey A Jones; College of Medicine, MUSC, Cardiothoracic Surgery, MUSC, Ralph H. Johnson VA.

2:15 - 2:30
098 Modification of Temozolomide to Improve Therapeutic Efficacy in Glioblastoma Cells, John H Rainwater, Daniela Ramos Mendoza, Yu Lin Jiang, Ann-Marie Broome; College of Medicine, MUSC, South Carolina Governor's School for Science and Mathematics, Cell and Molecular Pharmacology & Experimental Therapeutics, MUSC.

2:30 - 2:45
099 Preoperative Smoking Cessation As a Durable Form of Long-term Smoking Cessation, Jacob C Balmer, Ashley B Anderson, William R Barfield, Harry A Demos; COM, MUSC, Walter Reed Medical Center, Orthopaedic Surgery, MUSC.

2:45 - 3:00
100 The Use of Complementary and Alternative Medicine (CAM) Among Black/African-American Patients Managing Diabetic Foot Ulcers, April Stubbs, Theresa Kelechi; Medicine, MUSC, Nursing, MUSC.
12:00 - 12:15

101 Comparing Post-Operative Wound Complication Rates for Neoadjuvant Interdigitated Chemoradiation Versus Neoadjuvant Radiation Alone, Jonathan Pire¹, Stephanie Terezakis², Adam Levin¹, Chengcheng Gui⁴, Carol Morris¹; ¹College of Medicine, MUSC, ²Radiation Oncology, Johns Hopkins University School of Medicine, ³Orthopedic Surgery, Johns Hopkins University School of Medicine, ⁴School of Medicine, Johns Hopkins University

12:15 - 12:30

102 Does the Integrity of Specific White Matter Tracts Relate to Early and Late Motor Performance in Preterm Neonates?, Sybil K Hallman¹, Danielle Lowe¹, Hunter Moss², Patty Coker-Bolt³, Dorothea Jenkins⁴; ¹College of Medicine, MUSC, ²Occupational Therapy, MUSC, ³Biomedical Imaging, MUSC, ⁴Pediatrics, MUSC.

12:30 - 12:45

103 Predictors of Disclosure in the Forensic Interview in Pediatric Abuse and Maltreatment Cases, Trevor Morris¹, John D Melville³, Kathy Quinones³, Carole C Swiecicki³; ¹College of Medicine, MUSC, ²Pediatrics, MUSC, ³Dee Norton Child Advocacy Center.

12:45 - 1:00

104 A Tailored Tube-Voltage Adapted Contrast Media Injection Protocol for Coronary CT Angiography, Hubert E Smith, Philipp von Knebel Doeberitz, Domenico De Santis, Damiano Caruso, Carlo N De Cecco, Akos Varga-Szemes, Moritz H Albrecht, Joseph U Schoepf; Radiology, MUSC.

1:00 - 1:15

105 Treatment of Early Onset Scoliosis and Its Emotional Effects on Patients and Their Families: An EOSQ Analysis, Thomas L Offerle, James F Mooney, Murphy F Robert; Orthopaedics, MUSC.

1:15 - 1:30

106 The Effect of Shoulder Position on Capsular Measurements with Magnetic Resonance Arthrogram (MRA), Charles C White¹, Meghana Rao², Alyssa Greenhouse², Harris S Sloane⁶, Richard J Friedman⁷, Josef K Eichinger²; ¹COM, MUSC, ²Orthopaedics, MUSC.

1:30 – 1:45 BREAK

1:45 - 2:00

107 Cross-Sectional Analysis of Anterior Cruciate Ligament Injury in Elite Soccer Players in the Top Five European Leagues, Alexandra M Moreira¹, Jonathan Bernard², Zhara Ismaeil⁶, Timothy Johnson⁷, David Johnson⁸; ¹MUSC, ²National Sports Medicine Institute; Lansdowne, VA.

2:00 - 2:15

108 The Need for Emergency Department Based Primary Care: A Study of the Factors Leading to Patient Perception of the Emergency Department to Be Their Medical Home, Cameron J Weekley¹, Steven Saef², Sarah Katchem¹; ¹COM, MUSC, ²Emergency Department, MUSC.

2:15 - 2:30

109 Optimizing Nutrition in Neonates with Kidney Disease, Joycelyn C Hardy, Katherine E Twombley, Sarah N Taylor, Carolyn W Finch; Pediatrics, MUSC.
2:30 - 2:45

110 **Comparison of the Pharmacodynamic Profiles of Delafoxacin and Levofloxacin Using Monte Carlo Analysis**, Mohammed Aldhaeefi, White Roger; Pharmacy, MUSC.

2:45 - 3:00

111 **Stakeholder Perspectives on Cervical Cancer Prevention From a Community Near Kolkata, India**, Shannon McGue¹, Suparna PhD Qanungo², Kathleen PhD Cartmell; ¹Medicine, MUSC, ²Nursing, MUSC.

**Session 14: Clinical / Professional / Masters VI**

12:15 - 12:30

112 **Incidence and Risk Factors for Deep Vein Thrombosis Following Isolated Acute Traumatic Extensor Mechanism Injury**, Alyssa Althoff¹, Vincent Pellegrini², Harris Stone², Daniel Stone¹, Walker Heffron¹; ¹College of Medicine, MUSC, ²Orthopedics, MUSC.

12:30 - 12:45

113 **Interactions of Fork Barrier Protein Fob1 with Subunits of the MCM2-7 Helicase and Their Biological Significance**, Chris J Danielson, Deepak Bastia; Biochemistry and Molecular Biology, MUSC.

12:45 - 1:00

114 **Using Complement Modulation to Dampen Microglial Activity After Stroke and Enhance Neuronal Recovery and Regeneration**, Ali Alawieh, E Farri Langley, Stephen Tomlinson; Microbiology and Immunology, MUSC.

1:00 – 1:15 BREAK (Abstract 117 Withdrawn)

1:15 - 1:30

115 **Clinical Indicators of Admission for Pediatric Cochlear Implant Procedures**, Terral A Patel¹, Shaun Nguyen², David White²; ¹College of Medicine, MUSC, ²Otolaryngology, MUSC.

1:30 - 1:45

116 **Targeted Gene Expression in Mice and Placental Tissue**, Oyinda D Awe¹, Kyu-Ho Lee²; ¹COM, MUSC, ²Pediatric Cardiology, MUSC.

1:45 - 2:00

118 **Appropriate Screening for Urologic Complications After Spinal Cord Injury in a Non-Designated SCI Center Veterans Affairs Hospital**, Rohail Rashid Kazi, Alyssa Greiman, Lindsey Cox; Urology, MUSC.
Session 15: PhD IV: Years 1-2

12:15 - 12:30
119 The Adherens Junctions Suppress Pro-tumorigenic Colon Cell Transformation Via Long Non-coding RNAs, Mary C Bridges, Joyce U Nair-Menon, Antonis Kourtidis; Regenerative Medicine and Cell Biology, MUSC.

12:30 - 12:45
120 TLR9 Agonist Expands CD8+ T Cells with Robust Anti-melanoma Activity, Aubrey Smith, Michelle Nelson, Marshall Diven, Chrystal Paulos; Microbiology and Immunology, MUSC.

12:45 - 1:00
121 How Do Patients Perceive the Character of Care They Receive For Ambulatory Care-Sensitive Conditions in the Emergency Department?, Virginia B Shipes¹, Sarah Katchen², Steven Saeft³, Renee Martin¹; ¹Public Health Science, MUSC, ²Medicine, MUSC, ³Emergency Medicine, MUSC.

1:00 - 1:15
122 Identification of Polo-like Kinase and Retinoic Acid Receptor Pathways As Therapeutic Targets in Malignant Peripheral Nerve Sheath Tumors., Ralph Tanios¹, Amanda Prechtl¹, Stephen Guest¹, Elizabeth Garrett-Mayer², Steven Carroll¹; ¹Pathology, MUSC, ²Public Health Science, MUSC.

1:15 – 1:30 BREAK

1:30 - 1:45
123 The Role of Lysyl Oxidase in Systemic Sclerosis-Associated Lung Fibrosis, Xinh-Xinh M Nguyen¹, Tetsuya Nishimoto¹, Logan Mlakar¹, Ellen Riemer², Jonathan Heywood¹, Amy Bradshaw¹, Carol Feghali-Bostwick¹; ¹Medicine, MUSC, ²Pathology, MUSC.

1:45 - 2:00
124 Shorter Ex Vivo Expansion of Th17 Cells Mediates Potent Anti-tumor Regression in Melanoma, Hannah M Knochelmann, Michelle H Nelson, Jacob S Bowers, Daniel J Neitzke, Megan M Wyatt, Aubrey S Smith, Daniel J Salas-Escabillas, Chrystal M Paulos; Microbiology and Immunology, MUSC.

2:00 - 2:15
125 Mechanisms Underlying Sex Discrepancy in Bladder Cancer Outcome, Hyunwoo Kwon¹, Ching Ying Lin¹, Guillermo Rangel Rivera¹, Satoshi Kaneko², Caroline Wallace¹, Mohammad Salem¹, Xue Li², Zhai Li¹; ¹Microbiology and Immunology, MUSC, ²Urology and Pathology, Boston Children's Hospital.

Session 16: PhD V: Years 3+

12:00 - 12:15
126 First Trimester Prediction of Pre-eclampsia in Women with Type 1 Diabetes, Clare B Kelly¹, Michelle B Hookham¹, Jeremy Y Yu¹, Mei Du³, Alicia J Jenkins¹, Samar M Hammah⁴, James A Scardo⁵, Timothy J Lyons¹; ¹Endocrinology, MUSC, ²Clinical Biochemistry, Royal Victoria Hospital, Belfast, N. Ireland., ³Endocrinology, University of Oklahoma Health Sciences Center, ⁴Regenerative Medicine and Cell Biology, MUSC, ⁵Spartanburg Regional Hospital.
12:15 - 12:30
127 Does PKC Mediate the High Risk of Preeclampsia in Pregnant Women with Diabetes?, Rebecca P Chow¹, Jiawu Zhao², Tim M Curtis², Timothy J Lyons¹, Jeremy Y Yu¹; ¹Endocrinology and Diabetes, MUSC, ²Centre for Experimental Medicine, Queen's University of Belfast, UK.

12:30 - 12:45
128 Opportunistic Pathogen P. Gingivalis Modulates Danger Signal ATP-Mediated Antibacterial NOX2 Pathways for Successful Survival in Primary Epithelial Cells, JoAnn S Roberts¹, Kalina R Atanasova², Nityananda Chowdhury¹, Chul Hee Choi³, Ozlem Yilmaz¹; ¹Oral Health Sciences, MUSC, ²Periodontology, University of Florida, ³Microbiology and Medical Science, Chungnam National University.

12:45 - 1:00
129 Label-free and Nondestructive Method for Cell Viability Assessment in Tissue with Two-photon Fluorescence Microscopy, Yang Li¹, Neal Saini², Xun Chen¹, Tong Ye¹; ¹Clemson-MUSC Bioengineering Program, ²COM, MUSC.

1:00 - 1:15
130 Exploring the Geography of Pediatric Asthma Using Emergency Department Visits in South Carolina, Matthew Bozigar¹, Kathryn Cristaldi², John Pearce³; ¹Public Health Sciences, MUSC, ²Pediatrics and Telehealth, MUSC.

1:15 – 1:30 BREAK

1:30 - 1:45
132 Single Cell Genomic Profiling of Human B Cells Responsible for Immune Response Against Pneumococcal Polysaccharides in Aging Healthy and HIV-positive Individuals, Myra Happe, Samuvel Devadoss, Julie Westerink; Immunology and Microbiology, MUSC.

1:45 - 2:00
133 Lower Axon Density in Residual Temporal White Matter is Related to Semantic Paraphasia Prevalence, Emilie T McKinnon¹, Jens H Jensen², Julius Fridriksson³, Chris Rorden⁴, Joseph A Helpern², Vittoria Spampinato⁵, Leonardo Bonilha¹; Neurology, MUSC, ¹Neuroscience, MUSC, ³Communication Sciences and Disorders, USC, ⁴Psychology, USC, ⁵Radiology, MUSC.

2:00 - 2:15
134 Physical Activity, Cardiovascular Risk Factors and Brain Health: Impact on Long Range Mono-synaptic Connections, Modular Organization of Cortical Regions, and Verbal Fluency, Barbara K Marebwa¹, Robert J Adams¹, Gayenell S. Magwood², Leonardo Bonilha¹; ¹Neurology, MUSC, ²Nursing, MUSC.

2:15 - 2:30
135 Three Dimensional Molecular Diffusion Measurement in Collagenous Tissue with FRAP, Peng Chen¹, Xun Chen¹, Richard G Hepfer¹, Ye Tong¹, Hai Yao²; ¹Clemson-MUSC Bioengineering Program, CU, ²Oral Health Sciences, MUSC.

2:30 - 2:45
131 CRISPR-Cas9 Targeting of 16q12.1 Breast Cancer Susceptibility Locus to Generate Allelic Series of Rat Mutants Results in Altered Tox3 Expression, Lauren B Shunkwiler¹, Royal Pipaliya², Cody C Ashy², Benjamin Van Peel¹, Jan Guz³, Michael J Kern¹, Yang Zhao¹, Bart MG Smits¹; ¹Pathology, MUSC, ²Biology, CofC, ³Regenerative Medicine, MUSC.
12:00 - 12:15
136 Multivariate Air Pollutant Exposure Prediction in South Carolina, Ray Boaz, Andrew Lawson, John Pearce; Public Health Sciences, MUSC.

12:15 - 12:30
137 Kallistatin Attenuates Endothelial Senescence By Inhibiting Oxidative Stress and Inflammation, and Stimulating Let-7g-Induced SIRT1-eNOS Pathway, Youming Guo, Lee Chao, Julie Chao; Biochemistry and Molecular Biology, MUSC.

12:30 - 12:45
138 Use of KDM4B Inhibitors to Target Periodontal Disease Progression, Joy Kirkpatrick¹, Jonathan Turner², Rachel Wilkinson³, Bethany Herbert⁴, Keith Kirkwood⁵, Patrick Woster¹; ¹Drug Discovery and Biomedical Sciences, MUSC, ²Biochemistry, MUSC, ³GSSM, ⁴Oral Health Sciences, MUSC, ⁵Oral Biology, University at Buffalo.

12:45 - 1:00
139 Evaluating 2 RTMS Strategies for Pain Reduction in Controls and Individuals with Non-Medical Prescription Opiate Use, Logan T Dowdle, Sarah E Hamilton, Jeffrey J Borckardt, Sudie E Back, Colleen A Hanlon; Psychiatry and Behavioral Sciences, MUSC.

1:00 - 1:15
140 Practical Elicitation and Implementation of Toxicity Scores to Represent Patient Toxicity Burden in Cancer Clinical Trials, Nathaniel S O’Connell, Elizabeth Garrett-Mayer, Andrew Lawson; Public Health Sciences, MUSC.

1:15 – 1:30 BREAK

1:30 - 1:45
141 Development of Novel Penicillin Binding Protein 2 (PBP2) Inhibitors As Drug Candidates for Penicillin- and Cephalosporin-resistant Neisseria Gonorrhoeae, Jonathan M Turner¹, Patrick M Woster², Christopher Davies¹; ¹Biochemistry and Molecular Biology, MUSC, ²Drug Discovery and Biomedical Sciences, MUSC.

1:45 - 2:00
142 The Impact of Mitochondrial Fusion/Fission on Endothelial Cell Immunogenicity, Danh T Tran¹, Scott Esckilsen², Carl Atkinson¹, Satish N Nadig³; ¹Microbiology & Immunology, MUSC, ²College of Medicine, MUSC, ³Surgery, MUSC.

2:00 - 2:15
143 Anastomosis and Vascular Patterning of Scaffold-free, Prevascular Endothelial-fibroblast Constructs, Sanket Pattanaik, Chase Arbra, Heather Bainbridge, Sarah Grace Dennis, Jacob Brack, Stephen A Fann, Michael J Yost; General Surgery, MUSC.

2:15 - 2:30
144 Development and Characterization of a Novel Wound Dressing for the Treatment of Chronic Wounds, Sarah G Dennis, Heather Bainbridge, Sanket Pattanaik, Michael Yost; Surgery, MUSC.
**Assessment of NT108, a Vitamin K Analog, in the Recovery of Mitochondrial DNA Depletion Syndromes**, Tucker Williamson, James Chou, Sherine Chan; DDBS, MUSC.

**Session 18: PhD VII: Years 3+**

12:15 - 12:30

**Eukaryotic Initiation Factor 4E-Binding Protein (EIF4EBP1, 4EBP1, BP-1, 4E-BP1, and PHAS-I) is a Driver of Breast Cancer**, Alex C Rutkovsky, Stephen P Ethier; Pathology, MUSC.

12:30 - 12:45

**Identification of Circulating Murine CD34+OCN+ Cells**, Ryan R Kelly¹, McDonald T Lindsay², Vincent D Pellegrini³, James J Cray⁴, Amanda C LaRue⁵; ¹Pathology, MUSC, ²Ralph H. Johnson VAMC, ³Orthopaedics, MUSC, ⁴Oral Health Sciences, MUSC.

12:45 - 1:00

**CD26high T Cells Have a Natural Capacity to Migrate and Persist in Multiple Tumor Models**, Stefanie R Bailey, Michelle H Nelson, Megan M Wyatt, Jacob S Bowers, Lillian R Neal, Kinga Majchrzak, Chrystal M Paulos; Microbiology & Immunology, MUSC.

1:00 - 1:15

**Optogenetic Stimulation of Capillary Pericytes Reduces Cerebral Blood Flow in Vivo**, David A Hartmann, Andy Y Shih; Neuroscience, MUSC.

1:15 – 1:30 BREAK

1:30 - 1:45

**Inflammation in the Aging Mouse and Human Temporal Bone**, LaShardai N Brown¹, Ting Liu¹, Clarisse H Panganiban¹, Jeremy L Barth², Hainan Lang¹; ¹Pathology, MUSC, ²Regenerative Medicine, MUSC.

1:45 - 2:00

**Structural and Functional Analysis of an Essential Cell Cycle Regulator Reveals a Novel Mechanism of Action**, Katelyn M Williams, James H Atkison, Sabrina Salazar-Arango, Shuo Qie, J Alan Diehl, Shaun K Olsen; Biochemistry & Molecular Biology, MUSC.

2:00 - 2:15

**Propensity Score Matching for Multilevel Spatial Data: Accounting for Geographic Confounding in Health Disparity Studies**, Melanie L Davis¹, Brian Neelon¹, Paul Nietert¹, Kelly Hunt¹, Lane Burgette², Andrew Lawson¹, Leonard Egede³; ¹Public Health Sciences, MUSC, ²Rand Corporation, ³Internal Medicine, Medical College of Wisconsin.

2:15 - 2:30

**The Role of FABP7 Upregulation in ALS Models**, Kelby Killoy, Ben Harlan, Mariana Pehar, Marcelo Vargas; Pharmacology, MUSC.
12:00 - 12:15
154 **MiR-146a Is An Endogenous Regulator Of Both Hematopoiesis And Bone Mass**, Blake E Hildreth¹, Jennifer A Geisler², James Lee³, Albert de la Chapelle⁴, Prosper N Boyaka², Adam C Soloff⁵, Michael C Ostrowski¹, Sudarshana M Sharma¹;¹Biochemistry and Molecular Biology, MUSC, ²College of Veterinary Medicine, Ohio State University, ³Cancer Biology and Genetics, Ohio State University, ⁴Molecular Virology, Immunology & Medical Genetics, Ohio State University, ⁵Microbiology and Immunology, MUSC.

12:15 - 12:30
155 **School Racial Factors in Teacher Zero-Tolerance Policy Endorsement: Links to Student Perceived Climate and Internalizing Symptoms**, Katherine A Perkins¹, Charity Brown Griffin², Joni D Splett³, Mark D Weist⁴, Colleen A Halliday-Boykins⁵;¹Psychiatry, MUSC, ²Psychology, Winston-Salem State University, ³Education, University of Florida, ⁴Psychology, USC, ⁵MUSC.

12:30 - 12:45
156 **Sexual Dimorphisms of the Human Temporomandibular Disc: A Potential Mechano-Electro-Chemical Etiology for the Increased Prevalence of Temporomandibular Joint Disorders in Women**, Matthew C Coombs¹, Gregory J Wright², Xingju Nie³, Thierry H Bacro⁴, Michael K Lecholop⁵, Elizabeth H Slate⁶, Michael J Kern⁷, Hai Yao⁸;¹Oral Health Science, MUSC, ²Bioengineering, Clemson, ³Biomedical Imaging, MUSC, ⁴Anatomical Studies and Education, MUSC, ⁵Oral and Maxillofacial Surgery, MUSC, ⁶Statistics, Florida State University, ⁷Regenerative Medicine and Cell Biology, MUSC.

12:45 - 1:00
157 **Molecular Chaperone is Required for Gut Tolerogenic Dendritic Cell Development and Function**, Stephen Iwanowycz, Yi Yang, Zihai Li, Bei Liu; Microbiology and Immunology, MUSC.

1:00 - 1:15
158 **Viral-mediated Rescue of Arc/Arg3.1 knock-out Demonstrates a Requirement for Function in the NAc in Regulating Mood and Drug-related Behaviors.**, Rachel D Penrod¹, Laura N Smith², Jaswinder Kumar³, Brandon Hughes¹, Gabriella Barry⁴, Daniel Wood⁵, Makoto Taniguchi¹, Christopher Cowan¹;¹Neuroscience, MUSC, ²Psychiatry, McLean Hospital, ³Neuroscience, College of Charleston, ⁴MSTP, MUSC.

1:15 – 1:30 BREAK

1:30 - 1:45
159 **Endothelial Progenitor Cell Exosomes Are Beneficial in Murine Model of Sepsis**, Yue Zhou¹, Pengfei Li¹, Andrew J Goodwin², James A Cook³, Perry V Halushka⁴, Hongkuan Fan¹;¹Pathology and Lab Medicine, MUSC, ²Pulmonary, Critical Care, Allergy and Sleep Medicine, MUSC, ³Neurosciences, MUSC, ⁴Medicine and Pharmacology, MUSC.

1:45 - 2:00
160 **Antibiotic-Disruption of Gut-Microbiota Dysregulates Osteoimmune Crosstalk in Postpubertal Skeletal Development**, Jessica Hathaway-Schrader, Nicole Poulides, Heidi Steinkamp, Michael Chavez, Emily Huang, Lixia Zhang, Keith Kirkwood, Chad Novince; Oral Health Science, MUSC.

2:00 - 2:15
161 **Effects of Environmental Levels of EE2 on the Zebrafish Embryo: a Systems Level Analysis**, Ludivine Renaud¹, Bailey Glen², William da Silveira², Starr Hazard², Seok-Hyung Kim¹, Gary Hardiman¹;¹Medicine, MUSC, ²Center for Genomic Medicine Bioinformatics, MUSC.
2:15 - 2:30

**162 A Novel Myc-Zeb Regulatory Axis Promotes EMT By Co-Operatively Repressing E Cadherin**, Jasmine Kaur, Jennifer Isaacs; Pharmacology, MUSC.

2:30 - 2:45

**163 Application of Deacetylated-poly-N-acetyl Glucosamine (DEAC-pGlcNAc) Nanoparticles for the Delivery of MicroRNA MiR-126 for the Treatment of Cecal-igation Puncture (CLP) Induced Sepsis**, Joy N J Buie¹, Andrew Goodwin², James Cook³, John Vournakis⁴, Marina Demcheva⁴, Ann-Marie Broome⁵, Perry Halushka⁵, Hongkuan Fan⁶; ¹Neurology, MUSC, ²Pulmonary, Critical Care, Allergy and Sleep Medicine, MUSC, ³Neuroscience, MUSC, ⁴Marine Polymer Technologies, Inc, ⁵Cell and Molecular Pharmacology and Experimental Therapeutics, MUSC, ⁶Pathology and Laboratory Medicine, MUSC.

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**Session 20: Postdoc / Resident / Fellow / Staff Scientist III** EL 121

12:00 - 12:15

**164 S1P/PPARγ Axis Metabolically Reprograms the T Cells to Modulate Their Anti-Tumor Potential**, Paramita Chakraborty¹, Krishnamurthy Thyagarajan¹, Shilpak Chatterjee¹, Shanmugam Panneer Selvam¹, Mahvash Husain¹, Amir Al-Khami¹, Besim Ogretmen²; ¹Surgery, MUSC, ²Biochemistry and Molecular Biology, MUSC.

12:15 - 12:30

**165 Assessment of Brain Structural Changes in the Astronauts Using Magnetic Resonance Imaging**, Davud Asemani, Donna Roberts; MUSC.

12:30 - 12:45

**166 Transdiagnostic Effects of Ventromedial Prefrontal Cortex TMS on Drug Cue Reactivity: Sham-controlled Studies in Cocaine Users and Heavy Alcohol Users**, Tonisha E Kearney-Ramos, Logan T Dowdle, Mark S George, Raymond Anton, Colleen A Hanlon; Psychiatry and Behavioral Sciences.

12:45 - 1:00

**167 Testing a Novel Nanofiber Scaffold for Utility in Bone Tissue Regeneration**, R Nicole Howie¹, Emily Durham¹, Zach Grey¹, Braydon Oakes², Reed Houck², Amanda LaRue³, Martin Steed⁴, Robin Muise-Helmeriks⁵, James Cray¹; ¹Oral Health Sciences, MUSC, ²Dental Medicine, MUSC, ³Pathology and Laboratory Medicine, MUSC, ⁴Oral and Maxillofacial Surgery, MUSC, ⁵Regenerative Medicine, MUSC.

1:00 - 1:15

**168 Rising to the Challenge: Developing a Method to Measure and Adjust Challenge in Stroke Rehabilitation**, Kelly R Anderson¹, Deanna Adkins², Annie Simpson³, Jill Stewart⁴, Michelle Woodbury¹; ¹Health Science and Research, MUSC, ²Neuroscience, MUSC, ³Healthcare Leadership and Management, MUSC, ⁴Physical Therapy, USC.

1:15 – 1:30 BREAK

1:30 - 1:45

**169 Fli-1 Modulates Pericyte Loss in Murine Sepsis**, Pengfei Li¹, Yue Zhou¹, Andrew J Goodwin², James A Cook³, Perry V Halushka⁴, Xian K Zhang⁵, Lynn M Schnapp⁵, Hongkuan Fan¹; ¹Pathology and Lab Medicine, MUSC, ²Pulmonary, Critical Care, Allergy and Sleep Medicine, MUSC, ³Neurosciences, MUSC, ⁴Medicine and Department of Pharmacology, MUSC, ⁵Rheumatology and Immunology, MUSC.
1:45 - 2:00
170 Glycosphingolipid Catabolism Mediates Mesangial Cell IL-6 Production, Kamala Sundararaj, Jessalyn Rodgers, Tamara Nowling; MUSC.

2:00 - 2:15
171 Exosomes Derived From Retinal Pigment Epithelial Cells Mediate Cell-cell Communication Under Oxidative Stress Conditions in Age Related Macular Degeneration, Navjot Shah Saxena¹, Masaaki Ishii¹, Ablonczy Zsolt¹, Yutao Liu², James Chou³, Barbel Rohrer¹; ¹Ophthalmology, MUSC, ²Cellular Biology & Anatomy, Augusta University, ³Pharmacy, MUSC.

2:15 - 2:30
172 Targeting Sphingosine Kinase 2/S1P Axis Decreases Immunosuppressive Potential of Myeloid Derived Suppressor Cells (MDSCs) and Improves Tumor Control, Shilpak Chatterjee¹, Paramita Chakraborty¹, Selvam Panee Shanmugam², Besim Ogretmen², Shikhar Mehrotra¹; ¹Surgery, MUSC, ²Biochemistry and Molecular Biology, MUSC.
POSTER ABSTRACTS

001-A BMP-Notch Interaction in the Endocardial Lineage Plays an Essential Role for AV Endocardial Cushion Maturation and Remodeling. Miriam M Atteya, Patrick Smith, Thomas Trusk, Yukiko Sugi, College of Charleston, Honors College, Regenerative Medicine and Cell Biology, MUSC.

Valvuloseptal defects are among the most common and serious congenital heart defects (CHDs). In the atrioventricular (AV) canal, mesenchymalized AV endocardial cushions undergo distal outgrowth/elongation, maturation and remodeling into the membranous ventricular septum and striated AV valves. In our previous work we demonstrated that BMP2 expression in the endocardial lineage is required for AV endocardial cushion maturation and remodeling. In the present work we explored regulatory molecules that interact with BMP signaling in the endocardial cushions. Our data indicate that BMP2 ligands and receptors, as well as Notch 1 & 2, are expressed in the AV endocardial cushion and that BMP2 promotes expression of a Notch pathway effector, Hey1 in AV cushion mesenchymal cell (ECMC) cultures. These data lead us to hypothesize that BMP2 activates Notch signaling to coordinate BMP regulation of ECM differentiation into prevalvular fibroblasts during AV endocardial cushion maturation and remodeling. To test this hypothesis in an in vivo context, we investigate the effect of combining upregulated BMP signaling and downregulated Notch signaling in the endocardial lineage by using genetic activation of BMP signaling using conditionally activating Alk3 and disrupting the key Notch signaling transcription factor, RBPJ with an endocardial lineage specific cre-driver line, Nfatc1Cre. Resultant caAlk3; RBPJflox/+; Nfatc1Cre mice, which have combined up-regulation of smad-dependent BMP signaling and down-regulation of Notch signaling exhibit loss of normal stratification of mitral AV valves and up-regulation of Aggrecan in the mitral AV valves, indicating aberrant up-regulation of osteochondrogenic gene expression in 8 weeks old young adult mice. On the contrary, caAlk3; Nfatc1Cre mice do not exhibit valvular defects or aberrant up-regulation of osteochondrogenic gene expression in the valve. These data indicate that BMP-Notch interaction in the endocardial lineage plays essential roles in AV endocardial cushion maturation and remodeling into normal mitral AV valves. NIH/NIGMS P20 GM103499 DRP, AHA Grant-in-Aid, 15GRANT25710305

002-A The Relationship Between Quadriceps Strength and Size Following Anterior Cruciate Ligament Reconstruction. Kelli B Adams, Jennifer L Hunnicutt, Chris M Gregory, Michelle M McLeod, Harris S Slone, Health and Human Performance, CofC, Health Science and Research, MUSC, Orthopedics, MUSC.

Introduction: Anterior cruciate ligament (ACL) injuries are one of the most costly and debilitating knee joint conditions. Following ACL reconstruction (ACLR), individuals face several neuromuscular consequences in the quadriceps muscles that contribute to risk of re- injury and early-onset osteoarthritis. Quadriceps atrophy may play a significant role in strength deficits observed following ACLR. The purpose of this study is to describe the interlimb differences and relationships between quadriceps size and function. Methods: Individuals with history of primary, unilateral ACLR participated in this study consisting of muscle strength and imaging assessments. Peak knee extensor strength (Nm) was measured bilaterally with an isokinetic dynamometer. Maximal cross-sectional area (cm2) was measured bilaterally for each of the quadriceps muscles via magnetic resonance imaging. Between limb comparisons were made using paired samples t-tests. Relationships between variables were investigated with Pearson product-moment correlations. Results: Data from five individuals (24 years; 3 females; 8 mo. post-ACLR) is presented. The involved limb was significantly weaker (p=0.004) than the uninvolved limb. The involved limb also demonstrated significantly smaller vastus medialis (p=0.004), vastus intermedius (p=0.017), and rectus femoris (p=0.031) cross-sectional area. Muscle strength and size were strongly correlated in the involved limb (r=0.92). Conclusion: Based on the results, it is apparent that the cross-sectional area and strength are significantly lesser and strongly related in the reconstructed limb. These results are concerning because many individuals return to pre-surgery activity levels with lingering weakness and atrophy. Further work is needed to identify optimal treatment strategies aimed at addressing these deficits. MUSC TL1 TR001451; UL1 TR001450; NATA Foundation Award #1617DGP005


Microgravity (μXg) experienced by astronauts during space flights causes accelerated bone loss. However, the molecular basis of μXg induced bone loss in space is unclear. Osteoclast (OCL) is the primary bone-resorbing cell. We previously demonstrated that simulated μXg promotes OCL formation. In this study, we identified that μXg induces syncytin-A expression
in RAW264.7 preosteoclast cells without RANKL stimulation. We further tested the effect of osteotropic factors such as CXCL5 and 1,25(OH)2D3 to regulate the syncytin-A expression in preosteoclast cells subjected to μXg compared to ground based (Xg) cultures. CXCL5 increased syncytin-A expression under Xg. In contrast, μXg induced syncytin-A expression compared to Xg control in the absence of CXCL5. Furthermore, 1,25(OH)2D3 treatment did not affect syncytin-A expression in preosteoclast cultures in normal Xg. Interestingly, 1,25(OH)2D3 significantly increased syncytin-A expression in cells subjected to μXg. Confocal microscopy using Lyso-Tracker identified syncytin-A expression co-localized with lysosomes in preosteoclast cells. Acidine orange staining showed RANKL elevated autophagy activity in these cells. Further, siRNA suppression of syncytin-A significantly inhibits autophagy activity in RAW264.7 cells. In addition, knockdown of syncytin-A expression inhibits μXg increased OCL formation in mouse bone marrow cultures. Thus, our findings suggest that targeting syncytin-A expression may be an effective countermeasure to control bone loss under microgravity conditions. Palmetto Academy

004-A Mechanism of TGFβ-induced Cancer Stem Cell Formation Through ILEI and LIFR, Sean M Bloos¹, Annamarie C Dalton², Alec N Woosley², Philip Howe²; ¹Biochemistry, USC, ²MUSC.

Abstract not available.

005-A Tuning Micelle Composition to Improve Targeted Delivery of Chemotherapy to Brain Tumors, Stephen C Frederico, Suraj Dixit, Yu Lin Jiang, Ann-Marie Broome; Pharmacology, MUSC.

Therapeutic drug delivery across the blood-brain barrier (BBB) is not only inefficient, but also nonspecific. Nanoparticle composition plays a significant role in determining uptake efficiency and therapeutic efficacy. To understand the fundamental aspects of micelle assembly and dynamics, encapsulation efficiency, and therapeutic efficacy, micelle mixtures composed of different lipid constituents, namely PEG-PE-Amine, N-palmitoyl homocysteine (PHC, pH sensitive lipid breaks in endosome pH ~5.5) or D-α-tocopheryl polyethylene glycol succinate (TPGS), were investigated. Differences in the dependencies of the micelle size parameters (core radius and overall micelle radius) on the composition originated from the differing trends in aggregation number for the two micelle series. Conjugation of targeting moieties and contrast imaging agents was quantified using high-performance liquid chromatography. Preliminary cellular uptake studies via fluorescence imaging of glioblastoma cells treated with targeted and untargeted micellar particles demonstrate considerable uptake with PDGF-micellar PHC showing highest uptake as compared to PDGF-micellar TPGS. Our results show a strong correlation between the number of targeting monomers per micelle and the activity of uptake. In summary, the two micelle series showed similar uptake that was independent of the lipid structure or molecular weight yet significantly different dependencies of their aggregation number and size parameters.

006-A Factors That Predict Likelihood of Breastfeeding Among Women with Lupus, Priyanka K Fernandes, Jim C Oates, Gary S Gilkeson, Diane L Kamen; Medicine, MUSC.

BACKGROUND: Reasons for low rates of breastfeeding among women with systemic lupus erythematosus (SLE) are multifactorial, including medication contraindications and increased disease activity complicating pregnancy; despite the many health benefits of lactation for the mother and child. We evaluated factors affecting a woman’s decision to breastfeed and the association between breastfeeding and disease severity. METHODS: Data from 628 African American (AA) and Caucasian female patients with SLE from the MUSC lupus research registry were included. Patients were classified as “moms” (n=328), those with live births, and “never moms” (n=350). Among the moms, “breastfeeders” were defined as breastfeeding any of their children (n=86) and “non-breastfeeders” (n=242). Factors such as race, age, insurance status, education level and employment status were analyzed between these groups and SLICC Damage Index was used as a surrogate for SLE severity. RESULTS: AA women represented 77% in both the ‘never moms’ and ‘moms’ subgroup. Among 328 ‘moms’ there were 874 pregnancies with 733 live births. The “moms” group had an older age at SLE onset (34.66 vs. 27.85 years) compared to ‘never moms’ (P<0.005). Factors like high school graduation (85.33% vs. 89.77%), insured (92.78% vs. 94.04%), and employed (24.86% vs. 30.49%) were not significantly different between the ‘moms’ and ‘never moms’ subgroup. In the breastfeeding group (n=86) and non-breastfeeder group (n=242), AA were less likely to breastfeed (70.93% vs. 79.75%). Age of SLE onset (35.01 ± 12.74y vs. 14.55 ± 12.05y), high school graduation (88.89% vs. 90.09%), insurance status (95.06% vs. 93.67%), and employed status (36.05% vs. 28.51%) were not significantly different. The SLICC damage index (60% any damage, 40% high damage) was similar between breastfeeders and non-breastfeeders. CONCLUSION: Among women with SLE followed in the MUSC registry, AAs were less likely to breastfeed compared to Caucasians and education/insurance/employment status did not influence likelihood of pregnancy or breastfeeding.
Breastfeeding did not appear to impact disease damage, although the proportion of women breastfeeding was small.

007-A Varenicline and N-acetylcysteine: A Better Treatment for Nicotine Addiction? J. Jade D Doolittle¹, Lauren N. Beloate², Peter W Kalivas²; ¹CofC, ²Neurosciences, MUSC.

Varenicline tartrate (Chantix) is the most commonly used treatment for smoking cessation. However, relapse rates are as high as 50-60% three months after the attempt to quit with varenicline (VRN). Our lab has previously shown that N-acetylcysteine (NAC) prevents cocaine cue-induced reinstatement in rodents. Therefore, the hypothesis for the current study is that a mixture of VRN and NAC will more effectively block drug-seeking behavior. Adult male Sprague Dawley rats learned to self-administer nicotine for 10 2-hr sessions, in which the active lever press resulted in a nicotine infusion, tone, and light. The rats then remained in home cages for 10 days (abstinence) before being placed back into the chamber for a 30-min reinstatement session. Right lever presses resulted in cues, but no drug. Saline, VRN (0.3, 1, 3 mg/kg), NAC (10, 30 mg/kg) or VRN/NAC (1/10, 3/10, 3/30 mg/kg) mixture was administered on the last four days of abstinence and 2 hours prior to reinstatement. The VRN (3 mg/kg) + NAC (30 mg/kg) mixture significantly blocked active lever responding compared to the saline group. However, this effect is only due to the 30 mg/kg NAC, as none of the VRN doses alone blocked reinstatement. These results further support the role for NAC as a relapse prevention drug, not only for cocaine, but for nicotine as well. We hypothesize that VRN will instead be more effective when administered as the end of nicotine self-administration and beginning of operant extinction. Future studies include examining the neural mechanisms underlying the effects of NAC on reinstatement and VRN’s effects on nicotine self-administration and extinction. These studies are important for furthering our understanding of nicotine addiction and leading to the creation of a drug that is more effective in treating nicotine addiction and preventing relapse. NIH R01 DA038700

008-A Relationship Between Frequency of Keratinocyte Carcinoma Lesions and Strength of the Association Between History of Keratinocyte Carcinoma and Risk for Another Type of Cancer: A Case-control Study, Ashley Wilson¹, James Small², Catherine Flanagan³, David Perry⁴, Richard Marcheli⁴, Bruce Thiers⁴, Anthony Alberg⁴; ¹College of Medicine, MUSC, ²Public Health Sciences, MUSC, ³Hollings Cancer Center, MUSC, ⁴Dermatology and Dermatologic Surgery, MUSC.

It has been well-documented that keratinocyte carcinoma (KC) is associated with increased risk of other types of cancers. However, whether or not this association exhibits a dose-response relationship has yet to be explored. This case-control study formed matched pairs based on age and sex between two n=48 groups: those with a history of keratinocyte carcinoma only and those with a history of keratinocyte carcinoma plus another type of malignancy. These two groups were compared to see if greater frequency of keratinocyte carcinoma lesions leads to greater risk for other types of cancer. Compared with the KC only group, those with KC plus another cancer had a greater mean number of lesions by 43% for BCC (p=0.22), 35% for SCC (p=0.36), and 41% for total KC (p=0.19). When adjusted for lifestyle factors, the odds ratio (OR) of developing another type of cancer was increased from 1.0 (referent) to 1.09 (95% CI 0.48-2.48) to 1.39 (95% CI 0.29-6.61) according to whether the patient had zero, one, or ≥ two lesions (p for trend = 0.18). For SCC, the OR of developing another type of cancer increased from 1.0 (referent) to 1.09 (95% CI 0.50-2.24) to 2.12 (95% CI 0.50-9.08) according to whether the patient had zero, one, or ≥ two lesions (p for trend = 0.18). For SCC, the OR of developing another type of cancer increased from 1.0 (referent) to 1.24 (95% CI 0.48-3.24) to 1.39 (95% CI 0.29-6.61) according to whether the patient had zero, one, or ≥ two lesions (p for trend = 0.60). This pattern did not hold true for total KC, as the OR of developing another type of cancer went from 1.0 (ref) to 3.03 (95% CI 0.86-10.64) to 2.15 (95% CI 0.62-7.47) according to whether the patient had one, two, or ≥ three lesions (p for trend=0.18). None of the associations described above were statistically significant, but these hypothesis generating results hinted that increased number of SCC and BCC lesions were associated with increased risk of other cancers. Future research to resolve this question is warranted. NIH UL1 TR000062; NCI P30 CA38313; Dept of Dermatology.
Introduction/Rationale: Increased independence in activities of daily living (ADLs) is strongly related to lower healthcare costs (Sands et al., 2006) and likelihood of hospital readmission (Galloway et al., 2016). To date, there is a lack of evidence-based clinical decision-making supports to guide ADL intervention. One potential solution to this problem is to identify a common contributing factor that underlies all ADLs and explains why some ADLs are more challenging than others. Metabolic equivalents (METs), which are physiological measures of energy expenditure during an activity, may serve as an underlying physiological mechanism to explain observed similarities in ADL item difficulties. The objectives of this study are to: 1) illustrate the relationship between METs and ADL item difficulties, and 2) demonstrate the use of the MET/ADL item difficulty relationship as a basis for individualized intervention planning. Methods: For objective 1, item calibrations for the National Health and Examination Survey (NHANES) ADL items were generated from 1,306 individuals aged 65+ using Rasch analysis. MET values corresponding to NHANES ADL items were identified from published MET tables (Ainsworth et al., 2011). Simple linear regression was used to quantify the relationship between METs and ADL item difficulties. For objective 2, a patient at a local occupational and physical therapy clinic will complete the NHANES ADL items. Rasch person measures along with item difficulties will be used to identify activities that align with the just right challenge for the individual. Results: MET values explained 70.2% of the variance in item difficulty; accordingly, higher MET values significantly predicted higher item difficulty (coefficient=0.588, p<0.001). A case-study will be used to illustrate how the relationship between MET levels and ADL item difficulties can guide clinical reasoning. Conclusions: By identifying activities at the client’s just-right-challenge from MET tables, clinicians can develop personalized intervention plans to optimize functional recovery.
011-A Radiology Perspective on Long-Term Monitoring of Colonic Interposition As a Treatment for Esophageal Atresia: A Case Report, Dani C Inglesby¹; Meryle J Eklund²; ¹College of Medicine, MUSC, ²Radiology, MUSC.

Colonic interposition, or the use of the transverse colon and possibly parts of the ascending or descending colon to replace an incomplete esophagus, is a rare procedure that is used in pediatrics for patients with long gap esophageal atresia. Long gap esophageal atresia is a disorder of embryological origin, in which there is a separation disruption in the foregut, causing a long spanning gap between the upper esophagus and the lower esophagus or stomach. While other options for surgical treatment include grafts of the jejunum, gastric pull-up, and gastric tube reconstruction, colonic interposition is considered the best option for prevention of long term complications, such as anastomotic leak and respiratory complications. It is typically performed within the first 48 hours after birth, but can be earlier if respiratory distress is noted, such as in the case of tracheoesophageal fistula, which is related to esophageal atresia. From a radiology perspective, it is important to know which complications to look for, even years after the procedure. These include aspiration and associated respiratory pathology, anastomotic strictures and any ischemia or necrosis, gastric stasis, colon tortuosity, ulcers, and any native pathology of the colon such as diverticulitis, colitis, or Crohn’s. Evaluation for complications is performed via a variety of imaging modalities, including CT, MRI, and barium studies. This case follows an adult who underwent a colonic interposition procedure in the 1960’s with the goal of demonstrating characteristics that are important from an imaging standpoint. MUSC Department of Radiology

012-A Effects of Resveratrol on Endothelial and Glioblastoma Cells, Cameron E Callahan¹, Kendall Cole², Yu-Lin Jiang³; Ann-Marie Broome³; ¹MUSC, ²South Carolina Governor’s School of Science and Mathematics, ³Cell and Molecular Pharmacology, MUSC.

Glioblastoma multiforme (GBM) is the most common form of brain tumor in adults, as well as one of the most aggressive and difficult to treat. Survival rates after diagnosis remain at an average of 12-15 months even after standard-of-care treatment with resection surgery and chemotherapeutic drug temazololamide (TMZ), and recurrence rates are 80-90%. Thus, there is a need for a more effective chemotherapeutic drug—in particular, one with a side effect profile less toxic than that of TMZ. The present study investigates the cytotoxicity of R6A, a novel RSV analog, toward endothelial cells (mouse cardiac endothelial cells or MCECs) and glioblastoma cells (U118 line). Cells were grown at 37°C and 5% CO2, plated at a density of 5x10⁴ cells per well in a 24-well plate, and treated with increasing concentrations of R6A. Cell viability and cytotoxicity of R6A toward both endothelial cells and glioblastoma cells were assessed using a trypan blue viability assay. Results showed that R6A killed 50% of endothelial cells at concentrations between 1.641 and 2.369 μM and k50% of glioblastoma cells at a far lower concentration of 97 nM. These results suggest that R6A is far more toxic to glioblastoma cells than to endothelial cells, which could prove promising if R6A were injected locally such that in addition to killing tumor cells, the drug could kill local endothelial cells that provide critical nutrients and growth factors to the tumor. Despite the promising nature of these findings, they must be further replicated before generalities can be drawn regarding the cytotoxicity of R6A toward endothelial cells end glioblastoma cells. In addition, studies investigating the specific mechanisms by which R6A kills endothelial cells must be performed before the drug can be tested on living subjects. MUSC NIDDK for Health Professions Students

013-A Generation of T-Cells Expressing a Chimeric Antigen Receptor Targeting Stress Protein Gp96, Christopher Duckworth, Xingjun Wu, Zhai Li; Microbiology and Immunology, MUSC.

Cancer remains a top cause of mortality in the United States with 595,930 deaths in 2015 alone; recent treatment advances have sought to reduce nonspecific toxic effects and take advantage of the body’s own antitumor weapons – culminating in immunotherapeutic approaches like administration of chimeric antigen receptor (CAR) T-lymphocytes, including Kymriah, which in August 2017 was the first such drug to approved by the FDA. Some oral and hematologic cancers have previously been shown to express a normally intracellular ER chaperone, gp96 (a notable stress protein), on the cell surface – differentiating cancer cells from self in a way that a directed immune response (via CAR-T therapy) can target. Based on monoclonal antibodies previously developed by our lab, chimeric antigen receptor constructs against gp96 were synthesized and incorporated into T-cells. In our attempts to engineer model Jurkat CAR-96 T-cells, we found evidence of CAR-construct cell surface expression by direct flow cytometry; we also noticed signs of T-cell activation in the presence of target gp96 by examining secreted IL-2 levels. We also observed some evidence of CAR expression when engineering with mouse primary T-lymphocytes as well. To prepare for assessing cytotoxic effects of our CAR-T cells, we characterized a number of potential target cells and identified their
gp96 surface expression. When co-culturing mouse CAR-T cells with target Pre-B ALL, we noticed limited (but encouraging) evidence of cytotoxicity. Once the in-vitro killing potential of these murine CAR-96 cells has been established completely, subsequent in-vivo xenograft survival experiments will be underway – with the hope of eventually bringing yet another successful CAR-T therapy to clinical trials. *NIH 5T35DK007431-33; MUSC SHPRP*

014-A PGE2 Treatment of Bone Marrow Derived Macrophages Induces PD-1 Surface Expression, Alexander Oles, Dingzhi Wang, Raymond Dubois, *Biochemistry, MUSC.*

Abstract not available.

015-A HDAC1 and PKA Combination Therapy for Targeted Chemotherapy Resistant FLT3-IDT+ Acute Myeloid Leukemia., Guillermo O Rangel Rivera1, Besim Ogretmen2, Natalia Oleink2, Shanmugan Panneer Selvam2, Rose Waridi Ndeto2, Kyla Baron2, 1 College of Graduate Studies, MUSC, 2 Biochemistry and Molecular Biology, MUSC.

Abstract not available.

016-A Effect of Alcohol Septal Ablation on Renal Function of Patients with Hypertrophic Obstructive Cardiomyopathy. Does Relief of Obstruction Ameliorate Acute Contrast-Induced Nephropathy?, Alex Canova1, Mira Patel1, Billy Mullinax1, Ashley MD Waring1, Chris MD Capps1, Christopher MD Nielson1, Valerian MD Fernandes2, 1 MUSC, 2 Ralph H. Johnson VAMC.

BACKGROUND: Alcohol septal ablation (ASA), a catheter based treatment for hypertrophic obstructive cardiomyopathy (HOCM) uses contrast to visualize coronaries while targeting the septal artery for ablation. Alcohol infarcts the hypertrophied obstructive basal septum and relieves LV outflow obstruction. There is a risk of renal dysfunction and contrast induced nephropathy (CIN) with the use of angiographic contrast. This study evaluates the incidence of renal dysfunction after ASA in our center. METHODS: Renal function data of consecutive patients who underwent ASA at MUSC between January 2007 and May 2017 were retrospectively analyzed. CIN was defined as ≥0.5mg/dL or ≥25% increase in serum creatinine after the procedure. RESULTS: A total of 218 patients (age 60.39 ± 14.08y, 124F, 111M) who underwent 235 ASA procedures were included in this study. Alcohol (2.10 ± 0.68 cc) was injected into 1.22 ± 0.52 septal arteries, thereby relieving LVOT gradient from 71.65 ± 41.27mmHg at baseline to 5.68 ± 11.16mmHg after ablation. A mean volume of 114.4 ± 56.2mL of contrast (Omnipaque/Visipaque) was used for ASA. In the entire cohort there was a significant decrease in serum creatinine and BUN after ASA. Creatinine decreased from 1.05 ± 0.68mg/dL to 1.00 ± 0.72mg/dL while BUN decreased from 16.32 ± 9.09mg/dL to 14.91 ± 8.25mg/dL after procedure (P<0.05 for both). Predefined CIN was seen in 10/233 (4.3%) cases. The creatinine in these patients increased from 0.86 ± 0.23mg/dL to 1.29 ± 0.51mg/dL after ASA. None of these patients needed renal support. CONCLUSION: The use of contrast with ASA did not have a detrimental effect on renal function. Renal indices improved after ASA suggesting that the relief of LVOT obstruction and thus improvement in renal perfusion may have ameliorated the detrimental effect of contrast on the kidneys. The incidence of CIN was low at 4.3% with no one needing renal support.

017-A Primary Cilia, Ka’la D Drayton1, Russell Norris2, Katelynn Toomer2, Diana Fulmer2, 1 College of Medicine, MUSC, 2 Regenerative Medicine and Cell Biology, MUSC.

Cardiac valve disease is a major health burden. Mitral valve prolapse (MVP) is one of the most common forms of cardiac valve disease and affects ~2-3% of the human population. MVP can lead to secondary complications such as arrhythmias, heart failure, and sudden cardiac death and 1 in 10 patients will require valve surgery. There are no effective nonsurgical treatments for MVP and therapeutic efforts have been hindered by an incomplete understanding of its fundamental causes. One accessible source of such information may come from genetic studies of MVP. We previously reported familial and GWAS studies that identified genetic mutations and/or excellent candidate targets as causal to MVP. Pathway analyses suggested a common cellular and molecular thread between these studies and invoke the primary cilia as potential unifying mechanism. This discovery is further bolstered by our recent identification of a mutation in a cilia gene in a large family with MVP, DZIP1. Our data show genetic haplinsufficiency of primary cilia in cardiac valves leads to a non-syndromic mitral valve disease in mouse models whereas complete genetic ablation enhances mitral valve phenotype severity. We present, for the first time, a potential common cellular and molecular thread through which MVP can arise. These studies define the primary cilia as a critical, and previously unrecognized facet of cardiac valve development. Uncovering how valve disease genes regulate downstream signaling cascades will provide key mechanistic insights into MVP pathogenesis at a cellular and molecular level using 3D reconstruction models and In-Situ Hybridization to localize primary
Bone healing is a rapid, natural process that occurs spontaneously upon injury at any bony location. This delicate process can be hindered by systemic or external factors, and occasionally is inexplicably impaired in healthy individuals. In order to enhance bone healing, we investigated the efficacy of an FDA approved matrix (Talymed) currently used for cutaneous wound healing and application to bone regeneration. A 5 mm defect was created in the skulls of mice and treated with either an absorbable collagen sponge or the Talymed matrix loaded with BMP2. The mice were sacrificed at 4 and 8 weeks and their skulls were harvested for histological analysis by hematoxylin and eosin, Masson’s trichrome, picrosirius red, and tartrate-resistant acid phosphatase. Selected markers for each stain were analyzed and quantified using Visiopharm software. Quantification of these stains showed greater amounts of bone, collagen, and osteoclast activity generated by the collagen sponge compared to Talymed. These results suggest a lack of efficacy for Talymed to robustly regenerate bone as sole therapy in the context of bone tissue therapies. Medtronic Inc. and Marine Polymer Technologies; AO Foundation S-16-108C; NIH NIDCR 5T32DE017551; NIH NIGM P30GM103331; SCTR NIH/NCATS UL1TR000062

018-A The FPR1 and Activation of Fibroblasts, Aariel L Dees, Titus A Reaves; Regenerative Medicine and Cell Biology, MUSC.

Fibroblasts are mesenchymal cells that release collagens, laminins, and proteoglycans, which are essential for functional connective tissue. Myofibroblasts are activated-fibroblasts that express α-smooth muscle actin and contract during wound healing. If activation continues, myofibroblasts may become fibrotic resulting in fibrosis (excessive and dysregulated deposition of extracellular matrix that affects the function of target organs). Despite this information, the molecular events of fibrosis are not completely understood. Previously, we show that fibroblasts express the Nα-formyl-L-methionyl-L-phenylalanine receptor (FPR1). FPR1 is a 7TM spanning G-protein coupled receptor that regulates the leukocyte response to bacterial formylated peptides by facilitating activation of such peptides. We exposed intestinal fibroblasts to inflammatory cytokines IL-6 and IL-8 respectively. Interestingly, treatments with IL-6 resulted in minimal changes in FPR1. However, treatments with IL-8 resulted in an up-regulation of FPR1 and increased adhesion to fibrinogen (CD11b ligand). We then used inhibitors of G-protein coupled receptors and siRNA studies to examine FPR1 further. Studies reveal that reducing FPR1 exacerbates the inflammatory response of fibroblasts. Taken together, FPR1 appears to modulate the activation of fibroblasts. Down regulation of FPR1 may lead to a better understanding of the fibrotic response and better treatments of dysregulated inflammatory conditions involving fibroblasts. NSF R-II

019-A A Novel PGlcNAc Nanofiber Scaffold Used to Augment Bone Healing: A Histological Analysis, Brayden Oakes¹, R Nicole Howie², Emily Durham², Zachary Grey², R Amanda LaRue³, Martin Steed⁴, Robin Musie-Helmericks⁵, James Cray², ¹College of Dental Medicine, MUSC, ²Oral Health Sciences, MUSC, ³Pathology and Laboratory Medicine, MUSC, ⁴Oral and Maxillofacial Surgery, MUSC, ⁵Regenerative Medicine, MUSC.

Bone healing is a rapid, natural process that occurs spontaneously upon injury at any bony location. This delicate process can be hindered by systemic or external factors, and occasionally is inexplicably impaired in healthy individuals. In order to enhance bone healing, we investigated the efficacy of an FDA approved matrix (Talymed) currently used for cutaneous wound healing and application to bone regeneration. A 5 mm defect was created in the skulls of mice and treated with either an absorbable collagen sponge or the Talymed matrix loaded with BMP2. The mice were sacrificed at 4 and 8 weeks and their skulls were harvested for histological analysis by hematoxylin and eosin, Masson’s trichrome, picrosirius red, and tartrate-resistant acid phosphatase. Selected markers for each stain were analyzed and quantified using Visiopharm software. Quantification of these stains showed greater amounts of bone, collagen, and osteoclast activity generated by the collagen sponge compared to Talymed. These results suggest a lack of efficacy for Talymed to robustly regenerate bone as sole therapy in the context of bone tissue therapies. Medtronic Inc. and Marine Polymer Technologies; AO Foundation S-16-108C; NIH NIDCR 5T32DE017551; NIH NIGM P30GM103331; SCTR NIH/NCATS UL1TR000062

020-A The Relationship Between Posttraumatic Stress Disorder, Executive Function, and the Dopamine Receptor D4 Exon 3 Variable Number of Tandem Repeat Polymorphism, Allen Green, Zhewu Wang; Psychiatry, MUSC.

Posttraumatic stress disorder (PTSD) has been associated with dysfunction in several neurocognitive processes including impairments in response inhibition and attention regulation. Empirical evidence also indicates that there is a significant genetic component to both PTSD and executive function. While the dopamine receptor D4 gene (DRD4) has been implicated in a multitude of neuropsychiatric disorders and personality traits, the research regarding a possible role in PTSD is lacking. The current study analyzed the association between the variable number tandem repeat (VNTR) DRD4 exon III polymorphism, PTSD, and executive function in veterans and non-military volunteers (N=299). Participants were interviewed by a board certified psychiatrist, assessed for executive function via a cued Go/No-Go task, and were genotyped for the DRD4 polymorphism. Statistical analysis was then conducted. Results indicated a significant difference between participants with PTSD and those without it in all areas assessed by the Go/No-Go task; GNG latency F(1,206) = 17.82, p < .001, slow errors F(1,206) = 14.69, p < .001, response errors F(1,206) = 11.19, p = 0.001, and total errors F(1,206) = 19.08, p < .001, slow errors F(1,206) = 14.69, p < .001. Further analysis indicated a significant difference between DRD*4R homozygotes and all other genotypes for GNG latency F(1,208) = 5.89, p = .016, response errors F(1,208) = 3.63, p = 0.012, and total errors F(1,208) = 6.27, p = .013. Additionally, the results indicated a significant difference in the rate of PTSD diagnosis amongst DRD4*4R homozygotes compared to all other genotypes 2 (1, N=295) = 10.36, p = .001. These findings complement previous studies on the
Introduction: Individuals with high levels of anxiety, stress, and/or trauma exposure are more likely to report hypersensitivity to environmental odors. While preliminary evidence indicates a possible link between anxiety and blunted detection of neutral odors, correlations between psychological factors and threat-related odor detection are not well established. Combat veterans with PTSD, compared to healthy combat veterans and civilians, are much more likely to rate burning odors as intense and unpleasant. This study sought to examine the relationship between objectively measured burning odor detection and anxiety, stress, and sleep quality in a non-clinical adult sample. Methods: Thirty-three participants were recruited through community advertisement seeking adults with odor sensitivity. Odor detection thresholds for phenylethyl alcohol (PEA), a rose-like odorant, and guaiacol, a smoky odorant, were determined with Smell Threshold TestsTM, standardized sets of sniff wands containing serial dilutions of the corresponding odorant. Participants then completed multiple questionnaires assessing anxiety (Anxiety Sensitivity Index-3), stress (Holmes-Rahe Stress Inventory), and sleep quality (Pittsburgh Sleep Quality Index). Results: The 33 participants were primarily white, women (67%, 85%, respectively), with a mean age of 37±13.6 years. Threshold scores for guaiacol, but not PEA, were inversely related to anxiety sensitivity and sleep dysfunction (r=-.39, p<.05; r=-.36, p<.05), indicating a potential association between anxious arousal and sensory hypervigilance to threat-related odors. Participants with greater sensitivity to guaiacol than PEA (N=19), compared to those more sensitive to PEA than guaiacol (N=11), had significantly increased risk for illness/psychological disorder related to their stress load (chi-squared=5.69, p<.05), anxiety sensitivity (chi-squared=4.59, p<.05), and sleep dysfunction (chi-squared=3.45, p=.07). Conclusions: These data show that lower burning odor detection thresholds are associated with higher anxiety sensitivity, poorer sleep quality, and higher risk for stress-related illnesses and psychiatric disorders. Individuals with increased sensitivity to certain environmental odors may suffer from previously undiagnosed anxiety disorders or stress-related illnesses. NIH R25 DA020537.

Opioid use disorder (OUD) has become a major national crisis. Recent studies have shown that Emergency Department (ED)-initiated buprenorphine with primary care follow-up was more beneficial than a brief intervention or referral alone. The purpose of this study was to evaluate the willingness of ED providers to initiate buprenorphine for ED patients with OUD. We also evaluated barriers and facilitators for buprenorphine use in ED settings. Utilizing the theory of planned behavior, we designed a structured interview that was administered to 10 ED providers from Medical University of South Carolina. We utilized open-ended and Likert-type questions to examine self-reported measures of attitude, self-efficacy, controllability and intention to prescribe buprenorphine in ED settings as well as facilitators and barriers to buprenorphine use. We received structured interview information from 9 ED providers: 4 physicians, 3 Physician Assistants, and 2 Residents. The average age of the participants (7 male, 2 female) was 36 years old, 88% were Caucasian, 77% reported currently treating patients with OUD, and zero had a buprenorphine waiver. On average, participants reported seeing 9.7 OUD patients per week. In general, providers had a favorable opinion of buprenorphine, but were neutral with respect to intention to obtain buprenorphine waiver. The most commonly reported barrier to using buprenorphine was the lack of hospital endorsement and the most frequently cited facilitators to buprenorphine use were receiving paid time off for training and availability of outpatient follow-up. ED providers report generally favorable opinions about the use of buprenorphine in ED settings, but feel neutral about obtaining a waiver to prescribe buprenorphine. All providers agreed that they would be more willing to prescribe buprenorphine if outpatient follow-up were available. This study provides valuable information regarding areas for education and practice facilitation to expand access to evidence-based and life-saving treatment for OUD. NIH R25 DA020537.
023-A Safety and Efficacy of Combined Liver Transarterial Embolization and Ablation Using Cone Beam CT Navigation, Beatriz Bassaco¹, Ricardo Yamada², Juan Camacho³, Bret Anderson², Chris Hannegan², Marcelo Guimaraes², †COM-MPH, MUSC, ²Vascular & Interventional Radiology, MUSC.

Purpose: To assess the safety and efficacy of combined liver transarterial embolization (TAE) and radiofrequency ablation (RFA) during a single session using Cone Beam CT (CBCT) navigation. Materials and methods: Nineteen cases treated between May 2014 and January 2017 for liver cancer with transarterial embolization and radiofrequency ablation were studied. Twelve patients underwent TAE and RFA during two sessions on sequential or non-sequential days under fluoroscopy and CT guidance (Group 1). Seven patients underwent a one day single session of combined therapy under fluoroscopy and CBCT with real time needle guidance (Group 2). Tumor size, total procedure time (PT), patient effective dose (ED), number and purpose of CBCT and CT were examined. Immediate technical success and local recurrences using mRECIST criteria at 1-month follow-up were recorded. Mann Whitney U test and 2-sample t-test were used, with 0.05 significance levels.

Results: Mean tumor size was comparable in both groups (2.5cm [1.0 – 7.3] vs 2.8cm [1.1 – 5.1], p=0.74). An average of 9.58 CT scans were performed for RFA in Group 1 vs. 5.13 CBCT in Group 2 (p<0.001). Mean PT was shorter in Group 1 (120’ vs 190’, p=0.009), however; median ED was more than two times lower in Group 2 (66.8 vs 28.4 mSv in Group 1, p=0.07). Technical success was reached in all procedures. Complete responses were comparable between groups (67% vs 71%, p=1). No major complications were observed; one death occurred in Group 1 before follow-up from unrelated causes.

Conclusion: CBCT navigation for TAE and RFA during single session is safe and effective for combined directed liver therapy in patients with hepatic cancer.

024-A Custom 3D Printed Total Talar Prostheses Restore Normal Joint Anatomy Throughout the Hindfoot, Joseph A Tracey¹, Danny Arora², Christopher E Gross³, Selene G Parekh³, †MUSC, ²Duke.

Background: Third generation total talar prostheses (TTP) are viable options for talar avascular necrosis (AVN) in the absence of neighboring joint pathology. The use of modern three-dimensional (3D) printing allows for the production of custom implants that exactly mimic the patient's anatomy. The aim of this study is to determine the accuracy of 3D printing in reproducing a synthetic talus, and in doing so, restoring more normal anatomical relationships. We hypothesize that this mode of replication will restore and maintain normal radiographic alignment of the ankle, subtalar, and forefoot joints in the setting of talar AVN. Methods: A retrospective analysis was performed on all patients undergoing TTP implantation for the treatment of talar AVN between 2016 and 2017. Pertinent demographic and operative factors were recorded. Radiographic measurements were taken pre- and post-operatively to determine native talar dimensions, TTP implant dimensions, and the corresponding radiographic alignment about the forefoot and hindfoot. Results: Fourteen patients, treated for AVN between 2016-2017, were identified in our cohort. Talar arc length and width were not found to be significantly changed, however talar height was significantly increased with use of TTP. Five alignment dimensions were measured (tibiotalar alignment, talar tilt angle, Boehler’s angle, talar declination angle, and Meary’s Angle), of which, only talar tilt angle was significantly changed. Instances of Meary’s angle correction were observed in cavus and planus foot deformity. Conclusion: This study represents the largest case series of TTP performed in the United States, and is the first to investigate the 3D printed TTP. As a proof-of-concept, 3D printed TTP was successful in restoring talar height and talar tilt in the setting of AVN. Additionally, the procedure maintained normal alignment in non-pathologic joints. Total talar prosthesis, based on our cohort, is a viable option to restore more normal anatomic alignment.

025-A The Development and Utilization of an Online Professional Medical Series Addressing the Knowledge Gaps in the Management of Hypertension, Allyson Hill¹, Vanessa Diaz², Donald DiPette³, Robert Malcolm⁴, Jenifer Voeks⁵, Daniel Lackland⁶¹, College of Medicine, MUSC, ²Family Medicine, MUSC, ³Internal Medicine, USC, ⁴Psychiatry and Behavioral Sciences, MUSC, ⁵Neurology, MUSC.

While clinical trial and study evidence have demonstrated an impact on blood pressure reduction and control, population hypertension control remains suboptimal. There are many disparities in hypertension control among racial/ethnic minorities and among geographical areas in the United States. Reasons for inadequate blood pressure control may be patient or provider related. To address the issue of inadequate knowledge of appropriate hypertension treatment in health care providers, a gaps analysis was performed. An enduring, online continuing education series was designed based on these knowledge gaps. Education programs for health care practitioners have proven to be effective in changing practice. Such education programs should be readily accessible to the entire health care team and made available to primary healthcare providers in all areas, including high-risk
rural settings. In addition to improving the knowledge of current evidence-based practice in different types of health care providers, this program could also be a convenient, low cost, and nationally available program. NIH 5T35DK007431-33; MUSC SHP

026-A Do Patients, Visitors and Staff Perceive a Safety Benefit From the Use of Metal Detectors At an Urban, Academic Emergency Department?\textsuperscript{1}, Patricia Jokl\textsuperscript{1}, Russell Allinder\textsuperscript{2}, Steven H Saeff\textsuperscript{2}, Diann M Krywko\textsuperscript{2}; \textsuperscript{1}College of Medicine, MUSC, \textsuperscript{2}Emergency Medicine, MUSC.

Metal detectors (MD) are widely utilized in public places where there is raised concern for violence, such as in political arenas and airports. The presence of a MD may imply that increased risk exists. We wondered if openly acknowledging that potential risk by using MDs would increase or decrease perceptions of safety at an urban, academic emergency department (ED). This study was conducted from June through August, 2017 by medical students on a summer rotation. We surveyed patients, visitors and staff regarding their perception of safety and how it was affected by the presence of a MD at the ED entrance. Eligible participants included all adults willing and able to complete the survey. Our index question was “Would having a metal detector in use make you more likely to feel safe?” We reported descriptive statistics and compared responses to the index question with other survey items using Chi Square. In our data, a majority of participants responded they would feel safer with use of a MD. Overall: 75%; Staff: 82%; Patients, Families & Visitors: 74%; African American (AA): 87%; Caucasian: 64%; Women: 78%; Men: 71%. AA patients reported a greater perceived safety benefit than Caucasian patients (87% vs 64%; p<0.001). No difference was noted based on age, time of arrival, or placement in a hall- versus room-bed. Only five percent of all candidates reported feeling any sense of danger during their ED visit. The overwhelming majority of patients, visitors and staff at our urban, academic ED believed that their safety would be increased by the use of a MD at the ED entrance. Concerns that a MD would cause patients to avoid the ED seem unjustified.

027-A Qualitative Review of Publications Regarding Quadriceps Tendon Autograft Use in ACL Reconstruction, Walker M Heffron\textsuperscript{1}, John W Xerogenes\textsuperscript{2}, Jennifer L Hunnicut\textsuperscript{3}, Shane K Woolf\textsuperscript{1}, Harris S Stone\textsuperscript{1}; \textsuperscript{1}Orthopaedics, MUSC, \textsuperscript{2}Orthopaedics, Emory, \textsuperscript{3}Health Science and Research, MUSC CHP.

Introduction: Anterior cruciate ligament (ACL) reconstruction is one of the most common orthopedic surgeries performed in the United States. It involves use of allografts or autografts from various host tissue sites. Therefore, one of the most important surgical decisions is graft type for use in the reconstruction. A technique for use of the quadriceps tendon as an autograft harvest site for reconstruction of the ACL was introduced in 1979 by Marshall et al. Since its introduction, quadriceps tendon has gained popularity for use as a graft source. As the use of quadriceps tendon in ACL reconstruction increases, so does its interest as a topic of research. The purpose of this study was to perform a qualitative analysis of publications to date focusing on the use of quadriceps tendon grafts for ACL reconstruction. Methods: The PubMed database was queried for journal articles relating to quadriceps tendon autografts being used for ACL reconstruction. These publications were filtered for relevance, then analyzed and differentiated by publication characteristics. Results: After sorting the publications, the data not only showed a recent increase in the number of publications regarding quadriceps tendon as a choice for autograft harvest site in ACL repair over time, but also yielded informative data with regards to publication journal, country/region, and publication type. Conclusion: This evaluation shows the increasing interest in quadriceps tendon as a source for autograft tissue. Increased research production will allow surgeons to feel more confident about the use of the quadriceps tendon as an autograft option in ACL reconstruction.

028-A Evaluation of Machine Learning Algorithm to Convert Unstructured to Structured Radiological Reports in Patients with Pulmonary Embolism, Adam J Spandorfer\textsuperscript{1}, Cody Branch\textsuperscript{1}, Puneet Sharma\textsuperscript{2}, Pooyan Sahbaee\textsuperscript{3}, Taylor Duguay\textsuperscript{3}, U Joseph Schoepf\textsuperscript{4}, James Ravenel\textsuperscript{5}, John Nance\textsuperscript{2}; \textsuperscript{1}Medicine, MUSC, \textsuperscript{2}Radiology, MUSC.

Abstract not available.

029-A Open Versus Minimally Invasive Decompression and Stabilization for the Treatment of Thoraco-lumbar Traumatic Spine Fractures, Gibson AE Klapthor\textsuperscript{1}, Mohammed Alshareef\textsuperscript{2}; \textsuperscript{1}COM, MUSC, \textsuperscript{2}Neuroscience, MUSC.

Introduction: The treatment of patients with traumatic fractures affecting the axial spine, can be approached in a variety of ways. To reduce surgical-related patient morbidity in multiple system injured trauma patients, we employed several posterior less-invasive techniques to decompress and stabilize the thoraco-lumbar spine. Methods: The authors retrospectively reviewed the charts of patients who underwent posterior less invasive methods (MIS) of decompression due to traumatic spinal injury over the
Opioid addiction is an increasingly prevalent problem. Patients prescribed higher doses of opioids are at added risk of overdose. Opioid prescriptions for musculoskeletal pain, acute and chronic, increased from 2001-2010. It has never been examined which medical specialties are prescribing the patients of South Carolina opioid prescriptions for low back pain. We examined opioid prescribing habits of different specialties for non-surgical low back pain at MUSC. The sample size was 2790 patients (age >18) diagnosed with ICD-9 codes 724.2, 724.3, 724.5, or 54.5 and who were prescribed an opioid during outpatient visits between 1/01/2013-12/31/2016. De-identified data was stratified examining the most commonly prescribed opioids and the prescribing specialty. This overview explored the gross numbers associated with low back pain and opioid prescription habits without additional statistical analysis. For 2790 patients there were 5303 opioid prescriptions. Only 3861 prescriptions had a prescribing specialty listed. Thus, prescriptions with no specialty assigned were the largest group in the study (1442 prescriptions written (27%)). Family medicine wrote 986 (18.5%) of the prescriptions, followed by Internal Medicine with 795 (15%), Anesthesiology with 419 (8%), Neurosurgery with 283 (5.5%), and Pain Medicine with 230 (4.5%). These five specialties comprised 51.5% of the total prescriptions. Combining the top five prescribing specialties and prescriptions with no specialty listed yields ~78% of the total prescriptions written for low back pain. Interestingly, only 65 prescriptions (1.2%) were written by orthopedic surgeons for non-surgical low back pain. The three most commonly prescribed opioids were Oxycodone (29%), Hydrocodone

**301-A Opioid Prescribing Habits of Different Specialties for Non-surgical Low Back Pain, Matthew T DeMarco¹, Elizabeth C Durante¹, Christopher E Gross²; ¹College of Medicine, MUSC, ²Orthopaedics, MUSC.**

Introduction: Cadaver models have been used to help train emergency physicians in arthrocentesis using both ultrasound (US) and landmark techniques. By using US to confirm joint effusions prior to aspiration, it is possible to ensure that the effusions are a similar size between participants. In our experience, repeated needle sticks of the same ankle resulted in leakage from the joint, creating inconsistently sized effusions after injecting the same volume. We describe a novel method of creating - and replicating - consistently sized US confirmed ankle effusions in a cadaver.

Methods: A total of 14 different ankle joints - seven left and seven right - were used from seven different cadavers. Cadavers were prepped in advance by the investigators. A 20G 1.75inch (Braun) catheter was placed in the ankle joint from the lateral position under US guidance. 22 medical students and 13 emergency medicine faculty completed both, US and LM techniques, in a randomized fashion following a brief five-minute video outlining each procedure. Ankle joints were filled with normal saline prior to the start of each procedure. Throughout the procedure, investigators held gentle pressure on a 60cc syringe filled with normal saline and attached to the catheter. Participants proceeded to aspirate at least 1cc of fluid to be considered successful. Investigators confirmed with US the presence of fluid along the anterior talus immediately before, and after, aspiration. Results: A total of 70 ankle joint effusions were aspirated - all but two of them successfully. Joint effusions were measured prior to, and after, aspiration. All ankle joints held the effusion for the duration of the procedure, requiring at most 20cc of additional saline during aspiration. Conclusion: We describe a novel method of creating - and replicating - consistently sized US confirmed ankle effusions in a cadaver.

**030-A A Novel Approach for Creating and Maintaining Ankle Joint Effusions in a Cadaver Model, David Wynn¹, Graeme Ross², Nick Ashenburg², Alex Clendening², Jordan McCarthy², Brad Presley², Steven Kubalak³, Ryan Barnes³; ¹Medicine, MUSC, ²Emergency Medicine, MUSC, ³Regenerative Medicine and Cell Biology, MUSC.**

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(26.5%), and Tramadol (15.5%). More analysis is still being performed; however, this could potentially lead to more effective education and interventions to prevent opioid abuse and overdose. By elucidating which specialties are prescribing, focused education pertaining to each specialty will aid in decreasing rates of unnecessary opioid prescriptions.

032-A Effectiveness of the GoCheck Kids Vision Screener in Detecting Amblyopia Risk Factors, Rupa N Patel¹, Sarah Logan², Ryan Rhodes¹, Luke Edmondson³, Edward Cheeseman⁴, Rupal H Trivedi⁵, Mae M Peterseim⁶; ¹College of Medicine, MUSC, ²Ophthalmology, MUSC, ³Pediatrics, MUSC.

Abstract not available.

033-A Does a Patient's Use of a Primary Care Physician Impact Their Use of the Emergency Department?, James W Infanzon¹, Sarah Katchen¹, Warren Harvey¹, Steven Saeft²; ¹College of Medicine, MUSC, ²Emergency Medicine, MUSC.

Background: Through the Affordable Care Act, patients have had increased access to a primary care physician (PCP) and theoretically require fewer trips to the Emergency Department (ED). Capp, et al, in 2013 reported a trend towards increased use of the ED despite having insurance and access to a PCP. This study sought to determine if a similar pattern existed in a sample of patients coming to an urban, academic ED. Methods: We surveyed ED patients about a variety of factors including having a regular doctor, payer classification, and where they considered to be their medical home (MH): ED or PCP. Eligible patients were adults (>=18yrs old) who were willing and able to cooperate with an interview. Data was entered into REDCap © Vanderbilt University and uploaded into SAS, Cary, NC for analysis. Results: Seventy-two percent of patients who had a regular doctor expressed a belief that the ED was their MH. Only 15% of patients who reported having a regular doctor chose the ED because they will see you regardless of ability to pay. A significantly greater number of patients with private insurance (61%) reported having a regular doctor than those with no insurance (9%) or public insurance (30%); p<0.001. 73% percent of patients who had a regular doctor believed the ED was the place where they received the best treatment to prevent heart attacks, strokes, kidney failure and cancer. Conclusions: Many patients consider the ED to be their MH despite having a regular doctor or being insured. Patients with insurance were more likely to have a PCP than those without. We believe it would be prudent to expand emergency services to offer rudimentary PC to those who treat the ED as their MH.

034-A PD71-04 An Independent, Multi-Institutional, Prospective Study in the Veterans Affairs Health System Confirms the 4Kscore Accurately Predicts Aggressive Prostate Cancer, Edward L Held⁴, Sanoj Punnan², Stephen Freeland³, Thomas Polascik⁴, Stacy Loeb⁵, Edward Uchio⁵, Sharad Mathur⁷, Stephen Savage⁸, ¹MUSC, ²University of Miami, ³Cedars-Sinai, ⁴Duke Cancer Center, ⁵New York University, ⁶University of California Urvine, ⁷Kansas City Veterans Center, ⁸Urology, MUSC.

The 4Kscore test was previously validated in a large, prospective trial to predict aggressive prostate cancer, however, the study population had a limited number of African American (AA) men. We conducted an independent multi-institutional, prospective trial to validate the 4Kscore test within the Veterans Affairs (VA) Health System, where a large proportion of the men getting care are AA. We prospectively enrolled men who were referred for biopsy of their prostate at 8 diverse VA sites throughout the nation. All men underwent phlebotomy for 4Kscore ascertainment prior to prostate biopsy. We assessed the discrimination, calibration, and clinical utility of the 4Kscore test for predicting Gleason 7 or higher (G7+) prostate cancer, and compared it to a base model consisting of age, digital rectal exam findings, and PSA. Additionally, we compared the performance of the 4Kscore test in AA and non-AA men. Among 403 men who were enrolled in the trial, we had 366 men with a 4Kscore and complete data available for analysis. Among these men, 208 (56%) were AA, and 134 (36%) had G7+ prostate cancer. The 4Kscore exhibited better discrimination (AUC: 0.81 vs. 0.74, p=0.011) and higher clinical utility on decision analysis than the base model for deciding on the need for biopsy. Calibration plots of the 4Kscore for the entire cohort afforded predictions that closely matched the observed risk of G7+ prostate cancer in the population (Figure 1). There was no difference in the discrimination of the 4Kscore test between AA and non-AA men (0.80 vs. 0.84; p=0.32). While we found some evidence that the 4Kscore underestimates the risk of G7+ prostate cancer in AA men, discrimination (0.80 vs. 0.72, p = 0.013) and clinical utility for the 4Kscore test were still higher than the base model. In an independent, multi-institutional, prospective trial of the 4Kscore test in the VA health system, we confirmed that the 4Kscore accurately predicts the likelihood of aggressive prostate cancer and outperforms standard clinical information for biopsy decision making in both AA and non-AA men. Charleston Research Institute
MUSC, Alvarado Investigators and 'Team Science'

Abstract not available.

036-A An Assessment of Clinical Investigators and 'Team Science', Brenda A Alvarado¹, Daniel T Lackland²; ¹Medicine, MUSC, ²Neurology, MUSC.

Hypophosphatasia (HPP) is rare inheritable disorder characterized by defective bone mineralization. HPP is caused by a defect in tissue non-specific alkaline phosphatase (TNSALP), an enzyme responsible for clearing inorganic phosphate. HPP has a heterogeneous presentation ranging from early dental loss, fractures, to in utero death (1). Studies estimate severe forms of HPP to be present in 1:100,000-300,000 and moderate forms may be present in 1:6,370 (2,3). Persistent low alkaline phosphatase (ALP) can be used to screen for HPP. This study was performed to define the possible prevalence of HPP in the Medical University of South Carolina’s (MUSC) pediatric population. A retrospective chart review was conducted on pediatric patients who had ALP levels taken between 2014-2017 at MUSC. ICD-10 criteria were applied to exclude non-HPP causes of low ALP. Patients with the consistently low ALP levels, were reviewed for symptomatology suggesting possible HPP diagnosis. 274,642 pediatric patient encounters with ALP testing occurred between 2014-2017 at MUSC. Of these encounters, 679 patients had low ALP for age and gender. 63 of these patients were identified as having consistently low ALP, and were subsequently reviewed for symptomatology associated with the disorder. 8 patients were classified as “potential HPP patients” because they experienced both low ALP and associated symptomatology. The average age of the potential HPP patients on the date of their lowest ALP drawing was 1.77 ± 1.21 years. The potential prevalence of the disorder is approximately 1:25,000. HPP is considered a rare disorder however less severe forms may be more common. Recognizing low ALP for age and gender in the setting of associated symptomatology is crucial for early evaluation for a diagnosis of HPP. In 2015, TNSALP enzyme replacement therapy for HPP was FDA approved and thus treatment may be considered (4). NIH 5T35DK7431-33, MUSC SHP

037-A Alterations in Phosphorylated Substrates in Nucleus Accumbens Tissue of Rats in a Self-Administration Model of Alcohol Addiction, Helen L Martin¹, Clemence Obellianne², Joachim D Uys²; ¹College of Medicine, MUSC, ²Cell and Molecular Pharmacology, MUSC.

Alcohol use disorder (AUD) is associated with an increased risk for a number of health conditions and nearly 6% of deaths globally each year are associated with alcohol use. According to the National Institute on Alcohol Abuse and Alcoholism, more than 15 million people in the United States alone abuse or are addicted to alcohol. Currently, the molecular basis of AUD is not completely understood and there is great potential for identification of novel therapeutic targets. Further delineation of cell signaling mechanisms involved in addiction requires investigation of protein expression and posttranslational modifications (e.g. phosphorylation) in the nucleus accumbens (NAc), the reward center of the brain. In this study, a self-administration model of alcohol addiction was used followed by extinction training and reinstatement of alcohol seeking behavior. Animals were divided into two groups for the purpose of comparing differences in NAc protein phosphorylation between the extinction and reinstatement groups. The NAc of each of these animals was removed and tissue was homogenized for protein extraction. Western blot analysis of these extracts was performed to determine relative amounts of phosphorylated substrates of 6 highly utilized Ser/Thr kinases. Data showed significant increase (p<0.05) in phosphorylated substrates of Protein Kinase A (PKA) and Protein Kinase B (Akt/PKB) in the extinction group. Continued analysis was performed to determine which downstream proteins are involved in this change in PKA and Akt phosphorylation. This experiment provides insight into specific changes in protein modifications in the NAc that are associated with addicted phenotype. Additional research is necessary to understand the implications of this change in the posttranslational modification of the NAc and the potential impact on other brain areas of the reward pathway. Determination of molecular mediators that are directly involved in addicted phenotype will allow for exploration of novel therapeutic targets for AUD. MUSC COM Summer Research Stipend; NIH AA024426

038-A Diffusion Kurtosis Parameters in Pediatric Diffuse Intrinsic Pontine Gliomas, Kristen Herring¹, Vittoria Spampinato², Milad Yazdani²; ¹College of Medicine, MUSC, ²Neuroradiology, MUSC.

The goal of this study was to compare diffusion kurtosis parameters of pediatric patients diagnosed
with diffuse intrinsic pontine gliomas to see if there was any correlation between the initial magnetic resonance imaging kurtosis parameters and the overall length of survival of the patient after the initial diffusion kurtosis scan. We used MRICron software and Diffusion Kurtosis Estimator Software to find that there were negative correlations between mean kurtosis values and patient’s length of survival after initial scan. We also found that there was a positive correlation between the mean diffusivity values and patient’s length of survival after initial scan. NIH NIDDK 5T35DK007431-33

039-A Association Between Magnesium Intake, Serum Magnesium Levels, and Depression in an At-Risk Population, Emily A Young¹, Kristen B Johnson², Bernadette P Marriott³, ¹COM, MUSC, ²University of Tennessee, ³Gastroenterology and Hepatology, MUSC.

Intro: Over the past century, dietary magnesium (Mg) intake has significantly decreased alongside increased consumption of processed grains. Decreased Mg intake, decreased serum Mg levels, and a reduced serum magnesium/calcium (Mg/Ca) ratio have been implicated in the pathogenesis of chronic disease, including depression. Using a group of at-risk suicide patients in the BRAVO study, we explored the relationship between serum Mg levels, the serum Mg/Ca ratio, and measures of psychiatric symptomatology. Methods: Under the BRAVO protocol, serum Mg and Ca levels were measured after a baseline blood sample collection. Psychiatric symptoms were assessed using the Patient-Reported Outcomes Measurement Information System (PROMIS) for Anxiety, Depression, Pain, Fatigue, Physical Health, and Life Satisfaction and the Beck Depression Inventory (BDI-II). Pearson product-moment correlation analyses were used to examine association between the serum Mg level and psychiatric symptoms. Independent sample t-test were used to examine differences in serum Mg levels between those endorsing mild depressive mood symptomatology on the BDI-II (total score 14-19) versus severe depression (total score >28). Results: Serum Mg levels did not decrease with increasing depression; on the contrary, higher BDI-II scores were significantly associated with higher serum Mg levels (r = .241; p = .014). No statistically significant associations between serum Mg levels and other measures of psychiatric functioning were observed. The mean level of serum Mg in those endorsing mild depression on the BDI-II (mean=21.47 units, SD=2.18) was not significantly different from those endorsing severe depression (mean=20.90 units, SD=1.62; t=.887, p=.383). Conclusion: Contrary to expectations, in this sample of patients at elevated risk for suicide, higher levels of serum Mg were associated with less self-reported depressive mood symptomatology. Serum magnesium was not associated any other aspect of psychiatric functioning. Heterogeneity in this sample may independently affect depression and magnesium status. Future analyses will consider the relationship of dietary Mg intake with serum Mg levels and the serum Mg/Ca ratio.

040-A Characterizing Macrophage Polarization in Bone Wounds Following Administration of RhBMP2 and PGlcNAc, Zachary J Grey¹, R Nicole Howie¹, Emily Durham¹, Sarah Rose Hall¹, Martin Steed², Robin Muise-Helmericks³, James Cray¹; ¹Oral Health Sciences, MUSC, ²Oral & Maxillofacial Surgery, MUSC, ³Regenerative Medicine, MUSC.

Bone possesses the innate capacity for complete regeneration following injury or surgery, though this is highly dependent on the degree of injury and volume of ablated tissue. Several therapeutics are used clinically to precipitate healing by regeneration of like tissues while minimizing scarring, e.g. autologous bone grafts. While effective, limited supply of donor site grafts and associated harvest site morbidity have necessitated a search for alternative means of increasing bone repair efficiency. Among these is INFUSE Bone Graft, a combination therapy delivering osteoinductive bone morphogenetic protein 2 (rhBMP2) to the wound site via an osteoconductive scaffold (absorbable collagen sponge, ACS). Adverse side effects associated with rhBMP2 administration, such as rampant inflammation and clinical failures, have brought its efficacy into question. Although acute inflammation is absolutely necessary for proper healing in bone, inflammatory cascade dysregulation can result in further or sustained tissue damage. To study the effects of rhBMP2 administration on early acute inflammatory response following bone wounds, wild-type mice underwent a 5mm calvarial defect creation which were subsequently treated with ACS and clinically relevant doses of rhBMP2. Another group of mice were treated with a PGlcNac nanofiber scaffold, a US-FDA approved material that has been shown to decrease inflammation in cutaneous wounds. 3 and 7-day time points were used to assess the role that these biomaterials play in modulating inflammation. Specifically, immunohistological techniques were used to identify macrophage polarization following therapeutic intervention with either ACS/rhBMP2 or PGlcNac scaffolds. Increases in M1 markers in response to rhBMP2 delivery are indicative of a prolonged pro-inflammatory macrophage phenotype. Furthermore, data suggests that PGlcNac polarizes macrophages to a reparative M2 phenotype earlier in the signaling cascade. Better understanding of the mechanisms by which ACS, rhBMP2, and PGlcNac regulate
ADAMANTINOMA, A RARE PRIMARY BONE TUMOR OF THE TIBIAL DIAPHYSIS, Ashley S Williams, Meryle Eklund; Medicine, MUSC, Radiology, MUSC.

Adamantinoma is a rare malignant primary tumor of the bone that most commonly develops in the tibial diaphysis. Epidemiological findings indicate that adamantinomas typically appear in males in their 2nd to 5th decades of life, and present as an aggressive mass localized to the anterior cortex of the mid-tibia with a diameter of 3 to 15 cm and a gradual onset of dull pain. On radiograph and CT, lesions appear osteolytic with an eccentric focus. On MRI, adamantinomas have been characterized as having a focus of high signal intensity on T2-weighted images or T1-weighted images enhanced with contrast. Treatment involves performance of a surgical, en bloc resection due to the fact that it is a locally aggressive bone tumor with the possibility for metastasis to the lung, lymph nodes, liver, pericardium, and other bones. This case involves a 29-year-old male who presented with pain in the right lower leg. Plain film radiograph images revealed proximal anterior tibial destruction and fracture. A multiplanar MRI of the right lower leg with and without contrast (18 cc of MultiHance) demonstrated a 4.3 x 4.2 x 7.1 cm cortically-based lytic lesion involving the proximal tibial metadiaphysis. Edema and hemorrhage surrounding the fracture site was also noted, as well as edema in the fibular head as a likely result of stress from altered biomechanics at the proximal tibiofibular joint. The lesion did not invade the neurovascular bundle; however, there was an extension of the lesion to the adjacent tibialis anterior muscle with mild enhancement that extended to the posterior tibialis muscle belly. There was also trace fluid in the infrapatellar bursa. Surgical resection of the lesion was performed along with the placement of proximal metaphyseal and diaphyseal tibial osteotomies with plate and screw fixation. Follow-up radiographic studies indicate bony callus formation consistent with continued healing and no evidence of hardware complication.

AGE INGESTION DURING PUBERTY ALTERS THE BREAST MICROENVIRONMENT TO CREATE POTENTIAL PRE-NEOPLASTIC LESIONS VIA METABOLIC IMPRINTING, Jaime F Randise, Bradley A Krisanits, Lourdes M Nogueira, Kristi Helke, Taaliah Campbell, Victoria J Findlay, David P Turner; Pathology, MUSC, Biology, Claflin University.

Increased consumption of processed food and a sedentary lifestyle can lead to the accumulation of exogenous advanced glycation end products (AGEs) in the body. These reactive sugar metabolites are formed as a consequence of sugar metabolism and heat treatment of protein rich foods containing sugars and/or lipids. Accumulation of AGEs in the body can contribute to pathological consequences as they have been shown to be pro-inflammatory and pro-oxidant when signaling through the receptor for advanced glycation end products (RAGE). AGE;RAGE signaling also leads to a feed forward loop causing an increase in RAGE expression and further AGE production. Our data shows that consumption of a high AGE diet in pubertal mice causes the formation of mammary pre-neoplastic like lesions. In attempt to reverse the effects caused by a high AGE diet, mice were fed a regular diet after a pubertal high AGE diet. Hyperplastic lesions persisted despite diet intervention. Our findings along with studies in metabolic memory supports the concept that early glycemic environment is remembered or imprinted leading to disease complications and disease progression. Oxidative stress, non-enzymatic glycation of proteins, epigenetic changes, and chronic inflammation are thought to contribute to the role of metabolic memory. It is through the consumption of AGEs that we hypothesize that these events may occur and may lead to pathological consequences, such as increased risk of breast cancer.

IMPACT OF ROTAVIRUS VACCINE INTRODUCTION ON DIARRHEAL HOSPITALIZATIONS IN CHILDREN UNDER 5 YEARS OLD IN HAITI, Emily A Cloessner, Stanley Junin, Eleanor Burnett, Dante Bugli, Eyal Leshem, Negar Aliabadi; MUSC, Centers for Disease Control and Prevention, Haiti, Centers for Disease Control and Prevention.

Abstract not available.

IMPACT OF SENSORY STIMULATION ON IMPROVING POST-STROKE UPPER EXTREMITY THERAPY OUTCOMES, Caroline M Roark, Lauren E Landers, Sarah K Phillips, Ryan J Downey, Leonardo Bonilha, V Ramakrishnan, Na Jin Seo; Occupational Therapy, MUSC, Health Professions, MUSC, Neurology, MUSC, Public Health Sciences, MUSC.

Abstract not available.
Background: Stroke survivors with neglect demonstrate a lack of attention to one side of the body/space. This impairs perception and/or motor planning on the side opposite the lesion. Those with neglect experience more severe motor impairments and less motor recovery than those without neglect. The behavioral mechanisms underlying different patterns of motor recovery is unclear, but paretic arm non-use may play a role. Evidence regarding real-world paretic arm use behavior in survivors with neglect is limited. Real-world paretic arm use in survivors with/without neglect can be objectively measured and compared using accelerometers.

Hypotheses: (1) Stroke survivors with neglect will demonstrate significantly less (p<.05) paretic arm use than survivors without neglect (2) There will be a moderate positive correlation between paretic arm use (Arm Activity Ratio [AAR]) and neglect severity (Virtual Reality Lateral Attention Test [VRLAT]).

Methods: Participants with/without neglect (≥18 years of age, unilateral stroke, able to initiate forward shoulder movement) wore bilateral wrist accelerometers to record real-world arm use for 3 days. Accelerometry data were used to calculate the AAR. The AAR is the ratio of paretic/non-paretic accelerometry counts and smaller values indicate less paretic arm use. The VRLAT was used to determine the presence/severity of neglect. We compared the AAR values between groups using a two-tailed Mann-Whitney U-Test (p<.05). We examined the relationship between AAR and VRLAT scores using a Spearman’s Rank Correlation. Results: Twenty-one participants (11 with neglect) were enrolled. There was no significant difference (U=37.5, p =.22) in AAR for those with (Mdn=.26) and without neglect (Mdn=.34). The relationship between AAR and VRLAT values was fair (rs=.33, p=.16).

Conclusion: While there was not a significant difference between the groups in this small sample, individuals with neglect did have a lower mean AAR and there was a fair relationship between AAR and neglect severity which warrants further investigation.

045-A The Relationship Between Neglect and Real-World Paretic Arm Use in Stroke Survivors, Kristin B Housholder¹, Nicole T Bertolino¹, Roblin F Lynch¹, Myra L Nicks¹, Michelle L Woodbury², Sara Kraft³, Emily S. Grattan², ¹Occupational Therapy, MUSC, ²Health Science and Research, MUSC, ³Physical Therapy, MUSC.

046-A Alcohol Use During a Cannabis Cessation Trial: Evaluating N-acetylcysteine Treatment, George A Book¹, Nathaniel L Baker¹, Jason A Tran², Rachel L Tomko¹, Erin A McClure¹, Kenvin M Gray¹, Lindsay M Squeglia¹, ¹Psychiatry and Behavioral Sciences, MUSC, ²University of California Riverside.

Individuals with alcohol use disorder (AUD) do not always respond to currently available treatments, and evaluation of new candidate pharmacotherapies is indicated. N-acetylcysteine (NAC) has shown promise as a treatment option to help individuals with a variety of substance use disorders, but little research has evaluated its merits as a treatment option for AUD. This secondary analysis examined the effects of NAC versus placebo on co-occurring alcohol use among participants with cannabis use disorder (CUD) enrolled in a 12-week, multi-site cannabis cessation trial. Participants (N=302, ages 18-50) were randomized to double-blind NAC (1200mg, twice daily) or placebo. Neither alcohol use nor desire for alcohol cessation were requirements for participation. Participants (n=277) that returned for at least one treatment visit and had recorded alcohol use data, even when abstinent, (i.e., total drinks per week, drinking days per week, and binge drinking days per week) were included in the analysis. Participants in the NAC group had reduced risk of any alcohol consumption [RR=0.73; 95% CI=0.56-0.95], decreased drinks per week [RR=0.69; 95% CI=0.48-0.99], and decreased drinking days per week [RR=0.69; 95% CI=0.51-0.92], compared to those in the placebo group. Changes in concurrent cannabis use amounts were not correlated to reported drinks per week, drinking days per week, or binge drinking days per week. These findings suggest that NAC may be effective at reducing consumption of alcohol among treatment-seeking adults with CUD. This suggests a need for further trials focused on the effects of NAC on alcohol consumption among individuals seeking treatment for AUD. NIH R25DA020537; UG1 DA013727

047-A Module-based Analyses of Lower Extremity Muscle Coordination During Walking in Individuals Post-Stroke: A Systematic Review, Bryant A Seamon¹, Richard R Neptune², Steven K Kautz³, ¹Health and Research, MUSC, ²Mechanical Engineering, The University of Texas at Austin.

Decomposing electromyographic signals through factorization allows for grouping of muscle activation patterns into modules. Modules may help explain underlying muscle coordination impairments related to biomechanical deficits during gait, leading to development of more targeted interventions for walking performance post-stroke. The purpose of this
review is to summarize current evidence for module number, composition and control during post-stroke gait while reporting on module relationships with gait mechanics, rehabilitation outcome measures and response to intervention. We searched databases for studies decomposing electromyography into modules during walking tasks for individuals post-stoke and used a modified Downs and Black checklist to evaluate methodological quality. Methods were completed in collaboration between the Ralph H. Johnson VA Medical Center and Medical University of South Carolina. Ten articles matched our inclusion criteria. Methodological quality was high (6/10). A majority of studies used non-negative matrix factorization (9/10) to identify the number of modules needed to explain 90% of the EMG variability. Reduced ability to individuate the timing of muscle activity during stance phase of the paretic leg often resulted in individuals using fewer than four modules post-stroke. Fewer modules correlated with poor walking performance as assessed by biomechanical and clinical measures. There was evidence stroke also reduced module quality with respect to timing and that rehabilitation can lead to the use of more and/or higher quality modules. Stroke reduces the number and quality of modules, with decreased walking performance related to increased module impairment. Module number and quality appear to respond to rehabilitation aimed at improving muscle coordination. Future work will need to establish the ability of modules to identify impairment mechanisms. VA/ORD Rehabilitation R&D Service 1101RX001935; NIH P20 GM109040


050-A The Effect of Vibratory Sensory Stimulation on Cortical Activity During Grip in Stroke Survivors: an FMRI Study, Amanda A Vatinno1, Leonardo Bonilha2, Na Jin Seo1; 1Health Sciences and Research, MUSC, 2Neurology, MUSC. Abstract not available.

051-A The Role of Histone H4 in Regulated Repair of DNA Crosslinks, Colleen E Quaas, David T Long; Biochemistry and Molecular Biology, MUSC. Histones are highly modified protein octamers that are used to package and organize chromatin in eukaryotic cells. Histone tails also provide a scaffold for protein modifications (acyetylation, ubiquitylation, phosphorylation, and methylation) that are used to regulate various aspects of DNA replication and damage response signaling. SET8 (PR-SET7) is a histone lysine methyltransferase that plays important
roles in genome stability and cell cycle control in S phase by specifically mono-methylating histone H4 at lysine 20 (H4K20). Here, we show that introduction of exogenous SET8 into Xenopus egg extracts prevents damage signaling required to remove DNA inter-strand crosslinks (ICLs) from chromatin. ICLs are an extremely toxic form of DNA damage that covalently links together both strands of DNA. ICLs create an impassable barrier to DNA replication and must be removed to complete DNA synthesis. Defects in ICL repair can lead to genomic instability and several cancer predisposition syndromes, including Fanconi anemia and hereditary breast and ovarian cancer. Based on this data, we aim to answer several key questions about how H4K20 methylation regulates DNA processing and preserves genome integrity. R35GM119512

052-A Functional Characterization of Mutant BRCA1, John Barrows, David Long; Biochemistry and Molecular Biology, MUSC.

BRCA1 (breast cancer susceptibility protein 1) plays a major role in preserving genome integrity through its involvement in various aspects of the DNA damage response. BRCA1 mutations are the primary cause of hereditary breast and ovarian cancers, with patients exhibiting ~80% lifetime risk of developing these cancers. In addition, many sporadic breast tumors lack functional BRCA1, further implicating BRCA1 dysfunction in tumorigenesis. Clinical mutations in BRCA1 cluster within three highly conserved functional domains: the N-terminal RING domain, a central coiled-coil domain, and a C-terminal tandem BRCT domain. However, the role that each BRCA1 functional domain plays in DNA repair and tumor suppression remains unclear. By developing a new method to isolate intact BRCA1-mutant complexes, we will identify the molecular consequences of specific BRCA1 clinical mutations. These studies will elucidate how BRCA1 defects lead to cancer and support the development of new therapeutic strategies for different BRCA1-mutant tumors. NIH TL1 TR001451 and UL1 TR001450; MUSC SCTR

053-A High-Throughput Glycoprotein Biomarker Discovery By MALDI Mass Spectrometry Imaging of Antibody Arrays, Alyson P Black, Richard R Drake, Peggi M Angel, Anand S Mehta; Pharmacology, MUSC.

The vast majority of biomarkers used in the detection of cancer are glycoproteins and recent reports have indicated that the glycan component of the glycoprotein can act as a better marker of cancer than the protein component. However, accurate glycoprotein biomarker assays are lacking, and there is a need for higher throughput biomarker discovery. Patient sample volume and accuracy of glycoprotein detection are two limiting factors in assay development. Here we propose a novel method for glycoprotein biomarker discovery using antibody microarrays coupled with MALDI Imaging Mass Spectrometry. This technique allows us to specifically capture glycoproteins and then detect all the N-linked glycans on a specific protein with high accuracy. Initial experiments have been performed using serum proteins Alpha-1-antitrypsin and Fetuin-A. Glycan signatures from these glycoproteins are accurately detectable at 10 ng. Preliminary data suggest that this method would be suitable for using small amounts of patient serum samples and assaying for 100s of glycoproteins in one run. SmartState; U01CA168856; R01CA120206

054-A Akt3 Links Mitochondrial Homeostasis and Mitosis Via the Regulation of WDR12 and Aurora B Kinase, Zachary J Hough, Robin C Muise-Helmericks; Regenerative Medicine and Cell Biology, MUSC.

We have previously demonstrated that Akt3 is required for mitochondrial biogenesis in primary endothelial cells. Akt3 indirectly affects the subcellular localization of PGC-1α, a master regulator of mitochondrial biogenesis; blockade of Akt3 expression results in a cytoplasmic accumulation of PGC-1α, thus affecting its nuclear activity. Akt3 depletion results in a marked inhibition of mitochondrial homeostasis. Additionally, we have shown that Akt3 depletion results in a mitotic phenotype specified by multi-nucleation and micro-nuclei accumulation, suggesting an inhibition of appropriate chromosome segregation. The concurrent control of mitosis and mitochondrial homeostasis by Akt3 led us to test if disrupted mitochondrial function would also result in mitotic disruption. We discovered that mitochondrial complex one inhibition via rotenone causes an apparent disruption in chromosome segregation and accumulation of multinuclear cells containing micro-nuclei similar to that shown for Akt3 depletion. These results indicate that the mitotic disruption resulting from Akt3 depletion is likely due to the negative impact on mitochondrial homeostasis. Proteomic analysis has demonstrated an interaction between WDR12, a nucleolar scaffold protein and Akt3. We demonstrate that Akt3 depletion controls WDR12 protein expression and that WDR12 depletion phenocopies the mitotic effects of mitochondrial dysfunction. We show that WDR12 and Aurora B co-immunoprecipitate suggesting that they associate. Importantly, inhibition of mitochondrial homeostasis with rotenone disrupts the Akt3/WDR12/Aurora B pathway suggesting a direct link between mitochondrial homeostasis and mitosis through Aurora B. Current studies focus on whether WDR12 and Aurora B are co-localized during mitosis and the mechanism by which Akt3 controls WDR12 protein expression. Additionally, quantification of multinuclei is
being performed via flow cytometry following nuclear isolation.

055-A Effects of Modified Lipoproteins in First Trimester Trophoblast Cells: a Role in Pre-eclampsia in Pregnancies Complicated By Diabetes?, Rebecca H McLeese1, Jiawu Zhao2, Jeremy Y Yu3, Derek P Brazil2, Timothy J Lyons4; 1Endocrinology, MUSC, 2Experimental Medicine, Queen’s University Belfast.

Introduction: Pre-eclampsia (PE) complicates 2–8% of pregnancies worldwide. In women with diabetes, the risk for PE is increased 4-fold. Trophoblast cells are involved in angiogenesis, producing growth factors to promote vascularization of the developing placenta. In women destined to develop PE, trophoblast invasion is impaired, leading to incomplete spiral artery remodelling. Soluble fms-like tyrosine kinase (sFlt–1) and soluble endoglin (sEng) are anti-angiogenic factors, secreted from many cell types and tissues including placental trophoblast. Evidence suggests that increased release of these factors from the trophoblast into the maternal circulation may promote endothelial dysfunction associated with the development of PE. In this study, we investigated sFlt–1 and sEng release from the placental trophoblast cell line, HTR8/svneo, in response to modified lipoproteins (which accumulate in vascular tissues of patients with diabetes) and/or elevated glucose. Methods: HTR8/svneo cells were exposed to highly oxidized glycated low density lipoprotein (HOG–LDL) (0–200μg protein/ml) for 24h. To investigate the effect of hyperglycaemia, HTR8/svneo cells were pre-treated (72h) with 30mM glucose followed by exposure to HOG–LDL vs N–LDL for 24h. Transcriptional expression of the two main sFlt–1 isoforms, i13 and e15α, endoglin and its major shedding protease, MMP–14, were measured by RT–PCR. sFlt–1 and sEng secretion in cell supernatants were measured by ELISA. Results: HOG–LDL increased sFlt–1 mRNA expression (i13, p<0.05; e15a, p<0.01) and protein secretion (p<0.05). HOG–LDL increased mRNA expression of endoglin and MMP–14 (p<0.05) and secretion of sEng (p<0.01). N–LDL had no effect on HTR8/svneo cells. High glucose potentiated the effects of HOG–LDL, but alone had no effect. Conclusion: Exposure of trophoblasts to modified lipoproteins may contribute to the development of PE in diabetes, and the presence of high glucose may amplify the effect. These findings may explain the increased risk of PE in women with diabetes.

056-A Direct Conversion and Detection of Reactive Oxygen Species on a Cathodically-biased Metallic Surface, Michael J Wiegand, Jeremy L Gilbert; Bioengineering, Clemson.

Reactive oxygen species (ROS) can be produced both physiologically due to cellular aerobic activity or chemically from the reduction of water and oxygen molecules adjacent to an electron rich metallic surface. Because of their high toxicity and reactivity, ROS are a source of oxidative stress that can harm key cellular components as well as alter the corrosion resistance of alloys. Terephthalic acid (TA) converted to fluorescent 2-hydroxyterephthalate (HTA) can be used to measure ·OH production from local reduction reactions or from the cleaving of mitochondrial produced H2O2 by Fenton-like reactions. CoCrMo discs (n=3) with an exposed surface area of 0.641 cm2 were tested at room temperature using a 1 mL stock solution of 2 mM TA + 15 mM H2O2. Discs were held potentiostatically at -1 V from the reference electrode and maximum fluorescence intensity values were measured following tests at the emission wavelength, and the log of the average intensity was plotted against time. Fluorescence intensities (I/Io), the ratio between the measured maximum and untested stock solution intensities, increased rapidly between 0 and 1 hr, linearly between 1 and 16 hrs of applied voltage and then tapered off. There was a significant effect (p < 0.05) between time and measured fluorescence intensity. These findings indicate that there is an increase in ·OH production over time, as well as a significant interaction between solution H2O2 and a cathodically-biased surface. Further work has been done to study reduction reactions at the surface using the same experimental set-up, however the stock solution is saline based (0.9% NaCl) and free of initial H2O2. Fluorescent spectroscopy and ROS specific fluorescent molecules can help characterize solution chemistry during corrosion and in vitro inflammatory models. Hansjörg Wyss Endowed Fund for Regenerative Medicine

057-A Targeting Fli-1 in T Cells Prevents Chronic Graft-versus-Host Disease, Steven D Schutt1, Anusara Daenthanasanmak1, Wu Yongxia1, Hung Nguyen1, M. Hanief Sofi1, David Bastien1, Supinya Iamsawat1, Carole Wilson2, Lynn M Schnapp2, Zhang K Xian2, Xue-Zhong Yu2; 1Microbiology and Immunology, MUSC, 2Medicine, MUSC.

Allogeneic hematopoietic stem cell transplantation (allo-HCT) is a curative procedure for hematological malignancies. However, chronic graft-versus-host disease (cGVHD) is a lethal complication that often develops after allo-HCT. Few significant improvements have occurred in past decades for the
prevention of cGVHD, resulting in an urgent need for novel pharmacological or immunotherapeutic interventions. Friend Leukemia Virus Integration 1 (Fli-1) is an aberrantly expressed transcription factor in several types of cancers including erythroleukemia and melanoma. While also being implicated in the pathogenesis of systemic lupus in mice and humans, a disease with marked similarity to cGVHD. Due to these findings and the high level of Fli-1 expression on lymphocytes of the adaptive immune system—critical mediators of cGVHD—we hypothesized that targeting Fli-1 would prevent cGVHD after allo-HCT in mice. Hematopoietic cells from conditional knock-out mice deficient for the fli-1 gene specifically on T cells were used as a donor source to induce cGVHD. Progression of cGVHD in murine allo-HCT recipients was monitored using a clinical scoring system, and changes in activation status of hematopoietic cell populations were quantified using flow cytometry. Recipients transplanted with donor grafts containing hemizygous fli-1 deficient T cells exhibited improved survival and reduced cGVHD clinical scores compared to wild-type littermates. Donor-grafts containing hemizygous fli-1 deficient T cells were associated with restrained T-cell responses including reduced Interferon-γ cytokine production, PD-1 expression, and differentiation into follicular helper T cells. Hemizygous fli-1 T-cell deficient donor-grafts also improved donor B-cell reconstitution and reduced plasma cells in allo-HCT recipients relative to littermate wild-type control donor-graft recipients. Thus, inhibiting Fli-1 represents a promising therapeutic strategy for the goal of preventing cGVHD after allo-HCT while also directly targeting cancers which aberrantly express Fli-1. NIAID R01AI118305; NCI R01CA169116; NHLBI R01HL137373; TL1 TR001451

058-A Defining the Tissue N-Glycome of Genomic Subtypes of Breast Cancer. Danielle A Scott1, Rita Casadonte2, Laura Spruill3, Anand Mehta4, Nicole Simone5, Mark Kriegsmann6, Joerg Kriegsmann6, Richard Drake8, 1Pharmacology, MUSC, 2Proteopath GmbH, 3Radiation Oncology, Thomas Jefferson University, 4Pathology, University of Heidelberg, 5Pathology, MUSC.

We have applied a recently developed matrix-assisted laser desorption/ionization imaging mass spectrometry (MALDI-IMS) method to spatially profile N-linked glycans in human breast cancer formalin-fixed paraffin-embedded (FFPE) tissue sections and tissue microarrays (TMA). Routinely, 40–50 N-glycans are detected per FFPE tissue, and this number increases significantly with disease severity. Through the combined analysis of breast cancer FFPE tissues and TMAs we have been able to identify histopathology co-localized glycan structural classes specific to stromal, necrotic and tumor regions. N-glycan panels derived from TMAs representing HER2 receptor positive and triple negative breast cancers were compared to identify shared and divergent glycosylation patterns between the two genetic sub-types. Within the tissues, we have identified a series of high-mannose glycans that are predominantly associated with tumor regions, as well as more highly branched and fucosylated glycans in higher grade tumors. While high mannose and bi-antennary core fucosylated glycans maintained a fairly consistent distribution throughout the HER2+ and triple negative tissues, a series of polylactosamine glycans appeared to be highly specific for the triple negative samples. Several branched fucosylated glycans were also detected at higher levels in Her2+ tumors. Additionally, imaging of matched triple negative breast cancer biopsy and lumpectomy FFPE sections analysis revealed a vast diversity of N-glycan localizations, resulting in panels of glycans representing distinct structural regions in stroma, necrotic and tumor. Non-fucosylated bi- and tri-antennary glycans were specifically detected in regions of tumor necrosis. The results in these samples also further supported the TMA data in that the same polylactosamine glycans were detected in the triple negative tumor regions. Because triple negative breast cancer represents a subtype of breast cancer that is highly aggressive with poor clinical outcomes, we believe the presence of polylactosamine glycans could be associated with more aggressive cancers. NCI R21CA207779, NCI R21CA186799-01

059-A DZIP1-KIAA2026 Interactions Are Required for Normal Mitral Valve Development. Lilong Guo, Diana Fulmer, Katelynn Toomer, Joshua Lipschutz, Russell Norris; Regenerative Medicine and Cell Biology, MUSC.

Mitral Valve Prolapse (MVP) is a common cardiac disease that affects 1 in 40 individuals and is associated with secondary complications (e.g. arrhythmia’s, heart failure, and sudden death). Genetic analyses by our group and colleagues have resulted in the first identification of MVP genes. One of these genes, DZIP1, was previously reported to be involved in primary cilia structure and function, implicating a role for cilia in mitral valve development and disease. To initially identify the function of DZIP1 in promoting cilia function, we performed proteomics based approaches with the goal of identifying unique binding partners for DZIP1. These studies revealed a direct interaction between DZIP1 and a protein of unknown function, KIAA2026 that was previously shown to interact with CDC42. Our previous studies showed CDC42 facilitates localization of an octameric shuttling complex, known as the exocyst, to the primary cilium and then targets and docks vesicles carrying proteins necessary for ciliogenesis. Thus, we hypothesized that DZIP1 interacts with CDC42 and the exocyst through a KIAA2026 linker and stabilizes this complex at the
membrane to initiate ciliogenesis. Interestingly, this function is developmentally restricted, as primary cilia are not observed during postnatal life. Genetic and epistasis experiments in mice and zebrafish reveal pathway convergence during mitral valve morphogenesis. Biochemical approaches further demonstrated an interaction between this complex and the interaction domain between DZIP1 and KIAA2026. Live-image analyses further support our hypothesis that DZIP1 is required for promoting normal trafficking of exocyst to the primary cilia intermediated by KIAA2026. These data support a molecular interaction between DZIP1-KIAA2026-CDC42 to stabilize the exocyst complex at the membrane, a critical initial step in the generation of primary cilia. AHA-15GRNT25080052;NIH-P20 GM103444;RO1HL127692;RO1HL131546;VA-Merit Award I01 BX000820 ;NIH-P30DK074038

060-A Proteomic Imaging Analysis of Injured Cochlear Tissues, Kenyaria V Noble, Michelle Reyzer, Jeremy Barth, Kevin Schey, Edward Krug, Hainan Lang; 1Pathology, MUSC, 2Tissue Core, VU, 3Regenerative Medicine, MUSC.

Exposure to noise or ototoxic-drugs often results in degeneration of cells in the sensory epithelium, auditory nerve, and supporting cells of the cochlear lateral wall. However, the molecular mechanisms underlying this pathology remain unclear. Coupling gene arrays with matrix-assisted laser desorption/ionization-time of flight imaging mass spectrometry (MALDI-TOF IMS) offers high resolution spatial signatures of the molecular responses to cellular alterations. Thus, the purpose of this study is to identify and characterize regulatory proteins in the cochlea responsive to noise or ototoxic-drug exposure using this complementary proteo-transcriptomics approach. Young adult CBA/CaJ mice were subjected to octave-band noise at 106 or 112 dB SPL for two hours. Auditory brainstem responses were recorded immediately (< 1 hr), and 1-4 days post-noise exposure. Microarray analysis was performed on mRNAs of the cochlear lateral wall and auditory nerve. dChip analysis identified differentially expressed mRNAs meeting the criteria of a) increase in expression and b) statistically significant difference (p < 0.05). Gene expression results indicate that 394 genes are significantly upregulated in response to injury in both models. MALDI imaging was conducted on cochlear sections prepared from both noise- and ouabain-exposed mice and putative identifications for observed m/z ratios were compiled using established proteomic databases. MALDI imaging of cochlear sections revealed 14 proteins exhibiting spatially distinct patterns localized to various cochlear regions in both cochlear injury models. Convergent analysis of the mRNA and protein data yielded 15 candidates, including molecules related to chemotaxis, apoptosis and protein processing. Immunohistochemical analysis of one candidate, the neuropeptide nociceptin revealed localization to the neural cells of the auditory nerve and non-sensory cells of the spiral ligament and stria vascularis. The combined analysis of MALDI imaging with gene expression data provides a new strategy to acquire molecular regulators responsive to cochlear injury. NIH R01 DC007506, NIH P50 DC00422, NIH P30 GM103342, NIH P20 GM103499, NIH P41 GM103391, and NIH R25 GM072643

061-A Modeling Regulatory T Cell (Treg) Immunosuppression, Ravyn M Thompson, Cara Coleman, Dolloff G Nathan; Cellular and Molecular Pharmacology and Experimental Therapeutics, MUSC.

Immuno-oncology (IO) approaches have demonstrated promising clinical activity in a variety of solid and hematological malignancies, including multiple myeloma (MM). A limitation for successful and durable responses to IO strategies includes natural regulatory T cell (Treg) immunosuppression of effector T cells (CD8+) and helper T cells (CD4+). The long-term goal of this study is to first model Treg immunosuppression in vitro, and then use these model systems to discover and evaluate molecular strategies that dampen Treg function and ultimately improve IO. MM was chosen as our cancer disease model. We show results of successful activation and expansion of human Tregs from primary peripheral blood mononuclear cells (PBMCs) with IL-2, a CD3/CD28/CD2 trivalent antibody, and TGF-beta. Tregs were immunophenotypically verified as CD4+CD25+FOXP3+. Functionally, carboxyfluorescein succinimidyl ester (CFSE) labeling experiments revealed suppression of CD4+ and CD8+ T cell proliferation by Tregs at ratios as low as 1:4 (Treg : T cell) after 5 days of co-culture. Additionally, our induced Treg populations suppressed the secretion of IFN-gamma by effector T cells, as further evidence of immunosuppressive function. To directly measure anti-MM T cell responses, we developed a MM/T cell coculture system, and adapted this assay for high throughput in microtiter plates. The viability of MM cells is monitored by Gaussia luciferase (GLuc) activity, as cells stably express this secreted and highly sensitive luciferase enzyme. We were able to quantify T cell-induced death in MM cells and show decreased anti-MM T cell responses after pre-incubation with Tregs. Characterizing induced Tregs in vitro provides us with a model to better discover and evaluate future therapeutics including small molecules and biologics that inhibit Treg function. These studies will support drug discovery efforts that will ultimately improve IO therapies for patients with MM and other forms of cancer. TL1 TR001451, UL1 TR001450, ACS RSG1415601CDD, NIH P20GM103542
062-A Physical and Self-Reported Function Following Anterior Cruciate Ligament Reconstruction with Quadriceps Tendon Autografts, Jennifer L Hunnicutt¹, Kelli B Adams², Michelle M McLeod², Chris M Gregory¹, Harris S Slone³, ¹Health Science and Research, MUSC, ²Health and Human Performance, CofC, ³Orthopedics, MUSC.

Introduction: Following anterior cruciate ligament reconstruction (ACLR), individuals face deficits in quadriceps function that contribute to long-term consequences, such as early-onset osteoarthritis. One of the underlying contributors to long-term quadriceps dysfunction may be the various procedures performed during the reconstruction. The purpose of this analysis is to compare quadriceps tendon (QT) and bone-patellar tendon-bone (BPTB) autograft procedures and their effects on both muscular and self-reported function. Methods: Individuals with history of primary, unilateral ACLR participated in this study. Outcome measures include knee extensor isokinetic strength, dynamic knee function, and patient-reported knee function. Peak knee extensor strength was measured bilaterally with an isokinetic dynamometer and normalized to body mass. Dynamic knee function was measured bilaterally via the single leg hop test. Patient-reported knee function was measured with the International Documentation Knee Classification (IKDC) questionnaire. Results: Data from six individuals (29 years; 3 QT, 3 BPTB; 9 mo. post-ACLR) is presented. Individuals with QT autografts demonstrated less knee extensor strength (1.5 vs 2.4 Nm/kg) and dynamic knee function (129 vs 168 cm) in the surgical limb compared to the uninjured limb. This presents as an interlimb deficit of 60% in strength and 77% deficit in dynamic function. When compared to the surgical limb of the BPTB group, the QT group exhibited similar outcomes in strength (1.7 vs 1.5 Nm/kg), dynamic function (126 vs 130 cm), and IKDC scores (64 vs 70). Conclusion: Based on these pilot analyses of individuals following ACLR, similar outcomes are observed between QT and BPTB autograft groups. One limitation worthy of noting is that the QT group is older (36 vs 19 years) with longer chronicity (10.7 vs 7.3 months) than the BPTB autograft group. Additional participants will be included and specific data analyses will be conducted and presented in future work. MUSC TL1 TR001451 and UL1 TR001450; NATA Foundation 1617DGP005

063-A The Role of the BAF/VRK1 Signaling Axis on the DDR in Nestor-Guillermo Progeria Syndrome (NGPS), Maya F El-Sabban, Aye Mon, Paula Traktman; Biochemistry and Molecular Biology, MUSC.

The nuclear envelope is a dynamic structure involved in the regulation of nuclear function and architecture. The inner leaflet of the nuclear membrane is comprised of lamins, which provide structural scaffolding and an interface with chromatin. BAF is an important component of the lamina that binds to the proteins of the nuclear envelope and contributes to the architecture of the nucleus. Furthermore, BAF binds with the chromatin and chromatin domain-containing proteins, such as Lap2 and emerin, acting as a bridge that “snaps” DNA to the nuclear lamina. A subset of diseases called laminopathies or envelopopathies result from mutations in the components of the nuclear lamina or envelope, highlighting the importance of the nuclear envelope’s structural integrity in normal cell function. Nestor-Guillermo Progeria Syndrome (NGPS), a recently discovered novel progerioid syndrome and envelopopathy resulting from the homozygous inheritance of a mutation that causes an amino acid substitution in BAF from Ala-12 to Thr (A12T). The mechanism of disease pathology is still unclear and the role of the BAF A12T mutation in the disease phenotype has yet to be characterized. Envelopopathy is also observed in cells deficient in VRK1, a nuclear kinase that phosphorylates BAF. The literature describes BAF A12T mesenchymal stem cells as displaying a defect in their ability to maintain stemness and to differentiate into their known lineages in vitro. We aim to understand whether BAF and VRK1 signaling pathways are affected by the A12T mutation and whether disruption of these pathways in mesenchymal stem cells contributes to the differentiation defect. The literature further indicates that VRK1 depletion results in a dampened DNA damage response, and that BAF interacts with DNA damage response proteins. Therefore, we propose that the DNA damage response pathway may contribute to the NGPS phenotypes.

064-A Mitral Valve Prolapse: A Congenitally-based Disease of Primary Cilia. Katelynn Toomer, Diana Fulmer, Guo Lilong, Hughes Michaela, Brooks Brittany, Norris Russell; Regenerative Medicine and Cell Biology, MUSC.

Cardiac valve disease is a major health burden. Mitral valve prolapse (MVP) is one of the most common forms of cardiac valve disease and affects ~2-3% of the human population. MVP can lead to secondary complications such as arrhythmias, heart failure, and sudden cardiac death and 1 in 10 patients will require valve surgery. There are no effective nonsurgical
066-A Effect of Oxytocin on Stress-Induced Reinstatement of Alcohol-Seeking Behavior in Male and Female Mice, Courtney E King¹, Howard C Becker²; ¹Charleston Alcohol Research Center, MUSC, ²VA Medical Research Center. Alcoholism is a chronic relapsing disease characterized by periods of abstinence followed by return to heavy use. While many factors contribute to increased relapse vulnerability, stress is considered to play a prominent role in triggering relapse. A growing body of literature suggests that the oxytocin (OT) system plays a role in a number of stress-related psychiatric disorders including alcohol addiction. Work from our lab has demonstrated that systemic administration of OT reduced binge-like alcohol drinking and operant oral self-administration in male C57BL/6J mice. The present study was designed to extend these findings by examining the effects of OT treatment on alcohol relapse-like behavior. Adult male and female were trained to acquire stable rates of lever responding 12% ethanol in daily 20 min operant conditioning sessions. Once lever responding and alcohol intake stabilized (<15% variability over 3 consecutive days) mice entered into the extinction phase of the study (responding yields no alcohol delivery) for 14 days before reinstatement testing. All mice underwent stress-induced reinstatement testing using either predator odor (2,3,5-Trimethyl-thiazoline; TMT) or the α-2 adrenergic receptor agonist yohimbine. At 30 min prior to the reinstatement test session, separate groups of mice were injected (ip.) with vehicle (saline) or OT (0.1, 0.5, 1 mg/kg). Systemic OT administration attenuated stress (TMT)-induced reinstatement of alcohol seeking behavior in a dose-related manner in male and female mice. Further, female mice showed greater sensitivity to OT.

treatments for MVP and therapeutic efforts have been hindered by an incomplete understanding of its fundamental causes. One accessible source of such information may come from genetic studies of MVP. We previously reported familial and GWAS studies that identified genetic mutations and/or excellent candidate targets as causal to MVP. Pathway analyses suggested a common cellular and molecular thread between these studies and invoke the primary cilia as potential unifying mechanism. This discovery is further bolstered by our recent identification of a mutation in a cilia gene in a large family with MVP, DZIP1. Our data show genetic haploinsufficiency of primary cilia in cardiac valves leads to a non-syndromic mitral valve disease in mouse models whereas complete genetic ablation enhances mitral valve phenotype severity and generation of bicuspid aortic valve (BAV). We present, for the first time, a potential common cellular and molecular thread through which MVP and potentially BAV can arise. These studies define the primary cilia as a critical, and previously unrecognized facet of cardiac valve development. Uncovering how valve disease genes regulate downstream signaling cascades will provide key mechanistic insights into MVP and potentially BAV pathogenesis at a cellular and molecular level. AHA-16PRE30970048

065-A Heroin Self-administration and Extinction in Rats Alter Prefrontal Cortical Astroglial Synaptic Contacts Which is Normalized By Chronic N-acetylcycteine Treatment During Extinction, Ben M Siemsen¹, Michael D Scofield², Jacqueline F McGinty¹; ¹Neuroscience, MUSC, ²Anesthesiology, MUSC. Cocaine and heroin self-administration followed by extinction training in rats has previously been shown to decrease astroglial synaptic contacts in the nucleus accumbens core (NAcc). This retraction is associated with decreased expression of the glutamate transporter, GLT1, and elevated extracellular glutamate during cue-induced reinstatement following extinction, adaptations that are prevented by chronic treatment with the cysteine pro-drug, N-acetylcycteine (NAC). However, it is not known whether heroin self-administration and extinction alters astrocytic synaptic contacts within the prelimbic (PrL) cortex, and whether such a change would be affected by chronic NAC treatment. Rats were microinjected with AAV5-GFAP-Lck-GFP within the PrL cortex and received i.v. catheterization. Rats self-administered heroin (n=10), or yoked saline (n=5) for 14 daily sessions followed by extinction training. During the final 10 days of extinction, heroin rats (n=5) received injections of NAC (100 mg/kg, i.p.) 30 minutes prior to daily extinction sessions. Rats were perfused 24 hours after the final injection, and coronal sections of the PrL cortex were immunohistochemically processed for GFP, the presynaptic marker Synapsin I, and the post-synaptic marker GluA2. Confocal Z-stacks were 3D reconstructed with Imaris software, and the colocalization module of Imaris was used to assess the degree to which GFP co-registers with Synapsin I and GluA2 immunoreactivity. Results indicate that heroin self-administration followed by extinction increases the colocalization between GFP positive voxels and Synapsin I, as well as GluA2, positive voxels. Both effects were prevented by NAC treatment in heroin self-administering rats. These results suggest that, unlike NAcc astrocytes, PrL cortical astrocytes increase their contact to synapses following extinction, potentially to facilitate glutamatergic neurotransmission by preventing glutamate overflow to extrasynaptic sites. Current experiments are investigating whether astrocyte complexity, indexed by branching of the cytoskeletal protein GFAP, is increased in heroin rats and whether this is also prevented by chronic NAC treatment during extinction. R01-DA033479, F31-DA041021
Conclusions Noise exposure rapidly affected myelinating glial cells, causing abnormal molecular and cellular consequences. Aberrations in myelin and hearing loss in QKI-deficient mice support QKI’s importance in normal ANs. Our findings implicate that QKI dysregulation is a critical early component in noise trauma, influencing cochlear glia function that leads to AN demyelination and, ultimately, hearing deficiency. 

Background Noise exposure can lead to auditory nerve (AN) degeneration and hearing deficiency, though causal molecular mechanisms are not entirely understood. Most spiral ganglion neurons are ensheathed by myelinating glia which facilitate rapid transmission of nerve impulses from the cochlea to the brain. Here we show that noise exposure causes glial dysfunction leading to myelin abnormality and altered expression of numerous genes in AN, including quaking (QKI), a gene implicated in regulating myelination. Methods Young-adult CBA/CaJ mice were exposed to 8-16 kHz octave-band noise at either 106 or 112dBsPL for 2 hours, and paired with non-exposed controls. Auditory brainstem response tests were performed pre- and post-noise. Histological and microarray studies were performed on AN samples from these noise-exposed mice and on AN samples from postnatal CBA/CaJ mice. To analyze effects of QKI deficiency on the cochlea, young-adult QKIFL/FL;PLPCreERT mice were used with QKIFL/FL; controls. Results Noise-exposed ANs compared to controls showed increased demyelination and nodal abnormalities, which contributed to significant declines in hearing function. Microarray analyses in noise-exposed ANs showed widespread expression changes in myelin-related genes, including QKI and numerous QKI target genes. Expression profiling of these myelin-related, QKI target genes responsive to noise showed that changes in their expression patterns post-noise largely did not recapitulate changes in their expression patterns during postnatal development. In QKIFL/FL;PLPCreERT mice, protein expression of QKI isoforms were ablated in AN glia, and extensive dysmyelination, disruption of paranodal structures, and hearing loss were seen compared to control mice.

Conclusions Noise exposure rapidly affected myelinating glial cells, causing abnormal molecular and cellular consequences. Aberrations in myelin and hearing loss in QKI-deficient mice support QKI’s importance in normal ANs. Our findings implicate that QKI dysregulation is a critical early component in noise trauma, influencing cochlear glia function that leads to AN demyelination and, ultimately, hearing deficiency. NIH R01 DC012058; NIH P50 DC00422; NIH R25 GM072643; NIH F31 DC015741; NIH T32 DC014435; NIH P30 GM103342; NIH P20 GM103499; NIH P30 CA138313; NIH S10 OD018113; NIH C06 RR014516; MUSC
that Sirt6 could be a potential therapeutic target in ALS.

**070-A Differential AKT Signaling in PTEN Null Triple Negative Breast Cancer Cells**, Ericka L Smith, Christiana S Kappler, Stephen P Ethier; Pathology, MUSC.

Triple negative breast cancer is an aggressive molecular subtype of cancer with poor clinical outcome. A subset of these cancers overexpress epidermal growth factor receptor (EGFR), and are PTEN null. Despite overexpression of EGFR, therapies targeting EGFR have performed poorly in clinical settings. Therefore, understanding the mechanisms of resistance in these cells is critical for improved patient care. The SUM-149 and MDA-MB-468 cell lines overexpress EGFR and are PTEN-null; these cell lines both have elevated levels of phosphorylated AKT compared to control MCF-10A cells. However, while treatment of SUM-149 cells with inhibitors targeting EGFR (Gefitinib), type-1 PI3K (BKM120), mTOR (KU-0063794) and pan-AKT (MK2206) did not reduce p-AKT levels, MCF-10A and MDA-MB-468 cell lines treated with the same panel of targeted inhibitors showed marked inhibition of p-AKT. Although re-expression of PTEN alone in SUM-149 cells had little effect on p-AKT, these cells displayed decreased AKT phosphorylation following treatment with Gefitinib, BKM, KU, and MK. There are three isoforms of AKT (AKT1, AKT2 and AKT3) of which, AKT3 has been implicated in the aggressive nature of some cancers. SUM-149 cells have higher levels of AKT3 message and protein compared to the other AKT isoforms, and higher levels than the MDA-MB-468 and MCF-10A cells. Immunoprecipitation analysis in PTEN re-expressing SUM-149 cells showed that PTEN re-expression resulted in decreased phosphorylation of AKT1 but not AKT3. In addition, AKT3 phosphorylation displayed retained signaling to the PI3K type-I pathway inhibition, but sensitivity to a low dose of Wortmannin, a pan PI3K inhibitor, suggesting that AKT3 may be regulated by non-canonical PI3K signaling. Taken together, these data indicate that in this subset of basal breast cancers with overexpression of EGFR, loss of PTEN expression and increased expression of AKT3, oncogenic signaling involving activation of AKT3 contributes to the aggressive and drug-resistant phenotype observed in this subset of TNBC. NIH R01CA130933; MUSC IMSD


Evidence from human and animal studies indicates that the prefrontal cortex (PFC) is especially vulnerable to repeated episodes of binge alcohol exposure. Animal studies have reported that adolescent binge-like exposure to alcohol is associated with cognitive dysfunction in adulthood. In this study, we examined the effect of adolescent intermittent ethanol (AIE) exposure by vapor inhalation on performance of a probabilistic reversal learning (PRL) task in adult Long-Evans rats. This task requires rats to complete serial reversals within an operant learning session using probabilistic reward reinforcement. Compared to controls, AIE-exposed rats were moderately impaired on the first discrimination of the first day of PRL testing, indicating that AIE is associated with mild deficits in probabilistic reinforcement learning. We did not observe any effects of AIE on reversal learning. This was unexpected in light of previous studies using various non-operant procedures that reported deficits in reversal learning. To determine whether the lack of effect we observed on PRL could be strain-specific, we examined the effect of AIE on performance of the PRL task using Sprague-Dawley (SD) rats. These follow-up studies revealed that SD rats subjected to AIE-exposure displayed retarded acquisition of the PRL task, indexed by the number of reversals completed over 16 days of training, when compared to controls. In addition, AIE treatment also caused a trend (p = 0.06) towards reduced win-stay/lose-shift behavior, suggestive of impairments in sensitivity to both rewards and negative feedback. This same impairment of win-stay/lose-shift behavior has been demonstrated following inactivation of the medial orbitofrontal cortex, which contributes to decision-making involving reward uncertainty. Together, these results are consistent with studies showing that AIE alters prefrontal function in adulthood and that some of these impairments may be mediated by perturbed orbitofrontal functioning. Furthermore, these findings identify potential strain differences in the impact of AIE on cognitive function. NIH AA019967; NIH AA022701, NIH 4T32AA007474-29

**072-A Stromal Platelet Derived Growth Factor Receptor-Beta (PDGFRB) Promotes Breast Brain Metastasis**, Katie A Thies, Anisha M Hammer, Blake E Hildreth III, Luke O Russell, Steven T Sizemore, Anthony J Trimboli, Gina M Sizemore, Michael C Ostrowski; 1Biochemistry & Molecular Biology, MUSC, 2The Comprehensive Cancer Center, The Ohio State University, 3The Hollings Cancer Center, MUSC.

Abstract not available.
073-A Progressive Decrease in Left Atrial Volume Over 8 Years Following Alcohol Septal Ablation for Hypertrophic Obstructive Cardiomyopathy, Ashley A Waring, John Lecluyse, Amy Wahlquist, Alexander Canova, Mira Patel, Valerian Fernandes, Christopher Neilsen, Sheldon E Litwin; MUSC.

Background: Alcohol septal ablation (ASA) has been proven to be a safe and effective interventional treatment for hypertrophic obstructive cardiomyopathy (HOCM). Increased left atrial volume (LAV) is a marker of chronically elevated LV filling pressures and a strong predictor of adverse outcomes. We assessed long-term changes in LAV after ASA. Methods: We retrospectively studied 98 HOCM patients who underwent ASA (55 women; age 60±13; 80 white, 9 black, 9 other) and had serial transthoracic echoes performed following the procedure (mean follow-up 388±529 days, max 8.5 years). A repeated measures mixed model was used to determine changes in left ventricular outflow tract (LVOT) gradients and LAV over time. Results: There were significant reductions in resting LVOT gradient (44.9±7.0 to 19.9±3.4 mmHg, p=0.00) and LAV (86.4±2.6 to 74.7±1.9 ml, p=0.00) after ASA. The repeated measures mixed model for long-term changes in LVOT gradient (y=44.27-4.1x, p=0.00) and LAV (y=82.845-1.275x, p=0.027) showed significant negative trends. Conclusions: The findings suggest that improvements in LVOT gradients after ASA lead to progressive reductions in LAV that continue long-term after the procedure.

074-A Changes in Left Hemisphere Perilesional Grey and White Matter Predict the Evolution of Language Abilities in Chronic Stroke Aphasia, Alexandra Basilakos1, Lisa Johnson1, Grigori Yourganov2, Leonardo Bonilha3, Chris Rorden2, Julius Fridriksson1; Communication Sciences, USC, 2Psychology, USC, 3Neuroscience, MUSC.

Rationale: Language abilities are often assumed to remain relatively stable once an individual reaches the chronic stage of aphasia recovery. However, recent studies show that clinically relevant improvements and declines in language abilities are possible, and that these changes may be driven by neuroplastic changes in specific grey matter regions in the contralesional right hemisphere (Holland et al., 2017; Hope et al., 2017). The integrity of left hemisphere perilesional tissue is also important for recovery (Fridriksson, 2006), but the effects of longitudinal perilesional changes have not been systematically investigated in a large sample of individuals with aphasia. Accordingly, this study investigated whether changes in grey and white matter (GM, WM) tissue volume in left hemisphere perilesional areas predict changes in language. Methods: 26 participants with chronic aphasia caused by stroke (9 female, mean stroke age=54.4±9.5) were identified from databases of behavioral and neuroimaging data obtained in collaboration between USC and MUSC. Participants were included if they had structural neuroimaging data and aphasia testing (Western Aphasia Battery) acquired at two time points at least six months apart (mean inter-test interval=38.1±26.6mos). Perilesional GM and WM volumes were computed for Time 1 and Time 2 scans, and tissue changes were related to language changes. Results: Thirteen participants demonstrated an improvement in aphasia severity, seven declined, and six remained stable (>±3 point change in WAB-Aphasia Quotient). Lesion size did not differ between improvers and decliners (p=0.45). Perilesional WM changes predicted changes in object naming performance (R-squared=0.30;F(1,16)=6.3,p=0.02), and GM changes predicted changes in auditory comprehension (R-squared=0.24;F(1,16)=4.8,p=0.046). Specific regional analyses will be reported at time of presentation. Conclusion: Results confirm prior studies that refute the notion of a recovery plateau and suggest that changes in perilesional tissues account for some of the variance in symptom evolution. Results can inform neural plasticity, with implications for aphasia management. NIH T32DC014435; NIH P50DC014664; NIH U01DC011739

075-A MiRNA Expression Shifts As an Initiator Event in Carcinogenesis Induced By Bisphenol A in Human Prostate Cells., William A da Silveira1, Ludivine Renaud2, Jonathan Simpson1, Matthew Huff1, W Bailey Glen Jr1, Hazard E Starr1, Dongjun Chung2, Gary Hardiman1; 1Bioinformatics, MUSC, 2Medicine, MUSC, 3Library Science and Informatics, MUSC, 4Public Health Sciences, MUSC.

Introduction: Bisphenol A (BPA) is a chemical used in the production of polycarbonate plastics and is notable for its endocrine-disrupting effects acting as a xenoestrogen. Its ubiquitous nature in the environment is highlighted by the fact that 92.6 % of adults excrete BPA. Recently estrogens have been implicated as potential agents in the development and progression of prostate cancer. miRNAs act as gatekeepers in transcription modules, increasing the robustness of transcription networks. Objectives: We hypothesize that BPA exposure negatively impacts transcriptional programs via alterations in miRNA expression, resulting in less robust biological circuits that are more prone to unstable outputs that can ultimately lead to prostate cancer. Materials and Methods: We extracted RNA from Human Prostate Epithelial Cells (CloneticsTM), derived from a 23 year old male, and cultured in the presence or absence of two BPA doses (5 and 25 nM) and ethinylestradiol EE2 (0.1 nM) for 24
Moreover, we found that eHsp90 elicited Src/RhoA and GBM, indicating a conserved mode of action. In the current study, we aimed to further define the molecular and functional relationship between EphA2 independently of its cognate ligand ephrin A1. Hsp90 (eHsp90) exhibits functional collaboration with and eHsp90 within the context of ligand activation and altered cell morphology to favor rounded, retraction, and ECM detachment. Conversely, eHsp90 blockade impaired ephrin A1-mediated Src activation and formation of an EphA2-Src complex. Further, eHsp90 signaling via this axis stimulated activation of the myosin pathway, culminating in formation of an EphA2-myosin complex central for cytoskeletal remodeling. Inhibition of either eHsp90 or Src was sufficient to impair ephrinA1 mediated activation of myosin, and EphA2-myosin complex formation. Collectively, our data support a paradigm whereby eHsp90 and EphA2 exhibit molecular crosstalk and functional cooperation within a ligand dependent context to orchestrate cytoskeletal events controlling cell morphology and attachment. NCI RO1 CA187342

078-A Perturbation of Hedgehog Signaling in The Mesothelial Cell Lineage Results in Severe Congenital Heart Defects, Emilye Hiriart, Tara Burns, Ray Deepe, Turner Rainwater, Andy Wessels; Regenerative Medicine and Cell Biology, MUSC.

The epicardium is a mesothelially-derived epithelium that covers the surface of the heart. An epithelial to mesenchymal transition (epiMT) of the epicardium is responsible for the generation of a population of epicardially-derived cells (EPDCs). EPDCs contribute to a number of cell types in the developing heart including the interstitial fibroblasts, coronary smooth muscle cells, the mesenchyme of the annulus fibrosis, and a subset of fibroblasts in atrioventricular valve leaflets. In earlier studies from our lab we have used the mWt1Cre mouse to perform epicardial cell fate tracing studies and to investigate the role of BMP signaling in epicardial development. In the current study we have used this mouse model to investigate the role of mesothelial/epicardial Hedgehog (Hh) signaling in heart morphogenesis by targeting the Hh-dependent activator Smoothened (Smo). Preliminary results show that mWt1Cre:Smofl/fl offspring is characterized by having severe cardiac defects including Atrioventricular Septal Defects (AVSDs) and Right Atrial Isomerism (RAI). Given the fact that the transcription factor Wt1 is known to be expressed in the mesothelium at early embryonic stages, we infer from the nature and severity of the malformations observed in the mWt1Cre:Smofl/fl mouse that the observed defects result from perturbation of Hh signaling in the mesothelial cell lineage prior to the establishment of the epicardium. Specifically, it points at a critical role for Hh signaling in mesothelial cells for a proper establishment of (cardiac) laterality and atrioventricular septation.

076-A Modeling Metabolic Acidosis Disorders Using Human Induced Pluripotent Stem Cells, Behshad - Pournasr, Stephen A Duncan; Regenerative Medicine And Cell Biology, MUSC.

Abstract not available.

077-A The Modulation EphA2-induced Cytoskeleton Re-organization: a New Insight Into the Role of Extracellular Hsp90, Abdelkader Daoud1, Udhayakumar Gopals, Jasmine Kaur2, Jennifer S Isaacs3; 1Pharmacology, MUSC, 2Pathology, DUSM, 3Pharmacology, MUSC.

The Eph tyrosine kinase receptor A2 (EphA2) has emerged as key participants in the progression of a wide range of malignancies. EphA2 modulates the cytoskeletal dynamics to control cancer cell motility and invasion. We previously showed that extracellular Hsp90 (eHsp90) exhibits functional collaboration with EphA2 independently of its cognate ligand ephrin A1. In the current study, we aimed to further define the molecular and functional relationship between EphA2 and eHsp90 within the context of ligand activation. It is known that ephrinA1 signaling promotes RhoA activation and altered cell morphology to favor transient cell rounding, retraction, and diminished adhesion. Our findings reveal that eHsp90 neutralization via either blocking antibodies or cell-impermeable Hsp90-targeted inhibitors significantly attenuated ligand dependent cell rounding in diverse cancer models including breast, prostate, melanoma and GBM, indicating a conserved mode of action. Moreover, we found that eHsp90 elicited Src/RhoA activation and enhanced ligand dependent cell
079-A Ultrasound Capability and Patient Volume in Two Urgent Care Clinics in Nicaragua, Kyle Emberton, Lacey MenkinSmith; Emergency Medicine, MUSC.

Objectives Ultrasound is useful in urgent and emergent diagnosis and management of patients in resource limited settings. Our objective was to evaluate whether a correlation exists between ultrasound study capability and patient volume. We also wanted to determine how patient perception of ultrasound capability might affect clinic selection.

Methods We performed a retrospective longitudinal observational study of data collected in clinics in El Viejo and Sébaco, Nicaragua. We compared the amount of time per month ultrasound diagnostics were available, the number of ultrasound studies performed each month and the total number of monthly patient visits using Pearson correlation coefficients. We then performed a two-question qualitative survey of adult clinic patients presenting in the first two weeks of May 2017 to determine how ultrasound capability affected their selection of clinics. Results In the El Viejo clinic there was a small correlation between number of hours per month ultrasound was available and number of patients seen (r = 0.49). In the Sébaco clinic there was no correlation (r = 0.14). A total of 401 patients participated in the survey. In Sébaco 96% and in El Viejo 94.4% of patients reported that they were more likely to choose a clinic that performs ultrasounds. In Sébaco 23/32 (72%) and in El Viejo 34/42 (81%) patients who did not previously know about ultrasound services reported that they were more likely to come to a clinic that performs ultrasounds. In both clinics 100% of the patients who reported awareness of ultrasound capability also reported that it affected their likelihood of choosing a clinic. Conclusions This study showed that patient perception of ultrasound capability may have an effect on clinic selection. However, response biases may have played a role in questionnaire responses. Further investigation may benefit not only patient volume but also sustainability of the clinics.

080-A Long-Term Outcomes Outcomes of Alcohol Septal Ablation for Hypertrophic Obstructive Cardiomyopathy: A 16 Year Study, Christopher D Capps, Jeremy Rier, Ashley Waring, Justin Heizer, Barbara Griffin, Shaji Shawn, Billy Mullinax, Valerian Fernandes; Cardiology, MUSC.

Background: Alcohol septal ablation (ASA) is an accepted treatment for symptomatic patients with hypertrophic obstructive cardiomyopathy (HOCM). Even though the outcomes at 10 years are similar to septal myectomy there are still concerns about the long-term prognosis of alcohol induced septal scar. Objective: This study sought to determine the long-term outcomes of ASA over a 16-year time period at a high-volume ASA referral center. Methods: Five hundred and ninety-three (593) consecutive patients who underwent 673 ASA procedures at MUSC from 1999 to 2015 were enrolled in this long-term follow-up study. Evaluation included: procedural deaths, pacemaker requirement, repeat ASA and long term mortality. Results: The cohort included 274 males and 319 females. The majority 85% were Caucasian, 10% African American and 5% other. The mean age was 57.1 +/- 15.3 years (range 13.5y to 89y). During ASA, absolute alcohol (2.3 +/- 0.25 cc) was injected into 1.2 +/- 0.3 septal arteries inducing a septal infarct with a mean CK of 1239 U/L. Procedural mortality was 1% (6 of 578) and occurred early in the cohort. There were no procedural deaths after the year 2008. Permanent pacemaker implantation (PPI) was needed in 54 patients (9.1%). Seventy-five patients (12.6%) required repeat ablations. The follow-up was 100% complete for mortality. The mean follow-up was 7.8 +/- 4.3 years. (Range: 3months-16.2 years). Over the 16 year period 91 patients had died (15.3%) The survival estimates at 1, 5 and 10 and 15 years were 97%, 92%, 89% and 81% respectively which was similar to national age, gender and race matched controls. Survival after ASA was similar to septal myectomy. Conclusion: In contemporary practice at a high-volume center, Alcohol septal ablation has a high success rate, low procedural mortality and low pacemaker implantation rate. The temporal decline in procedural mortality and pacemaker requirement reflects the learning curve and the institutional expertise. The long term survival at 16 years is similar to national survival curves for normal population suggesting that there is no detrimental effect of the alcohol induced septal scar.

081-A Role of EphB1 in Axon Guidance and Learning and Memory, Ahlem Assali1, Benjamin Zirlin1, George Chenaux2, Michael Robichaux3, Mark Henkemeyer4, Christopher Cowan1; 1Neuroscience, MUSC, 2UC Davis, 3Baylor College of Medicine, 4UT SouthWestern Medical Center.

Abstract not available.

082-A The Neurodevelopmental Disorder-linked Gene, MEF2C, Regulates PCDH17 to Control Cortical Synapse Density, Adam J Harrington, Aram Raisi, Carly Hale, Kayla Blankenship, Alexandra Bowen, Jennifer Darnell, Kimberly Huber, Christopher Cowan; Adam Harrington.

Abstract not available.
083-A Age-related Differences in Time-compressed Sentence Identification Are Predicted By Cognitive Processing Speed and Cortical Oscillatory Activity, James W Dias, Carolyn M McClaskey, Kelly C Harris; Otolaryngology, MUSC.

Older adults typically have more difficulty than younger adults identifying spoken time-compressed sentences, which present information faster than normal conversational speech. The difficulty experienced by older adults may originate from a deficit in the ability to adequately process fine-grained sensory information, introducing ambiguity when processing the rapidly unfolding phonetic details within time-compressed sentences. However, this difficulty may also be accounted for by age-related slowing of cognitive processing, which can interfere with the ability to track, store, and process information over time. Previous research suggests that cortical neural processing speed, quantified as the peak frequency in the alpha band (8Hz – 14Hz), can predict both processing of fine-grained sensory detail and cognitive processing speed. Peak alpha frequency also slows with age, and has been associated with the deterioration of cortical white matter microstructure. The current investigation examines the extent to which age-related differences in the identification of time-compressed sentences are accounted for by peak alpha frequency and cognitive processing speed. A group of 15 younger adults between the ages of 19 and 30 (7 female) and 25 older adults between the ages of 57 and 82 (17 female) participated in this study. All participants were native English speaking with pure-tone hearing thresholds ≤ 25dB HL between 250Hz and 3000Hz. 50% and 60% Time-compressed sentences were constructed from low-probability Speech-In-Noise sentences. Peak alpha frequencies were determined from electroencephalographic (EEG) recordings taken during a period of quiet rest, eyes closed, as the frequency at which amplitude peaked between 8hz and 14hz. Cognitive processing speed was measured behaviorally using the Connections Test. Replicating previous studies, older adults exhibited poorer time-compressed sentence identification (p < .05). Older adults also exhibited slower peak alpha frequencies and slower cognitive processing (p < .05). Further, the results suggest that age-related differences in time-compressed sentence identification are mediated by cognitive processing speed and peak alpha frequency. NIH R01DC014467 NIH T32DC014435 NIH P50DC00422 NIH UL1RR029882 NIH C06RR14516

001-B Assessing Cognitive Changes Due to Microgravity Using Windows Spaceflight Cognitive Assessment Tool (WinSCAT), Kaylen B Bradley¹, Donna R Roberts², Davud Asemani², Biology, Clemson University, Radiation, MUSC.

NASA utilizes the Windows Spaceflight Cognitive Assessment Tool (WinSCAT) as a means to monitor astronauts’ neurocognitive performance while in space. The scores presented by WinSCAT provide insight into the astronauts’ cognitive condition which can be used for a variety of purposes. Many previous studies have utilized WinSCAT to analyze spaceflight simulations or high-stress activities on cognitive performance but not much work has done with scores from astronauts that were actually in space. NASA provided WinSCAT scores of 19 different astronauts who were in space anywhere from 125 to 200 days. The subjects consisted of four females and 14 males. WinSCAT is taken six times preflight, every 30 days in space and once when the astronauts return to Earth. WinSCAT has five subtests: code substitution, continuous processing, mathematics, match to sample, and code substitution delayed. Each time WinSCAT is taken it provides 20 scores: accuracy, response time, lapses, and throughput for each of the five subtests. The median of the preflight scores and the average of the during flight scores were used for analysis. Overall there were 23 instances of subjects having decrements in their scores once they were in space. Accuracy scores on all subtests stayed stable throughout each subject’s time in space. Frequencies of lapses decreased once the subjects were in space. Overall, depending on the subtest and timing considered, there was high variability in cognitive performance both pre and during flight. South Carolina Space Grant Consortium

002-B The Impact of Denomination on Participation in Faith Based Blood Pressure Measurement, Ciara Wilson; Public Health, CSU.

Hypertension, also known as high blood pressure, is a major but modifiable risk factor. This occurs when the force of blood is consistently too high. Of the nearly 80 million adults diagnosed with hypertension; 46% are not controlled. Studies have shown that home blood pressure monitoring can be affective and provide an alternative to traditional ambulatory monitoring as well as identifying masked hypertension. Faith based programs have continually been shown to have success rate when implementing programs. Therefore a feasibility study was developed to implement home blood pressure monitoring and increase awareness of hypertension. An unanswered question that arose was “Does denomination of the church effect participation in faith based blood pressure measurement?” Three very diverse churches participated in this feasibility
study including a Lutheran, United Methodist and Catholic Church. Participants for the study included 13 individuals from the Lutheran and United Methodist Church and 15 from the Catholic Church. The study design included three important steps by first holding a discussion with the clergy of each church to identify a convenient sample. Then participants were trained then given new home blood pressure monitors and Check.Change.Control protocol. Finally, participants were followed up with within one week to discuss how the program went. The program resulted in 39 out of 41 participants being compliant and successfully participating in the program. Denomination showed to not effect participation in faith based blood pressure measurement. The program showed to be extremely successful and future aims look for increasing the program a longer time length and expanding to further denominations. Keywords: faith based, hypertension NIH NHLBI R25 HL092611

003-B Feasibility of Including Women of Childbearing Age in a Faith-based Study, Alondra DeSantiago¹, Daniel T Lackland²; ¹Public Health Sciences, Clemson University, ²Neurology, MUSC.

About 85 million or one out of every three adults in the United States over age 20 have high blood pressure with nearly half of all adults with high blood pressure being women. This pilot study focuses on women of childbearing age which the CDC defines as women between the ages of 18 and 44. This feasibility study seeks to answer the question: Can faith-based home blood pressure monitoring programs be applied to women of childbearing age? It was hypothesized that faith-based programs can effectively encourage women of childbearing age to self-monitor their blood pressure at home. This study involved three Charleston, SC area churches of differing denominations and with parishioners of a variety of demographics. Methods included providing a brief training for a selected group of parishioners at each church on how to self-monitor blood pressure using an automatic blood pressure monitor. A follow up meeting was conducted in order to investigate whether participants complied to taking their blood pressure once at the same time for a week. Results demonstrated that none of the 50 participants were women between the ages of 18 and 44. This study concluded that although female participants of the target age group did not participate in this pilot study, it is feasible to create faith-based programs that include women of childbearing age to self-monitor their blood pressure at home. NHLBI R25 HL092611; MUSC SURP

004-B Molecular Basis Underlying Calcium-dependent Regulation of Cardiac and Skeletal Muscle Calcium Release Channels (ryanodine Receptors), Hannah G Addis¹, Jordan S Carter², Naohiro Yamaguchi³, ¹Biology, CofC, ²Regeneteive Medicine and Cell Biology, MUSC, ³Regenerative Medicine and Cell Biology, MUSC.

Ryandine receptor (RyR) calcium release channels play a pivotal role in skeletal and cardiac muscle contraction by releasing massive amounts of Ca2+ from an intracellular Ca2+ store, the sarcoplasmic reticulum, during muscle action potentials. RyR channel activity is enhanced by micromolar Ca2+ and inhibited by millimolar Ca2+. Over 200 missense mutations in human skeletal RyR (RyR1) have been reported to be associated with malignant hyperthermia (MH) and central core disease. Similarly, a number of mutations in the cardiac isoform of RyR (RyR2) have been identified in human patients with catecholaminergic polymorphic ventricular tachycardia (CPVT). We found that two domains in RyR, the EF hand domain and the second transmembrane segment, are important for Ca2+-dependent inactivation. Other studies with cryo-electron microscopy showed proximity between the EF hand domain and the cytoplasmic loop between the second and the third transmembrane segments (S2-S3 loop). Therefore, we introduced human disease-associated mutations in the EF hand domain and S2-S3 loop of wild type RyR cDNAs, expressed them in HEK293 cells, and characterized channel function of the recombinant mutant RyRs by [3H]ryanodine binding assay. Three RyR1 mutations in the EF hand domain (T4082M, S4113L and N4120Y) did not significantly alter the Ca2+-dependent activation/inactivation profile of RyR1. Four mutations (F4732D, G4733E, R4736W, and R4736Q) in the S2-S3 loop drastically impaired Ca2+ inactivation, while Ca2+ activation of these mutants remained unchanged. A CPVT-associated RyR2 mutation, G4663S, corresponding to the RyR1-G4733E site, did not cause a substantial change in Ca2+-dependent regulation of RyR2. The results suggest the S2-S3 loop is crucial for Ca2+-dependent inactivation of RyR1, and the regulatory mechanism underlying Ca2+-dependent inactivation could depend on RyR isoforms. We are extending our studies through the construction of additional mutants focusing on another potential Ca2+ regulatory domain that was recently reported in the near-atomic level structure of RyR1. NIH UL1TR001450, R03AR061030; CofC Honors Summer Enrichment Grant
005-B Neonatal Abstinence Syndrome: A Look At The Maternal-Infant Dyads At The Medical University of South Carolina, Susan Fields1, Olivia Kapera2, Price Ward3, Dorothea Jenkins3, 1Washington and Lee University, 2CofC, 3Neonatology, MUSC.

Neonatal Abstinence Syndrome (NAS) is a drug withdrawal syndrome infants experience after birth when they are exposed to opiates in utero with the mainstay of treatment morphine therapy. The rate of NAS in South Carolina has increased considerably— from 0.9 to 3.9 per 1000 births from 2000 to 2013, respectively. Discovering the maternal and fetal demographics, as well as, characteristics of hospital treatment for these infants affected by NAS at the Medical University of South Carolina (MUSC) will result in a deeper and more knowledgeable understanding of the impacts of opiate drug use during pregnancy on our maternal-infant dyads here in Charleston, SC and the surrounding area. A retrospective chart review using the perinatal information system (PINS) was used to identify 111 infants diagnosed with NAS over a five-year period (02/2012-02/2017). Thirty-two infants were excluded. Analysis of the remaining 79 infants showed the average gestational age of 37.9 weeks (±1.2 weeks), average birth weight of 2930 grams (±434 grams), 49 male infants (62%) and 83% inborn (66 of 79). The average age at start of morphine treatment was 2.4 days (±1.6 days). Although morphine is the mainstay of treatment, clonidine was used as an adjunct therapy in 20 infants (25.3%) with all being discharged home to finish a clonidine wean. The median length of treatment (LOT) 16 days (9.5-26 days) and subsequent median length of stay (LOS) 20 days (13.5-30 days). Future studies will aim to compare these NAS treated maternal-infant dyads to maternal-infant dyads who were exposed to opiates in utero but ultimately did not undergo treatment for NAS with the hopes of better understanding the differences between these two populations and why some exposed infants do not require pharmacologic therapy for NAS.

006-B Neural Circuit Disruptions in Emotional Processing Across Psychiatric Disorders, James W Lopez1, Benjamin M Rosenberg2, David M Carreon3, Julia M Huemer4, Ying Jiang5, Simon Eickhoff6, Amit Etkin3, Lisa M McTeague1; 1College of Charleston, 2University of California-Los Angeles, 3Stanford University School of Medicine, 4Medical University of Vienna, 5Washington University in St. Louis, 6Heinrich-Heine University Düsseldorf, 1MUSC.

In a recent transdiagnostic meta-analysis of regional gray matter volume, reduced gray matter was observed across patient groups in nodes of the salience network (i.e., bilateral insula and dorsal anterior cingulate cortex) (Goodkind et al., 2015). In a follow up functional neuroimaging meta-analysis of cognitive control tasks (McTeague et al., 2017) we observed transdiagnostic deficits largely overlapping with regions prone to gray matter loss in conjunction with a broader fronto-parietal network impairment. In the current study, we investigated these patterns during emotional processing. Articles on functional neuroimaging of emotional processing (n=290) including patients across a range of Axis I diagnoses (bipolar, depression, anxiety, substance use, schizophrenia, psychosis) and control participants were submitted to meta-analysis with the revised Activation Likelihood Estimation algorithm (Eickhoff et al., 2009) implemented in MATLAB. Deficits common across disorders and pooled across hypo- and hyper-activation were observed in anterior dorsal cingulate and right anterior insula extending to ventrolateral prefrontal cortex, bilateral amygdala extending to hippocampus and parahippocampal gyrus as well as left caudate and right thalamus. Accounting for hypo- and hyper-activation separately revealed that the impairment pattern was due to patient hyper-activation, with the exception of hypo-activation of right ventrolateral prefrontal cortex. Considering psychotic and non-disorders separately, revealed that these deficits were more specific to non-psychotic disorders, particularly anxiety disorders. In conclusion, consistent with our prior evidence of structural integrity disruptions and cognitive processing impairments, the salience network showed prominent disruption during emotional processing tasks—across Axis I disorders. Emotional processing disruptions were also evident in a broader limbic network, which was more pronounced in non-psychotic than psychotic disorders and most severe in the case of anxiety disorders. NIMH 1 K23 MH104849

007-B A Regional Analysis of Healing in Large Cranial Defects Augmented with BMP2 and an Osteoconductive Matrix, Reed A Houck1, Nicole Howie2, Emily Durham2, Zachary Gray2, Amanda LaRue8, Martin Steed8, Robin Muise-Helmericks8, James Cray8, 1College of Dental Medicine, MUSC, 2Oral Health Sciences, MUSC.

Bone regeneration in large craniofacial defects is a great challenge for clinical practice. The osteogenic front surrounding the defect, the underlying dura mater, and the cranial suture area may all play a role in this healing process, but are often insufficient. Thus, osteoconductive matrices as well as osteoinductive cues (e.g. rhBMP2 peptide) are often employed to help augment healing in large bony defects. In this investigation, we hypothesized that the healing along the bony edges of a 5mm murine critical sized cranial
defect would be greater than the center of the defect due to the contribution of the osteogenic surgical front. To assess this healing, 155 adult wild-type mice were randomly arranged in 16 groups by time, 4 weeks and 8 week, and treatment, a standard acellular collagen sponge (ACS) or a quasi-barrier matrix, Talymed, loaded with control, low, medium or high dosages of BMP2. The skulls were then subjected to histological and microCT analysis looking for bone regeneration in three locations: the entire 5mm defect, the 2mm center of the defect, and the remaining outer ring of the defect. The ACS groups showed greater cellular infiltration and healing in general by 4 weeks post-op compared to Talymed confirming its transient ability to inhibit cell migration from the dura mater. Medium and high doses of BMP2 showed higher levels of bone regeneration throughout the entire 5mm defect, and ACS performed better than Talymed. Both BMP2 dose and matrix contributed to healing within the center of the defect, but only dose affected bone regeneration along the outer ring. In conclusion, healing was greater along the outside of the defect, most likely due to the contribution of the surgical osteogenic front. Medtronic Inc. and Marine Polymer Technologies; AO Foundation S-16-108C; NIH NIDCR 5T32DE017551; NIH NIGM P30GM103331; SCTR NIH/NCATS UL1TR000062

008-B Too Fat for Joint Replacement: The Fate of the Morbidly Obese Patient with Joint Pain, Glenn D Heftet1, Russell A Reeves2, Richard D Williams3, Sarah M Guess3, Jacob C Balmer3, Bennett L Haskins3, Vincent D Pellegrini Jr2, Harry A Demos2, 1Bioengineering, MUSC, 2Orthopaedics, MUSC, 3College of Medicine, MUSC.

Background: Weight loss is a recommended for osteoarthritis (OA), but the effectiveness an orthopaedic surgeon’s recommendation to lose weight is unknown. Methods: Data from 298 obese patients (BMI >40), seen in arthroplasty clinic were obtained for analysis. Patients were divided into three groups based on their chief orthopaedic complaint: knee (78.5%), hip (18.8%) or combined hip and knee OA (2.7%). Descriptive statistics were reported per group and a cox proportional hazards model was used to assess the rate of total knee arthroplasty (TKA) and total hip arthroplasty (THA). Significance is reported as p < 0.05. Results: Of the patients with knee OA, 2.9% lost weight preoperatively, 10.1% lost weight postoperatively. Weight loss measures included: diet and exercise (29%), pharmacologic (14%), bariatric surgery (29%) and unknown (29%). For patients with knee and combined knee and hip OA, the majority (53.0% and 75%) received intra-articular injections for 16-24 and 25 months, respectively. The largest non-operative treatment group for hip OA was 16.1%, using nonsteroidal anti-inflammatory drugs for an average duration of 11-25 months. No patients with hip or combined knee and hip osteoarthritis lost weight preoperatively or postoperatively. The rate of TJA was assessed using a cox proportional hazards model, demonstrating radiographic OA grade to have a positive correlation on the rate of knee (HR 1.66, p = 0.003) but not hip arthroplasty (HR 1.83, p = 0.278). The use of intra-articular steroids correlated with a decrease in rate of knee (HR 0.34, p <0.001) but not hip arthroplasty (HR 0.27, p = 0.167). Conclusion: Weight loss efforts are minimally successful which suggests that weight may not be a modifiable risk factor for obese patients with knee or hip OA.

009-B Adoption of the ACMG-AMP Standards and Guidelines for the Interpretation of Sequence Variants, Annie Niehaus1, Danielle Azzariti2, Harrison Steven2, DiStefano Marina2, Hemphill Sarah2, Senol-Cosar Ozlem2, Rehm Heidi3, 1Medicine, MUSC, 2Partners Healthcare Personalized Medicine, 3Brigham & Women's Hospital and Harvard Medical School.

In March of 2015, the ACMG-AMP Standards and Guidelines for the Interpretation of Sequence Variants (Richards et al., Genetics in Medicine) recommended the following terminology for sequence variant interpretation in Mendelian genes: pathogenic, likely pathogenic, uncertain significance, likely benign, and benign, as well as a set of evidence criteria and combining rules to evaluate variants. To evaluate the utilization of these guidelines, the NIH-funded Clinical Genome Resource (ClinGen) surveyed the 195 US-based and 170 International clinical testing laboratories registered in the Genetic Testing Registry. Representatives from 65 laboratories responded, including individuals from 33 international labs representing 15 different countries. Analysis of survey responses demonstrated high adoption of the ACMG-AMP terminology, with a few notable areas for improvement. 95% of surveyed labs use the ACMG-AMP five-tiers for classifying variants in Mendelian genes. While 78% of labs just use these five-tiers for classifying variants, 22% indicated using additional terms, such as the use of subcategories (e.g., uncertain significance – favor benign), to further classify variants. 86% of surveyed labs classify variants with respect to a condition and mode of inheritance in a uniform and structured manner, and 89% of labs routinely avoid the use of ‘mutation’ or ‘polymorphism’ in clinical reports in favor of ‘variant.’ 36% of labs use the evidence criteria exactly as described (Figure 1, Richards et al.), 44% use an approach that is roughly consistent, and 17% use an approach that they consider a more advanced version than the ACMG-AMP guidelines. While this survey has demonstrated widespread adoption of the recommendations in just three years, future efforts by
The purpose of this study is to track the effectiveness of ergonomics education on promoting proper posture and body mechanics in dental students at the Medical University of South Carolina. Musculoskeletal disorders are common within the population of working dentists, nearly two thirds complain of at least one issue. 1 Chronic low back, wrist and hand, cervical, and shoulder pain are frequent problems. 2 These are due to awkward static posture, prolonged back and neck flexion, repetitive and strenuous motions, usage of vibrating tools, and extended work periods without stretches or breaks. 1 Ergonomics, or the study of people's efficiency and body mechanics in their working environment, can help prevent many of these issues by increasing awareness of job hazards and promoting healthier posture and work habits. Ergonomic training can potentially improve the longevity of these future dentists' careers. This project was inspired by an interprofessional dialogue, in which occupational therapy students saw an opportunity to assist dental students in circumventing these musculoskeletal pitfalls. Dental students' ergonomic habits were initially evaluated to assess body positioning while treating patients. After initial assessment, ergonomic intervention was implemented progressively, including an ergonomic lecture, simulation lab sessions, and pre- and post-tests. Our research team has observed and tracked the effect of this ergonomics education in improving body mechanics and posture within each year's senior class of dental students. The Rapid Upper Limb Assessment (RULA) was conducted in the dental clinic, both in-person and video recorded. As this project continues, successive classes of students will be evaluated and feedback will be provided to them. As this project continues, successive classes of students will be evaluated and feedback will be provided to them. Statistical analysis will be performed to validate the success of the intervention. It was hypothesized that increased ergonomic intervention to the dental students would improve their posture and positioning in the dental clinic and would potentially carry over throughout their future careers.

Introduction: Mobile applications are becoming the preferred method of all types of digital technology due to ease of use and speed of accessing information (Bowen & Pistilli, 2012). Today's students are opting for immediate answers through mobile and digital technology instead of textbooks (Skiba & Barton, 2006). Mobile applications allow users to access instruction through video, pictures, and text, which “bridge the gap between text-based knowledge and practical application” (Sandholzer, Rurik, Deutsch, & Frese, 2014). Digital-based instructional methods offer students and educators significant savings related to cost, resources, and time (Avers, Maraschiello, van Melle, & Day, 2009; Bureau of Labor Statistics, 2016). Purpose: The purpose of this study was to explore student perceptions related to using a mobile application in an occupational therapy lab setting. Hypotheses: Students will report greater preference for both using an app for studying and purchasing an app over a textbook. Additionally, students will agree that the MOBI app is user-friendly, accessible, useful as a study tool, and provides additional clarity over a textbook. Methods: MOBI, a mobile application on ambulatory assistive devices, was created by occupational therapy and physical therapy faculty. Participants used MOBI to review ambulatory device content prior to arrival in lab. Student perceptions were gathered using an anonymous survey via REDCap software. Results: Quantitative and qualitative data were analyzed. Students preferred to study an app over a textbook (77.5%) and purchase an app over a textbook (72.5%). Students reported that MOBI is user friendly (100%), easily accessible (100%), increased confidence (95%), and provided additional clarity over a textbook (92.5%). Based on thematic analysis, students believed that MOBI made content easier to visualize and understand through the use of pictures and videos. Discussion: Current trends in student learning preference indicate that students desire the implementation of technology in course instruction. MUSC Department of Health Professions Interdivisional/Interdepartmental/Intercollege Seed Grant

010-B Effects of Interprofessional Education on Dental Students’ Ergonomics, Payton A Donley¹, Rachel E Crossland¹, Madison L Farrell¹, Madison E Smith¹, Joe Vuthiganon², Peter J Bowman¹, ¹Occupational Therapy, MUSC, ²Dental Medicine, MUSC.
Leading organizations in healthcare have advocated for culturally based initiatives to reduce health disparities and improve national health indicators, including cultural competency training. Research has demonstrated that patients have better outcomes when health care providers are able to provide culturally competent care. This pilot study examines the effectiveness of a newly created mixed methods course elective for students in the MUSC College of Health Professions. The course utilized cognitive, psychomotor, and affective approaches to improve knowledge, confidence, and skills in working with diverse and underserved communities. The semester long course employed a didactic classroom portion with group discussion and presentations as well as hands-on, community-based experiences and reflective writing about working with diverse and underserved communities in Charleston. Survey responses (n=21) were compared from students who took the course elective to those who did not within the same graduating class. The study will consist of the Health Student Attitudes Toward the Underserved (HSATU) survey and an original addendum. Several themes existed in the results. All students that took the survey strongly agreed that they want to work with diverse/underserved communities. In order to support these ambitions, current literature asserts that it is necessary to teach cultural competency, which supports this course as an intervention for students. Following the 2010 earthquake in Haiti, public health response has focused on disaster relief and disease management. While these needs are critical, recent studies report that women remain concerned about unmet basic health needs, i.e. menstrual education and affordable sanitary products. The Days for Girls (DFG) International Program is a non-profit organization striving to help young women stay in school through reusable feminine hygiene kits and promotion of women’s health issues. The goal of this study is to translate the DFG program into a culturally sensitive format for Haiti. The study aims to identify the perceived benefits and challenges to using the DFG program kits and determine ways to adapt the current DFG program for Haitian culture. We hypothesized that the program will be well-accepted, yet require adaptations to fit Haitian cultural needs. There may be differences in the perceptions of high school and college women after using the kits due to age, knowledge of women’s health, and experience using feminine hygiene products. A post-use survey design was used to study the perceptions of the program for women at the Episcopal University of Haiti (18-24 years; n=44) and the Ecole Sainte Croix High School (12-17 years; n=48). The DFG kits were distributed and used by women in the two cohorts for 2-months. A likert scale questionnaire was administered after use of kits. Independent samples t-test revealed no significant differences in perceptions of using the DFG kits, although thematic analysis of open-ended questions revealed differences in perceptions related to benefits and challenges of using the kits. Focus group interviews will be conducted with participants from each cohort to further identify ways to adapt the DFG program for the Haitian culture. Results of this study could support a larger funded trial of the DFG program, especially for young women in rural Haiti. MUSC Center for Global Health Faculty
Tumors inhibit effector function of T cells through multiple mechanisms, but the specific effect of tumor microenvironments on T cell metabolic activity has not been assessed. Assays that directly measure the level of T cell metabolic fitness in patient tumors have not been developed. We hypothesized that reactive oxygen species produced within the mitochondria (mtROS) as a byproduct of oxygen consumption within the electron transport chain may be an indicator of metabolic fitness of T cells in tumors. We used the fluorescent dye mitosox red to measure accumulation of superoxide anions within mitochondrial membranes of T cells. We found that antigen-specific activation of mouse or human T cells led to accumulation of mtROS in CD8+ T cells. Glutathione, a key cell-intrinsic antioxidant necessary for T cell inflammatory function, was preferentially consumed by mtROS+ T cells. Treatment of T cells with extrinsic anti-oxidant N-acetylcysteine reduced mtROS production in T cells, extinguished glutathione uptake, and reduced inflammatory function. Assessment of mtROS in CD8+ TILs from multiple patient tumor types and mouse models showed a consistent lack of mitochondrial function of T cells in tumors. Importantly, PD-1+ CD8 TILs expressed low levels of mtROS. We found that tumor microenvironment conditions of hypoxia and nutrient deprivation extinguished mtROS expression and this led to loss of inflammatory cytokine production. Inhibition of tumor nutrient supply through angiogenic inhibition led to a 4-fold increase in mtROS in CD8+ TILs. Increased metabolic fitness of effector T cells promoted response to anti-PD-1 therapy in a mouse melanoma model. Therapies that remodel tumor microenvironments to restore T cell metabolic function may improve the efficacy of anti-PD-1 treatment and expand the range of patients able to respond to such therapy. *NCI Paul Calabresi Clinical Oncology K12 2015-2018 American Cancer Society Institutional Research Grant 2015-2016, 2017-2017*
018-B Extended Post-Exposure Effects on Human Neurons and Preliminary Astrocyte Migration Studies Using a Novel Ex-Vivo Hydrocephalus Model, Ryan Gedney, Ramin Eskandari, Michael Smith; MUSC.

Abstract not available.

019-B Radiologic Evaluation of Cardiac Sarcoidosis: Prognostic Value of FDG-PET/CT in Clinical Management, Paul H Hargrave, Philip Burchett, Carlo De Cecco; Radiology, MUSC.

Sarcoidosis is a multisystem inflammatory granulomatous disease of unknown etiology characterized by non-caseating granulomas in involved organs. Given the challenges associated with a definitive diagnosis of cardiac sarcoidosis, MRI and FDG-PET/CT are non-invasive radiologic imaging techniques crucial for ruling out cardiac involvement, especially in patients with a confirmed diagnosis of extra-cardiac sarcoidosis. Though current research points toward the efficacy of FDG-PET in the diagnosis and evaluation of this disease process, the relationship of these findings compared with MR is not yet clear. A 10-year retrospective chart review revealed a lack of available data that prevents a more extensive comparison at this time. Based on the findings of the original research question, a meeting of cardiologists and nuclear radiologists was convened and the direction of study pivoted towards the identification of predictors of positive treatment response in cardiac sarcoidosis, where “positive treatment response” is defined by improvement on consecutive PET imaging. Future chart review will focus on integrating patient radiologic findings with clinical management in the context of disease progression to ascertain the factors contributing to the change in imaging findings. NIH NIDDK 5T35DK007431-33

020-B Neonates Who Get G-tubes At MUSC, Katherine A George1, Kristen Morella2, Anbesaw W Selassie3, Aaron P Lesher3, Alison Chapman4, Rita M Ryan4; 1College of Medicine, MUSC, 2Public Health Sciences, MUSC, 3Surgery, MUSC, 4Pediatrics, MUSC.

Background: Some premature infants are unable to take all of their feedings by mouth prior to discharge from the neonatal intensive care unit (NICU) and therefore need a feeding gastrostomy tube (G-tube). We would like to identify these babies in advance but needed to describe the population as our first step. Methods: Infants in the NICU with G-tubes placed for feeding were identified using the local NICU “PINS” data base comprised of prospectively collected data by research personnel. All infants who were born in 2015 or 2016 and had a G-tube placed were identified. Results: There were 116 babies who received a G-tube in 2015-2016. After assessment of the medical indication for a G-tube for each infant, it was determined that infants born ≥30w gestation were receiving G-tubes due to congenital anomalies and not simply due to problems related to their prematurity. For those <30w gestation at birth, the average weight at the time of the G-tube procedure was 4.6 kg, the average corrected gestational age (CGA) was 47.2w and the average CGA at discharge was 52.0w, respectively. In comparison, the infants who were ≥30w and received a G-tube were 43w CGA at procedure and 47w at discharge. Infants who were <30w (n=282) and did not receive a G-tube were discharged much earlier at 35w CGA and weighed 2363g at discharge. Conclusion: The average weight at the time of G-tube placement was 4.6 kg, which is well above the minimum 2.8 kg necessary for the procedure. Therefore, developing a predictive model to identify infants in advance who may ultimately need a G-tube may be advantageous in allowing for earlier G-tube placement and associated earlier discharge home. PHS 5T35DK7431-33; MUSC SHP

021-B Observational Analysis of Near Vision in Monofocal Pseudophakic Children, Hallie R Hahn1, Rupal Trivedi2, Marion E Wilson2; 1College of Medicine, MUSC, 2Ophthalmology, MUSC.

Abstract not available.
022-B Geographic Variation in Total Hip and Knee Arthroplasty Utilization is Influenced by the Presence of Orthopaedic Residency Programs, James J Gregory1, Russell Reeves2, Alexander Chiaramonti2, Keith Orland2, William Barfield2, Jacob Drew2, Vincent Pellegrini2; 1Medicine, MUSC, 2Orthpaedics, MUSC.

Indications for total hip (THA) and knee (TKA) arthroplasty vary among surgeons and patients, and utilization of these procedures depends upon supply and demand factors. We investigated influence of orthopaedic surgeon density and presence of orthopaedic residency programs on THA and TKA rates across the United States to analyze variability between regions. Using the Dartmouth Atlas we obtained Medicare data for 2012 rates of THA and TKA for 306 Hospital Referral Regions (HRR). HRRs were divided into four quartiles based on descending populations per HRR; quartiles were chosen such that total numbers of Medicare beneficiaries per quartile were approximately equal. The American Medical Association residency database provided the number of orthopaedic programs per HRR. Pearson’s correlations were performed with Bonferroni correction using surgeon density and number of orthopaedic residency programs as explanatory variables. A positive correlation was found between THA rate and increasing orthopaedic arthroplasty subspecialist density (r=0.354, p<0.0001); this was strongest in the first (largest population) quartile (r=0.640, p=0.001), accounting for two-thirds of observed rate variation. A negative correlation was observed between the number of orthopaedic residency programs per HRR and TKA and THA rates, nationally (r=-0.267, p<0.0001; r=-0.135, p=0.018) and in the first population quartile (r=-0.644, p=0.001; r=-0.436, p=0.043). Both THA and TKA rates vary substantially among HRRs in the US, suggesting influence of non-medical factors in utilization. Orthopaedic surgeon density was positively correlated with THA rates, particularly for higher population HRRs, but not TKA. The number of orthopaedic residency programs per HRR had an inverse relationship with TKA and THA rates. These findings suggest that indications for elective THA and TKA vary based on patient and provider characteristics in a population-dependent manner. Our data suggests operative indications may be more relaxed in areas with increased surgeon density and more stringent in areas with increased orthopaedic residency programs. MUSC Department of Orthopaedics

023-B The Correlation Between Pre-Operative Cochlear Implant Patients’ Quality of Life and Speech Perception Ability, Nicholas B Aizcorbe, Jonathan Hatch, Shaun A Nguyen, Theodore R McRackan; Otolaryngology.

Abstract not available.

024-B Piece It Together: Testing Balance of Youth with Autism Spectrum Disorder and Other Neurodevelopmental Disorders in a Novel Wellness Program, Conner McDonald1, Eve Spratt2, Carrie Papa3, Jessa Norton3, Janis Newton3, Alicia O’Connor4; 1College of Medicine, MUSC, 2Developmental Pediatrics, MUSC, 3College of Charleston, 4Wellness Center, MUSC.

Piece It Together is a comprehensive wellness program designed for transitional age youth with Autism Spectrum Disorder (ASD) or other mild neurodevelopmental disorders (NDD) that is a collaboration with MUSC Wellness Center and the Division of Developmental Pediatrics. 20 participants with an average age of 19.7 years (11 male, 9 female, 16/20 diagnosed with ASD) completed a 6-week wellness program, consisting of 2 classes each week for 1.5 hours each and completed pre and post measures. The program focuses on increasing exercise, nutrition, stress management, socialization and getting out of your comfort zone. While ASD is generally viewed as a disorder affecting social skills and behavior, deficits in motor function, balance, and coordination have also been recognized despite not being included in the diagnostic criteria. This study assessed the improvement in balance of participants in this fitness program using the miniBEST before and after the wellness program. The Mini Balance Evaluation Systems Test is a clinical balance assessment tool that aims to target and identify 4 balance control systems to better design specific rehabilitation approaches based on deficits. From our sample, 16/20 (80%) pre-intervention measures indicated at least some balance deficit compared to normative data. Average total miniBEST score increased from 24.2 to 25.2 (N=20, p=.028, max score of 28) after the wellness program, with higher scores indicating better balance, and a maximum score of 28. Scores for four types of balance (sensory orientation, dynamic gait, reactive postural control, and anticipatory) were also analyzed, with conflicting results, however, the greatest improvement occurred in reactive postural control. This study highlights that increasing exercise and balance activities can improve balance deficits in transitional age youth with ASD and other mild NDD.
025-B Do Patients Who Come to an Urban, Academic ED Consider the Emergency Physician to Be the Doctor They Trust the Most?, Elizabeth Dawley1, Sarah Katchen1, Warren Harvey1, Steven Saef2; 1Medicine, MUSC, 2Emergency Medicine, MUSC.

Title: Do patients who come to an urban, academic ED consider the Emergency Physician to be the doctor they trust the most? Dawley, E, Saef, S Background: Many patients seem to consider the Emergency Department (ED) to be their affirmative choice for healthcare. This is a complex decision driven by a large mix of patient characteristics leading them to trust the Emergency Physician (EP) as their doctor. We chose to identify patient characteristics associated with that choice. Methods: Eligible participants included all adults (>18 years old) at an urban, academic ED who were willing and able to complete a survey. Patients were surveyed by student teams who entered responses on tablet computers, after which data was uploaded into SAS, © Cary, NC, for analysis. Our dependent variable was the following survey item: “Did you choose the ED because you consider the doctors here to be the ones you trust the most?” We performed bivariate and multivariate analyses. Results: In bivariate analysis we noted the following associations with trust of the EP: Race other than white (p=0.02); Believing the ED provided the best preventive care (<0.0001); The ED will see you regardless of ability to pay (<0.0001); Self-pay or Medicaid (0.002); You can be seen anytime (0.002); Appointment not needed (<0.0001); Not having a regular doctor (<0.0001); Sent to ED by a doctor (0.0002); No wait for special studies (<0.0001); Considering the ED to be a Medical Home (<0.0001). In multivariable analysis confounding was noted leaving only “considering the ED to be one’s MH” to be associated with trust of the EP [OR 4.4 (2.7-7.2)].

Conclusions: Among ED patients, the decision to place one’s trust in the EP above other doctors appeared to be multifactorial involving convenience issues, financial issues, and believing the ED to be a MH. Our findings suggest that “Trust of the EP” is a surrogate for other patient priorities which are personal or cultural.

026-B The Effect of Socioeconomic Status on Patient-Reported Outcomes After Renal Transplantation. Andrew J Cole, David J Taber, Prabhakar K Baliga; Surgery, MUSC.

Research analyzing the effect socioeconomic status (SES) has on renal transplant outcomes has demonstrated conflicting results. However, recent studies demonstrate that certain patient-reported outcomes (PROs), such as depression, medication non-adherence, health literacy, social support, and self-efficacy can influence clinical outcomes in renal transplant recipients. Our objectives were to examine the effect SES has on PROs, and determine if there is an association between SES, patient-reported outcomes, and healthcare utilization. This study was a post-hoc analysis of 52 patients enrolled in an ongoing prospective trial aimed at improving cardiovascular disease risk factor control in renal transplant recipients. As part of the study, at baseline, patients completed detailed surveys assessing SES and PROs. Patients were divided into low and high SES cohorts based on income, education, marital status, insurance, and employment. All patients were given 12 self-reported surveys in the domains of medication-related issues, self-care and knowledge, psychosocial issues, and healthcare. Analyses included the associations between 12 PRO surveys, SES measures, and healthcare utilization, including the rate of hospitalizations, ED visits and clinic visits that occurred between the date of transplant and enrollment in the trial. The low SES cohort (n=16, 30.8%) experienced more severe depression (5.75 vs 3.0, p=0.022), higher rates of inadequate health literacy (3.42 vs 1.68, p=0.022) and perceived stress (2.743 vs 3.266, p=0.027), along with significantly less self-efficacy (6.971 vs 8.214, p=0.006) and social support (3.86 vs 4.408, p=0.012). Low SES was associated with a 60% higher rate of hospitalization and 90% higher rate of ED visits per patient-year. Medication non-adherence was also associated with more hospitalizations and ED visits. This analysis demonstrates that low SES was significantly associated with negative PROs, including depression, health literacy, stress and self-efficacy. Further, low SES and medication non-adherence was associated with higher rates of healthcare utilization. NIH 5T35DK007431-33; MUSC SURP

027-B Gastrointestinal Complaints in Williams Beuren Syndrome and Supravalvular Aortic Stenosis Suggest a Vascular Contribution, Alexandra O Hamberis1, Phoebe CR Parrish2, Michael Lugo1, Mark D Levin2, Beth A Kozel2; 1College of Medicine, MUSC, 2NHLBI, NIH.

Abstract not available.

028-B Utilization and Efficacy of Staged US/CT Algorithm in Suspected Appendicitis in MUSC Pediatric Patients, Caroline E Hubbard1, William S Russell2, Robert A Cina3, Jeanne G Hill4; 1College of Medicine, MUSC, 2Pediatric Emergency Medicine, MUSC, 3Surgery, MUSC, 4Radiology and Radiological Science, MUSC.

In keeping with the goals of providing the highest level of care, a multi-disciplinary team at MUSC developed
a clinical practice guideline pathway in June 2010 in an effort to standardize the diagnosis and management of suspected appendicitis in pediatric patients. The objective of this study was to evaluate the utilization and efficacy of this refined algorithm, which incorporates Pediatric Appendicitis Score and staged ultrasound (US) and computed tomography (CT) imaging, in the diagnosis and management of pediatric patients that presented to the Medical University of South Carolina with suspected appendicitis from 1/1/13-12/31/16. A retrospective chart review was conducted utilizing patient data obtained from Epic and AGFA Impax 6.6.1.3525. We analyzed the utilization and efficacy of US, CT, and the staged US/CT approach in addition to determining the sensitivity, specificity, and positive and negative predictive values. From 2013-2016, 1,466 patient encounters representing 1,390 different patients met inclusion criteria. 1,466 US and 261 CT scans were performed, 6 of which were excluded as they were not used to specifically evaluate the appendix but to investigate other etiologies. There were 350 US and 41 CTs (11.7%) in 2013, 353 US and 53 CTs (15.0%) in 2014, 385 US and 76 CTs (19.7%) in 2015, and 378 US and 85 CTs (22.5%) in 2016. 219 US were interpreted as positive, 1,085 as negative and 162 as equivocal for appendicitis. Of the 219 total positive US scans, 17 (7.8%) had a follow up CT due to a clinical picture inconsistent with the imaging results. Of the 1,085 total negative US scans, 174 (16%) had a follow up CT scan due to continued clinical concern, and of the 162 equivocal US scans, 64 (39.5%) had a follow up CT. The sensitivity and specificity of the staged US/CT clinical algorithm were 97.9% and 97.96% respectively. NIH NIDDK; Grant #: 5T35DK007431-33; PI-Raymond N. DuBois, M.D., Ph.D. Dean, College of Medicine. Grant Support for RedCap Data entry form provided by SCTR-Biomedical Informatics Center (BMIC)- NIH/NCATS UL1 TR001450

029-B Self-reported Pain Vs Discomfort Levels in Emergency Room Patients with Chest or Abdominal Pain, Joshua Shaffer1, Shilpa Sreedharan1, Trinh Chu1, Steven Sae2; 1Medicine, MUSC, 2Emergency Medicine, MUSC.

Background: Previous studies have reported that patients, such as women with cardiac ischemia, will deny being in pain but report feeling uncomfortable. We seek to determine if there is a significant difference in how patients with noxious conditions in the Emergency Department (ED) report pain vs. discomfort, and whether this correlates with their clinical presentations to further distinguish their conditions and improve quality of care. Methods: This was a prospective cohort study conducted at an urban, academic ED. Adult patients (>=18yrs old) with a chief complaint that included pain of any sort, who were willing and able to participate without duress, were eligible. Surveys were administered by student teams asking patients to separately rate their pain and discomfort from 1-10 on visual analog scales. Patient characteristics including demographics, types of pain, duration of pain, location of pain, quality of pain or discomfort, and pain-modifying conditions were recorded on tablet computers. Data was entered into REDCap ©, Vanderbilt University and uploaded into SAS, Cary, NC for analysis. Results: There were 289 patients enrolled in the study. Overall, 58% reported no difference between their discomfort and pain. 21% reported their discomfort to be greater than pain and 21% reported their discomfort to be less than their pain. Fifty-two (18%) of patients reported chest pain. Of these, 52% saw no difference between pain and discomfort, 25% reported discomfort to be greater than pain and 23% reported discomfort to be less than pain. Conclusions: ED patients with chest and abdominal pain showed a clinically significant difference in their self-reporting when given the opportunity to quantify their pain and discomfort separately. Understanding how patients perceive noxious symptoms can lead to more robust descriptions of disease processes and ultimately better care.

030-B Case Study of a Small Bowel Angiodysplasia Via Computer Tomography, Ian C Miller1, Meryle Eklund2; 1College of Medicine, MUSC, 2Radiology, MUSC.

Abstract: Angiodysplasia are among risk factors for a lower GI bleed with an increasing prevalence with ageing. 1 This abnormality is defined as malformed submucosal and mucosal vasculature. Though the pathogenesis of angiodysplasia are still undefined, it has been proposed that normal distention and contraction associated with bowel function may result in intermittent occlusion of the submucosal veins that penetrate the muscularis propria. The result of which may be tortuosity and focal dilation of upstream mucosal and submucosal vasculature. 2 Angiodysplasia is typically identified using endoscopy; however, in this case report, described is an incidental finding wherein small bowel angiodysplasia were identified in the arterial phase of an abdominal Computer Tomography (CT) study. 1 1. Gómez SQ, Lafuente MP, Abadía MA-S, Conesa JC. Gastrointestinal bleeding: The role of radiology. Radiologia (English Edition). 2012;53(5):406-420. doi:10.1016/j.rxeng.2011.03.003. 2. Klatt EC. Robbins and Cotran Atlas of Pathology. Elsevier Health Sciences; 2015. Dept of Radiology.

031-B The Esophageal Sweep: Inter-observer Variability, Accuracy, and Utility of Inclusion of Limited Upright Single Contrast Esophagram As Part of Modified Barium Swallow Studies, Brenton G Davis1, Douglas H Sheafor2; 1Medicine, MUSC, 2Radiology, MUSC.
The modified barium swallow study (MBSS) is a fluoroscopic radiology exam, used to evaluate dysphagia, performed by speech-language pathologists (SLP) with a radiologist. The purpose of this study was to assess the sensitivity, specificity and accuracy of one of the components of the MBSS, the esophageal sweep, for diagnosing esophageal dysmotility. 35 consecutive adult patients who underwent diagnostic MBSS from March 2016 to February 2017 were included in the study. MBSS was performed using the MBSIMP standardized protocol, including an esophageal sweep (ES). The ES consisted of an anterior-posterior fluoroscopic view of the esophagus during oral contrast transit from the oropharynx through the gastroesophageal junction and recorded digitally. MBSS prospective clinical reads were assessed for diagnosis of esophageal dysmotility based on review of the initial SLP report. Subsequently, in a blinded fashion, 2 radiologists retrospectively reviewed all ES. Without radiologist input, two speech language pathologists also retrospectively reviewed each ES by consensus. Each ES was graded on a scale of 0 - 4 describing dysmotility as follows: 0 – normal, 1 – mild (breakup of primary stripping wave), 2 – moderate (intramural reflux), 3 – severe (tertiary contractions), 4 – cannot evaluate. The sensitivity of the esophageal sweep was compared to the gold standard of correlative manometry or a standard diagnostic esophagram. The initial prospective clinical read by an SLP demonstrated a sensitivity of 64% and specificity of 33%. The retrospective consensus SLP read showed sensitivity of 55% and specificity of 42%. Both radiologists had 91% sensitivity for detection of esophageal dysmotility using the esophageal sweep. Specificity for esophageal dysmotility was substantially less, at 17% and 21%. When read by radiologists, the ES component of the MBSS shows high sensitivity for detection of esophageal dysmotility compared to standard esophagram and manometry. However, specificity was low. Conversely, SLP’s evaluation of the ES showed higher specificity than sensitivity. Future studies will be required to assess whether combined SLP and radiologist reads could improve the accuracy of the esophageal sweep. NIH 5R25HL096316-08; MUSC SHP

032-B Surgical Skills in Video Recordings of ENT Procedures. Ryan Metts1, Ted Meyer2, Heather Schopper2, 1College of Medicine, MUSC, 2Otolaryngology, MUSC.

Introduction: Surgical competency is essential, yet trainees in otolaryngology continue to be evaluated based on number of cases performed and/or subjective evaluations of overall surgical performance by a supervising attending physician. Currently available assessment tools focus on outcomes or use cadaveric specimens or simulation, settings which lack the authenticity of a real surgery. Real-time feedback during an operative procedure is often difficult due to the requirements of patient care and the length of many procedures. An evaluation tool assessing a surgeon’s actions during surgery would be a helpful tool and could give residents a better understanding of ways in which to improve in the future. Thus, the goal is to create a validated and standardized system to describe and track surgical process skills during a mastoidectomy. Methods: The first step in creating an evaluation tool is validating the evaluation items. Residents and faculty have been recorded performing surgeries, and surveys have been created that include questions about process rather than overall performance. The videos have been edited for time and will be simple for evaluators to view and offer feedback. Results: Moving forward, the videos and surveys will be sent to otolaryngologists nationally and responses will be pooled and assessed for interrater reliability and validity. Conclusion: We hope to find objective measurement metrics which reliably distinguish between surgeons of different experience level and provide concrete aspects of surgical skill about which to give useful feedback to trainees.

033-B A Fatal Case of Necrotizing Pancreatitis in Sickle Beta Thalassemia Zero. Taylor L Turnbull1, Peter Houston2, Nicholas Batalis2; 1College of Medicine, MUSC, 2Pathology, MUSC.

Sickle Beta Thalassemia Zero (Sβ0) is a variant of Sickle Cell Disease (SCD) that results in the complete absence of the beta globin gene, and thus no production of HbA. While the prevalence of Sβ0 is only one tenth that of homozygous sickle cell disease (SS), this variant is noted to be just as severe. As with SCD, Sβ0 patients are plagued with chronic hemolytic anemia and vaso-occlusive pain crises. High rates of hemolysis put these patients at increased risk of developing bilirubin gallstones, one of the most common causes of acute pancreatitis. SCD can also lead to acute pancreatitis via direct microvessel occlusion. Here we examine the case of an Sβ0 patient with fatal necrotizing pancreatitis that went undiagnosed until the time of autopsy and argue that acute pancreatitis should be on the differential diagnosis of all sickle cell patients presenting with acute abdominal pain.

034-B Alcohol Septal Ablation (ASA) Produces Similar Changes to CBC As Atherosclerotic Myocardial Infarction (MI) But Platelet Counts Are Not Elevated. Is There Less Inflammation With ASA?, Billy J Mullinax1, Patel Mira1, Canova Alex1, Waring Ashley1, Nielsen Christopher2, Fernandes Valerian3, 1Medicine, MUSC, 2MUSC, 3Ralph H. Johnson VA Medical Center.
Objectives: To study blood cell count changes after alcohol induced septal infarct in Hypertrophic Obstructive Cardiomyopathy (HOCM) patients.

Background: Atherosclerotic MI is a pro-inflammatory and prothrombotic state associated with neutrophilic leukocytosis, anemia, and increased platelet count and platelet size. The degree of leukocytosis correlates with infarction size and, together with increased platelets, amplifies myocardial inflammation. ASA produces a targeted infarction in the hypertrophied septum to reduce left ventricular outflow obstruction. The inflammatory effects of this iatrogenic alcohol induced infarction have not been studied. Methods: We evaluated 109 consecutive patients who underwent ASA with pre- and post-ASA Hemoglobin, WBC count, platelet counts, and troponin. Results: A total of 109 patients (age 62.57 ± 12.41, 38M, 71F) who underwent ASA were included in the study. Alcohol (2.11 ± 0.78cc) was injected into a targeted septal artery producing a peak troponin of 58.81 ± 74.25 ng/ml. After ASA, WBC increased from 7.44 ± 2.15 to 8.27 ± 2.49 (p<0.001), hemoglobin decreased from 13.27 ± 1.87 to 12.04 ± 2.13 (p<0.001), and platelet counts decreased from 210 ± 55 to 186 ± 45 (p<0.05). Patients with lower baseline WBC (<6.5) had a significantly lower troponin peak (31.65 ± 0.25) compared to patients with higher baseline WBC (>6.5) (troponin 68.82 ± 66) (p<0.05). This was independent of the volume of alcohol injected with no significance difference across all levels of post-ASA WBC. Patients with higher troponin level had a higher post-ASA WBC. Conclusions: Compared to atherosclerotic MI (historical controls), alcohol induced infarction also leads to increase in WBC count and anemia but unlike atherosclerotic MI there is a reduction in platelet count. This could suggest a similar pro-inflammatory response with a reduced pro-thrombotic state. Lower baseline WBC count led to a significantly less infarct size. Post-ASA infarct size correlated positively with higher WBC count.

036-B Superiority of Remnant Clostridium Difficile Diarrhea Specimens in Detecting Carbapenem-Resistant Enterobacteriaceae (CRE) Colonization in a Tertiary Care Hospital with Low Endemicity, Fadyah Albalawi, Lisa L Steed, Michael G Schmidt; *Microbiology & Immunology, MUSC.*

Background: Carbapenem-Resistant Enterobacteriaceae (CRE) have emerged as a significant cause of healthcare associated infections (HAI) resulting in significant morbidity and mortality. Identification of CRE colonized and/or infected patients early during care enables implementation of comprehensive infection control measures. Methods: Remnant diarrhea specimens, submitted for *C. difficile* toxin production-PCR (n=600), were compared to remnant *VRE* surveillance perianal swabs (n=600) to determine the superiority of one specimen type over the other for assessing CRE carriage. Specimens were analyzed using both the disk method and broth method recommended by CDC. Carbapenem resistance was confirmed by disk diffusion testing. Carbapenem resistant isolates were identified by Matrix Assisted Laser Desorption/Ionization-Time of Flight Mass Spectrometry (MALDI-TOF). Results: 1.8 % of the patients (11/600) from the universal surveillance arm from within VRE high risk units were found to harbor CRE. 6.2% of the patients (37/600) from the targeted surveillance arm (C. difficile) were found to harbor CRE. This difference was significant (p value of <0.0002, Fisher Exact Test). Conclusions: Use of targeted surveillance through screening remnant *C. difficile* diarrhea specimens was superior in its ability to identify CRE colonized patients than was universal surveillance using remnant VRE perianal swabs in facilities with low clinical incidence of these microbes. This approach may offer a cost-effective alternative to detect changes to the CRE colonization pressure within hospitals where CRE incidence is low.

035-B Infantile Scimitar Syndrome Leading to Surgical Repair, Michael N Melson1, Merle Eklund2; *1COM, MUSC, 2Pediatric Radiology, MUSC.*

Scimitar Syndrome (Hypogenetic Lung Syndrome) is a rare syndrome characterized by anomalous pulmonary venous return in which the anomalous vein(s) cause a left to right shift of blood within the heart. The name originates from the curvilinear shape of the anomalous veins which resemble that of a curved middle eastern sword, the scimitar. The anomalous pulmonary vein/s often leads to hypoplastnic lung(s) and/or pulmonary hypertension. In this case, we present an 8 month old male initially presented with Respiratory Distress Syndrome. This patient was followed until the age of 6, at which point he began having complaints of fatigue with exertion, exertion at baseline levels, along with a dry cough. He was assessed as a surgical candidate and ultimately had surgery to relocate the anomalous right pulmonary vein. Our goal is to review the radiographic and presenting features of this syndrome, and to present an unusual case where surgical treatment of Scimitar Syndrome is postponed until later in life when severe symptoms become more pronounced. *Dept of Radiology Summer Immersion Program*
Patients 18-65 years old with both ASD and MDD by DSM-V without any medication changes in the last month who are eligible for an open label trial with a goal recruitment of 15 subjects. Once consented, 10 Hz rTMS at 100-120% of motor threshold was provided on the left dorsolateral prefrontal cortex (DLPFC) for 3000 pulses per session for 25 sessions. Pre- and post-rTMS assessments of depressive and autism symptoms were collected and preliminary analyses were completed with t-test of pre- and post-TMS behavioral tests. Results: To date, ten patients have been enrolled with seven completing the rTMS treatment, two withdrawing, and one currently undergoing treatment. Preliminary analyses of the seven patients with pre- and post-rTMS behavioral scores suggest a reduction in the Hamilton Depression Rating Scale (-11.7±7.39, p=0.006). There is also a reduction in the informant-reported Aberrant Behavior Checklist (-29.29±18.81, p=0.006).

Conclusions: Preliminary data from this novel trial of rTMS in Autism Spectrum Disorder and Major Depressive Disorder suggest an improvement in depressive and core autism symptoms after completion of a standard depression rTMS treatment series. Thus, rTMS may be a viable treatment option for both depression and aberrant behaviors in the autism population.

039-B MRI Utilization By Orthopaedic and Non-orthopaedic Providers for Acute or Chronic Ankle Pain, Elizabeth C Durante1, Russel Chapin2, Ariel Palanca3, David Hocking1, Julia Hermann3, Christopher Gross4; 1College of Medicine, MUSC, 2Radiology, MUSC, 3Orthopaedics, Stanford University, 4Orthopaedics, MUSC.

Healthcare costs are an increasingly significant burden on society. Advanced imaging comprises a large component of these costs. Many professional groups (American Academy of Family Physicians (AAFP), American College of Radiology (ACR)) recommend use of plain film radiographs prior to magnetic resonance imaging (MRI). We examined the compliance rate of this recommendation at our institution between orthopaedic providers (Orthopaedic surgeons, non-operative physicians employed in the Department of Orthopedics, and Orthopaedic Physician Assistants) compared to other physicians. We hypothesized that there is an over utilization of resources by non-orthopaedic providers. This was a retrospective chart review of patients who had had MRIs of their ankles from April 2015-June 2016 (total of 721 charts). We assessed whether the ordering physician had obtained an ankle radiograph prior to the MRI. The diagnosis listed as the reason for the study was also recorded. We determined that 222 of the 259 (85.7%) of the orthopaedic providers obtained radiographs prior to MRI while only 271 of 462 (58.7%)
between impairment and perceived difficulty using ability; a strong/significant relationship $rp=0.70\ (p<0.01)$ $0.87\ (p<0.01)$ between impairment and functional strength.

Results showed a strong/significant relationship $rp=0.00$ throughout the testing process. Hypotheses were tested with Pearson correlational analyses (SPSS v.24); correlation strength defined as $rp=0.00$ having no association, $0.25$ low, $0.50$ moderate, and $>0.75$ strong.

Introduction: Functional upper extremity (UE) movement skill is crucial for efficiency in everyday activities. Stroke causes UE movement impairment, resulting in functional deficits and perceived difficulty completing activities. Occupational therapists assume that reducing impairment will increase survivors’ ability to complete activities. However, some research contradicts this assumption. Thus, the relationship between impairment and both function and perceived difficulty performing activities is unclear. The aims of this study are to clarify these relationships. We hypothesized a strong relationship between stroke constructs consistent with clinical assumptions driving practice.

Methods: Secondary analysis of baseline VA-funded rehabilitation RCT data. Participants provided informed consent, the study was IRB-approved. Inclusion: ≥3 months post-stroke, with at least minimal UE paresis, and without severe cognitive/communicative deficits, or pain.

Outcome measures: Fugl-Meyer UE Assessment to define impairment, Wolf Motor Function Test to define function, and Stroke Impact Scale to define difficulty performing everyday activities. Hypotheses were tested with Pearson correlational analyses (SPSS v.24); correlation strength defined as $rp=0.00$ having no association, $0.25$ low, $0.50$ moderate, and $>0.75$ strong.

Results: $N=103$ survivors, 3 months-11 years post-stroke, with mild (28%), moderate (33%) and severe (39%) UE impairment completed the study. Results showed a strong/significant relationship $rp=0.87\ (p<0.01)$ between impairment and functional ability; a strong/significant relationship $rp=0.70\ (p<0.01)$ between impairment and perceived difficulty using the impaired hand for activities; and a fair/significant relationship $rp=0.36\ (p<0.01)$ between impairment and perceived difficulty performing activities.

Conclusion: The hypotheses were partially supported; there was a strong relationship between impairment and both functional ability and hand use, but only a fair relationship between impairment and ability to complete activities. This suggests improving impairment is not the sole factor contributing to survivors’ ability to complete activities. Thus, therapists’ clinical assumption to target impairment is not entirely misguided, but therapists must address other factors to enhance survivors’ functional ability. VA NO799-R; NIH P20GM10940;

041-B When Worlds Collide: Th17 Cells in Cancer Immunotherapy and Autoimmunity, Sierra Amaya$^1$, Stefanie Bailey$^1$, Hannah Knochelmann$^2$, Dirk Elston$^1$, Joni Mazza-McCrann$^1$, Chrystal Paulos$^1$; $^1$Microbiology and Immunology, MUSC, $^2$Medicine, MUSC.

Abstract not available.

042-B The Impact of Early Neuroimaging and Developmental Assessment in a Preterm Infant Diagnosed with Cerebral Palsy, Lily Gullion$^1$, Jennifer Stansell$^1$, Katy Hallman$^2$, Hunter Moss$^2$, Patty Coker-Bolt$^1$, Dorothea Jenkins$^2$; $^1$Occupational Therapy, MUSC, $^2$Medicine, MUSC.

Preterm infants who are at a high risk for brain injury and disorders such as cerebral palsy (CP) are typically diagnosed at 18-24 months. A combination of neuroimaging and developmental assessment may improve earlier detection and treatment for children with CP. We have shown that DTI fractional anisotropy (FA) and MRS metabolites are associated with below average scores on developmental assessments at 0-3 months corrected age. Our premise is that FA and brain metabolites in white matter and basal ganglia reflect early delays and deficits seen in motor, self-care, and communication skills later in life.

The infant in this case report had no neurological deficits at discharge, but neurological imaging at term showed bilateral periventricular leukomalacia. We evaluated the relationship between neuroimaging abnormalities and functional developmental trajectory with assessments at term, 3, 12, and 45-months. The infant had low FA in the corticospinal tract, inferior fronto-occipital fasciculus, posterior limb of the internal capsule, and posterior thalamic radiations compared with a group of typically developing infants without neuroimaging abnormalities. Surprisingly, abnormal brain metabolites were found in frontal white matter distant to site of PVL for NAA/Cr, Cho/Cr, ml/Cr. The infant was below average on assessments at term, 3
Recent findings have suggested that therapeutic emotional processing of the foreground pictures. Furthermore, the comparison of blocks with and without TMS revealed that TMS pulses did not disrupt emotional processing of the foreground pictures. Recent findings have suggested that therapeutic benefit of rTMS is in part reflected in increased anticorrelation of the DMN and CEN (Liston et al., 2014). These findings suggest that modulating state-dependence during rTMS administration might enhance treatment outcomes.

043-B Perturbing Emotion Neurocircuits: A Concurrent TMS-fMRI Investigation, Oliver J Mithoefer¹, James W Lopez², Logan T Dowdle¹, Bashar W Badran¹, Philipp M Summers¹, Mark S George¹, Lisa M McTeague¹, Psychiatry & Behavioral Sciences, MUSC, Psychology, CofC.

Transcranial magnetic stimulation delivered concurrent with functional magnetic resonance imaging (TMS-fMRI) extends conventional correlational imaging to causal neurocircuit mapping. That is, single pulses of TMS can be delivered to superficial cortical regions, and the activity in the connected networks mapped with the BOLD response. In the current study, we investigated whether state dependence, particularly emotional arousal, would influence the responsiveness of the central executive network (CEN) to single pulse TMS. We also examined whether its interactions with the default mode network (DMN) and salience network (SN) varied with emotional arousal. Twenty-four individuals free of medical or psychiatric illness completed a picture-viewing paradigm. Pleasant, neutral and unpleasant pictures from the International Affective Picture System were presented in blocks. Low, moderate and high arousal blocks stratified emotional pictures equally. While pictures were presented in the foreground, jittered, single pulses of TMS were presented intermittently. TMS was targeted to left dorsolateral prefrontal cortex, a node in the CEN. As a control site, participants also received TMS to primary motor cortex (M1). TMS site and stimulus orders were counter-balanced across participants. In terms of findings, the DMN is typically anticorrelated with the CEN and SN. In the current study, the anticorrelation between the CEN and DMN as well as the DMN and SN during single pulse TMS, increased as the arousal of foreground pictures increased. No such interactions were revealed in relation to M1 stimulation, although connectivity within the somatomotor network increased with arousal. Furthermore, the comparison of blocks with and without TMS revealed that TMS pulses did not disrupt emotional processing of the foreground pictures. Recent findings have suggested that therapeutic

044-B Monte Carlo Analysis of Aztreonam-avibactam and Ceftazidime-avibactam Against Wild-type and Carbapenem-resistant Gram-negative Pathogens, Aaron T Smith, Roger L White; MUSC College of Pharmacy.

Purpose: The new beta-lactamase inhibitor, avibactam (AVI) has been recently combined with ceftazidime (CAZ) as CAZ-AVI. AVI is also currently being investigated in Phase 2 clinical trials with aztreonam (ATM) as ATM-AVI. Methods: Monte Carlo Analysis (MCA) was performed for both drug combinations utilizing pharmacokinetic parameters, pharmacodynamic (PD) targets associated with clinical efficacy, protein binding, and MIC data from peer-reviewed literature. An inpatient creatinine clearance (CrCl) distribution was used to assess clearance of each drug utilizing a CrCl vs. Clearance regression. For CAZ-AVI, the product label dosing, and for ATM-AVI dosing from phase 1 and 2 trials were used in the analysis. Dose regimens were adjusted for CrCl per each drug’s labeling/trial protocol. MCA was performed using two volumes of distribution reflective of normal and patient volumes. Target Attainment (TA) for %fT>MIC≥40 was used for both drugs as a low PD target. The high PD target for ATM-AVI and CAZ-AVI were %fT>MIC≥60 and %fT>MIC≥70, respectively. The 5 organisms studied included wild-type P. aeruginosa (WT-PA), wild-type E. coli (WT-E. coli), carbapenem-resistant E. cloacae (CR-E. clo), carbapenemase-producing K. pneumoniae (CP-KP), and metallo beta-lactamase producing Enterobacteriaceae (MBL-ENT). Results: TA for both ATM-AVI and CAZ-AVI was 100% for both PD targets at both the normal and patient volumes for WT-E. coli, CR-E. clo, and CP-KP. CAZ-AVI had 100% TA at both PD targets for both volumes for WT-PA. ATM-AVI had 75-78% TA for both targets and both volumes for WT-PA. For MBL-ENT, ATM-AVI had 100% target attainment for the low target and 99% target attainment for the high target. CAZ-AVI had very low TA (3-5%) for all targets and volumes for MBL-ENT. Conclusions: As resistance mechanisms become more prevalent, it will be important for the clinician to understand the differences in agents that can be used to effectively treat these resistant organisms.
045-B Monte Carlo Analysis of Plazomicin in a Representative Tertiary Care Inpatient Population, Sahand Askarian1, Roger L White2; 1SCCP, MUSC, 2Clinical Pharmacy and Outcome Sciences, MUSC.

Introduction: The rise of aminoglycosideresistance mechanisms and multiple drugresistant (MDR) Gram-negative organisms has called for new agents in infectious disease. Plazomicin (formerly ACHN490) has been granted fast-track designation by the FDA for the potential treatment of severe carbapenemresistant Enterobacteriaceae (CRE) infections. Monte Carlo analysis (MCA) was performed to predict the potential efficacy of plazomicin in a representative tertiary care hospital inpatient population. Methods: MCA (n = 10,000) was performed using wild-type MIC distributions collected from USA hospitals of K. pneumoniae, P. aeruginosa, E. coli and S. aureus. Population pharmacokinetic parameters were used to simulate free (unbound) serum concentration time profiles (Vss of 0.255 L/kg and a CrCl vs. drug clearance regression, 16% protein binding). Dosing regimens of 15 mg/kg and 10 mg/kg, adjusted for body weights of 60, 70, 80, and 90 kg and adjusted for renal function were evaluated. Pharmacodynamic (PD) targets of fAUC24/MIC of 161 (stasis) and 279 (optimal killing) were used to assess target attainment (TA%). Results: For 90 kg subjects, Plazomicin MCS achieved ≥98% (%TA) for K. pneuomo at both target fAUC24/MIC, ≥96%TA for E. Coli at low target, and ≥92%TA at both targets for S. aureus (15mg/kg). MCS for P. aeruginnosa achieved low %TA (<30) at both targets for both regimens. Conclusion: Plazomicin at both the higher and lower doses achieved target attainment greater than 90% for the high and low targets for K. pneumoniae, E. coli and S. aureus, suggesting that it may be a clinical option for the treatment of infections caused by these organisms. However, target attainment was much lower for P. aeruginossa suggesting that treatment may require combination therapy with another agent. Ongoing research is underway to compare plazomicin with amikacin using both wildtype and resistant subpopulations of organisms.

047-B The Rational Design of Peptidomimetic Inhibitors of PD-1, Thomas Z Benton1, Pieter Burger1, Yuri K Peterson2, Patrick M Woster1; 1Drug Discovery, MUSC, 2Pharmacy, MUSC.

Programmed death 1 (PD-1) is a cell surface receptor responsible for promoting immune tolerance, organ development and regulation of apoptosis. PD-1 has been validated as a therapeutic target in lung cancer, and several monoclonal antibodies that target PD-1 have been approved by the FDA for use in lung cancer. To date, no small molecule inhibitors that target PD-1 have been described. To address this problem, we have proposed a small molecule-peptidomimetic of PD-L1, the naturally occurring ligand of PD-1. We have analyzed the published X-ray structural data, mapped and identified the binding pocket interface and identified residues essential for receptor interaction. Annotation of the binding pocket interface revealed a contiguous strand from PD-L1 interacting with a Tyr68 centered-hydrophobic pocket surrounded by several polar residues from the receptor. This analysis served to inform the generation of several geometric and electrostatic based queries, which were used to virtually screen 612,698 conformers of the Chembridge Macrocycle library. The results were refined using pharmacophore and docking surface models, leading to 10 compounds with suitable theoretical binding energies. These compounds will be used to probe the PD-1/PD-L1 interaction, be validated as select PD-1 inhibitors, and move forward as potential experimental therapeutics. NIH R01CA204345

048-B Chemogenetic Inhibition of Prelimbic Cortical Pyramidal Neurons Blocks BDNF-mediated Attenuation of Cocaine-seeking, Giuseppe Giannotti, Sarah M Barry, Ben M Siemsen, Jacqueline F McGinty; Neuroscience, MUSC.

Our lab has shown that a single BDNF infusion into the prefrontal (PrL) cortex immediately after the last cocaine self-administration (SA) session attenuates reinstatement of cocaine-seeking. Moreover, inhibition of AMPA/NMDA receptor function prevents BDNF's ability to attenuate relapse, indicating a relationship between BDNF-mediated suppression of cocaine-seeking and synaptic activation. Based on this evidence, we employed a chemogenetic approach to modulate glutamatergic activity in the PrL cortex by infusing an adeno-associated virus to drive the expression of inhibitory m4D(Gi)-DREADD or eGFP in pyramidal neurons of the PrL cortex. Immediately after the last cocaine SA, all rats received an injection of CNO followed by an infusion into PrL cortex of PBS or BDNF 30 min later. Rats then underwent 6 days of abstinence followed by a post-abstinence test under extinction conditions, extinction training to criterion, a cue-induced reinstatement test, re-extinction, and a final cocaine prime-induced reinstatement test. Infusion of BDNF in the eGFP-expressing rats attenuated relapse and activation of the Gi-DREADD blocked BDNF's ability to attenuate cocaine-seeking. Surprisingly, the Gi-DREADD, in the absence of BDNF, induced a long-lasting attenuation of relapse, raising the possibility that multiple brain regions receiving glutamatergic afferents from the PrL cortex contribute to subsequent relapse. To explore this possibility, we selectively inhibited glutamatergic activity in PrL neurons that project to the nucleus accumbens (NAc) core by infusing an AAV5 carrying a
CRE-dependent Gi-DREADD into PrL cortex and a CAV2-Cre virus into the NAc core of the same rats. Infusion of BDNF in the eGFP-expressing rats attenuated relapse and CNO-mediated activation of the Gi-DREADD blocked BDNF’s ability to suppress cocaine-seeking. However, activation of the Gi-DREADD in the absence of BDNF did not affect relapse. Future experiments will explore the contribution of different brain regions receiving glutamatergic projection from the PrL cortex that may be involved in attenuation of relapse. P50 DA15369, R01 DA033579, F31 DA039709, F31 DA041021

049-B N-Linked Glycan Imaging By MALDI FT-ICR for Early Biomarker Detection in Hepatocellular Carcinoma, Connor A West¹, Harmin Herrera¹, Yuko Kono², Peggi M Angel¹, Richard R Drake¹, Anand Mehta¹; ¹Pharmacology, MUSC, ²Medicine, University of California San Diego.

Hepatocellular carcinoma (HCC) is the second leading cause of cancer death worldwide and one of the fastest rising cancers in the USA, with high recurrence rates and limited therapeutic options for advanced disease stages. There is a strong correlation between survival rates and detection time, thus early detection has become crucial. To identify new potential biomarkers of HCC, a recently developed matrix-assisted laser desorption/ionization imaging mass spectrometry (MALDI-IMS) approach targeting N-linked glycans in formalin-fixed paraffin embedded (FFPE) clinical tissues and tissue microarrays (TMA) was done. Two tissue microarray slides were purchased from US Biomax (Rockville, MD): the first containing HCC and normal adjacent tissue (n=90 cases) the second containing HCC, cirrhotic, cholangiocellular carcinoma and normal cases (n=80 cases). HCC samples were also received from the University of San Diego to perform orthogonal analysis alongside the TMAs. The slides underwent antigen retrieval, enzymatic digestions and CHCA matrix, all applied using a HTX TM-Sprayer. Data was collected using a Bruker 7T solarIX MALDI FT-ICR then analyzed using flexImaging and SCiLS lab software. We used this methodology in the analysis of over 140 HCC samples on the TMA slides and compared the N-linked glycans in cancer tissue with either adjacent tissue or tissue from patients with just liver cirrhosis and no cancer. Following MALDI-IMS and data analysis, thirteen N-glycans were identified as being elevated in HCC samples (AUC > 0.75). Many of these tumor glycans are also detected in serum from HCC patients. These tumor glycans represent greater distributions of branched and fucosylated species in cancerous regions as opposed to normal or cirrhotic regions, confirmed through lectin staining. These tissue glycan changes will be leveraged for evaluation of the same changes in matched serum samples. With larger sample cohorts, biomarker possibilities can be assessed for monitoring HCC progression and therapeutic targeting. NCI 5R21CA207779-02

050-B The Role of a Host Adenosine-generating Ectoenzyme CD73 in Modulating Porphyromonas Gingivalis Survival and Growth in the Oral Epithelium, Jaden S Lee, Nityananda Chowdhury, JoAnn S Roberts, Zachary Messick, Özlem Yilmaz; Oral Health Sciences, MUSC.

Abstract not available.

051-B Behavioral Testing in a Murine Maternal Immune Activation Model of Neurodevelopmental Disorders, Catherine Svetcharkin¹, Adam Harrington², Christopher Cowan²; ¹MSTP, MUSC, ²Neuroscience, MUSC.

Abstract not available.

052-B Understanding Hospice Family Preferences and Needs Related to Time of Death Visits, Kathy S Katzenberger, Michelle Nichols; Nursing, MUSC.

Hospice patients die in various settings, including their home, with family caregivers. Hospice can conduct a time of death (TOD) visit to provide support and confirm death, although not a requirement in all states. To date, there have been no systematic studies conducted in the United States among non-mandated TOD visit states to explore family member experiences with the death of their loved one, preferences and understanding related to TOD visits by home hospice personnel or how it may have affected their grieving process. To better understand the family’s experience regarding the TOD of their loved one, we conducted a qualitative exploratory study using a hermeneutic phenomenological approach. Participants were recruited using purposeful sampling of home hospice families that had experienced a death within the last 6-13 months and had not received a TOD visit. Eligible families were invited by mail to participate. Seven reflective, in-depth interviews were conducted and audio recorded. Data were analyzed using NVivo, a qualitative software application, using an emergent thematic approach. Major themes emerged including caregiver roles and responsibilities, prior experience with end of life, disease progression, hospice experience and support, final hours and emotionality. Results indicated that families with strong social support coped relatively well throughout without having the addition of a TOD visit. This study conveys the importance of allowing home hospice families a choice regarding TOD visits. Through understanding TOD
needs of the home hospice families, researchers and clinicians can improve the death experience and identify families in need of additional support through the grieving process. Future studies will further explore social support on the grieving process and identify the TOD activities most meaningful and supportive to hospice families.

053-B Regulation of Cue-induced THC Seeking in the Nucleus Accumbens, Vivian C Chioma, Peter W Kalivas; Neurosciences, MUSC.

Marijuana is the most widely used illicit drug in the United States. Thus, there is a demand for further research to understand the neurobiological effects of cannabis. Our lab has recently established a rodent model of operant Δ9-tetrahydrocannabinol + cannabidiol (THC+CBD) self-administration. With this model, we can examine the neuroadaptive mechanisms underlying daily THC+CBD use and relapse to drug-associated cues. We previously found that cocaine cue-induced relapse involves transient-synaptic potentiation (t-SP) at glutamatergic synapses on medium spiny neurons (MSNs) in nucleus accumbens. t-SP is initiated by spillover of synaptically released glutamate from cortico-accumbens synapses to stimulate neuronal nitric oxide synthase (nNOS) interneurons and the release of nitric oxide. Subsequently, activation of matrix metalloproteinase-9 (MMP-9) by S-nitrosylation results in cleavage of the extracellular matrix. It is unknown whether this cascade of events necessary for cue-induced cocaine seeking also mediates cue-induced THC+CBD seeking. Here, we hypothesize that pharmacological antagonism of nNOS and MMP-9 by microinjecting N-propyl-L-arginine (NPLA) and MMP-9 inhibitor, respectively, into the accumbens attenuates cue-induced THC+CBD reinstatement. We pretreated male Sprague-Dawley rats with NPLA (0.1 nmol) or vehicle 10 minutes prior to the reinstatement test and observed inhibited cue-induced reinstatement in NPLA-treated rats. Similarly, rats were pre-treated with MMP-9-inhibitor (0.1 nmol) or vehicle 15 minutes prior to the reinstatement test and we observed suppressed cue-induced reinstatement in MMP-9-inhibitor treated rats. The role of nNOS and MMP-9 in cue-induced THC+CBD seeking supports the likelihood that like all other addictive drugs tested to date, the desire to seek and use marijuana activates an intra-accumbens microcircuit involving nNOS interneurons and MMP activation. NIH R01DA003906; MUSC IMSD Program R25GM072643; MUSC MSTP.

055-B The Role of Transcription Factors in Sinoatrial Node Differentiation, Yunkal Dai¹, Kemar Brown², Rich Robinson³, Ann Foley¹; ¹Bioengineering, Clemson, ²Mount Sinai College of Medicine, ³Columbia University.

Pacemaker cells are rare, accounting for <10,000 of the approximately 10 billions cells of the heart. Damage to the sinoatrial node (SAN) leads to bradyarrhythmias and eventual heart failure. The molecular mechanisms that drive the SAN fate are poorly understood, although a transcriptional program that mediates this fate has been identified. Our previous studies showed that Map3K7/TAK1 is expressed in the embryonic myocardium with stronger expression in the atria and the presumptive SAN. Overexpression of Map3K7 in differentiating mouse embryoid bodies (EBs) drives myocardial differentiation toward a pacemaker-like fate. This includes activation of transcription factors (TFs) that mark the SAN, such as Tbx3, Tbx5 and Shox2. This suggests that TAK1 is upstream of the known SAN transcriptional program. We hypothesize that genetic manipulation of target TFs will direct SAN-like differentiation, alone or in synergy with Map3k7. I tested this by doxycycline inducible cell lines to overexpress the TFs Tbx3, Tbx5, Shox2, Tbx18, Isl1, and Map3k7. Several phenotypic hallmarks of pacemaker cells will be examined, for example, fast beating rate, diastolic depolarization, HCN4-mediated increase in If density, automaticity and marker expression. I have determined an optimal doxycycline dose to overexpress Tbx5 overexpression during EB differentiation. I assessed TurboRed expression (as an indicator of construct activation) and have found that overexpression of Tbx5 from day 2-day 16 of EB differentiation increases the percentage of cells with rapid beat rate (greater than 100 bpm at RT). Further analysis of markers and electrophysiology will be required to confirm SAN identity in these cells.

056-B The Role of ADAMTS5-mediated Aggrecan Turnover in the Development of the Mandibular Condyle in the Temporomandibular Joint, Alexandra W Rogers, Sarah E Cisewski, David L Billings, Christine B Kern; Regenerative Medicine and Cell Biology, MUSC.

Abstract not available.
057-B Delivery of Therapeutic Doxorubicin Dose Across the Canine Blood-brain Barrier with Hyperthermia and Temperature-sensitive Liposomes, Anjan Motamarry1, Amy-Lee Bredlau2, Chao Chen3, Ann M McCracken4, Kris Helke4, Ann-Marie Broome3, Dieter Haemmerich1, 1Pediatrics, MUSC, 2Regeneron Pharmaceuticals, 3Pharmacology, MUSC, 4Comparative Medicine, MUSC.

Background/Purpose: Delivering chemotherapeutic drugs across the blood brain barrier (BBB) is a major challenge in the treatment of brain tumors. The BBB can be transiently opened by the application of hyperthermia (>40 °C). Thermosensitive liposomal doxorubicin (TSL-Dox) is a drug delivery system that rapidly releases the contained drug in response to hyperthermia. The goal of this study was to demonstrate delivery of doxorubicin across the BBB by TSL-Dox combined with local hyperthermia. Methods: TSL-Dox was infused intravenously over 30 min at a dose of 0.94mg/kg in anesthetized beagles (age ~17 months). Following, a hyperthermia probe was placed 5-10 mm deep through one of 4 skull burr holes. Hyperthermia was performed randomized for 15 or 30 minutes, at either 45 or 50 °C. Blood was drawn at baseline, immediately after completion of doxorubicin infusion, and then every 30 min for up to 180 minutes. Non-survival studies were performed in four dogs, where brain tissue at the hyperthermia location was extracted following treatment to quantify doxorubicin uptake via HPLC, and to visualize cellular uptake via microscopy. Survival studies for 6 weeks were performed in 5 dogs treated by a single hyperthermia application. Results: Local doxorubicin delivery ranged from 0.11 to 0.74 ng/mg of brain tissue at the hyperthermia locations, with undetectable drug uptake in unheated tissue. Fluorescence microscopy demonstrated cellular doxorubicin uptake. Histopathology in H&E stained samples demonstrated localized heat-induced damage near the probe. No animals in the survival group demonstrated significant neurological deficits. Conclusion: Localized doxorubicin delivery to the brain can be facilitated by TSL-Dox with localized hyperthermia with no significant neurotoxicity.

058-B Relationship Power Imbalance and History of Partner HIV Testing Among Pregnant Women in Uganda, Caroline J Vrana1, Jeffrey Korte1, Angela Malek1, Esther Buregyeya2, Joseph Matovu3, Harriet Chemusto2, William Musoke3, Rhoda Wanyenze2, 1Pediatrics, MUSC, 2Regeneron Pharmaceuticals, 3Pharmacology, MUSC.

In some societies, greater power/resources are given to males over females, and this imbalance can have a negative impact on HIV prevention. We investigate the association between relationship power imbalance and male partner HIV testing among pregnant women attending antenatal care (ANC) in central Uganda. This analysis uses baseline data from a cluster-randomized HIV self-testing intervention from three ANC clinics in central Uganda. Pregnant women with HIV- male partners were recruited and randomized by day into standard of care or intervention arm. Women were asked about history of partner testing, characteristics of their relationship, and other factors using REDCap software on electronic tablets. Analyses were performed in SAS (9.4), with chi-square tests and p-value <0.05 for significance. 1,514 women were recruited across the three sites in July-November 2016 (737 standard of care, 777 intervention). 18.2% of the women’s partners had ever accompanied them to ANC, and only 39.6% of male partners had ever tested for HIV. Among women under 26, women’s contributions to household expenses differed by partner testing (overall p<0.001), with 47.6% of women whose partners tested making no contribution to expenses compared to 63.2% of women whose partners did not test. Relationship status differed by partner testing (overall p=0.02), but 12.4% of women whose partners tested had a sometimes difficult relationship with their partner vs. 5.7% of women whose partners did not test. Among women aged 26+, decision making for visiting family differed by partner testing (p=0.005), with 52.9% of women making joint decisions with partners who tested compared to 36.5% whose partners did not test. Higher relationship power balance is significantly associated with increased HIV testing among male partners when measured by household expenses and decision making, but not relationship status. Interventions aiming to increase relationship power balance could increase HIV testing among males in Uganda. NIH/NCATS UL1 TR001450; International Initiative for Impact Evaluation, TW2.2.28; NIH TL1 TR001451 and UL1 TR001450
059-B Maternal Cardiometabolic Determinants of Breastfeeding Noninitiation in South Carolina By Maternal Race and Ethnicity. Danielle R Stevens, Kelly Hunt; Public Health Sciences, MUSC.

Introduction/Rationale: One in five infants born in the US have never been breastfed, with non-Hispanic blacks (NHB) having lower rates of breastfeeding. This is extremely problematic as a lack of breastfeeding has been associated with increased risk of adverse health problems for both offspring and mother. Current evidence suggests that women with metabolic disorders (diabetes, obesity, etc.) are less likely to initiate breastfeeding, though recent evidence from several large-scale studies have found nonconforming results. In order to inform targeted clinical interventions, we sought to identify maternal cardiometabolic determinants of breastfeeding noninitiation by race/ethnicity. Methods: Our study population is comprised of live singleton births in South Carolina delivered at a gestational age between 28-42 weeks from January 2004 to 2008. Logistic regression was used to evaluate the association between maternal cardiometabolic factors and breastfeeding noninitiation by hospital discharge, with stratification by race/ethnicity to examine race/ethnic differences in this population. Results: Analyses were conducted on 131,683 non-Hispanic whites (NHW) and 76,045 NHB. NHB were more likely to be obese (NHW: 10.1%, NHB: 18.9%, p<0.001) or diabetic (NHW: 10.2%, NHB: 12.0%, p<0.001) entering the pregnancy, but were just as likely to develop gestational diabetes during the course of the pregnancy (NHW: 6.3%, NHB: 6.1%, p=0.09). Breastfeeding noninitiation was higher among NHB than NHW (57.4% and 32.3%, respectively). Despite lower rates of breastfeeding noninitiation, NHW women were less likely to initiate breastfeeding if affected by obesity (OR: 1.32, 95% CI: 1.26, 1.38) or pre-gestational diabetes (OR: 1.16, 95% CI: 1.05, 1.27) whereas NHB women were more likely to initiate breastfeeding if affected by a metabolic disorder. Conclusions: Our study shows that breastfeeding noninitiation in South Carolina varies by maternal cardiometabolic factors and race/ethnicity. This study can aid in the development of tailored clinical and public health breastfeeding interventions and improve maternal and child health. SCTR NIH TL1 TR001451 and UL1 TR001450

060-B Inhibition of the Central Amygdala Selectively Decreases Alcohol Consumption in Mice with a History of Stress and Alcohol Dependence, Harold L Haun¹, William C Griffin ², Marcelo F Lopez², Howard C Becker³; ¹Neuroscience, MUSC, ²Psychiatry, MUSC, ³Ralph H. Johnson VA Medical Center.

Stress exposure has been observed to contribute to high levels alcohol consumption and dependence in humans yet the underlying neuronal influence of stress on alcohol intake is poorly understood. Our lab has developed a mouse model of stress enhanced alcohol (ethanol) intake utilizing repeated exposure to forced swim stress (FSS). In this model, repeated cycles of chronic intermittent ethanol (CIE) vapor exposure result in increased ethanol intake compared to air exposed controls (CTL). Furthermore, exposure to FSS prior to ethanol drinking selectively increases intake in CIE-exposed mice generating blood ethanol concentrations (BECs) in the 200mg/dL range, well exceeding the 80mg/dL legal limit of intoxication. Our goal in the present study is to chemogenetically inhibit the central amygdala (CeA), a stress and ethanol sensitive structure, to return intake to baseline levels in these high drinking mice. The CeA of male C57BL6-J mice was infused with an inhibitory Designer Receptor Exclusively Activated by Designer Drugs (AAV8-hSyn-hM4Di) and baseline ethanol (15% v/v) intake was established. Subjects then received CIE exposure (16 hr/day x 4 days/week) to ethanol vapor (CIE group) or air (CTL group). Weekly cycles of inhalation exposure were alternated with 5-day, 1-hour limited access drinking tests. FSS (10 min) occurred 4 hr prior to each daily drinking session. CIE exposure resulted in increased drinking compared to CTL while FSS alone did not affect CTL intake. As expected, CIE+FSS increased ethanol intake compared to both CIE and CTL+FSS. For CeA inhibition, clozapine-N-oxide (3mg/kg) was delivered systemically 30min prior to drinking which resulted in attenuated ethanol intake in both CIE and CIE+FSS groups but had no effect on both CTL and CTL+FSS drinking. This reduction in intake points to plasticity within the CeA as a driving force in stress-enhanced ethanol consumption. NIAA F32 023700, U01 014095, U01 020929, and P50 07061; and VAMC

061-B A Theory of Mental Imagery, Jesse Breedlove¹, Ghislain St-Yves¹, Cheryl Olman², Thomas Naselaris¹; ¹Neurosciences, MUSC, ²Psychology, Univ. Minnesota.

INTRODUCTION: We present a theory of vision that offers a functional rationale for mental imagery and an explanation for why mental images are experienced as vague and weak. The theory assumes a hierarchical network of recurrently connected brain areas that perform probabilistic inference over retinal input. To
test this theory we directly measured imagery receptive fields, an analog of the population receptive field measured during vision. METHODS: We measured whole-brain BOLD activity as participants viewed and then imagined previously memorized objects at 8 distinct locations in the visual field. We then estimated for each voxel a visual receptive field model (vRF) and an imagery receptive field model (iRF) using the activity generated during visual perception and mental imagery, respectively. The fitting procedure assigned a receptive field size and center to each voxel, as well as a spatial frequency tuning profile. RESULTS: We found that it is possible to predict imagery activity using the iRF, with accuracy increasing with ascension of the visual hierarchy. Following this pattern, we found that receptive field model characteristics, such as eccentricity and tuning functions, become more similar between imagery and vision in higher visual areas. To rule out the possibility of these RF patterns being attributed to spatial attention or eye movements, we also showed that iRF models can be used to identify the content and the location of a left out collection of imagined scenes, while eye movements do not permit such identification. CONCLUSIONS: These findings demonstrate the feasibility and utility of imagery receptive fields to quantitatively characterize mental imagery. Consistent with major predictions of the theory, our results suggest that during mental imagery, activity is propagated toward early visual areas from higher-level areas. NEI RO1 EY023384

063-B Intracellular Calcium Stores in the Prelimbic Cortex Regulate Drug Related Behaviors, Paul Culver, Carrie Bailes, Bethany Pavlinchak, Jeffrey Parrilla-Carrero, William Butcha, Arthur Riegel; Neuroscience, MUSC.

Cocaine addicts display increased sensitivity to drug associated cues, due to pathological cellular changes in the prelimbic cortex (PLC). Preclinical rodent models of addiction implicate dysfunction in signaling mechanisms regulating intracellular calcium. To what extent repeated cocaine administration influences calcium release from intracellular stores is poorly understood, but may involve the endoplasmic and perinuclear ryanodine receptor Ca2+ channels (RYR). Low to normal levels of intracellular calcium release from RYRs facilitate neuronal inhibition by activation of inhibitory Kv7 channels. In contrast, high levels of calcium suppress Kv7 channels and facilitate LTP. Thus, RYRs are known to play a role in dendritic remodeling, synaptic plasticity, and potentially learning and memory important for drug related behaviors. Here, using behavioral, physiological, and immunohistochemical techniques, we tested the hypothesis that repeated exposure to cocaine suppresses PLC inhibition in a manner dependent on intracellular calcium. Electrophysiological studies showed attenuated Kv7 channel currents and hyperexcitable PLC pyramidal neurons in brain slices from rats with a history of cocaine self-administration. Inhibitory Kv7 currents and hyperexcitability were normalized by pharmacological stabilization of Kv7 channels with retigabine. Preliminary immunofluorescence data suggests that repeated administration of cocaine decreases PLC expression of FK506 binding protein (FKBP12.6), an immunophilin protein known to bind and stabilize the closed probability of RYRs. Pharmacological replacement of FKBP12.6 with bath applied S107 or JTV-5119 also reduced hyperexcitability. When microinjected bilaterally into the PLC 10 minutes prior to cued reinstatement testing, both S107 or retigabine reduced cocaine seeking. In contrast, cocaine seeking was potentiated by microinjections of thapsigargin which was expected to block Ca-ATPases, indirectly elevating intracellular calcium levels. Similar PLC microinjections of thapsigargin or the RYR agonist caffeine potentiated cocaine-induced locomotion in cocaine-sensitized rats. Taken together, these studies suggest that hyper-sensitivity of PLC neurons to drug related cues may reflect increases in intracellular calcium transmission from RYRs. NIDA RO1DA033324A, P50DA015369

064-B Inhibition of Protein Synthesis in Adoptively Transferred T Cells Promotes Complete Tumor Response, Katie E Hurst, Kiley A Lawrence, Lee R Leddy, Jessica E Thaxton; Orthopaedics, MUSC.

Protein synthesis and folding occur in the endoplasmic reticulum (ER) on ribosomes to catalyze assembly of amino acids into protein chains. This process engages ER stress sensors and chaperones for protein folding and disulfide bond formation. We previously demonstrated that ER stress elements are critical to tune T cell activation and anti-tumor function. However, the role of protein synthesis in T cell function has not been studied. We hypothesized that the ER guides T cell development, metabolism, and inflammatory function through synthesis of proteins. We used a cell-permeable puromycin analog, O-Propargyl-puromycin, to detect translating polypeptide chains in T cells using flow cytometry. We found that upon activation, Pmel-1 TCR transgenic T cells undergo high levels of protein synthesis over the course of differentiation. This process required T cells to consume ATP and deplete mitochondrial energy stores. Using a protein synthesis inhibitor (Homoharringtonine, HHT) we show that protein synthesis in T cells requires upregulation of ER protein chaperones (glucose regulated protein 78, grp78), mediators of disulfide bond formation (ER oxidoreductin-1, ERO1), and drives expression of mitochondrial-associated apoptosis through increased expression of BIM. Treatment of T cells with HHT resulted in depression of inflammatory function as measured by reduced mitochondrial reactive oxygen
species (mtROS), glutathione (GSH) uptake, glucose dependence, and IFN-γ production. HHT-treated T cells showed enhanced in vivo persistence upon adoptive transfer to T cell deficient RAG1-/- mice. Strikingly, the enhanced in vivo persistence of adoptively transferred HHT-treated T cells promoted complete tumor regression and indefinite survival in 30% of tumor-bearing mice in a melanoma mouse model. Together, our data suggest that protein synthesis inhibition of adoptively transferred T cells is a viable strategy to promote complete tumor regression in patients. 


065-B Patient-derived Xenograft Model to Advance Rectal Cancer Personalized Therapy. Scott A Becker1, Yun Zhu1, Cindy Wang2, Katie E Hurst1, Brenda J Hoffman2, Elizabeth G Hill2, Victoria J Findlay4, Ramsey Camp1; 1Surgery, MUSC, 2Medicine, MUSC, 3Public Health Sciences, MUSC, 4Pathology, MUSC.

Neoadjuvant 5-fluorouracil chemoradiation (5FU/RT) has established benefits in locally advanced rectal cancer (LARC) patients; however, therapeutic resistance is observed in ~70% of the cases. To advance care, predictors of 5FU/RT response still need to be identified and novel personalized approaches are desperately needed. We hypothesized that a unique "bedside-to-bench" LARC patient-derived xenograft model established from pre-neoadjuvant 5FU/RT LARC endoscopic biopsy samples could serve as a therapy predictive platform used for testing future personalization strategies. Mouse xenografts were created by mixing dissociated cancer cells with Matrigel (1:1 ratio) and subcutaneously injected into NSG mice to yield the passage 0 (P0) tumors. Dissociated tumor cells were passaged in an expanded number of mice to create subsequent passages for investigation. P2-3 xenografts were used for histologic characterization and for in vivo therapy experiments. Therapy groups include 1) DMSO control; or 2) 5FU/RT 3) Cetuximab + 5FU/RT. Xenograft response, as measured by tumor weight and serial volume measurements, was compared to the corresponding human LARC. After optimization, we achieved an outgrowth (human tumor to P0) rate of 73% (n=19/26) and engraftment (P0 to P1) of 85%. Clinical factors did not predict outgrowth but tumors with distant metastasis demonstrated increased xenograft doubling times. Xenograft histology was conserved in 88% of cases compared with the human LARC tumor. Xenograft 5FU/RT response based on tumor volume correlated with clinical tumor regression grading response to neoadjuvant 5FU/RT. Additionally, KRAS wild type tumors demonstrated response to Cetuximab in addition to 5FU/RT (p<0.05). This novel LARC patient-derived xenograft platform maintains the biology, architecture, and therapy heterogeneity observed in LARC patients suggesting our model represents an effective platform to develop future personalization therapeutic strategies. MUSC Department of Surgery; Hollings Cancer Center 

066-B Hypovitaminosis D and Risk Factors in Pregnant Women and Their Newborns in the Middle East: a Systematic Review. Shayesteh Hajizadeh, Judy R Shary, Susan Reed, Carol L Wagner; Children’s Hospital, MUSC.

Pregnant women and newborns are at risk for vitamin D deficiency. Poor health outcomes for pregnant women with VDD have been reported. We undertook a systematic review of the literature on hypovitaminosis D and risk factors in pregnant women and their newborns in the Middle East. This study is a review of the existing literature about vitamin D status in pregnant women and their newborns in the Middle East. It was conducted by exploring international electronic databases Pubmed and Scopus. Finally, 52 papers were included in this study. This review revealed the prevalence of 25(OH)D <50 nmol/L in pregnant women and their newborns was between 24.5–98%, and 22–100%, respectively. The prevalence of 25(OH)D <25nmol/L in pregnant women and their newborns was over a wide range between 16.7-80%, and 22-82%, respectively . Predictors for low maternal and neonatal 25(OH)D levels included decreased vitamin D synthesis due to reduced exposure to sunlight and decreased nutritional intake of vitamin D. Decreased vitamin D synthesis due to reduced exposure to sunlight included personal factors such as lifestyle that decrease the time spent outdoors and the use of sunscreen and cultural practices when clothing covers more of the body surface, environmental factors influencing the amount of UVB radiation reaching earth such as air pollution and season. Decreased dietary sources of vitamin D were due to dietary habits and the lack of vitamin D replacement. A predictor of low neonatal 25(OH)D levels included maternal vitamin D status and correlation between vitamin D levels in maternal and cord blood. Public health awareness about predictors of low maternal and neonatal 25(OH)D levels in the Middle East and the need to encourage modest sunshine exposure and adequate maternal vitamin D intake during pregnancy are needed.
067-B IL-15 Superagonist and Anti-PD-1 Monoclonal Antibody Combination Therapy Leads to Enhanced CD8+ T Cell Functionality, Luis E Cardenas1, Marzena Swiderska-syn1, Samantha Suriano1, Kristina Andrijauskaite1, Caroline Mart1, John Wrangle2, Mark Rubinstein1; 1Surgery, MUSC, 2Medicine, MUSC.

Abstract not available.

068-B S1P Secretion By Hematopoietic Stem Cell-Derived Osteoblasts Enhances Osteosarcoma Progression, Uday K Baliga1, Inhong Kang1, Shikar Mehrotra2, Ogretmen Besim3, Meenal Mehrotra3; 1Pathology, MUSC, 2Surgery, MUSC, 3Biochemistry, MUSC.

Osteosarcoma is the most common primary malignant bone sarcoma but mechanisms underlying progression remain elusive. Tumor microenvironment is a promising avenue of research to hinder tumor progression. In osteosarcoma, the non-malignant osteoblasts also form a part of tumor microenvironment but their role has not been investigated. We have previously shown that, contrary to the popular belief, osteoblasts can be derived from hematopoietic stem cells (HSC) also. We also demonstrate, for the first time, that non-HSC-derived osteoblasts significantly increased migration and invasion of osteosarcoma cells and that this effect is enhanced with HSC-derived osteoblasts when compared to stromal-derived ones. Differences in these two osteoblast populations is an untapped resource for further understanding their role in osteosarcoma progression. Unbiased screening using RNA sequencing of HSC and stromal-derived osteoblasts demonstrated that one of the pathways significantly up-regulated in HSC-derived osteoblasts, as compared to the stromal-derived ones, was the sphingolipid signaling pathway. Thus, we hypothesized that sphingosine kinase-1 (SphK1)/ sphingosine 1-phosphate (S1P) pathway, prosurvival signaling axis, is involved in osteosarcoma progression by HSC-derived non-malignant osteoblasts in tumor microenvironment. SphK1 mRNA levels were almost 3-folds higher in HSC-derived osteoblasts as compared to the stromal-derived ones. Preliminary data demonstrates that endogenous S1P in HSC-derived osteoblasts decreases with time while the same is not seen with stromal-derived ones. The percentage of release of S1P increases considerably at 2h in HSC-derived osteoblasts while it remains constant in stromal-derived ones over entire time course. This indicates that HSC-derived osteoblasts release more S1P into the microenvironment. MUSC COBRE in Lipidomics and Pathobiology

069-B Determining the Role of CD26 in T Cell-Based Cancer Immunotherapy, Megan M Wyatt, Stefanie R Bailey, Michelle H Nelson, Chrystal M Paulos; 1Microbiology and Immunology, MUSC.

Adoptive T-cell immunotherapy (ACT), an exciting breakthrough in cancer treatment, utilizes patients' own tumor-specific T-cells to fight their cancer. However, not all T-cells are equal in their tumor-fighting ability. We have recently discovered that CD4+ T cells that express CD26 possess enhanced antitumor properties in three different aggressive models. Herein, we sought to determine whether the CD26 protein itself is responsible for these results, or if it is just a marker of an excellent memory cell population. To address this, CD4+ T cells from wild-type (WT) versus CD26/-/- mice were transduced with the T cell receptor TRP-1 that recognizes tyrosinase and infused into mice with established subcutaneous B16F10 melanoma tumors. We hypothesized that the CD26/-/- cells would be less successful in restraining tumor growth than their WT counterparts. Prior to infusion, the cells were indistinguishable phenotypically and functionally. While both B6 and CD26/-/- cells controlled tumor growth in vivo when compared to the untreated control, they were not significantly different from each other. These results are early indications that CD26 might not be important for tumor outcome but rather a marker of a superb cell population for ACT. NIH R01CA175061

070-B Lifestyle Associated Metabolites Drive Neuroendocrine Differentiation in Prostate Cancer, Lourdes M Nogueira1, Sean Cosh2, Michael B Lilly3, David P Turner1, Victoria J Findlay1; 1Pathology, MUSC, 2Biology, Clemson, 3Medicine, 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). The investigators have identified a lifestyle factor known as advanced glycation end-products (AGEs) that promote a more aggressive prostate cancer phenotype through the induction of a specific microRNA (miR-204) and MYC (a known driver of NEPC). The role of miR-204 in
prostate cancer was considered controversial with some groups reporting a tumor suppressor and others an oncogenic role. More recent studies now show that miR-204 plays an oncogenic role in AR negative cells representing NEPC and as a tumor suppressor in AR positive cells representing prostate adenocarcinoma. We show 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. We also show that inhibition of miR-204 can inhibit the neuroendocrine phenotype, including the downregulation of MYC. 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.

072-B Estimating Auditory-nerve Activity in Younger and Older Adults Using Forward-masked Recovery Functions, Carolyn M McClaskey, James W Dias, Judy R Dubno, Kelly C Harris; Otolaryngology, MUSC.

Older adults often have difficulty processing suprathreshold stimuli and listening in complex environments. These findings may relate to changes in the function of the auditory nerve (AN), specifically the loss or diminished activity of AN fibers with low spontaneous firing rates (SR). These low-SR fibers are thought to be primarily responsible for encoding sound in the presence of noise. Because these fibers also recover more slowly from prior stimulation, a forward masking paradigm was developed to characterize the function of AN fibers (Schmiedt et al., 1996). In this paradigm, AN responses are elicited by a signal ("probe") that is preceded by a masker, and the time interval (Δt) between the offset of the masker and the onset of the probe is varied. When this time interval is small, fibers with longer recovery periods are unable to respond to the probe and the neural response is diminished. To better understand how changes in AN function may contribute to listening difficulties in older adults, we adapted this paradigm to human listeners and assessed AN recovery in younger (aged 19-30) and older (aged 58-85) adults using the compound action potential (CAP). CAPs were elicited by interleaved blocks of a tonal probe presented in isolation or preceded by a tonal masker. Responses to the masked probe were normalized to the amplitude of the isolated probe, and Δt was varied between 30 ms and 700 ms. In both younger and older adults, mean normalized CAP amplitudes increased as Δt increased and the slope of this recovery function was steeper for Δt ≤ 100 ms than for Δt > 100 ms. Slopes were steeper for older than younger adults for Δt ≤ 100 ms and Δt > 100 ms. Results are consistent with a loss or inactivity of low-SR fibers in older adults. NIH/NIDCD R01 DC014467, NIH/NIDCD P50 DC00422, NIH/NIDCD T32 DC014435, NIH/NCRR C06 RR14516, and NIH/NCRR UL1 RR029882.

073-B Existence of Hematopoietic-derived Cells in the Periodontal Ligament, Inhong Kang, Katie Wilson, Meenal Mehrotra; Pathology, MUSC.

Periodontal disease is a chronic inflammatory disease that can result in irreversible destruction of tissues leading to loss of attachment of teeth. It affects up to 70% of Americans and is the major cause of tooth loss after 65 years of age. Identification of suitable cells for seeding into periodontal defects would be a powerful tool to promote regeneration and cells from periodontal ligament (PDL) have shown promise. While earlier studies have suggested that cells with hematopoietic markers (CD34, CD45) can be found in dental tissues, our study shows, for first time, existence of cells originating from hematopoietic stem cells (HSCs) in PDL. To conclusively demonstrate this, we utilized a unique transgenic model (VarV) in which all hematopoietic cells are GFP+. Analysis of PDL cultures demonstrated numerous GFP+ cells, which also stained positive for CD45 (indicating hematopoietic origin) as well as co-expressed markers of major cell populations (alpha smooth muscle actin [ASMA] and osteocalcin). Transplantation of clonal cells derived from a single GFP+ HSC into lethally irradiated recipient mice demonstrated numerous GFP+ cells within PDL of recipient mice. These GFP+ cells also stained for known markers for cell populations in PDL (periostin, ASMA, vimentin, osteocalcin) indicating that transplanted HSCs can differentiate into fibroblastic and osteoblastic populations. Our data also indicates that these hematopoietic-derived cells from PDL express stemness markers such as Nanog and Sox2, indicating that these cells are pluripotent. Almost 60-70% of these cells were Ki67+, indicating that they are highly proliferative. Hematopoietic-derived PDL cells can also undergo osteogenic differentiation and their percentage in PDL increases during recovery from ligature-induced periodontitis, indicating involvement of these hematopoietic-derived cells. Since, hematopoietic-derived PDL cells are a novel population, we believe that these studies yield important information about this population, potentially providing a new cellular component for translational approaches in treatment of periodontitis. MUSC COHR Pilot & Feasibility Project Program-P30GM103331, R03DE024536

NIH/NIDCD
074-B The Hepatic Nuclear Factor 1 Beta Is Required for the Hepatic Specification of Human Induced Pluripotent Stem Cell-Derived Endoderm, Francesca Di Furio, Stephen A Duncan; Regenerative Medicine and Cell Biology, MUSC.

Hepatic-like cells (HLCs) generated through the differentiation of human embryonic stem cells (hESCs) and induced pluripotent stem cells (hiPSCs) represent an advantageous alternative to the use of primary hepatocytes in a variety of applications, ranging from regenerative medicine to disease modeling, drug discovery and drug development. Several protocols have been established that generate cells with functional and gene expression characteristics associated with hepatocytes; however, since these HLCs share similarities with fetal hepatocytes, efforts are needed to further improve the methodologies. The understanding of the molecular mechanisms that control hepatocyte differentiation during embryogenesis provides useful information to develop and improve approaches for the differentiation of hESCs or hiPSCs into HLCs. The role of several transcription and growth factors has been investigated in the context of liver development. The Hepatocyte Nuclear Factors (HNFs) are a family of transcription factors that are enriched in the liver and regulate liver-specific gene transcription. HNF1beta, a member of the family, seems to have a conserved role in mouse and Zebrafish liver development, however no studies have been reported so far investigating its role in human hepatogenesis. In this study we investigate the function of HNF1beta during liver development using a cell model based on hiPSCs differentiated towards the hepatic lineage and the CRISPR/Cas9 technology to knockout the gene of interest. The loss of HNF1beta disrupts the expression of typical hepatic markers. We show that this phenotype can be rescued with ectopic HNF1beta, transiently expressed. Interestingly, the expression of HNF4alpha, which is a known crucial regulator of hepatic differentiation, is drastically reduced in the early stages of the specification in the HNF1beta knocked out cell line. We conclude that HNF1beta is required to establish the hepatic fate of the endoderm and further investigation on its mechanism of action will foster our understanding of how embryonic liver develops.

075-B Cortical Changes Following Concurrent Subthreshold Sensory Stimulation During Hand Task Practice, Ryan J Downey, Na Jin Seo; Health Professions, MUSC.

This study examined whether concurrent application of sensory stimulation during hand task practice can yield similar benefits, thereby reducing the time burden on patients. While the overall study investigated the effect of concurrent sensory stimulation on clinical hand function and neural plasticity, this abstract focuses on neural plasticity assessed by electroencephalography (EEG). A pilot double-blinded randomized controlled trial was employed. Thirteen chronic stroke survivors (>6 months post stroke) completed the study (n=6 treatment, n=7 control). All subjects practiced functional motor tasks with their paretic hand for 2 hours per session, for a total of 6 sessions, with a vibrotactile device on the wrist. The control group received no vibration, while the treatment group received random-frequency vibration at intensity below perception. This method was selected because the device placement does not interfere with hand use and because it was previously shown to yield immediate short-term improvements in sensation/motor function in chronic stroke. Before and after the 6-session task practice, cortical activity was assessed with EEG during repeated paretic hand grips and rest. Groups were compared in their changes (pre to post) in the cortical sensorimotor activity, specifically, EEG power during rest and grip-related power change in the alpha/beta frequency bands. Resting alpha power decreased bilaterally following intervention for the treatment group (p<.05), but not for controls. Changes in the other EEG measures did not significantly differ between groups. The result suggests that application of imperceptible vibration during hand motor task practice may lead to change in resting cortical activity. Alpha power reduction may be related to lessened cortical inhibition for sensorimotor activity. NIH P20GM109040

076-B A Novel and Versatile Fluorescent Sensor for the Detection of Alkylating Agents, Yu Jiang, Ann-Marie Lin Broome; Cell and Molecular Pharmacology and Experimental Therapeutics, MUSC.

Abstract not available.

077-B Extrarenal Malignant Rhabdoid Tumor of the Appendix: A Case Report, Ashley W Cross, M Tim Smith; Pathology & Laboratory Medicine, MUSC.

Extrarenal rhabdoid tumors are rare neoplasms, with gastrointestinal malignant rhabdoid tumors representing an exceedingly small proportion. To date, ten of these rare tumors have been described within the colon and rectum. We present a case of a young adult with weight loss, nausea, and abdominal pain. A diagnostic laparoscopic procedure demonstrated diffuse appendiceal thickening and numerous diffuse appendiceal thickening and numerous
fibroblasts or endothelial cells. We then designed
Unexpectedly, we observed that HDAC1 is present in
function and tissue viability attenuated I/R injury, as indicated by improved LV
ex vivo I/R injury +/-
Hearts from male Sprague
MS
that selective inhibition of class I HDACs with the drug
I/R injury have not been identified. We hypothesized
HDAC inhibition has not been tested during reperfusion. We have shown previously that
drugs have been shown to be cardioprotective
histone deacetylase enzymes (HDACs) contribute to
the ischemic region while the patient is in
A myocardial infarction occurs during reperfusion of
Approximately half of the damage done to the heart by
a myocardial infarction occurs during reperfusion of
the ischemic region while the patient is in the care of
the treatment team. Recent evidence indicates that
histone deacetylase enzymes (HDACs) contribute to
ischemia reperfusion (I/R) injury, and pan-HDAC
inhibitors have been shown to be cardioprotective when administered either before an ischemic insult or
during reperfusion. We have shown previously that
selective inhibition of class I HDACs provides superior cardioprotection when compared to pan-HDAC
inhibition in a pretreatment model, but selective class I HDAC inhibition has not been tested during
reperfusion, and specific targets of class I HDACs in
I/R injury have not been identified. We hypothesized
that selective inhibition of class I HDACs with the drug
MS-275 (entinostat) during reperfusion would improve
recovery from I/R injury in the first hour of reperfusion. Hearts from male Sprague-Dawley rats were subjected to
ex vivo I/R injury +/- MS-275 class I HDAC inhibition
during reperfusion alone. MS-275 significantly
attenuated I/R injury, as indicated by improved LV
function and tissue viability at the end of reperfusion. Unexpectedly, we observed that HDAC1 is present in
the mitochondria of cardiac myocytes, but not
fibroblasts or endothelial cells. We then designed
mitochondria-restricted and mitochondria-excluded
HDAC inhibitors, and tested both in our ex vivo I/R
model. The selective inhibition of mitochondrial
HDAC1 attenuated I/R injury to the same extent as
MS-275, whereas the mitochondrial-excluded inhibitor
did not. Further assays demonstrated that these
effects are attributable to a decrease in SDHA activity
and subsequent metabolic ROS production in
reperfusion. We demonstrate for the first time that
HDAC1 is present within the mitochondria of cardiac
myocytes, and mitochondrial HDAC1 contributes significantly to I/R injury within the first hour of
reperfusion. VA BX002327-01; NIH F30 HL129629,
T32 GM008716, T32 HL007260, SCTR NIH/NCATS
TL1 TR000061, UL1 TR000062

079-B Bilateral Transradial Approach to
Alcohol Septal Ablation for Symptomatic
Hypertrophic Obstructive
Cardiomyopathy, Thomas E Miller, Christopher
D Nielsen, Valerian Fernandes, Justin Heizer,
John M Neathawk, Jeremy Rier, Shawn Shaji,
Alexandria Panuccio, Internal Medicine, MUSC,
Drug Discovery and Biomedical Sciences, MUSC,
Cell and Molecular Pharmacology, MUSC.

Alcohol septal ablation (ASA) for hypertrophic obstructive cardiomyopathy (HOCM) has
conventionally been performed via transfemoral (TF) approach. TF procedures historically have higher
bleeding and vascular complications while transradial (TR) approach for PCI has led to reduction in bleeding
and vascular complications with better patient
satisfaction and with similar outcomes. The purpose of
this study was to evaluate feasibility, safety, and
results of bilateral TR access approach for ASA.
Bilateral TR ASA was attempted in 60 consecutive
patients (24M, 36 F) with average age 61.75 ± 12.84
years, compared to 65 consecutive patients (27M,
38F) with average age 61.69 ± 13.92 via TF approach.
2 patients in TR group required crossover to TF and
thus excluded from this study. Prism 7 software was
used to analyze procedural success, fluoroscopy time,
contrast use, and vascular complications using two
tailed t-test comparison of means and contingency
tables with Chi-squared tests assessing statistical
significance of categorical data. Procedural success
defined as ≥50% reduction in resting gradient was
similar at 98.33% in TR group (average post-ASA
gradient of 7.51) and 95.38% in TF group (average post
-ASA gradient of 5.56). There were no strokes or
deaths in either group. The TR group had 0 vascular
complications, whereas the TF group had 2. Length of
stay and average contrast use were equivalent.
Average fluoroscopy time was statistically higher in the
TR group (19.9±14.2 min vs. 13.8±7.5 min, p-value of
0.004). Bilateral TR approach ASA for symptomatic
HOCM is feasible, equally effective, with less vascular
complications, and a low rate of crossover to TF.
TR
Effective cancer therapy for the treatment of Glioblastoma Multiform (GBM, primary malignant brain tumor) still remains one of the most challenging areas in brain cancer research with little progress in GBM patient survival rate in the last few decades. One of the major limitations of chemotherapeutics for GBM in the clinic is the lack of tumor selectivity. Systemically delivered therapeutics cause cell death in healthy surrounding tissues and cells. The development of nanoparticles that act as drug delivery vehicles is critical for improving the treatment and monitoring of GBM. Reservatrol (RSV, 3,4′,5-trihydroxy-trans-stilbene) is a dietary polyphenol extracted from grapes, berries, and other plant sources. RSV impacts all three distinct stages of carcinogenesis (initiation, promotion, and progression) via modulating signal transduction pathways that control cell division and growth, apoptosis, inflammation, angiogenesis, and metastasis. The anti-cancer properties of RSV impede proliferation of a wide variety of human tumor cells in vitro. In this study, RSV derivatives in micelles composed of PEG-PE amine (1, 2-distearyl-sn-glycero-3-phosphoethanolamine-N-[amino(polyethylene glycol)-2000]) and PHC (N-palmitoyl homocysteine) were evaluated for encapsulation efficiency and stability. PEG-PE amine was labeled with fluorescent dye (Dylight 680) for tracking of the micelle in in vitro cellular uptake. PHC, a pH sensitive lipid, was utilized to assist in the rupture of the micelle at acidic pH to ensure the delivery of the cargo inside the cells. For RSV derivate containing micelles, the hydrodynamic diameter was 10-20 nm in size; UV-Vis absorbance spectra show a peak at 680 nm (Dylight 680) and a peak around 300 nm (RSV derivative). Preliminary cellular uptake studies via fluorescence imaging of glioblastoma cells treated with fluorescently labeled micellar particles demonstrate considerable uptake. Ongoing experiments include cellular cytotoxicity assays, pharmacokinetic analysis, and tissue distribution studies in vitro.

**082-B The EM*Ppowered (trademarked) Initiative: Can a Two Week Selective Be Effective in Promoting Wellness and Professional Development?**, Drew Johnson, Christina L Bourne, Diann M Krywko; Emergency Medicine, MUSC.

OBJECTIVES: Emergency medicine (EM) physicians have high rates of un-wellness. The ACGME RRC requires teaching wellness and professional development (W&PD) as core competencies. However, there is no national standard selective developed to teach W&PD. Our objective was to determine if the innovative EM*Ppowered (TM) Initiative (EM personal and professional wellness, renewed engagement and development) 2 week selective would be an effective avenue for teaching W&PD and met with positive evaluations. METHODS: The selective launched October, 2016 with EM program director and ACGME DIO approval. Emphasizing W&PD focus absent in traditional clinical rotations or didactics, it incorporates self-directed reading of a W&PD book and articles on sleep, exercise, curriculum vitae (CV) and personal statement (PS) writing. Required professional activities include: CV/PS composition, job application, residency program presentation of professional skill studied. Required personal activities include: maintenance of sleep/exercise logs; reconnection with one person medicine caused a drift from; one medical appointment if indicated; and one weekend with no work duties/electronic access. All seniors were eligible (n=6). Five enrolled/completed (83%). Identical six question pre- and post-tests covering literature were administered and scores compared. Our electronic residency management tracking system with open comment field was utilized for evaluation. RESULTS: Average scores were: pre-test 42%, post-test 100%, improvement 58%. Individual responses revealed solely positive comments. 100% of residents responded with the verbiage “awesome”. Selected comments were: “Felt like a new person”, “First time in residency I felt completely normal”, “…realized I should focus on looking at my phone way less”, and unexpectedly, "I met with a financial advisor... signed up for disability insurance." CONCLUSION: Development of an innovative two week selective designed to teach and promote mental, physical, and career wellness, as well as provide platform for acquisition in PD skills was successful in our sample. The experience was overwhelmingly positive for resident physicians.
**ORAL ABSTRACTS**

**084 Investigation Into Serotonylation of Extracellular Matrix Proteins in Periodontal Disease**, Nicolas G Shealy¹, Amy D Bradshaw²; ¹Biology, CofC, ²Gazes Cardiac Research Institute, MUSC.

The periodontal ligament (PDL) is the connective tissue between the alveolar bone and cementum of the tooth. It is rich in fibroblasts with a high rate of turnover of the extracellular matrix (ECM). It was previously reported that SPARC-null PDL had decreased volume and quality of collagen. One possible modality for the decrease in ECM quality is the effect of the enzyme transglutaminase (TG) on collagen. TG is able to modify ECM proteins in multiple ways including cross-link formation and by binding the free amine on serotonin (5-HT) to glutamine residues on ECM proteins. It was hypothesized that SPARC-null tissues would display differences in the serotonylation of ECM proteins, due alterations in TG activity in the PDL. To test the hypothesis, immunoblotting, immunohistochemistry, and immunofluorescence were conducted. SPARC-null PDL samples demonstrated stronger signals when stained for 5-HT. It was also hypothesized that PDL with ligature, a murine model of periodontal disease, would display differences in the serotonylation, however, results with ligature samples were inconclusive and require further investigation. NHLBI R25 HL092611; MUSC SURP

**085 CD8+ T Cells Mediate Immune Response to Combination Therapy with IL-15/IL-15Ralpha Complexes and Anti-PD-1 MAb**, Caroline S Mart, Marzena Swiderska-syn, Samantha Suriano, Luis Cardenas, Kristina Andrijauskaite, John Wrangle, Mark Rubinstei; Surgery, MUSC.

Abstract not available.

**086 Effect of Scent-Paired Restraint Stress on Heroin Reinstatement and Corticosterone Levels**, Jordan S Carter¹, Rachel A Weber², Carmela M Reichel; ¹Biology, CofC, ²Neuroscience, MUSC.

Withdrawal symptoms following substance use disorders and post-traumatic stress disorder (PTSD) reciprocally exacerbate one another. Withdrawal symptoms, induced by cessation of substance use culminate as stressors and lead to relapse. PTSD can be triggered by withdrawal-induced stress responses further increasing relapse potential. Here we paired a neutral odor (lemon or sandalwood) with restraint stress to test whether re-exposure to the stress-paired odor would impact heroin seeking during withdrawal. Rats in the stress group were restrained in a plastic tube that did not allow for mobility with exposure to a scent. Unstressed (control) rats were exposed to SW or lemon in a neutral cage. All animals underwent heroin self-administration and extinction followed by both an extinction test (Ext TEST) and a cued reinstatement test with exposure to the paired and unpaired scents. Blood was collected during extinction and after each test to assay corticosterone (CORT) levels. Male and female (stressed and unstressed) rats robustly self-administered heroin and extinguished responding at the same rate. On the Ext TEST, sex and stress conditions interacted. Males reinstated significantly above normal extinction rates in response to the stress paired odor. Only unstressed males generalized responding to a novel (unpaired) odor. CORT levels were constant in males across all sessions. For females on the Ext TEST, there were no differences in lever pressing on any tests; however, CORT levels were higher for both stressed and unstressed females on the Ext TEST regardless of the odor that was presented. There were no differences on the cued reinstatement tests as all rats robustly reinstated to heroin-conditioned cues. Interestingly, males had higher baseline CORT levels relative to females, which contrasts the notion that females are more sensitive to endogenous stressors. Future studies will explore this sex difference and the underlying neural mechanisms governing this difference. CofC Honors College Summer Enrichment Grant, MUSC SURP, SCOR P50DA016511

**087 Preclinical Approaches to Evaluate Radiation-induced Necrosis in Glioblastoma**, Indira S Kanginakudru¹, Daniel McDonald², Arindam R Chatterjee³, Sunil J Patel⁴, David Cachia⁴, Tyson McCormick¹, Arabinda Das¹; ¹Academic Magnet High School, ²Radiation Oncology, MUSC, ³Radiology & Radiation Science, MUSC, ⁴Neurosurgery, MUSC.

Progressing rapidly, glioblastomas are aggressive, WHO Grade IV brain tumors with a median survival rate, with irradiation and chemotherapy, of 14.6 months. Excessive radiation causes complications like recurrent glioma and radiation necrosis, with the latter being more severe. Late-delayed chronic necrosis, which occurs months to years post-irradiation, is prevalent in humans and is irreversible, causing permanent neurodegeneration. Although some characteristics of radiation necrosis have been discovered, other characteristics, such as standard latent period and radiation tolerance, remain a mystery. This study was conducted to identify a dosage of radiation that could induce acute necrosis, a lesser and reversible stage of radiation necrosis. Here, we investigated the molecular mechanism of necrosis.
glioma cells in both in vitro and in vivo (orthotopically allograft) models in response high doses of X-ray radiation. Overall, our data shed new light on the relationship between RIP1/RIP3-mediated programmed necrosis and AIF-mediated caspase-independent programmed necrosis in glioblastoma. At the same time, we specifically addresses the differentiation between radiation necrosis and glioma by comparing their respective imaging features with histology in animal models. We hope by identifying the distinction between radiation-induced necrosis and recurrent GB, the proposed studies may significantly enhance patient survival outcomes for an otherwise bleak prognosis of GB without adding to the burden of cost-of-care. MUSC Department of Neurosurgery

088 Oral Microbiota Has Osteoimmunomodulatory Effects Distinct From the Systemic Microbiome, Blakely E Graham¹, Chad Novince², Jessica Hathaway-Schrader², Nicole Poullides²; ¹Biology, Wofford College, ²Oral Health Sciences, MUSC.

Abstract not available.

089 FLI-1 Transcription Factor Increases IL-6 and VEGFα Production in Mouse Lung Pericytes, Valeria C Montalvo¹, Pengfei Li¹, Yue Zhou¹, Andrew J Goodwin², James A Cook³, Perry V Halushka⁴, Xian K Zhang⁵, Hongkuan Fan⁶; ¹Pathology, MUSC, ²Pulmonary, MUSC, ³Neuroscience, MUSC, ⁴Medicine, MUSC, ⁵Rheumatology, MUSC, ⁶Pathology, MUSC.

Sepsis is a leading cause of death in the Intensive Care Unit, and characterized by a dysregulated immune responses caused by an infection that leads to vascular leakage and organ failure. Pericytes are specialized cells embedded in the capillary basement membrane that wrap around endothelial cells of the microcirculation throughout the body and are thought to play a significant role in angiogenesis and immune responses. Friend leukemia virus integration 1 (Flt-1), a member of the ETS transcription factor family and a key regulator in modulating inflammatory response in endothelial cells. However, the role of Flt-1 on pericyte function in sepsis remains unknown. We hypothesize that Flt-1 regulates lung pericyte function in sepsis. Lung pericytes were isolated from mice and transfected with Flt-1 plasmid and stimulated with LPS. Our results show that cells transfected with the Flt-1 plasmid increases IL-6 and VEGFα mRNA levels (2.2 ± 0.2 fold and 2.2 ± 0.2 fold respectively; P<0.05). In another experiment, the transfected cells were stimulated with Gram negative bacterial component LPS (100 ng/ml) for 24 hrs. Pericytes did not show a further increase of IL-6 or VEGFα mRNA expression. This result suggests that the lack of further increase in IL-6 and VEGFα mRNA could be due to saturation in the Flt-1 binding site in these mRNAs. These results are complemented by increases in IL-6 and VEGFα mRNA in LPS-treated pericytes that were not transfected with Flt-1 plasmid. Our studies suggested that Flt-1 regulates inflammatory cytokine and growth factor production in lung pericytes, which may contribute to the pathogenesis of sepsis. NHLBI, R25 HL092611

090 Identifying the Role of Complement in Triggering Neuroinflammation After Traumatic Brain Injury, Farris Langley¹, Ali Alawieh¹, Shannon Weber¹, DeAnna Adkins², Stephen Tomlinson³; ¹Medical Scientist Training Program, MUSC, ²Neurosciences, MUSC, ³Microbiology and Immunology, MUSC.

Abstract not available.

091 Gut Flora Metabolites Modulate Autoimmune Inflammation in the Central Nervous System, Davis M Borucki¹, Veit J Rothhammer², Isabel M Garcia Sanchez³, Guillermo Izquierdo⁴, Howard L Weiner⁵, Francisco J Quintana⁶; ¹Medicine, MUSC, ²Neurology, Harvard Medical School, ³Physician, Universidad de Salamanca, ⁴Physician, Universidad de Sevilla, ⁵Neurologic Disease, Brigham and Women’s Hospital.

Astrocytes play important roles in the central nervous system (CNS) during autoimmune inflammatory diseases such as multiple sclerosis (MS). We have recently shown that the ligand-activated transcription factor aryl hydrocarbon receptor (AhR) in astrocytes reduces inflammation in experimental autoimmune encephalomyelitis, EAE, the animal model of MS. Ligands to AhR arise from multiple sources, including dietary ingredients and their interaction with the gut microbiome, as exemplified by tryptophan metabolism. However, the modulation of AhR ligands in MS is yet unknown. Dietary tryptophan is metabolized by gut microbiota into AhR agonists, which cross the blood brain barrier and activate AhR in astrocytes to limit CNS inflammation. Indeed, depletion of gut microbiota promoted disease activity in EAE depending on AhR in astrocytes. Conversely, administration of tryptophan metabolites or the bacterial enzyme tryptophanase reduced CNS inflammation. Thus, microbial metabolites of dietary tryptophan act on AhR in astrocytes to limit CNS inflammation. To test whether alterations in AhR ligands contribute to MS pathogenesis, we devised a bioassay to detect AhR agonist activity in sera from patients with relapsing-remitting MS (RRMS) or healthy controls. Indeed,
RRMS sera displayed decreased AhR agonistic activity as compared to healthy controls and in comparison to patients with mild clinical impairment despite longstanding disease. Finally, mass spectrometry of serum samples from RRMS patients revealed decreased AhR ligands derived from dietary tryptophan. Taken together, low levels of circulating AhR agonists in MS patients may suggest deficits in dietary factors and their interaction with the commensal flora, or in the pathways that control the production and degradation of AhR ligands. Conversely, unaltered serum AhR ligand levels in patients with a benign course of MS suggest a protective role of AhR ligands. These observations may be useful to develop biomarkers for MS and may guide the development of novel therapeutics. NIH ES025530, AI093903, and AI126880; National MS Society RQ4111A1, JF2161-A-5Q; Mallinckrodt Pharmaceuticals A219084; German Research Foundation DFG RO4866 1/1

092 The Impact of Advanced Glycation End Products (AGEs) to Prostate Cancer Disparity, Narges Anbardar, Danzell Smith, Dion Foster, Lourdes Nogueira, Laura Spruill, Thomas Keane, Steve Savage, Victoria J Findlay, David P Turner; MUSC.

Established factors such as low income, poor diet, drinking alcohol, smoking and a sedentary lifestyle are known socioeconomic and environmental risk factors that contribute to cancer health disparity. Such factors may have molecular effects on the inherent biological make-up of the tumor itself, possibly altering cell signaling events and gene expression profiles to profoundly alter tumor development and progression. The immune response has recently come to the fore as a biological mechanism implicated in cancer health disparity. An examination of expression differences based upon tumor composition shows that cytokine signaling associated with an increased immune response was found to be a predominant pathway increased in African American prostate cancer patients. Glycation occurs during metabolism and is the non-enzymatic glycosylation of sugars to protein and DNA. Glycation results in the accumulation of reactive metabolites known as advanced glycation end products (AGEs). Significantly, apart from their production during normal metabolism, AGE accumulation is also associated with the socioeconomic and environmental factors that drive cancer disparity. Based on links between AGE accumulation, immune response and established cancer health disparity factors we hypothesis that: Race specific elevations in AGEs alters tumor associated immune responses in prostate cancer. We are generating race specific primary and immortalized human epithelial prostate cancer cells which we will grow on micro-porous membranes in the presence and absence of stromal cells to simulate the in vivo tumor microenvironment. Cells will be treated with exogenous AGE and the effects on cytokine secretion and immune factor gene expression profiles examined. The goal is use the tumor cell culture model to define the contribution of the AGE signaling axis to the immune response and identify race specific immune response patterns. NIH/NCI P20 CA157071; NIH/NCI R21 CA176135

093 The Role of Ccdc117 in Modulating the Formation of Exosomes Via Hsp40., Timothy Jiang, Kyu-Ho Lee, Pamela Riggs-Gelasco; Pediatrics, MUSC.

Abstract not available.

094 Exploring the Role of MiRNA-204 in Low Milk Supply, Clare E Burton1, Jerrica Walden2, Martina Mueller3, David P Turner1, Sarah N Taylor4, Victoria J Findlay1, 1Pathology, MUSC, 2Biology, USC, 3Nursing, MUSC, 4Pediatrics, MUSC.

Breastfeeding is the optimal method for mothers to deliver nutrients to her newborn(s), as it not only provides key nutrients but improves their overall physical health. However, only 24% of infants receive exclusive breastfeeding for the first 6 months, as recommended by the World Health Organization, with the most often cited reason for stopping being “low milk supply”. The inability to sufficiently lactate (or Low Milk Supply, LMS) is a real and growing problem in the United States, with at least 5-10%, approximately 200,000, of mothers experiencing LMS in the US each year. We observed that overexpression of miR-204, using our unique dox-inducible miR-204 transgenic mouse model, during lactation results in reduced pup weight suggesting a lactation defect. This led to the hypothesis that dysregulation of miR-204 expression results in Low Milk Supply through the inhibition of the Milk Protein Synthesis (MPS) Pathway. We have collected mammary gland tissue and milk from miR-204 transgenic (204 Tg) and control (non Tg) mice at different stages of lactation and performed IHC and qPCR analysis. We collected milk from women with known sufficient milk supply (≥500 ml/day) and LMS (<300 ml/day) and extracted miRNA for qPCR analysis. We show that miR-204 is present and is temporally expressed in mouse tissue and milk. We show reduced activation of the MPS Pathway in miR-204 transgenic mice. Furthermore, we are able to detect miR-204 in human breast milk and demonstrate elevated miR-204 levels in women with LMS. Our data suggests that miR-204 may be a useful biomarker in milk to detect an LMS in women. Once detected, we can intervene in a timely fashion, with approved medications guided by the outcomes of our study, to maximize a successful lactation outcome in all women.
095 The Identification of Leukocyte Populations in the Synovial Fluid of Patients with Osteoarthritis, Thomas A Valente1, Kiley Lawrence2, Matthew Essman3, Katie Hurst3, Vincent Pellegrini Jr8, Jessica Thaxton8,1 COM, MUSC, 2Orthopedics, MUSC, 3Microbiology & Immunology, MUSC.

The pathogenesis of established osteoarthritis is driven by inflammation, as the condition is not simply a disease of “wear and tear” on the joint. We hypothesized that isolation and identification of leukocyte populations from synovial fluid of osteoarthritis patients may elucidate the major immune subsets responsible for disease progression. Identification of such populations may yield immunotherapeutic targets to diagnose and prevent progression of disease. In order to phenotype the cellular infiltrate in the joint-space environment, we performed immune cell subsets analysis by flow cytometry on synovial fluid samples taken from patients undergoing total joint arthroplasty for the treatment of osteoarthritis. We were able to consistently isolate and identify monocyte and lymphocyte populations found in patient synovial fluid samples. The majority of lymphocytes found were T cells, with slightly higher CD4+ populations compared to CD8+ subsets. Interestingly, the patients in the study could be stratified into two groups, those whose monocytes were HLA-DR+ or HLA-DR-. These differences indicate that patients may experience alternate forms of disease progression driven by differential immune populations. These variances could prove important in patient prognosis and the course of osteoarthritis progression. Together these data indicate that targeting immune cell populations may be an immunotherapeutic strategy useful in diagnosis and treatment of osteoarthritis.

096 Roles of an Nkx2–5 Target Gene in the Developing Placenta, Balakrishnan Pillai, Kyu–Ho Lee; Pediatrics, MUSC.

The Nkx2–5 transcription factor is expressed in cardiac progenitor cells, and regulates formation of the right ventricle and outflow tract. Prior studies have shown that Nkx2–5 directly regulates the gene ccdc117, which in turn interacts with MMS19 the cytoplasmic iron–sulfur cluster assembly (CIA) targeting complex. MMS19 CIA acts at the final step in Fe–S metabolism, to insert Fe–S clusters into a growing list of apoenzymes, including many DNA repair and replication enzymes. We have previously shown that ccdc117 knockdown in HeLa cells results in increased DNA damage, decreased DNA synthesis, and decreased proliferation. We also found that ccdc117 knockdown in HeLa cells caused a significant bioenergetic insult to the cell. In other prior studies, we found that both Nkx2-5 and Ccdc117 were also expressed in developing placenta, and that correlated elevations in the expression of Nkx2-5 and Ccdc117 mRNA were present placenta of women with early onset and severe pre-eclampsia. We therefore sought to determine whether ccdc117 similarly acts as a proliferation factor in HTR8 cells (as a model system for the developing placenta), and additionally if there are metabolic effects of ccdc117 knockdown in HTR8 cells. We found that ccdc117 knockdown in HTR8 cells caused a very significant increase in G1 phase population, with similar very significant decreases in S phase and G2/M phase populations. These findings support the overall G1/S stalling phenotype previously observed. Furthermore, we found that ccdc117 knockdown caused significant reduction in NAD/NADH and [ATP], however this was inconsistently observed and may be more sensitive to specific levels of ccd117 expression. Taken together, our findings support the hypothesis that ccd117 acts a proliferation factor in the developing placenta and may have cell–specific metabolic roles relevant to placent al health and disease. NIH 5 T35 DK 7431-33; MUSC SHP

097 Regulation of the TGF-Beta Pathway During Thoracic Aortic Aneurysm (TAA) Development, Megan G Gross1, Robert E Stroud1, Elizabeth K Nadeau1, Mukherjee Rupak2, Jeffrey A Jones3,1College of Medicine, MUSC, 2Cardiothoracic Surgery, MUSC, 3Ralph H. Johnson VA.

Thoracic aortic aneurysms (TAAs) develop as a consequence of abnormal remodeling of the aortic extracellular matrix (ECM). TAA development is influenced by mechanisms that disrupt ECM homeostasis in part through changes in the resident cellular constituents within the aortic wall. Recent suggests that aortic fibroblasts undergo a stable cellular phenotype transformation characterized by increased staining of myofibroblast markers. However, the mediator(s) regulating this fibroblast-to-myofibroblast transition during TAA development remain undefined. Transforming growth factor-beta is capable of regulating the structure and composition of the aortic ECM and is known to play a role in mediating cellular transdifferentiation. This study examines the role of TGF-beta in thoracic aortic aneurysm development by quantifying macrophages in the aorta during TAA development and seeing if delivery of a TGF-beta neutralizing antibody attenuates aortic dilatation during TAA development. Previously banked formalin-fixed aortic rings were used to complete histological examination with F4/80 staining across different time-points in TAA development. TAAs were induced in wild-type mice - TAA alone, TAA + TGF-beta neutralizing antibody, and TAA + nonspecific rabbit IgG; the outer thoracic aortic diameters were computed from calibrated intra-
operative digital images acquired at the time of terminal surgery. Macrophages were present in the tunica media and tunica adventitia of thoracic aortas with a significant increase in the number of macrophages between un-operated & 8-week TAA and un-operated & 16-week TAA. Further research needs to be conducted to see if the macrophages are responsible for the ECM breakdown and TAA development via their secretion of TFG-beta or if they are trying to repair the damaged aortic tissue. Preliminary data showed that administration of TFG-beta neutralizing antibody slightly attenuated aortic dilation in mice at 8-weeks post-TAA induction. Further studies need to be conducted to understand the extent that TGF-beta plays in TAA development. American Association of Thoracic Surgeons

098 Modification of Temozolomide to Improve Therapeutic Efficacy in Glioblastoma Cells, John H Rainwater¹, Daniela Ramos Mendoza², Yu Lin Jiang³, Ann-Marie Broome³; ¹College of Medicine, MUSC, ²South Carolina Governor’s School for Science and Mathematics, ³Cell and Molecular Pharmacology & Experimental Therapeutics, MUSC.

Aim: Temozolomide (TMZ) in conjunction with radiotherapy is the current gold standard for treatment of GBM. However, these methods only result in an average life expectancy of 12-15 months and the side effects of TMZ are especially harsh. Systemic administration of TMZ results in little drug accumulation across the blood brain barrier. However, encapsulation of TMZ is challenging. Therefore, development of a modified TMZ was evaluated for therapeutic efficacy and encapsulation efficiency. Further, encapsulation of a modified TMZ could reduce off-target side effects and target the therapy only to the GBM. Therefore, we created TMZ analogs that could be more easily encapsulated in micelles. We tested the modified TMZ for therapeutic efficacy using an in vitro human glioma cell line viability assay. Materials and Methods: Human glioblastoma cells, LN-229 cells, were treated with increasing concentrations of TMZ, TMZ-E, or TMZ-A. Cell viability was assessed 24 hours later using a trypan blue assay. Morphology was observed using phase contrast microscopy. Results and Conclusion: The modified analog, TMZ-E, was the most effective killer of LN-229 cells when compared to unmodified TMZ or acidified TMZ (TMZ-A). We now plan to test TMZ and its analogs on other cell lines and then encapsulate the analogs in micelles, which are then targeted specifically to the tumor cells. NIH 5T35DK007431-33; MUSC SURP

099 Preoperative Smoking Cessation As a Durable Form of Long-term Smoking Cessation, Jacob C Balmer¹, Ashley B Anderson², William R Barfield³, Harry A Demos³; ¹COM, MUSC, ²Walter Reed Medical Center, ³Orthopaedic Surgery, MUSC.

Background: Smokers who undergo total joint arthroplasty (TJA) face increased rates of medical and surgical complications. Smoking in the perioperative time is associated with increased pulmonary, cardiac, and local wound complications. Preoperative intervention for smoking cessation four to eight weeks prior to surgical operations reduces risk of operative complications in the immediate postoperative period. The purpose of this study was to investigate if preoperative smoking cessation is sustainable in total joint reconstruction patients. Methods: Following institutional review board approval, 27 patients from the Medical University of South Carolina (MUSC) who underwent TJA were included in the study cohort. Patients were counseled to quit smoking preoperatively and completed a 12-month postoperative telephone survey to evaluate if there was sustainable long-term smoking cessation. Their cessation rate was then compared to documented long-term cessation rates of pharmacological smoking cessation therapies with a 2 sample independent proportion z-test. Results: Out of 27 patients who met the inclusion criteria and were able to complete the telephone survey, 21 (77.8%) self-reported as having quit smoking for surgery. At 1-year post-op, 11 patients (40.7%) self-reported being abstinent from smoking, and 10 patients of the 21 who quit for surgery were still abstinent (47.6%). Compared with historical models the 1-year abstinence rate of our cohort was significantly higher (p<.05) than documented long-term abstinence rates due to currently available pharmacological treatments and other methods. Conclusion: Smoking cessation lowers post-operative morbidity and increases quality of life after surgery. Our results demonstrate that brief smoking-cessation counseling prior to elective total joint surgeries may have long-term sustainability and should be considered by orthopaedic surgeons as a standard of treatment prior to surgery.

100 The Use of Complementary and Alternative Medicine (CAM) Among Black/African-American Patients Managing Diabetic Foot Ulcers, April Stubbs¹, Theresa Kelechi²; ¹Medicine, MUSC, ²Nursing, MUSC.

Background: African American/Black patients are more likely to develop chronic diabetic foot ulcers than non-Hispanic Whites. While diabetic patients are more likely to use complementary and alternative medicine (CAM), little is known about the specific treatments patients choose to use. Because Black/African
American patients are more likely to suffer from ulcers that may lead to amputation, it is important to know how CAM therapies are incorporated. Objective: The aim of this study is to determine knowledge and attitudes about CAM, prevalence of its use, reasons for its use, and types of CAM used by African American/Black patients who are managing diabetic foot ulcers. Method: A cross-sectional, descriptive, hospital-based survey will be conducted to explore patients’ experiences and knowledge of CAM to manage their diabetic foot ulcers. Results: Previous studies concluded that over 30% of patients used CAM to treat diabetic foot ulcers. We anticipate that a majority of patients in the target population will report CAM use during the previous 12 months. Conclusions: Researchers and clinicians should more carefully consider patients’ use of CAM therapies when constructing care plans. Future research will explore feasibility of the CAM Use Questionnaire in measuring patient CAM use among African American/Black patients with diabetic foot ulcers. NIH R25HL096316-08

101 Comparing Post-Operative Wound Complication Rates for Neoadjuvant Interdigitated Chemoradiation Versus Neoadjuvant Radiation Alone, Jonathan Pire¹, Stephanie Terezakis², Adam Levin³, Chengcheng Guì⁴, Carol Morris⁵. ¹College of Medicine, MUSC, ²Radiation Oncology, Johns Hopkins University School of Medicine, ³Orthopedic Surgery, Johns Hopkins University School of Medicine, ⁴School of Medicine, Johns Hopkins University.

Interdigitated preoperative chemoradiation therapy is a treatment option for high-grade soft-tissue sarcomas (STS) to improve patients’ chances of local control and survival(7-11). Preoperative radiation alone has been shown to increase the risk of surgical wound complications(12). The purpose of this study was to investigate whether interdigitated preoperative chemotherapy-radiation was associated with a greater incidence of post-operative wound complications compared to preoperative radiation alone. We retrospectively reviewed records of patients who underwent surgery for high grade STS between 1999 and 2017. Patients that received pre-operative radiation alone or pre-operative interdigitated chemoradiation were included in our analysis. Ninety-nine patients met our inclusion criteria; 66 received preoperative radiation (RT) and 33 received interdigitated preoperative chemoradiation (ICRT). Wound complication was defined as previously described by O’Sullivan(12), including any secondary wound-related operation, invasive wound management procedure, readmission for wound care, or chronic wound-healing past 120 days. Outcomes were recorded binomially and analyzed using a Fisher’s exact test. Secondary outcome measures included information about demographics, medical history, tumor specificities, and surgical details. 14 (21.21%) of 66 patients in the RT cohort and 6 (18.18%) of 33 patients in the CRT cohort experienced major wound complications (p=0.7963). Median radiation dosages for the 2 groups were 50 Gy and 44 Gy respectively. The CRT cohort had an average 3.06 cycles of preoperative chemotherapy, ranging from 2 to 6. In multivariate analysis, race, specimen size, and anatomic location were found to be prognostic factors for the sample. Evidence showed no significant difference in major wound complication rates between patients treated with preoperative chemoradiation and radiation alone. This suggests that addition of chemotherapy to pre-operative radiation in an interdigitated fashion does not have an untoward effect on wound healing. Surgical wound complications may be one less consideration for interdisciplinary teams when deciding between the two preoperative treatment plans.

102 Does the Integrity of Specific White Matter Tracts Relate to Early and Late Motor Performance in Preterm Neonates?, Ñybil K Hallman¹, Danielle Lowe¹, Hunter Moss², Patty Coker-Bolt³, Dorothea Jenkins⁴. ¹College of Medicine, MUSC, ²Occupational Therapy, MUSC, ³Biomedical Imaging, MUSC, ⁴Pediatrics, MUSC.

The objective of this study was to determine if white matter tract fractional anisotropy (WM FA) with scores on the Specific Test of Early Infant Motor Performance (STEP), predict 12-month motor outcomes in preterm infants better than STEP alone and relate individual STEP item scores to specific WM FA. 23 preterm infants received DTI (term); STEP (term, 3months); and Bayley III (12-months). We tested WM FA with total STEP scores, in predicting Bayley Gross Motor Scaled Scores using generalized linear models. Individual STEP item scores (rolling leg, rolling arm, head movements in supported sitting) were related to WM FA. It was found that FA in left corpus callosum (CC) and inferior frontal-occipital fasciculus (IOF) at term contribute significantly to total STEP score in predicting 12-month motor outcomes. FA in left uncinate fasciculus (UF) also contributed to the term STEP model, and posterior limb of internal capsule (PLIC), to 3-month STEP model. Performance on rolling leg at term predicts CC FA, and at 3-months, right CC and PLIC. Performance on supported sitting at term predicts PLIC FA, and at 3 months, CC and left PLIC FA. At 3 months rolling arm predicts CC FA. Rolling leg and supported sitting require thoracic tone and head control, while rolling arm requires pelvic muscle control. We concluded that microstructural integrity in CC, IOF, UF and PLIC obtained at term with functional STEP scores at 0-3 month predict 12-
103 Predictors of Disclosure in the Forensic Interview in Pediatric Abuse and Maltreatment Cases, Trevor Morris¹, John D Melville², Kathy Quinones³, Carole C Święcicki³; ¹College of Medicine, MUSC, ²Pediatrics, MUSC, ³Dee Norton Child Advocacy Center.

Pediatric abuse and maltreatment are an unfortunate aspect of our society. Whenever a child discloses that it has occurred, the standard of care includes a forensic interview, an exam conducted by a trained professional to gather factual information regarding the allegations. Many researchers have studied what characteristics in children and their environment makes them more or less likely to disclose during a forensic interview, however there have been changes in interview protocols over the past decades. The purpose of this study is to identify predictors of disclosure during the forensic interview using a clinically representative sample using modern forensic interview techniques. 600 patient’s records were examined in this study. 18 records were removed due to the lack of written prior history. 291 (51.2%) cases disclosed some form of abuse or maltreatment during the forensic interview. In our study, prior disclosures, age, and witnessed abuse, were statistically significant increased the likelihood for disclosure during a forensic interview, while prior denials and sibling examination decrease the likelihood of disclosure during a forensic interview. Our study also shows that 43% of the patients disclosed at least 1 type of abuse not listed as the referral indication.

104 A Tailored Tube-Voltage Adapted Contrast Media Injection Protocol for Coronary CT Angiography, Hubert E Smith, Philipp von Knebel Doeberitz, Domenico De Santis, Damiano Caruso, Carlo N De Cecco, Akos Varga-Szemes, Moritz H Albrecht, Joseph U Schoepf; Radiology, MUSC.

Abstract not available.

105 Treatment of Early Onset Scoliosis and Its Emotional Effects on Patients and Their Families: An EOSQ Analysis, Thomas L Offerle, James F Mooney, Murphy F Robert; Orthopaedics, MUSC.

Background: Patients with early onset scoliosis and their families are exposed to significant emotional, psychological, and financial burdens. Many patients undergo years of multiple interventions, including casting, bracing, and surgery. The Early Onset Scoliosis Questionnaire (EOSQ-24) is a patient reported outcome measure which was developed and validated to measure quality of life and patient/parent reported outcomes in this population. The EOSQ-24 uses a 5-point scale and comprises 11 domains, including general health, pain, pulmonary function, transfers, physical function, daily living, fatigue, emotion, parental impact, financial impact, and satisfaction Methods: The EOSQ-24 was administered to all eligible patients with early onset scoliosis who qualified for inclusion into a multicenter registry at our institution. Scoliosis etiology (neuromuscular, idiopathic, congenital/other), treatment type, and length of time in the treatment plan were queried. Results of all answered questions from the EOSQ-24 domains were tabulated. Average reported scores were calculated and statistically analyzed for significance. Results: 42 total EOSQ-24 were collected from 27 patients, which included 12 patients with idiopathic, 13 patients with neuromuscular, and 2 patients with congenital/other scoliosis. Of these 27 patients, 3 were casted, 7 were braced, and 17 had surgical intervention. Fifteen were male and 12 were female. On average, patients were in a treatment plan for 37 months. For those patients who had multiple surgeries, the average was 4.8 surgeries over an average of 40 months (range of 1-13 surgeries and 1-102 months). The average scores for the daily living and physical function EOSQ-24 domains had the lowest values of 3.43 and 3.00, respectively. When comparing neuromuscular scoliosis patients to those with other etiologies, we found that they had statistically lower scores on the EOSQ-24. (Neuromuscular 3.29, Congenital 4.22, Idiopathic - 4.39) (Neuromuscular vs. non-neuromuscular p-value<0.000). Furthermore, those patients who have been in an active treatment plan for longer than 35 months had a trend toward lower EOSQ-24 scores. (Treatment length 35 months – 3.59, Treatment length < 35 months – 3.94, p-value 0.077). Conclusion: The EOSQ-24 is a reliable assessment of the patient and parent reported outcomes surrounding early onset scoliosis. Neuromuscular patients/parents report lower scores, likely reflecting a larger burden placed on these families. Further research is needed to understand this patient reported outcome measure and the effects of early onset scoliosis on patients and families. MUSC Department of Orthopaedics.
106 The Effect of Shoulder Position on Capsular Measurements with Magnetic Resonance Arthrogram (MRA), Charles C White¹, Meghana Rao², Alyssa Greenhouse², Harris S Sloane³, Richard J Friedman², Josef K Eichinger², ¹COM, MUSC, ²Orthopaedics, MUSC.

Previous research has identified linear and capsular area measurements measured on shoulder MRA to be an independent predictor of shoulder instability. The purpose of this study was to determine if changes in shoulder position during MRA affects capsular measurements. A retrospective study of 21 patients who underwent arthroscopic surgery and received a shoulder MRA with separate sequences for humeral internal (IR) and external rotation (ER) views in the axillary plane was performed. Differences in humeral rotation between ER and IR views, glenoid retroversion, humeral head subluxation, linear capsular size for both axillary and sagittal measurements, and two-dimensional capsular area using axillary views of the shoulder were recorded. Measurement comparison was performed between IR and ER views (n=21). Patients with >25° rotation (n=12) were compared to patients with <25° (n=9), and those with a diagnosis of instability (n=8) were compared to those with no instability (n=13). Inter-observer reliability was calculated for all measurements using the intra-class correlation coefficient (ICC). Humeral subluxation and linear capsular measurements were significantly greater with ER compared to IR (p<0.0002). Linear (p<0.02) and two-dimensional capsular area (p<0.01) in ER were significantly greater in patients with >25° of rotation. Patients with a diagnosis of instability had a significantly greater posterior subluxation (p<0.01) and linear capsule size (p<0.01). ICC values were good or excellent (ICC=.75-.90+) on all measurements except sagittal capsular measurement, which was rated moderate (ICC=.50-.75). Variance in humeral rotation during shoulder MRA significantly affects linear and area capsular measurements. Recognition of humeral rotation’s effect on previously established diagnostic parameters is important when interpreting shoulder MRA’s. The implementation of IR and ER views with 25 degrees of rotational difference may enhance the ability to examine capsular changes of the shoulder joint and assist in the diagnosis of instability.

107 Cross-Sectional Analysis of Anterior Cruciate Ligament Injury in Elite Soccer Players in the Top Five European Leagues, Alexandra M Moreira¹, Jonathan Bernard², Zhara Ismaeli², Timothy Johnson⁸, David Johnson⁸, ¹MUSC, ²National Sports Medicine Institute; Lansdowne, VA.

Anterior Cruciate Ligament (ACL) injuries are common and potential career threatening injury for professional athletes, despite many prevention interventions. Injury rates, return to play, and functional performance after ACL injury have been reported in numerous elite athletes in American sports specializations. There is a paucity of information regarding performance based outcome data reported for elite soccer players in Professional European Soccer. The purpose of this study was to determine the incidence of ACL injury in a single season across five professional soccer leagues, demographic information of injured players, and modifiable risk factors for injury prevention.

Literature was searched using previously established methodology to evaluate the 2016-2017 season. Players were identified via publicly available team press releases, injury reports, and player profiles through internet searches. Inclusion criteria included: ACL injury, knee operation and in one of the top five leagues in European soccer. Exclusion criteria included: non-ACL ligament injuries, fractures, meniscal tears, dislocation and tendon tears. Demographic information including age, position, BMI, league, number of games played that season before injury, career experience, and exposure condition were obtained after player selection. After exclusion criteria, 33 athletes were identified with ACL injuries. Most injuries occurred mid-season and during games. Rate of injury per game was 0.014 per game. The most common positions with ACL injuries were center forward and center midfield (15.15%). There was no association between position and risk of ACL injury. No player returned to play that season. After injury, athletes did not return to play that season. The most common injured positions were center forward and center midfield. Prospective studies on return to play metrics after two season status post injury will be conducted to better assess performance based outcomes. Nth Dimensions

108 The Need for Emergency Department Based Primary Care: A Study of the Factors Leading to Patient Perception of the Emergency Department to Be Their Medical Home, Cameron J Weekley¹, Steven Saef², Sarah Katchem¹, ¹COM, MUSC, ²Emergency Department, MUSC.

The modern Emergency Department (ED) is a place for acute treatment of unforeseen illnesses and
This study compared the pharmacodynamics of DELA and LEVO against Streptococcus pneumoniae, Methicillin-resistant Staphylococcus aureus (MRSA), and Klebsiella pneumoniae using Monte Carlo analysis (MCA). Methods: MCA (n = 10,000) was performed using PK parameters (Vss, protein binding of 84% for DELA and 25% for LEVO, and a CrCl vs. clearance regression), recent wild type MICs distributions, and pharmacodynamic targets from peer-reviewed literature. Regimens of IV DELA (300 mg and 450 mg q12h) and LEVO (250 mg and 500 mg) were used to simulate free serum concentration time-profiles. An inpatient CrCl distribution was used to adjust dosages for renal function. Free (fAUC0-24/MIC) targets for each drug/organism combination (lower targets for stasis of 4-10 for DELA and 25-100 for LEVO and higher targets for maximal bacterial killing of 24-60 for DELA and 20-125 for LEVO) were used to assess target attainment (TA%). Results: TA% at (high/low target) of DELA 450 mg against K. pneumoniae was ≥74/100 and DELA 300 mg was ≥71/96, and against S. pneumoniae the TA% of DELA 450 mg was 100/100 and DELA 300 mg was 100/100, and against MRSA the TA% of DELA 450 mg was ≥91/298 and DELA 300 mg was ≥89/96. On the other hand, TA% at (high/low target) of LEVO 500 mg against K. pneumoniae was 100/100 and LEVO 250 mg was 100/100, and against S. pneumoniae the TA% of LEVO 500 mg was ≥97/97 and LEVO 250 mg was 83/89, and against MRSA the TA% of LEVO 500 mg was ≥8/100 and LEVO 250 mg was ≥4/24. Conclusion: DELA had high target attainment for S. pneumoniae and MRSA; however, it was lower against K. pneumoniae. LEVO had high target attainment for K. pneumoniae and S. pneumoniae; however, it was much lower against MRSA. The differences between the drugs suggest that they will have different roles in the treatment of infections against these organisms and that DELA will likely be more useful where MRSA is a concern. Additional analysis and clinical trials are needed to confirm these results.

111 Stakeholder Perspectives on Cervical Cancer Prevention From a Community Near Kolkata, India, Shannon McGue1, Suparna PhD Qanungo2, Kathleen PhD Cartmell2; 1Medicine, MUSC, 2Nursing, MUSC.

Background: Cervical cancer is the second most common cancer diagnosed in Indian women. Effective primary and secondary prevention methods exist but have yet to be implemented on a large scale within India. This study explores perspectives on barriers, facilitators, and strategies for both vaccination and screening from diverse stakeholders within one community in Kolkata. Methods: Twenty-five in-person interviews were conducted with clinicians/administrators from a private cancer hospital in Kolkata (9), community women from the neighborhood around the hospital (10), and

109 Optimizing Nutrition in Neonates with Kidney Disease, Joycelyn C Hardy, Katherine E Twombley, Sarah N Taylor, Carolyn W Finch; Pediatrics, MUSC.

Neonatal kidney disease patients with acute kidney injury and chronic kidney disease are at great risk of undernutrition during their time in the hospital. In an effort to assess and monitor the nutritional delivery to MUSC NICU patients with kidney disease, we conducted a retrospective chart review and data collection on 10 neonate patients admitted to MUSC NICU from July to December 2014. Data collected during this retrospective chart review will be utilized to establish AKI/CKD feeding protocol guidelines to optimally feed infants suffering from kidney disease while in the care of MUSC NICU in the future. NIH/NHLBI R25HL096316

110 Comparison of the Pharmacodynamic Profiles of Delafloxacin and Levofloxacin Using Monte Carlo Analysis, Mohammed Aldhaeeefi, White Roger; Pharmacy, MUSC.

Introduction: Delafloxacin (DELA) is a novel fluoroquinolone antibiotic that has activity against Gram-positive and Gram-negative bacteria and is more potent than levofloxacin (LEVO) against MRSA.
professionals involved with advising or implementing cancer prevention programs (6). Thematic content analysis was performed, with the social ecological model (SEM) of public health serving as a conceptual model. Results: Participant described barriers at the individual level (literacy, knowledge, concerns about vaccine safety), interpersonal level (low prioritization of women in families), community level (lack of idea of routine health care, sexual health taboos, cancer stigma, poor view of public health services), organizational level (deficient public health services, low access to HPV vaccines and screening tests), and policy/enabling environment level (lack of prioritization of health, NCD’s, and women’s health, public health funding issues). For HPV vaccination, accessibility factors emerged as the most significant barriers and participants identified incorporation of HPV vaccines in the national immunization program as the most promising strategy. Barriers for screening mainly revolved around community norms and taboos and participants shared strategies for encouraging women to attend clinics and health camps. Participants emphasized that awareness strategies needed to target all members of the public, since women were not usually empowered to make their own health care decisions. Conclusion: This study provides in-depth perspectives on the situation within one community, offers experience from an area of the country with limited ongoing programs on cervical cancer, and addresses a broad range of topics relevant to cervical cancer prevention. 

New York Academy of Medicine

David E. Rogers Student Fellowship Award

112 Incidence and Risk Factors for Deep Vein Thrombosis Following Isolated Acute Traumatic Extensor Mechanism Injury, Alyssa Althoff1, Vincent Pellegrini2, Harris Slone3, Daniel Slone1, Walker Heffron1; 1College of Medicine, MUSC, 2Orthopedics, MUSC.

Introduction: Acute, traumatic extensor mechanism disruptions are relatively uncommon, yet disabling, injuries that have the ability to affect health-related quality of life3. Due to the commonly failed ability of conservative management to restore functional mobility following a primary disruption, surgical treatment is accepted as the gold standard to restore functional range of motion, eliminate pain and improve quality of life4,5. Despite use of thromboprophylaxis and post-operative preventative measures, orthopedic surgery is commonly associated with an increased risk for venous thromboembolism (VTE), potentially contributing to morbidity and mortality1,6. Even when current prophylactic protocols are strictly followed, fatal pulmonary embolisms remain a serious threat after surgery2. While comorbidities associated with primary extensor mechanism injury have previously been identified3, prior studies have yet to identify incidence and associations between prophylaxis as well as patient-related risk factors and potentially life-threatening postoperative complications such as deep vein thrombosis (DVT) and VTE. Accordingly, the purpose of this study was to: (I) determine the incidence of post-operative DVT at our institution in patients suffering from acute, traumatic extensor mechanism injuries, and (II) identify independent patient related risk factors that place patients at increased risk for these adverse outcomes. Methods: Using relevant injury mechanism CPT codes, patient records from 2009-2017 were identified from an internal database for patients undergoing operative and non-operative management of primary extensor mechanism injuries at our institution. Patients who did not have an isolated extensor mechanism injury or who were undergoing concomitant surgeries were excluded. Occurrence of DVT within 3 months of intervention was then recorded using manual chart review and CPT codes for diagnosis of DVT, or a procedure for this indication. Patient-related risk factors for postoperative complication, including demographic and comorbidity variables were also recorded for analysis. Adjusted odds ratios (OR) and 95% confidence intervals (CIs) were calculated for each risk factor, with P <0.05 considered statistically significant. Results/Discussion: 120 patients met all inclusion and exclusion criteria. There were 5 patients with a diagnosis of or a procedure for DVT. The incidence of DVT following an isolated acute, traumatic extensor mechanism injury at our institution is 4.16%. Patients with patella fractures were at a higher risk than those with other injuries. This study has the ability to direct future practice through identification of incidence, non-modifiable risk factors, and modifiable risk factors associated with DVT, aiding in efforts to minimize potentially fatal postoperative complications. 1. Geerts WH, Bergqvist D, Pineo GF, Heit JA, Samama CM, Lassen MR, Colwell CW. Prevention of Venous Thromboembolism: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). American College of Chest Physicians. Chest. 2008 Jun; 133(6 Suppl):381S-453. 2. Lapidus L, Ponzer S, Pettersson H, De Bri E. Symptomatic Venous Thromboembolism and Mortality in Orthopedic Surgery- an Observational Study of 45, 968 Consecutive Patients. BMC Musculoskeletal Disorders 2013. 4:177. DOI: 10.1186/1471-2474-14-177. 3. Garner MR, et al. Extensor Mechanism Injuries of the Knee: Demographic Characteristics and Comorbidities from a Review of 726 Patient Records. J Bone Joint Surg Am. 2015 Oct 7;97(19):1592-6. doi: 10.2106/JBJS.O.00113. 4. O Malley M, Reardon P, Pareek A, Krych A, Levy BA, Stuart MJ. Extensor Mechanism Disruption in Knee Dislocation. J Knee Surg 2016 May 29(4):293-9. doi: 10.1055/s-0035-1568991. 5. Grim C, Lorbach O, Engelhardt M. Quadriceps and patellar Tendon Ruptures. Orthopade 2010. Dec;39(12):1127-34. doi: 10.1007/s00132-010-1690-5. 6. Naess IA, Christiansen SC, Romundstad P, Cannegieter SC, Rosendaal FR, Hamnerstr.m J. Incidence and mortality of venous thrombosis: an
Interactions of Fork Barrier Protein Fob1 with Subunits of the MCM2-7 Helicase and Their Biological Significance, Chris J Danielson, Deepak Bastia; Biochemistry and Molecular Biology, MUSC.

Abstract not available.

Using Complement Modulation to Dampen Microglial Activity After Stroke and Enhance Neuronal Recovery and Regeneration, Ali Alawieh, E Farri Langley, Stephen Tomlinson; Microbiology and Immunology, MUSC.

Abstract not available.

Clinical Indicators of Admission for Pediatric Cochlear Implant Procedures, Terral A Patel¹, Shaun Nguyen², David White²; ¹College of Medicine, MUSC, ²Otolaryngology, MUSC.

A portion of pediatric cochlear implant (CI) patients are admitted for observation post-implantation, but there is little data on prognostic indicators. Our goal is to review national data to identify variables associated with admission post-implantation and identify effects on postoperative outcomes. We retrospectively analyzed data from the 2012-2015 American College of Surgeons’ National Surgical Quality Improvement Program-Pediatric. The database was queried for patients undergoing CI. Demographics, comorbidities, anesthesia time, total operation time, 30-day complications, and 30-day readmission were compared between ambulatory and admitted patients. 2943 CI patients (507/2436 inpatient/outpatient) were included, with 17.2% admitted post-implantation. Single variable analysis showed patients with longer anesthesia time, longer operation time, age < 12 months, premature birth, asthma, esophageal/gastric/intestinal disease, cardiac risk factors, seizure disorders, and CNS abnormalities were more likely to be admitted post-implantation. Multivariable logistic regression showed patients with asthma were 2.2 times (p < 0.001; OR = 1.484-3.227) and those with structural CNS abnormalities 2.1 times (p < 0.001; OR = 1.584-2.706) more likely to be admitted. Younger age (p = 0.002; OR = 0.995-0.999) and longer operation time (p < 0.001; OR = 1.003-1.006) were significant, but weak predictors. Interestingly, 216 patients lacked any of these factors but were admitted. They had similar outcomes to ambulatory healthy patients (p=0.269 and p= 1.000). We identified factors associated with post-CI admission and higher readmission rates. 60% of admitted patients lack any of these factors and have comparable outcomes to corresponding ambulatory patients. Asthma and CNS abnormalities are strong predictors of admission post-implantation. NIH T32DC0014435; MUSC SHP

Targeted Gene Expression in Mice and Placental Tissue, Oyinda D Awe¹, Kyu-Ho Lee²; ¹COM, MUSC, ²Pediatric Cardiology, MUSC.

Preeclampsia is a condition where pregnant women suffer from high blood pressure and sometimes kidney damage. It is prevalent in 2-8% of pregnancies and if left untreated, can be serious and sometimes fatal for the mother and child. This research focuses on linkages between target genes and their expression in the placental tissue of preeclampsia populations. A previous Vitamin D study examined the effects on Vitamin D on fetal growth in patients with early onset preeclampsia. The study showed a correlation between Vitamin D deficiency and fetuses that were small for gestational age. It was concluded that Vitamin D may impact fetal growth through placental mechanisms. Samples used in this experiment are from term pregnancy placenta with varied levels of vitamin D supplementation. Another study by Schulz et. Al showed a correlation with higher vitamin D supplementation and lower levels of S-flt1 mRNA. Therefore, the hypothesis is that S-flt1 mRNA levels may be correlated with Nkx2.5 and sam68 levels. Placental samples were examined using qPCR. The target genes examined were preeclampsia marker S-flt1, RNA splicing factor Sam 68 and Nkx2-5. Beta-actin was used as the control. MUSC SHP

Withdrawn

Appropriate Screening for Urologic Complications After Spinal Cord Injury in a Non-Designated SCI Center Veterans Affairs Hospital, Rohail Rashid Kazi, Alyssa Greiman, Lindsey Cox; Urology, MUSC.

Surveillance for common urologic complications after spinal cord injury (SCI) is not consistent, without consensus among clinical practice guidelines. The Paralyzed Veterans of America has issued a clinical practice guideline with recommendations including a yearly urologist visit, a serum creatinine, and a renal ultrasound. These recommendations are the least intensive urologic follow-up of the various other clinical practice guidelines for SCI. We present adherence to these screening guidelines at a non-designated SCI center as a bellwether for urologic care after SCI. We identified all patients with documented SCI seen at the Ralph H. Johnson VA Medical Center between...
January 2014 and December 2015 and evaluated whether patients received a urologist visit, serum creatinine measurement and upper tract imaging during the study period. 99 patients were identified with SCI [Demographics in Table 1]. 49% of patients had a complete urological surveillance. Those patients with a complete evaluation did not live closer to the care facility (p=0.40) or the designated SCI center in Augusta (p = 0.13). There was no difference in age (p=0.18), race (p=0.64), SCI level (p=0.16) ASIA impairment (p=0.39), ambulatory status (p=0.27), comorbidities (p=0.83) or bladder management (p=0.14). Those with a complete evaluation were more likely to have had a urology visit (p<0.0001), to have had cystoscopy (p=0.001), cytology (p=0.03), and urodynamics (p=0.00001). There was no difference in hospitalization for urinary tract infections in those who had a complete evaluation and those who did not (18.4%, p=0.09). Based on these data, there were no identifiable predictive factors to aid in determining who is most likely to receive a complete evaluation.

119 The Adherens Junctions Suppress Protumorigenic Colon Cell Transformation Via Long Non-coding RNAs, Mary C Bridges, Joyce U Nair-Menon, Antonis Kourtidis; Regenerative Medicine and Cell Biology, MUSC.

Loss of epithelial homeostasis and tissue integrity are associated with colon cancer, one of the most prevalent forms of the disease. The adherens junctions (AJs) are essential architectural elements of epithelial tissues. Recently, we identified a novel mechanism whereby the AJs of non-transformed colon cells suppress aberrant cell behavior by recruiting the RNAi machinery, mRNAs, and miRNAs, via the AJs component PLEKHA7. Our data reveal widespread dysregulation of PLEKHA7 and of this mechanism in colon cancer cell lines and patient tissues. Interestingly, RNA-CLIP and subsequent RNA-Seq identified association of PLEKHA7 with numerous long non-coding RNAs (lncRNAs). While a number of lncRNAs have been associated with tumorigenesis, the underlying mechanisms of their regulation are still largely unclear. We hypothesize that the AJs regulate the levels and function of lncRNAs via PLEKHA7 and its associated RNAi mechanism to suppress protumorigenic colon cell behavior. Comprehensive examination of the junction-associated lncRNAs by RNA-seq identified several whose expression levels are indeed regulated by PLEKHA7. One of top regulated IncRNAs is MIR17HG (miR-17-92; Oncorn-1), an oncogenic polycistronic host transcript of a set of miRNAs, including miR-17, miR-18a, miR-19a, miR-19b, miR-20a, miR-92a. Notably, the mature forms of these miRNAs also co-precipitate with PLEKHA7. PLEKHA7 knockdown results in increased levels of MIR17HG and of a specific set its hosted miRNAs, namely miR-19a, miR-19b and miR-20a. Our data suggest that two PLEKHA7-associated miRNAs, miR-203a and miR-372, mediate suppression of this IncRNA by PLEKHA7 and by its associated RNAi machinery. Re-expression of PLEKHA7 in aggressive colon cancer cells that lack PLEKHA7 suppressed expression of MIR17HG, as well as anchorage independent growth of these cells. Our present data point towards a novel mechanism of lncRNA regulation that tethers epithelial tissue integrity with protumorigenic cell transformation. SCTR Institute, NIH TL1 TR001451, UL1 TR001450; ACS Institutional Research Grant (ACS-IRG), Hollings Cancer Center

120 TLR9 Agonist Expands CD8+ T Cells with Robust Anti-melanoma Activity, Aubrey Smith, Michelle Nelson, Marshall Diven, Chrystal Paulos; Microbiology and Immunology, MUSC.

Toll like receptor 9 signaling via CpG has been shown to augment cancer vaccines by activating the innate immune system. However, the role of TLR9 activation in other immunotherapeutic strategies like checkpoint modulators or adoptive T cell transfer (ACT) therapy is incompletely elucidated. To determine the if innate immune activation via Toll Like Receptor 9 (TLR9) signaling augments antitumor T cell immunity, we used the pmel-1 melanoma mouse model. B16F10-bearing mice were preconditioned with 5Gy TBI and given a combination ACT therapy consisting of transferred pmel-1 CD8+ T cells primed in vitro with the TLR9 agonist CpG oligodeoxynucleotide (ODN). Here we report that simply adding CpG to a T cell culture dramatically augments their engraftment, function and antitumor activity when infused into tumor-bearing mice. In fact, this therapy was as effective and safer than exogenous administration of CpG. Moreover, we found that pmel-1 CD8+ T cells primed with CpG highly expressed CD25, the IL-2 receptor, and were overtly functional, co-secreting many cytokines including IFN-gamma, IL-10 and Granzyme B. Additional investigation implied that CpG indirectly enhanced these properties of pmel-1 CD8 T cells by directly activating dendritic cells. Therapeutic effectiveness of this therapy was associated with enhanced persistence of the infused T cells. Collectively, our results identify how to safely and more effectively use TLR agonists to enhance T cell-based immunotherapy. Our findings have clinical implications for the design of next generation immune-based therapies for cancer patients. R01 CA175061, R01 CA208514
121 How Do Patients Perceive the Character of Care They Receive For Ambulatory Care-Sensitive Conditions in the Emergency Department?, Virginia B Shipes1, Sarah Katchen2, Steven Saef3, Renee Martin1; 1Public Health Science, MUSC, 2Medicine, MUSC, 3Emergency Medicine, MUSC.

Background: The Framingham study provided evidence that prevention of serious outcomes from atherosclerotic disease and cancer requires longitudinal care. The Emergency Department (ED) is not designed to provide this care. Nevertheless, many patients seek the ED for treatment of Ambulatory Care Sensitive Conditions (ACSCs). We sought to determine characteristics of ED patients who believe the ED can replace Primary Care (PC). Methods: 384 adult patients were administered a twenty-two item survey in an urban, academic ED regarding perceptions about the benefit of ED-based treatment of ACSCs. The index question was “Where do you believe that you receive the best treatment to prevent heart attacks, strokes, kidney failure and cancer?” Surveys were administered by student teams via tablet computers and SAS version 9.4 was used to produce summary statistics and logistic regression analysis. Results: While controlling for perceived MH, Payor type, Trust in the EP, gender and race, there was no difference in perception of which locale provided best preventive care between those who had an ACSC and came to the ED for an ACSC and those who did not; OR 0.877; 95% CI 0.553-1.390. Overall patients saw no difference in the opportunity to obtain preventive care from the ED versus a PC clinic. However, men were more likely (OR 1.74; 95% CI 1.11-2.74) and Caucasians were less likely (OR 0.5; 95% CI 0.31-0.79) to believe the ED provided better care for ACSCs. Conclusions: Patients who come to an urban, academic ED with or because of an ACSC perceive equivalent preventive care with a PC clinic. This study showed that men and non-Caucasians were more likely to share this perception. This evidence supports the expansion of emergency services to include delivery of rudimentary PC which could be met by an ED Follow-up Office.

122 Identification of Polo-like Kinase and Retinoic Acid Receptor Pathways As Therapeutic Targets in Malignant Peripheral Nerve Sheath Tumors., Ralph Tanios1, Amanda Precht1, Stephen Guest1, Elizabeth Garrett-Mayer2, Steven Carroll1; 1Pathology, MUSC, 2Public Health Science, MUSC.

Malignant Peripheral Nerve Sheath Tumors (MPNSTs) are Schwann cell neoplasms and the most common malignancy seen in patients suffering from Neurofibromatosis Type I (NF1). They can also arise sporadically or at sites of previous radiation therapy. MPNSTs have been reported in patients as young as 11 months of age, but over 80% of cases occur in adulthood. The prognosis for patients with MPNSTs is abysmal with a 5-year survival rate of less than 50%. This largely reflects a lack of effective pharmacotherapies. We have conducted a genome-scale shRNA dropout screen in 2 NF1-associated (T265-2c, S462) and 1 sporadic (2XSB) human MPNST cell lines. We identified 210 genes that were the top 5% most depleted genes in all three cell lines. An Ingenuity Pathway Analysis of the 107 non-commonly essential genes identified the polo-like kinase (PLK) and the retinoic acid receptor (RAR) pathways as key survival/proliferation pathways. A search was performed to identify drugs targeting these pathways that are currently being used in clinical trials. Three drugs were selected that met these criteria: Rigosertib (inhibits PLK-1 and 2), Volasertib (inhibits PLK-1), and CD437 (targets RAR pathway). We found that treatment with Rigosertib, Volasertib, and CD437 resulted in a significant decrease in proliferation and/or survival in 5/5, 8/9, and 7/9 cell lines tested, respectively. In a subset of these cell lines, treatment with CD437 promoted caspase 3/7 activation, consistent with an apoptotic mechanism of drug action. These observations suggest that drugs targeting the PLK and RAR pathways may be effective for the treatment of patients with MPNSTs.

123 The Role of Lysyl Oxidase in Systemic Sclerosis-Associated Lung Fibrosis, Xinh-Xinh M Nguyen1, Tetsuya Nishimoto1, Logan Mlakar1, Ellen Riemer2, Jonathan Heywood1, Amy Bradshaw1, Carol Feghali-Bostwick1; 1Medicine, MUSC, 2Pathology, MUSC.

Introduction: Systemic sclerosis (SSc) is a connective tissue disease of unknown etiology characterized by progressive fibrosis of the skin and visceral organs. Effective therapies for SSc are needed. Lysyl oxidase (LOX) is a copper-dependent amide oxidase that plays a critical role in the crosslinking of the extracellular matrix (ECM). We investigated the role of LOX in the pathophysiology of SSc. Methods: LOX expression and protein levels were measured in vitro in primary human lung fibroblasts from patients with SSc and healthy controls (HC). The effects of recombinant LOX (rLOX) were measured in vitro in primary fibroblasts, ex vivo in human lung tissues and in vivo in mice given bleomycin in combination with rLOX. To differentiate the crosslinking activity of LOX from other potential effects, in vitro assays were done in the presence of the inhibitor, beta-aminopropionitrile (BAPN). The expression levels of ECM (collagen and fibronectin), pro-fibrotic factors (IL-6 and TGF-beta), and transcriptional factor (c-Fos) were examined by real-time PCR, ELISA, immunoblotting, or hydroxyproline assay. Results: rLOX induced ECM production in vitro and ex vivo. LOX mRNA levels were increased in lung
fibroblasts of SSc patients compared to HC. Additionally, TGF-beta and bleomycin induced ECM production, LOX mRNA expression and activity. In vivo, rLOX exacerbated bleomycin-induced lung fibrosis. Inhibition of LOX catalytic activity by BAPN failed to abrogate LOX-induced ECM production. LOX increased the production of IL-6. IL-6 neutralization blocked the effects of LOX suggesting that the fibrotic effects of LOX are mediated by IL-6. Further, LOX induced c-Fos expression and its nuclear localization. Conclusions: Our findings suggest that inhibition of LOX may be a viable option for the treatment of lung fibrosis. Further, the use of human lung in organ culture establishes the relevance of our findings to human disease. TL1 TR001451 and UL1 TR001450; SCTR

124 Shorter Ex Vivo Expansion of Th17 Cells Mediates Potent Anti-tumor Regression in Melanoma, Hannah M Knochelmann, Michelle H Nelson, Jacob S Bowers, Daniel J Neitzke, Megan M Wyatt, Aubrey S Smith, Daniel J Salas-Escabillas, Chrystal M Paulos; Microbiology and Immunology, MUSC.

Adoptive T cell transfer therapy mediates potent immunity in patients with bulky metastatic malignancies, but proves difficult to translate clinically due to production costs, time, and labor required to generate the large number of tumor-specific lymphocytes believed necessary to yield objective responses. To overcome such obstacles, we proposed a method of shortened ex vivo expansion using Th17 cells to treat melanoma. We found that as few as 400,000 Th17 cells expanded four days could robustly regress and clear large established melanoma as effectively as 10+ million Th17 cells expanded for two weeks. We discovered that younger cultures had a markedly reduced effector memory phenotype, yet persisted in the peripheral blood of mice as efficiently as long-term expanded Th17 cells. Importantly, Th17 cells expanded four days induced a unique cytokine storm in vivo, with heightened detection of IL-6 and IL-17, as well as chemokines G-CSF, MCP-1 and KC compared to Th17 cells expanded for two weeks. Our results indicate that fewer, younger Th17 cells can indeed regress large tumors, if they are more potent cells. We are now actively investigating if the cytokine storm induced by this Th17 cell therapy is responsible for their effectiveness or if young cells have an epigenetic advantage to older Th17 cells when infused into the host. Regardless, our findings have significant clinical implications as reducing expansion of T cells may alleviate current clinical barriers, and streamline the progression of immunotherapy to the clinic. NIH T32 GM08716-18, NCI R01CA175061, NCI R01CA208514

125 Mechanisms Underlying Sex Discrepancy in Bladder Cancer
Outcome, Hyunwoo Kwon¹, Ching Ying Lin¹, Guillermo Rangel Rivera¹, Satoshi Kaneko², Caroline Wallace¹, Mohammad Salem¹, Xue Li², Zihai Li¹; ¹Microbiology and Immunology, MUSC, ²Urology and Pathology, Boston Children’s Hospital.

Abstract not available.

126 First Trimester Prediction of Pre-eclampsia in Women with Type 1 Diabetes, Clare B Kelly¹, Michelle B Hookham², Jeremy Y Yu¹, Mei Du³, Alicia J Jenkins¹, Samar M Hammah ⁴, James A Scardo⁵, Timothy J Lyons⁶; ¹Endocrinology, MUSC, ²Clinical Biochemistry, Royal Victoria Hospital, Belfast, N. Ireland, ³Endocrinology, University of Oklahoma Health Sciences Center, ⁴Regenerative Medicine and Cell Biology, MUSC, ⁵Spartanburg Regional Hospital.

Introduction: Pre-eclampsia (PE) occurs ∼4× more frequently in diabetic than non-diabetic women (∼20% vs ∼5%). Early identification of women at highest risk is urgently needed. We investigated the predictive ability of plasma leptin, a marker of insulin resistance, and creatinine-corrected urinary neutrophil gelatinase-associated lipocalin (uNGALcc), a marker of kidney dysfunction. We used samples and clinical data from an established, prospective, complication-free cohort of type 1 diabetic (T1DM) women. Methods: The cohort comprised 23 T1DM women who developed PE, 24 who remained normotensive, and 19 non-diabetic women. Biomarkers were measured by ELISA (R&D Systems) in samples collected at three study visits (12.3 ± 1.8, 21.7 ± 1.4, and 31.4 ± 1.5 wks gestation; mean ± SD). Diabetic groups were matched for age, duration, HbA1c, and parity. All study visits preceded clinical onset of PE. Results: At first trimester (univariate analysis), in T1DM women with vs. without PE (primary analysis), leptin (p<0.01) and uNGALcc (p<0.05) were elevated. In normotensive T1DM vs. non-diabetic women (secondary analysis), there were no differences. At the second and third trimesters, findings for leptin persisted and there was no longer a difference in uNGALcc; secondary analyses again showed no differences. After adjustment for established maternal risk factors (HbA1c, BMI, insulin dose/kg/day, gestational age (weeks)), first trimester leptin and uNGALcc remained independently associated with PE outcome. Adding both to a model comprised of three simple maternal clinical risk factors improved the area under the ROC curve 0.778 to 0.948 (p=0.03). Conclusions: As early as the first trimester, plasma leptin and urinary NGAL may have utility as effective predictors of PE in women
with T1DM. Maternal insulin resistance and subclinical renal dysfunction may underlie these associations, and may predispose women with T1DM to PE.

**127 Does PKC Mediate the High Risk of Preeclampsia in Pregnant Women with Diabetes?**, Rebecca P Chow¹, Jiawu Zhao², Tim M Curtis³, Timothy J Lyons¹, Jeremy Y Yu¹; ¹Endocrinology and Diabetes, MUSC, ²Centre for Experimental Medicine, Queen’s University of Belfast, UK.

Introduction: Preeclampsia (PE) is a leading cause of maternal and perinatal morbidity and mortality, and its prevalence is 4-fold higher in women with diabetes than those without: the underlying mechanism is unclear. The anti-angiogenic factor soluble fms-like tyrosine kinase-1 (sFlt1) plays a key role in PE pathogenesis. Evidence suggests that PKC activation, which is associated with the development of diabetic vascular complications, may mediate enhanced sFlt1 release in non-trophoblast cells; but it is unclear whether this mechanism also occurs in the placenta and thus contributes to the high risk of PE in diabetes. We aimed to determine: 1) the role of PKC in the regulation of sFlt1 expression in placental trophoblasts; and 2) whether diabetic conditions upregulate sFlt1 expression via the PKC pathway. Methods: Quiescent human trophoblast HTR-8/SVneo cells were treated with the PKC activator phorbol-12-myristate-13-acetate (PMA), or the diabetes stimuli 'heavily oxidized, glycated' low-density lipoproteins (HOG-LDL) vs. native LDL ± high glucose (30 mM), over 24hrs, with or without the PKC inhibitor GF109203X. Both sFlt1 mRNA expression (RT-PCR) and protein release (ELISA) were measured. Results: PMA (5 nM) increased sFlt1 mRNA expression and protein release (both p<0.001) vs. vehicle control in trophoblasts; this effect was abrogated by the pre-treatment of 5 uM GF109203X (p<0.001 for both mRNA expression and protein release). Similarly, HOG-LDL (50 μg/ml) increased sFlt1 mRNA expression and protein release (both p<0.001), both again attenuated by GF109203X (p<0.05). However, high glucose did not appear to affect sFlt1 expression, or to enhance the effect of HOG-LDL. Conclusions: The results are consistent with the possibility that modified lipoproteins may promote PE development in women with diabetes, at least in part via PKC-mediated upregulation and release of sFlt1. These findings provide new insights into disease mechanisms, and may lead to new targets for prevention and treatment of PE.

**128 Opportunistic Pathogen P. Gingivalis Modulates Danger Signal ATP-Mediated Antibacterial NOX2 Pathways for Successful Survival in Primary Epithelial Cells**, JoAnn S Roberts¹, Kalina R Atanasova², Nityananda Chowdhury¹, Chul Hee Choi³, Ozlem Yilmaz¹; ¹Oral Health Sciences, MUSC, ²Periodontology, University of Florida, ³Microbiology and Medical Science, Chungnam National University.

Abstract not available.

**129 Label-free and Nondestructive Method for Cell Viability Assessment in Tissue with Two-photon Fluorescence Microscopy**, Yang Li¹, Neal Saini², Xun Chen¹, Tong Ye¹; ¹Clemson-MUSC Bioengineering Program, ²COM, MUSC.

Cell viability assessment is important in engineered tissue evaluation and cultured cell state monitoring. Most prevalent methods to assess cell viability rely on dye staining and/or destructive to the examined samples, thus cannot be performed for longitudinal monitoring, in-vivo assessment or use-after-assay applications. Here we demonstrate that cellular autofluorescence imaging with two-photon fluorescence microscopy distinguishes live cells from dead cells in intact ex-vivo tissues, which provides a non-invasive method to assess cell viability. The endogenous imaging contrast is primarily from nicotinamide adenine dinucleotide (phosphate) (NAD(P)H) and flavin adenine dinucleotide (FAD), which fluoresce at blue and red range respectively and are detected in separate channels. NAD(P)H and FAD are coenzymes relevant to cell metabolism and the concentration ratio of two are believed to reflect cell metabolism states and viability as well. In the experiment, rat tibia condyles were harvested immediately after the euthanasia and the superficial and mid zone of cartilages were imaged by a two-photon microscope (Olympus FV1200). We first imaged samples with two fluorescence channels that collected autofluorescence from NAD(P)H and FAD respectively at the excitation wavelength tuned to 740 nm. We then stained the same tissue with fluorescent dyes calcine-AM/live) and ethidium homodimer-1 (dead) (Invitrogen, Cell Live/Dead Assay Kit) to identify live/dead cells. While keeping the sample immobilized during the staining process, we imaged the exact same area as in the autofluorescence imaging. We found that live cells presented stronger NAD(P)H fluorescence than dead cells in general. The intensity ratio of NAD(P)H and FAD fluorescence could be used as a quantitative measure for viability assessment. Owing to its non-destructive nature, this method holds the potential value in assessing cell viability of engineered or living tissues without dye.
that has previously been found to regulate Estrogen Receptor (ER)-responsive genes in breast cancer cells. The risk allele of the variant strongly associated with ER+ breast cancer in women of European descent is associated with lower expression levels of TOX3. We hypothesize that non-coding breast cancer-associated polymorphisms on 16q12.1 regulate TOX3, subsequently modifying risk of developing ER+ breast cancer. To begin exploring TOX3 as a candidate breast cancer susceptibility gene, we used CRISPR-Cas9 technology to genetically engineer an allelic series of mutations in the rat genome. The rat is the preferred rodent model for ER+ breast cancer. Rats were generated with deletions or knock-in mutations in the portion of the Tox3 locus orthologous to the human risk-associated region. Functional studies are possible with these new rat models because we obtain viable mutants across all genotypes, despite partial embryonic lethality in homozygous Tox3 knockouts. The allelic series displays variable levels of Tox3 downregulation in the mammary gland, suggesting there are multiple Tox3-regulatory elements in this non-coding region. Mutants showing altered Tox3 expression also show significant effects on mammary gland development, namely on ductal elongation and the numbers of terminal end buds and branch points. The phenotypes implicate Tox3 in mammary stem/progenitor cell biology potentially through ER-alpha gene regulation. Interestingly, Tox3 knockout rats also present a morbid obesity phenotype and previous publications demonstrate the role of TOX3 in neuronal tissue, suggesting possible pleiotropic effects of mutations in the TOX3 locus. Ongoing studies are focused on the functional role of Tox3 in mammary gland biology and carcinogenesis to elucidate the mechanism of susceptibility to ER+ breast cancer. Understanding breast cancer risk will ultimately lead to innovative strategies and therapeutic approaches aimed at preventing the development of breast cancer. DoD W81XWH-11-2-0222; NIH P30 CA138313

130 Exploring the Geography of Pediatric Asthma Using Emergency Department Visits in South Carolina, Matthew Boziger1, Kathryn Cristaldi2, John Pearce1; 1Public Health Sciences, MUSC, 2Pediatrics and Telehealth, MUSC.

Emergency department (ED) visits for pediatric asthma are burdensome for both patients and healthcare systems. One aspect of this burden that is important to understand is the geography of asthma risk. The objective of this research is to explore the spatial distribution of pediatric asthma outcomes across South Carolina in order to identify areas of elevated risk, disparities, and to support hypothesis generation of spatially varying predictors. We map ED visit rates, the white/non-white ED visit rate ratio, and contextual factors including median family income and toxic pollution point sources by ZIP code tabulation area (ZCTA) in South Carolina for the period 2005-2015. We find that elevated ED visit rates exist in rural areas (specifically the Interstate-95 corridor, the Lower Savannah District, and northwest of Columbia), low income areas generally coincide with high rate areas, and there are striking statewide disparities between non-white and white residents. These findings lay a strong framework for future study as more complex analyses are needed to more clearly disentangle risk factors. Department of Public Health Sciences, NIH LRP

131 CRISPR-Cas9 Targeting of 16q12.1 Breast Cancer Susceptibility Locus to Generate Allelic Series of Rat Mutants Results in Altered Tox3 Expression, Lauren B Shunkwiler1, Royal Pipaliya2, Cody C Ashy2, Benjamine Van Peel1, Jan Guz3, Michael J Kern3, Yang Zhao1, Bart MG Smits1; 1Pathology, MUSC, 2Biology, CofC, 3Regenerative Medicine, MUSC.

As the incidence of breast cancer diagnoses continues to surge, it is imperative to understand mechanisms that underlie susceptibility to this disease. Genome-wide association studies (GWAS) have identified regulatory variants that influence likelihood of developing breast cancer. The human chromosomal locus 16q12.1 attracts attention for it contains GWAS-identified variants that uniquely associate with breast cancer risk in populations of European and African American women. The correlated polymorphisms comprising these variants exist in non-coding regions of this locus, providing the possibility that these mutations alter gene expression. The most likely candidate gene, TOX3, encodes a transcription factor that has previously been found to regulate Estrogen labeling. NIH GMS R21GM-104683 and P20GM-103499; NSF 1539034

132 Single Cell Genomic Profiling of Human B Cells Responsible for Immune Response Against Pneumococcal Polysaccharides in Aging Healthy and HIV-positive Individuals, Myra Happe, Samuvel Devadoss, Julie Westerink; Immunology and Microbiology, MUSC.

Background: Streptococcus pneumoniae is a leading cause of life-threatening infections among the elderly and HIV+ individuals. Despite preventative strategies, such as pneumococcal vaccination, it remains a challenge to induce potent and durable immune responses to pneumococcal polysaccharides (PCPs). Both aging and HIV result in significant B cell perturbations that, to date, are poorly characterized. The goal of this study is to characterize individual cellular changes in IgM memory B cell population that
is largely responsible for producing responses to PCPs, and identify variations in inter-cellular gene expression that shape polysaccharide–specific B cell responses. Methods: PBMCs were isolated from the whole blood collected from healthy or HIV+ individuals 50–65 years of age according to guidelines of institutional review board of Medical University of South Carolina. Cells were FACSorted based on the expression of CD19, CD27, and IgM. CD19+CD27+IgM+ single cells were reverse transcribed and preamplified using C1 Fluidigm. All preamplified products were pooled, harvested, and transferred to Biomark HD system for RT-PCR analysis. Results/Conclusions: Single-cell genomic studies of IgM memory B cells revealed important insights into cell-type specific signatures. The results showed that 4 genes have unimodal distribution (BCMA, CD80, IL-21R, IL-10), and 10 genes have a bimodal distribution including TACI, BAFF-R, CD86, and CD21. Bimodal distributions indicate that these genes are differentially expressed in at least two subpopulations within the singular cells that have been analyzed. Principal component analysis (PCA) of single-cell PCR gene expression further confirmed hierarchical clustering results, visualizing two cell subpopulations. Current studies involve single cell genomic profiling of IgM memory B cells isolated from HIV+ individuals as well as profiling of PcPs-specific IgM memory B cells. SCTR Institute; NIH TL1 TR001451 and UL1 TR001450

133 Lower Axon Density in Residual Temporal White Matter is Related to Semantic Paraphasia Prevalence. Emilie T McKinnon1, Jens H Jensen2, Julius Fridriksson3, Chris Rorden4, Joseph A Helpern5, Vittoria Spampinato3, Leonardo Bonilha1; 1Neurology, MUSC, 2Neuroscience, MUSC, 3Communication Sciences and Disorders, USC, 4Psychology, USC, 5Radiology, MUSC.

The impact Wallerian degeneration (WD) has on aphasia remains poorly understood. Diffusion MRI is ideally suited to study white matter (WM) integrity, admitting, results are hard to interpret as they characterize the generic physical process. Biophysical models, a simplification of complex biological systems, are necessary to overcome this drawback. Here we use the white matter tract integrity model (WMTI), which provides a biological interpretation to diffusional kurtosis images (DKI). Specifically, we focus on axonal water fraction (AWF), representing the percentage of water inside axons. We hypothesize that WD results in a decreased AWF, caused by diminished axon count. Additionally, we probe regional differences in AWF and the relationship to semantics during speech production. Twenty-four subjects with chronic post-stroke aphasia underwent the Philadelphia Naming Test and MRI (Structural images/DKI). In-house software was used to estimate tensors, from which AWF was calculated together with a probabilistic WM mask. The following regions of interest were defined for both ipsi- and contralateral sides: whole-hemisphere WM, temporal lobe WM and parietal lobe WM (all excluding lesioned WM). Simple correlations and t-tests were performed to study AWF behavior. Average AWF is significantly lower throughout the whole left-hemisphere, the left temporal and left parietal lobes compared to their right homologues. A decrease in AWF in the left compared to the right temporal, but not whole-hemisphere or parietal lobe, was associated with an increase in semantic paraphasias. Controlling for lesion size strengthened the correlation between temporal lobe AWF and semantic paraphasia prevalence. Biophysical models such as WMTI are promising techniques to study WM integrity since they provide interpretable parameters. Our results suggest widespread left hemisphere axonal degeneration, as quantified by AWF. Importantly, AWF shows regional specificity, as temporal lobe reduction relates to increases in semantic paraphasias. These results possibly reflect the process of WD occurring after ischemic incidents. NIH DC014021, DC01739, DC014664, DC0014435, GM008716; AHA SFDGN26030003; The Litwin Foundation

134 Physical Activity, Cardiovascular Risk Factors and Brain Health: Impact on Long Range Mono-synaptic Connections, Modular Organization of Cortical Regions, and Verbal Fluency. Barbara K Marebwa1, Robert J Adams1, Gayenell S. Magwood2, Leonardo Bonilha1; 1Neurology, MUSC, 2Nursing, MUSC.

It has been well documented that long standing cardiovascular risk factor burden in the absence of clear clinical or radiological “events”, is associated with mild cognitive impairment. New MRI techniques exploring the integrity of neuronal fiber connectivity within white matter networks supporting cognitive processing could be used to measure the impact of cardiovascular (CV) disease on brain integrity and brain health, which may in turn be used beyond bedside neuropsychological tests, to detect subclinical changes, and select or stratify participants for entry into clinical trials. In this study, we aimed to assess the relationship between CV risk factors and white matter network architecture using whole brain structural connectomes constructed from MRI diffusion images of 60 participants with various degrees of CV risk factors. The individual white matter networks topological organization was quantified using graph theory. Multivariate statistical analyses were used to evaluate the relationship between physical activity level, CV risk factors, white matter organization and verbal IQ. We observed that reduced physical activity and higher CV risk factors were associated with white
matter network fragmentation, which was in turn associated with decreased verbal IQ. Network fragmentation was related to a disproportionate loss of long-range white matter fibers. CV risk factors and decreased physical fitness have negative effects on cerebral circulation and reserve capacity. This may mediate negative effects on brain health via loss of energy dependent long range white matter fibers, which in turn leads to fragmentation of the topological organization of the white matter networks, and reduced cognitive function. White matter topological organization measured from the connectome could be used as a personalized biomarker for individual brain health.

135 Three Dimensional Molecular Diffusion Measurement in Collagenous Tissue with FRAP, Peng Chen¹, Xun Chen¹, Richard G Hepfer¹, Ye Tong¹, Hai Yao², ¹Clemson-MUSC Bioengineering Program, CU, ²Oral Health Sciences, MUSC.

Abstract not available.

136 Multivariate Air Pollutant Exposure Prediction in South Carolina, Ray Boaz, Andrew Lawson, John Pearce; Public Health Sciences, MUSC.

Introduction: Air pollution is associated with adverse health outcomes ranging from increased respiratory incidence to increased mortality; however, the health impacts from exposure to multiple pollutants remain unclear. Large gaps in knowledge remain for developing flexible models that address the decomposition of chemical mixtures in relation to health outcomes. In particular, application of complex fusion models, which combine observed and modeled data, to areas with sparse monitoring networks with multiple chemical components is under-developed. Such models could provide improved accuracy and coverage for air quality measurement predictions, an area greatly limited by the amount of missing data.

Methods: This project focuses on the development of methods for improved estimation of pollutant concentrations when only sparse monitor networks are found. Sparse monitoring networks are defined as areas where fewer than three criteria air pollutants (based on EPA standards) are monitored. Particularly, a multivariate air pollutant statistical model to predict spatio-temporally resolved concentration fields for multiple pollutants simultaneously is developed and evaluated. The multivariate predictions allow monitored pollutants to inform the prediction of non-monitored pollutants in sparse networks.

Results/Impact: These methods utilize only widely available data resources, meaning that the improved predictive accuracy of sparsely monitored pollutant concentrations can benefit future studies in any US area by improving estimation of health effects and saving resources needed for supplemental air pollutant monitoring campaigns. Our method for estimation attempts to improve predictive accuracy and data availability for sparsely monitored pollutants and areas. TL1 TR001451; UL1 TR001450

137 Kallistatin Attenuates Endothelial Senescence By Inhibiting Oxidative Stress and Inflammation, and Stimulating Let-7g-Induced SIRT1-eNOS Pathway, Youming Guo, Lee Chao, Julie Chao; Biochemistry and Molecular Biology, MUSC.

Kallistatin, a key component in the circulation, protects against vascular and organ injury in animal models. Our present study shows that kallistatin significantly inhibits H2O2-induced senescence, as indicated by reduced senescence-associated β-galactosidase (β-gal) activity, plasminogen activator inhibitor-1 (PAI-1) and p16INK4a expression, and elevated telomerase activity in human endothelial cells. Likewise, kallistatin suppresses oxidative stress and inflammation by reducing H2O2-induced NADPH oxidase expression and activity, superoxide levels, and VCAM-1 synthesis. Kallistatin stimulates eNOS, SIRT1 and catalase synthesis, and prevents H2O2-mediated inhibition on these antioxidant enzymes. Kallistatin-induced eNOS expression is blocked by NAM, a SIRT1 inhibitor, while kallistatin-mediated SIRT1 synthesis is not inhibited by L-NAME, a NOS inhibitor. Additionally, NAM attenuates kallistatin’s effects on β-gal activity and NADPH oxidase activity, indicating that kallistatin’s stimulation of SIRT1-eNOS pathway is essential for attenuating endothelial senescence and oxidative stress. Moreover, microRNA let-7g plays a crucial role in mediating kallistatin’s anti-senescence, as kallistatin stimulates let-7g synthesis, and let-7g inhibitor abolishes kallistatin’s stimulation of antioxidant genes, and its inhibition of H2O2-induced PAI-1, p16INK4a, and NADPH oxidase. Furthermore, lung endothelial cells isolated from endothelium-specific kallistatin knockout mice, display marked reduction of mouse kallistatin levels. Kallistatin deficiency in endothelial cells exacerbates senescence, oxidative stress and inflammation, and H2O2 treatment further worsens these effects, as evidenced by elevated β-gal activity, PAI-1, p16INK4a and VCAM-1 levels, NADPH oxidase activity, superoxide formation, and decreased let-7g, SIRT1, eNOS and catalase expression. Therefore, kallistatin exhibits novel mechanisms in protection against vascular endothelial senescence by inhibiting oxidative stress and inflammation, and stimulating let-7g-mediated SIRT1-eNOS pathway. NIH 118516
138 Use of KDM4B Inhibitors to Target Periodontal Disease Progression, Joy Kirkpatrick¹, Jonathan Turner², Rachel Wilkinson³, Bethany Herbert⁴, Keith Kirkwood⁵, Patrick Woster¹; ¹Drug Discovery and Biomedical Sciences, MUSC, ²Biochemistry, MUSC, ³GSSM, ⁴Oral Health Sciences, MUSC, ⁵Oral Biology, University at Buffalo.

Abstract not available.

139 Evaluating 2 RTMS Strategies for Pain Reduction in Controls and Individuals with Non-Medical Prescription Opiate Use, Logan T Dowdle, Sarah E Hamilton, Jeffrey J Borckardt, Sudie E Back, Colleen A Hanlon; Psychiatry and Behavioral Sciences, MUSC.

Rationale: Non-medical prescription opiate use (NMPOU) is a growing health crisis, driven in part by continued pain following pharmacological intervention. Prior work from our lab validated the use of repetitive transcranial magnetic stimulation (rTMS) to elevate pain thresholds in control and NMPOU populations, but the ideal stimulation target remains unknown. There are at least two competing strategies: 1) Excitatory rTMS to the left dorsolateral prefrontal cortex (LDLPFC), an executive node or 2) inhibitory rTMS to the left medial prefrontal cortex (LMPFC), an area involved in limbic processing. Methods: Healthy controls (n=13) and treatment enrolled, buprenorphine maintained individuals with a NMPOU history (n=3) were invited to MUSC and assigned to one of three treatments: intermittent (excitatory), continuous (inhibitory) or sham tethaburst stimulation (iTBS/cTBS/sham). An advanced fMRI-based thermal heat task (10 second blocks of stimuli on left wrist) was administered before and after the stimulation session. Quantitative Sensory Testing was also performed to evaluate sensory, pain and tolerance thresholds. Results: Stimulation was tolerable at both locations, in both groups. At baseline during thermal stimulation, we observed significant (FWE p<0.05) activation in standard areas of the pain network (ACC, insula, S1), and in areas in which detection is more difficult (STN, brainstem). Following cTBS, but not sham, there was both an elevation in pain thresholds (p <0.001) and a reduction in activity in the ACC (p <0.05). Conclusions: These early results show that cTBS delivered the LMPFC, an entirely novel target for pain, may be a more effective strategy for elevating pain thresholds. Imaging results suggest that this change is driven by the ACC, which is tightly connected with the LMPFC. These findings lay the groundwork for determining the effectiveness of these two strategies for reducing pain in a larger population with NMPOU. NIH T32DA007288; NIH F31DA043330

140 Practical Elicitation and Implementation of Toxicity Scores to Represent Patient Toxicity Burden in Cancer Clinical Trials, Nathaniel S O’Connell, Elizabeth Garrett-Mayer, Andrew Lawson; Public Health Sciences, MUSC.

Conventional dose-finding cancer trials simplify the comprehensive toxicity grading system defined by the National Cancer Institute’s Common Terminology Criteria for Adverse Events (CTCAE) guidelines into a single binary toxicity endpoint, treating low to moderate grade toxicities as irrelevant and ignoring combinations thereof. Addressing this, the concept of composite toxicity scores accounting for multiple toxicities of varying grades has been introduced in the literature, which requires prior specification of severity weights to represent the relative toxicity burden each observed toxicity contributes to a patient profile. Elicitation of weights generally rely on subjective specification, and resulting scores may be confusing in clinical settings. We propose the Toxicity Score Elicitation Method (TSEM), a statistical method for estimating toxicity severity weights to be used in cancer clinical trials. The TSEM is further adapted to take into account the opinions of multiple oncologists to determine an overall toxicity weighting scheme, which may then be applied to a cancer clinical trial for patient toxicity evaluation. With the rise of molecularly targeted agents, immunotherapies, and combination treatments, comes increasingly complex patient toxicity profiles. The need for an improved, more refined measurement for quantifying patient toxicity burden is of significant importance in the future of cancer clinical trials. The TSEM is among the first methods proposed that provides an objective tool for determining such toxicity scores, making their use and adoption into practice more feasible. NIH F31-CA210380

141 Development of Novel Penicillin Binding Protein 2 (PBP2) Inhibitors As Drug Candidates for Penicillin- and Cephalosporin-resistant Neisseria Gonorrhoeae, Jonathan M Turner¹, Patrick M Woster², Christopher Davies¹; ¹Biochemistry and Molecular Biology, MUSC, ²Drug Discovery and Biomedical Sciences, MUSC.

Abstract: Gonorrhea is the second most common sexually transmitted infection in the United States, with nearly 400,000 cases reported in 2015 by the Centers for Disease Control. Untreated infections can lead to pelvic inflammatory disease, infertility, gonococcal arthritis, and increased risk of contracting and transmitting HIV. Strains of N. gonorrhoeae with decreased susceptibility to extended-spectrum cephalosporins (ESC) have emerged, marking this
pathogen as a major public health concern. However, these resistant strains retain some susceptibility to ertapenem and meropenem, suggesting that discovery of new carbapenems is a viable approach to developing anti-gonococcal agents. The aim of this study is the design and synthesis of novel carbapenem-based compounds exhibiting greater PBP2 inhibition compared to known β-lactams. The Davies lab has solved a high-resolution crystal structure of a mutant of PBP2 in complex with meropenem, allowing for design of ligands with enhanced complementarity to the altered binding pocket. From the molecular structures of meropenem and ertapenem, a virtual library was designed employing functional group variation and isosterism. Each compound was docked to the PBP2 construct in silico to simulate binding. A facile synthetic route involving the reaction of thiols with p-nitrobenzyl-(4R,5S,6S)-3[(diphenyloxy)phosphoryloxy-6-[(1R)-1-hydroxyethyl]-4-methyl-7-oxo-1-azabicyclo[3.2.0]hept-2-ene-2-carboxylate was developed and adapted for the production of the selected compounds. Docking methods were validated by 1) correlation of docking score with activity for known carbapenems, as well as three synthesized derivatives, against mutant PBP2 and 2) correlation of docking score with activity against mutant verses wild-type PBP2. A preliminary 3.6 Å crystal structure of prototype JMT000 with mutant PBP2 has also been solved, showing acylation of the target. Using these data, and considering such factors as tractability of synthesis, a group of lead compounds was identified from the designed library. The first compound selected for synthesis is JMT001, with the goal of testing its ability to inhibit PBP2 and whether it exhibits antimicrobial activity against cephalosporin-resistant strains of N. gonorrhoeae.

142 The Impact of Mitochondrial Fusion/Fission on Endothelial Cell Immunogenicity, Danh T Tran¹, Scott Escalante², Cari Atkinson¹, Satish N Nadig³, ¹Microbiology & Immunology, MUSC, ²College of Medicine, MUSC, ³Surgery, MUSC.

Abstract not available.

143 Anastomosis and Vascular Patterning of Scaffold-free, Prevascular Endothelial-fibroblast Constructs, Sanket Pattanaik, Chase Arbra, Heather Bainbridge, Sarah Grace Dennis, Jacob Brack, Stephen A Fann, Michael J Yost; General Surgery, MUSC.

Introduction: Tissue engineered constructs (TECs) are designed to restore the function of dysfunctional native tissue; however, viability of these constructs is hampered by stressors including ischemia due to poor vascularization of TECs. To contend with this ischemia, a new network of blood vessels is needed. Vascularization is a multistep process requiring: (1) degradation of the connective tissue; (2) proliferation and migration of nearby endothelial cells; (3) tip to tip anastomosis of endothelial networks; (4) lumen formation; (5) stabilization of vessels. To investigate these steps, we employ our novel scaffold-free prevascular endothelial-fibroblast constructs (SPECs), a coculture of endothelial cells and fibroblasts which self-assemble into capillary-like tubules in vitro.

Materials and Methods: Rod-shaped SPECs and fibroblast-only spheroids were constructed within agarose molds with a 4:1 mixture of normal human dermal fibroblasts to human adipose-derived microvascular endothelial cells. Fifty-four Sprague-Dawley rats were engrafted with implants within a hind limb muscular pocket: eighteen with SPECs; eighteen with fibroblast spheroids; eighteen with silicone implants. Six rats from each cohort were sacrificed at 6h, 12h, and 24h intervals. Constructs were sectioned and stained for markers of vascular development, hypoxia, and markers of apoptosis/inflammation. Results and Discussion: Both SPECs and fibroblast-only spheroids were rapidly encapsulated by endothelial cells (CD31/vWF+ structures) within 6 hrs of implantation, suggesting that rapid migration of host endothelial cells to site of implantation. Capsules around the SPECs took the form of lacier, capillary-like structures. Differences in rate of tip-tip anastomosis and vessel penetration, were measured among the cohorts. Endothelial tubule formation was measurably faster (by 6hrs) in SPECs compared to Fibroblasts (12+hrs). Additionally, the SPEC endothelial branches interdigitated with construct-derived endothelial structures, with a consolidation of branches at 12-24 hours. NIH T32 GM08716-13

144 Development and Characterization of a Novel Wound Dressing for the Treatment of Chronic Wounds, Sarah G Dennis, Heather Bainbridge, Sanket Pattanaik, Michael Yost; Surgery, MUSC.

Wound healing is a vital process that is impaired in chronic wounds. Pressure ulcers, one of the most frequently observed chronic wounds, are caused by unrelieved pressure that disrupts capillary blood perfusion. The failed wound healing of pressure ulcers is attributable to the ischemic environment, impaired angiogenesis, copious wound exudate, and bacterial colonization. By combining a tissue engineered construct that resembles a nascent vascular bed with an ultrafiltration layer that controls effluent and prevents bacterial infection we aim to accelerate closure of chronic wounds. The Scaffold-free Prevascularized Endothelial-fibroblast Construct (SPEC) is comprised of endothelial cells and fibroblasts, and was shown to organize into cord-like vascular networks. Notably, the SPECs anastomosed
with the host vasculature and become perfused when implanted submuscularly. In this study, we determine the effects of the SPEC on cell migration in vitro. Additionally, an external layer comprised of regenerated cellulose sputter-coated in silver has been developed to filter wound exudate and act as an antibacterial component. Two silicone disks of 5mm diameter were placed on the bottom of a cell culture dish and seeded with fibroblasts. At 80% confluence, the disks were removed. Rod-shaped SPECTs and Fibroblast-Only Spheroids (FOS) were formed in linear 2% agarose molds with a mixture of 4:1 fibroblast to endothelial cells after 3 days. FOS lack prevascular networks and were created as a control. The migration of cells was examined using microscopy at 2, 5, and 7 days. Silver coated ultrafiltration membranes were assessed for effluent control by an aqueous protein size exclusion assay. This work suggests achievement of our two technological aims: rapid migration of endothelial cells to improve vascularization and selective filtration of damaged cytokines and proteases for proper wound healing. Our future work is to implant this device in a pressure ulcer model to analyze the rate of wound closure. South Carolina Clinical and Translational Research Institute Pilot Projects

145 Assessment of NT108, a Vitamin K Analog, in the Recovery of Mitochondrial DNA Depletion Syndromes. Tucker Williamson, James Chou, Sherine Chan; DDBS, MUSC.

Abstract not available.

146 Eukaryotic Initiation Factor 4E-Binding Protein (EIF4EBP1, 4EBP1, BP-1, 4E-BP1, and PHAS-I) is a Driver of Breast Cancer. Alex C Rutkovsky, Stephen P Ethier; Pathology, MUSC.

Eukaryotic Initiation Factor 4E-Binding Protein (4EBP1) is a repressor of translation that is expressed across human cell types, with especially high levels in normal breast tissue, and even higher levels in breast cancer. 4EBP1 is not essential for normal cell proliferation, as corroborated by our findings in normal mammary cells. Many cancers overexpress 4EBP1 at a high level (top 1% or 5% overexpressed genes comparing cancer to normal in >30 Oncomine data sets) and transcripts are rarely mutated. One mechanism causing increased 4EBP1 is through copy number amplification of the 8p11-12 locus. Genomic Identification of Significant Targets in Cancer (GISTIC) shows 4EBP1 is significantly focally amplified (12/33) but not deleted (1/33) across cancer types. 4EBP1 is amplified in >15% of breast tumors which are usually estrogen receptor positive (ER+), endocrine therapy resistant, have poor prognosis, and tend not to mutate PIK3CA. Consequently, when comparing patient breast tumors, 4EBP1 copy number levels trend higher in ER+ versus ER- patients, but this is contrary to 4EBP1 mRNA expression levels which are higher in ER- versus ER+ breast tumors. Our data show that short-hairpin knockdown of 4EBP1 in breast cancer cell lines, bearing the 8p11-12 amplicon or in those where 4EBP1 was identified as a positive hit in our genome-wide RNA-interference screens, inhibits cell proliferation. Analysis of apoptosis and cell-cycle using fluorescence-activated cell sorting will further resolve growth variations. Loss of 4EBP1 decreases the protein levels of key regulators such as ER, CyclinD1, and MYC, while levels of phospho-S6, BCL2, or BCLXL remain unchanged. Phosphorylated 4EBP1 is important to breast cancer prognosis, pathologically grade, is useful as a potential biomarker for drug efficacy (NCT02444390), and is robust in the 8p11-12 models. Here we show loss of 4EBP1 can be detrimental to breast cancer. Dept of Pathology and Laboratory Medicine

147 Identification of Circulating Murine CD34+OCN+ Cells. Ryan R Kelly¹, McDonald T Lindsay², Vincent D Pellegrini³, James J Cray⁴, Amanda C LaRue²; ¹Pathology, MUSC, ²Ralph H. Johnson VAMC, ³Orthopaedics, MUSC, ⁴Oral Health Sciences, MUSC.

Circulating osteoprogenitors are receiving increased attention for their potential to promote bony repair. Although the current paradigm suggests that bone marrow-derived (BM) adherent mesenchymal stem cells (MSCs) form osteoblasts and non-adherent hematopoietic stem cells (HSCs) form osteoclasts, a number of studies have shown that HSCs possess osteogenic potential. Circulating osteoprogenitors likely originate in the BM, from which they egress into circulation, suggesting they are non-adherent and, thus, may be of hematopoietic origin. Due to limitations in the therapeutic use of MSCs and the latest findings suggesting MSCs act as medicinal signaling cells, studying other populations with osteogenic potential, including HSCs, is warranted. Previous work from other groups identified a circulating human osteoblastic population that expressed osteocalcin (OCN) and alkaline phosphatase (ALP), increased during fracture repair and pubertal growth, and formed mineralized colonies in vitro and bone in vivo. Interestingly, a subpopulation also expressed CD34, a hematopoietic/endothelial marker. The present study extends these findings by identifying circulating CD34+OCN+ cells in mice by flow cytometry. These cells were confirmed to be of hematopoietic origin through demonstration of CD45 expression and by use of the VavR double transgenic mouse model. In a murine non-stabilized tibial fracture model, circulating CD34+OCN+ cells peaked at 3 weeks post-fracture, suggesting involvement in transformation of cartilage callus to bone and early mineralization. With regard to therapeutic potential, CD34+OCN+ cells were mobilized after 3 days of treatment with 10 mg/mL
AMD3100. Together, these data demonstrate a murine CD34+OCN+ circulating population similar to that published in human studies that may be directly involved in fracture repair. Future studies will examine if CD34+OCN+ cell number correlates with improved fracture healing outcomes in a murine atrophic non-union model. VA Merit Award BX000333; NIH T32HL007260; NIH T32DE017551

148 CD26high T Cells Have a Natural Capacity to Migrate and Persist in Multiple Tumor Models, Stefanie R Bailey, Michelle H Nelson, Megan M Wyatt, Jacob S Bowers, Lillian R Neal, Kinga Majchrzak, Chrystal M Paulos; Microbiology & Immunology, MUSC.

Abstract not available.

149 Optogenetic Stimulation of Capillary Pericytes Reduces Cerebral Blood Flow in Vivo, David A Hartmann, Andy Y Shih; Neuroscience, MUSC.

Vascular mural cells surrounding the cerebrovasculature are responsible for modulating blood supply in accordance with the metabolic demands of the brain. Although it is accepted that vascular smooth muscle cells on arterioles can regulate blood flow, the capacity for pericytes on capillaries to regulate blood flow is debated. To test the hypothesis that pericytes throughout the capillary bed can regulate blood flow, we stimulated channelrhodopsin (ChR2) in individual pericytes using two photon illumination, as done previously (Hill, et al. Neuron 2015). Although we used offspring of PDGFRBeta-Cre and Ai32 mice, which possess ChR2 in both smooth muscle cells and pericytes, the spatial selectivity of two photon excitation enabled selective stimulation of pericytes and not vascular smooth muscle cells. Simultaneously, with the same two photon laser used for excitation of ChR2 in pericytes, we measured capillary diameter and red blood cell velocity by using intravenous dextrans. We find that pericyte excitation for 60 seconds produced, on average, a ~20% reduction in diameter and velocity throughout the cortical microvasculature (1-9 branch points distal to the penetrating arteriole), including territories that lack alpha smooth muscle actin. Importantly, identical stimulation parameters did not produce hemodynamic changes in control mice with cytosolic YFP or membrane-bound GFP in vascular mural cells, in contrast to our observations in ChR2-YFP mice. Further, the observed decrease in velocity and diameter in response to pericyte ChR2 stimulation was inhibited when we applied fasudil, a Rho kinase inhibitor and vasodilator, to an intact dura (dose of 10 mM). Our results to date suggest that pericytes, even those in territories without alpha smooth muscle actin, have the capacity to modulate blood flow. NIH T32 GM08716, NIH - NCATS UL1 TR001450; TL1 TR001451; NIH-NINDS F30NS096868; NIH-NINDS NS085402, NS096997, NS097775

150 Inflammation in the Aging Mouse and Human Temporal Bone, LaShardai N Brown1, Ting Liu1, Clarisse H Panganiban1, Jeremy L Barth2, Hainan Lang1; 1Pathology, MUSC, 2Regenerative Medicine, MUSC.

Age-related hearing loss, or presbyacusis, is a leading chronic condition affecting older adults. Studies have shown that declines in auditory function seen in presbyacusis can result from loss of the peripheral auditory nerve and alterations of the cochlear microenvironment. Macrophages, immune cells of the inner ear, play a critical role in maintaining a healthy microenvironment by eliciting inflammatory responses and clearing apoptotic cells and cellular debris. Aging promotes chronic activation of the immune system and the proliferation of immune cells, such as macrophages, exacerbating the pathology of neurodegenerative disorders. Macrophages of the aged auditory nerve have not been well characterized. Furthermore, it is unknown whether macrophages are beneficial or detrimental to the health of the aged auditory nerve. In this study we used a combination of genomic and morphological assays to examine the inflammatory changes in the auditory nerve of the aged mice and human temporal bones from older donors. Our studies revealed that immune-related biological processes, such as complement activation, antigen presentation and macrophage activation, were enriched in auditory nerves of aged mice. Ultrastructure of auditory nerves revealed that aged nerves possess more macrophages than young nerves. Aged macrophages surveyed normal cells and were in contact with degenerating axons and cells. Immunohistochemistry analysis of macrophages from young and aged mice revealed an age-related increase in macrophage numbers and an increase in the presentation of macrophage-associated activation markers. Our results suggest that immune-related biological processes, including macrophage activation, are increased in the aged auditory nerve. Further studies of macrophages in the aging cochlea will provide insight into ways to use resident immune cells as therapeutic targets for presbyacusis. NIH F31DC015741, T32 DC014435, R01 DC7506, P50 DC000422, GM103342, GM103499, R25 GM072643, American Federation for Aging Research.
151 Structural and Functional Analysis of an Essential Cell Cycle Regulator Reveals a Novel Mechanism of Action, Katelyn M Williams, James H Atkinson, Sabrina Salazar-Arango, Shuo Qie, J Alan Diehl, Shaun K Olsen; Biochemistry & Molecular Biology, MUSC.

Abstract not available.

152 Propensity Score Matching for Multilevel Spatial Confounding in Health Disparity Studies, MELANIE L DAVIS¹, BRIAN NEELON¹, PAUL NIETERT¹, KELLY HUNT¹, LANE BURGETTE², ANDREW LAWSON¹, LEONARD EGEDE³, ¹Public Health Sciences, MUSC, ²Rand Corporation, ³Internal Medicine, Medical College of Wisconsin.

Motivated by a study exploring racial disparities in diabetes specialty care between non-Hispanic black and non-Hispanic white veterans, we aim to address a type of confounding that arises in spatially referenced observational studies. Specifically, we introduce a spatial propensity score matching method to account for “geographic confounding”, which occurs when the confounding factors, whether observed or unobserved, vary by geographic region. We augment the propensity score and outcome models with spatial random effects, which are assigned conditionally autoregressive priors to improve inference by borrowing information across neighboring geographic regions. Through a series of simulations, we show that ignoring spatial heterogeneity results in increased absolute bias and mean squared error, while incorporating spatial random effects yields improved inferences whether the treatment effect is estimated directly in the matched sample or whether further adjustment is performed through a regression model for the outcome. In the motivating application, we construct multiple global estimates of the risk difference in diabetes care: an unadjusted estimate, an estimate based solely on patient-level matching, and an estimate that incorporates both patient and spatial information. The unadjusted estimate suggests that specialty care is more prevalent among non-Hispanic blacks, while patient-level matching indicates that it is less prevalent. Hierarchical spatial matching supports the latter conclusion, with a further increase in the magnitude of the disparity. These results highlight the importance of accounting for spatial heterogeneity in propensity score analysis, and suggest the need for clinical care and management strategies that are culturally sensitive and racially inclusive. HSR&D CIN 13-418

153 The Role of FABP7 Upregulation in ALS Models, Kelby Killoy, Ben Harlan, Mariana Pehar, Marcelo Vargas; Pharmacology, MUSC.

Abstract not available.

154 MiR-146a Is An Endogenous Regulator Of Both Hematopoiesis And Bone Mass, Blake E Hildreth¹, Jennifer A Geisler², James Leo³, Albert de la Chapelle¹, Michael G Columns¹, Adam C Soloff⁵, Michael C Ostrowski¹, Sudarshana M Sharma¹, ¹Biochemistry and Molecular Biology, MUSC, ²College of Veterinary Medicine, Ohio State University, ³Cancer Biology and Genetics, Ohio State University, ⁴Molecular Virology, Immunology & Medical Genetics, Ohio State University, ⁵Microbiology and Immunology, MUSC.

miR-146a is a key regulator of inflammation and has been shown to have an endogenous protective effect against excessive immune activity, autoimmunity, and cancer. Osteoclasts are the principle bone-resorbing cell of the body. Bone loss associated with osteoporosis, autoimmune diseases, and primary or metastatic bone cancer results from dysregulated and excessive osteoclast activity. Osteoclasts share a common progenitor with macrophages within the hematopoietic myeloid lineage. miR-146a has been shown to negatively regulate osteoclast differentiation and function by our laboratory and others in vitro. Because of this, we wanted to investigate the role of miR-146a in bone biology and hematopoiesis in vivo.

Two mouse models were used for this purpose: a knock-out (KO) with global deletion of miR-146a and a knock-in (KI) overexpressing miR-146a. Male and female mice were aged 2-3 and 7-9 months at which time spleen and liver weights were obtained, femurs isolated for radiographic evaluation, and blood, spleens, and bone marrow collected for flow cytometric evaluation. Tissues from all organ systems were also collected for histologic and molecular phenotyping. In both male and female KO mice and male KI mice there was a significant increase in spleen weight. Female KO mice had significantly greater liver weights. These findings suggest altered cellularity. KO mice had decreased bone density whereas KI mice had increased density, suggesting miR-146a also negatively regulates osteoclast function in vivo. Flow cytometric analysis revealed marked differences in hematopoietic cell populations between genotypes. This was observed most notably within the myeloid compartment, where KI mice had significantly lower and KO mice had a significantly greater number of osteoclast precursors. These findings indicate that miR-146a regulates both hematopoiesis and bone mass. Negative regulation of osteoclast activity by miR-146a suggests a potential therapeutic role of miR-
Research on the impact of zero-tolerance policies shows higher rates of out-of-school suspension and expulsion at schools with principals who favor a zero tolerance approach, and evidence does not support safety benefits related to such policies (APA Zero Tolerance Task Force, 2006; Skiba & Rausch, 2006). These policies also disproportionately negatively impact students of color, even when controlling for socioeconomic status (Wallace et al., 2008). Little research has been conducted linking to zero-tolerance policy endorsement to structural antecedents, such as school racial factors, or to student academic and mental health outcomes. The purpose of the present study was to examine 1) The extent to which school race composition and discipline racial disproportionality predicts zero-tolerance policy endorsement among teachers, 2) the extent to which teacher reported attitudes on zero-tolerance policies positively predict student internalizing problems, and 3) The extent to which student perceptions of care from adults in the school explain the proposed relationship between zero-tolerance policy endorsement and student outcomes. Data were drawn from 1734 students and 754 adults in 24 schools in the southeast United States. Teachers indicated the extent to which they endorsed the effectiveness of exclusionary discipline on the authoritative school climate subscale. Student reports of supportive climate were assessed with authoritative school climate, and students and teachers reported on student internalizing symptoms on the SDQ. Discipline disproportionality is the proportion of potential to actual disciplinary referrals for African American students compared to that for European American students (see Boneshefski & Runge, 2014). Results of the conceptual structural equation model with aggregated data supported two hypothesized paths: race composition predicted lower student reported supportive climate and higher student-reported, but not teacher-reported, internalizing problems. Disaggregated data from a multilevel structural equation model along with academic outcomes will also be presented. Implications, limitations, and future directions will be discussed. NIJ 16-3017


Temporomandibular joint disorders (TMJDs) disproportionately affect women (3-8 times), with approximately 30% of TMJDs including disc degeneration. TMJD etiology is currently unknown. Sexual dimorphisms in temporomandibular disc mechano-electro-chemical properties could result in a loading environment which predisposes women to TMJD development. Intact human temporomandibular joints (TMJs) were excised and imaged using a preclinical 7T MR, and solid models of the temporomandibular disc were reconstructed for morphometric analysis. TMJ discs were extracted, and underwent an incremental stress-relaxation tensile testing protocol to determine disc viscoelasticity, and electro-chemical assays to determine disc extracellular matrix fixed charge density (FCD). Statistical modelling showed significant effects for donor sex for disc morphometry and FCD. When considering skull size and shape, female temporomandibular discs were proportionally larger than male discs in their anteroposterior length (p=0.0199), with no difference in their mediolateral width. Temporomandibular discs for male discs had higher FCD compared to females (p=0.007), with FCD twice as high for males compared to females in the disc posterior band. Human TMJ discs trended stiffer for females compared to males, with higher Young’s Modulus and Instantaneous Modulus, and relaxing proportionally less. These findings establish important sexual dimorphisms in temporomandibular disc mechano-electro-chemical properties. Differences in disc size and shape between males and females is anticipated to alter stress and strain patterns. Coupled with their increased stiffness and decreased viscoelastic response, the TMJ disc could experience higher stresses in females compared to males. Additionally, FCD is an important regulator of disc compressive modulus through osmotic swelling pressure, and could be an important contributor to tissue viscoelasticity. These findings build on our understanding of the structure-function relationships within the TMJ disc, and provide potential insights into etiological mechanisms behind the increased prevalence of TMJDs among women. T32DE017551
157 Molecular Chaperone is Required for Gut Tolerogenic Dendritic Cell Development and Function, Stephen Iwanowycz, Yi Yang, Zihai Li, Bei Liu; *Microbiology and Immunology, MUSC.*

The intestinal mucosa is continuously inundated with foreign antigens. Therefore, immune cells need to be tightly regulated to maintain tolerance against harmless dietary antigens and microbiota while responding to pathogens. Intestinal dendritic cells (DCs) play an integral role in regulating immunity and tolerance because of their unique position at the interface of innate and adaptive immunity. Multiple populations of intestinal DCs have been reported based on the expression of CD103, CD11b, and CX3CR1. However, the mechanism by which different DC subsets regulate intestinal homeostasis is still unclear. Heat shock protein gp96 is an essential chaperone for most TLRs, integrins, and other proteins important for DC functions. However, the role of DC-intrinsic gp96 in regulating gut tolerance has not been studied. Using a genetic strategy, we discovered that selective deletion of gp96 from CD11c+ cells in mice results in alterations of DC and T cell subsets predominately in the gut. There was a decrease in Irf8 dependent tolerogenic DCs and an increase in inflammatory DCs as well as the loss of antigen-specific regulatory T cell induction. Strikingly DC-specific gp96 knockout mice develop spontaneous colitis by 24 weeks of age. Differentiation of murine bone marrow-derived DCs revealed that gp96 depletion intrinsically and selectively inhibited the maturation of Irf8 dependent DC populations evidenced by reduced co-stimulatory protein expression and T cell induction capacity. Taken together, our results demonstrated that gp96 depletion from CD11c+ cells selectively inhibits tolerogenic DCs in the gut leading to decreased Treg cells, which indicates that DC-intrinsic gp96 plays essential roles in maintaining gut tolerance. *NIH T32CA193201 NIH R01CA193939 MUSC Bridge Funding*

158 Viral-mediated Rescue Of Arc/Arg3.1 knock-out Demonstrates a Requirement for Function in the NAc in Regulating Mood and Drug-related Behaviors., Rachel D Penrod, Laura N Smith, Jaswinder Kumar, Brandon Hughes, Gabriella Barry, Daniel Wood, Makoto Taniguchi, Christopher Cowan; *Neuroscience, MUSC, Psychiatry, McLean Hospital, Neuroscience, College of Charleston, MSTP, MUSC.*

A key feature of drug addiction is the persistent vulnerability to relapse, despite long periods of abstinence. This vulnerability is conferred by long-lasting, drug experience-induced plasticity in key brain regions such as the nucleus accumbens (NAc). The immediate early gene, activity-regulated cytoskeleton-associated protein (Arc/Arg3.1), is a known regulator of AMPAR surface expression, both through the promotion of endocytosis and the regulation of GluA1 expression. Given that AMPAR regulation is a key site of cocaine-induced glutamatergic plasticity, Arc/Arg3.1 has potential to be a molecular contributor to this plasticity. We discovered that Arc/Arg3.1-deficient mice (KO) display several cocaine- and mood-related behavioral phenotypes, including decreases in anxiety and increased locomotor responses to cocaine, but perhaps more interestingly, they show drug-experience dependent “reward sensitization”. We find that prior cocaine experience appears to enhance cocaine reward in non-contingent (conditioned place preference; CPP) and contingent (intravenous drug self-administration) assays. While these behavioral phenotypes are likely linked to Arc/Arg3.1’s regulation of AMPAR surface expression and/or GluA1 transcription, it is unclear what phenotypes are developmentally derived and which are dependent on Arc/Arg3.1’s function in the adult brain. Additionally, it is not yet clear where Arc/Arg3.1 is functioning in the brain to regulate any of these behaviors. Here, we examine the effects of viral-mediated, region-specific expression of Arc/Arg3.1 in KO and WT mice in anxiety and cocaine-related behaviors. We find that Arc/Arg3.1 expression within the NAc of Arc/Arg3.1 KO mice rescues some, but not all, of these behavioral phenotypes. Our results are consistent with a role for Arc/Arg3.1 in the NAc in regulating some of the phenotypes observed in the total Arc/Arg3.1 KO animals. To more clearly define the role of Arc/Arg3.1 in NAc-mediated drug-induced plasticity, future work will focus on spatially and temporally restricted knockdown of Arc/Arg3.1 and consequent behavioral and cell biological phenotypes. *R01 DA027664; F32 DA036319*

159 Endothelial Progenitor Cell Exosomes Are Beneficial in Murine Model of Sepsis, Yue Zhou, Pengfei Li, Andrew J Goodwin, James A Cook, Perry V Halushka, Hongkuan Fan; *Pathology and Lab Medicine, MUSC, Pulmonary, Critical Care, Allergy and Sleep Medicine, MUSC, Neurosciences, MUSC, Medicine and Pharmacology, MUSC.*

Abstract not available.
160 Antibiotic-Disruption of Gut-Microbiota Dysregulates Osteoimmune Crosstalk in Postpubertal Skeletal Development, Jessica Hathaway-Schrader, Nicole Poulides, Heidi Steinkamp, Michael Chavez, Emily Huang, Lixia Zhang, Keith Kirkwood, Chad Novince; Oral Health Science, MUSC.

Abstract not available.

161 Effects of Environmental Levels of EE2 on the Zebrafish Embryo: a Systems Level Analysis, Ludivine Renaud1, Bailey Glen2, Willian da Silveira2, Starr Hazard2, Seok-Hyung Kim1, Gary Hardiman1; 1Medicine, MUSC, 2Center for Genomic Medicine Bioinformatics, MUSC.

The synthetic derivative of the endogenous estrogen hormone estradiol, 17-alpha-ethynylestradiol (EE2), has been widely used as oral contraceptive since 1964. Given the importance of estrogens in controlling many physiological processes in vertebrates, including growth, differentiation, functioning of the reproductive, skeletal, cardiovascular and central nervous systems, and the fact that EE2 has made its way into the aquatic environment at concentrations ranging from 0.02 – 0.9 nM, it is essential to clearly define the adverse effects that EE2 could have on wildlife and human health. Several studies concluded that EE2 decreases breeding success in zebrafish (Danio rerio) by inducing complete sex reversal in males and inhibiting gametogenesis in both males and females. Because EE2 is able to activate both estrogen receptors and regulate genes in steroid-responsive tissues, we hypothesize that EE2 could disrupt other pathways and biological processes in developing embryos. Our laboratory exploited the unique advantages of zebrafish as a systems toxicology model to investigate the effects of EE2 (0.01nM-1microM range) on zebrafish embryos. RNA-sequencing was performed on Illumina HiSeq 2500. Gene and systems level analyses were performed along with a novel percolation clustering approach we have developed for modeling gene-gene and protein interactions. Our analyses revealed several significant [1] networks with hubs centered around myelin basic protein (mbp) as well as rhodopsin (rho) and retinoschisin-1 (rs1), suggesting perturbation of the central nervous system and retinal development respectively, and [2] biological processes, including Neurological System Process, Visual and Sensory Perception, Mitochondrial Dysfunction, and Cardiac Diseases. Eye measurements (short/long-axis, lens) and GFP signal in GFP mbp tagged zebrafish were significantly increased in 0.01nM EE2-treated group compared to control embryos. Our data suggests that environmentally relevant levels of EE2 (0.01-1nM) perturbed the transcriptome, and visual and nervous system signaling networks, in addition to several key biological processes in zebrafish embryos.

162 A Novel Myc-Zeb Regulatory Axis Promotes EMT By Co-Operatively Repressing E Cadherin, Jasmine Kaur, Jennifer Isaacs; Pharmacology, MUSC.

Metastasis is the leading cause of majority of cancer related mortalities. Despite its dire clinical implications, very little is known about the molecular events dictating the fate of tumor cells. Perturbation of the epithelial to mesenchymal transition (EMT) developmental program has been shown to play a critical role in promoting metastasis. Loss of E-cadherin is considered to be the hallmark of EMT process and thus, discerning the mechanisms responsible for E-cadherin regulation is critical for understanding tumor metastasis. Although the transcription factors c-Myc and Zeb1 have both been reported to transcriptionally suppress E-cadherin, no prior study has evaluated whether these effectors may act cooperatively. The present study describes a novel c-Myc-Zeb1 interdependent regulatory axis that cooperatively functions to repress E-cadherin. We employed co-immunoprecipitation technique to identify a novel protein interaction between c-Myc and Zeb1, and further demonstrated a critical role for c-Myc in maintaining Zeb protein expression. These findings suggest a unique role for c-Myc as a functional partner with Zeb1, resulting in the formation of a robust repressive complex at E-cadherin promoter which is capable of initiating a key metastasis-supporting EMT event. Collective, our data supports a new paradigm wherein c-Myc and Zeb1 cooperatively orchestrate the loss of epithelial characteristics, thereby directing them towards metastasis. Furthermore, our data highlight the conceptual possibility of disrupting Myc-Zeb1 association as a therapeutic approach for attenuating cancer progression. NIH RO1 CA187342
Abstract not available.

164 S1P/PPARγ Axis Metabolically Reprograms the T Cells to Modulate Their Anti-Tumor Potential, Paramita Chakraborty, Krishnamurthy Thyagarajan, Shilpak Chatterjee, Shanmugam Panneer Selvam, Mahvash Husain, Amir Al-Khami, Besim Ogretnmen, Shikhar Mehrotra, Surgery, MUSC, Biochemistry and Molecular Biology, MUSC.

Adoptive T cell transfer (ACT) holds promise in cancer therapy. However, various confounding factors as tumor induced immunosuppression, or activation induced cell death limit the favourable outcome of this therapy. Thus, strategies that enhance anti-tumor T cell functions could enhance the efficacy of ACT. Sphingosine 1-phosphate (S1P), generated by sphingosine kinase 1 (SphK1), regulates lymphocyte egress into circulation also plays a role in the differentiation of regulatory T cells and T helper-17 cells. Here, we examined the roles and mechanism of action of SphK1/S1P signalling in the regulation of antitumor potential of T cells using pharmacologic, molecular and genetic tools. To achieve this, we developed C57BL/6/pMel transgenic mice on Sphk1−/− background. Adoptive transfer of pMel-Sphk1−/− T cells to a recipient WT-syngeneic mouse with subcutaneous melanoma B16 inhibited its growth as compared to controls. Our data showed that pMel-Sphk1−/− T cells maintained central memory phenotype, showed higher mitochondrial respiration, and exhibited resistance to TGF-β mediated suppression. Importantly, pMel-Sphk1−/− T cells secreted higher levels of IL-17 compared to their wild type counterparts even without activation. Mechanistically, we demonstrate here that SphK1/S1P signaling regulates IL17 generation through attenuation of PPARγ (peroxisome proliferator-activated receptor gamma), which is downregulated in Sphk1−/− T cells as compared to controls. In reciprocal studies, addition of S1P in culture media enhanced PPARγ expression, resulting in decreased IL17 production in Sphk1−/− T cells. Furthermore, we also discovered that down-regulation of PPARγ in Sphk1−/− T cell increased lipolysis to produce free fatty acids, and metabolically reprogram T cells to induce mitochondrial metabolism to meet their energy demand. Thus, SphK1/S1P signaling regulates anti-tumor functions and persistence of T cells by controlling T cell energy metabolism through induction of lipolysis via PPARγ modulation. Overall, these data highlight the clinical potential of targeting SphK/S1P with ACT for the treatment of patients with solid tumors. Department of Surgery, MUSC, NIH/CA198646, NIH/P01CA203628, NIH/PO1CA154778

165 Assessment of Brain Structural Changes in the Astronauts Using Magnetic Resonance Imaging, Davoud Asemani, Donna Roberts; MUSC.

The effect of long-term microgravity during space mission on intracranial structures remains unknown. The impacts of spaceflight on the volume of cerebrospinal fluid (CSF) as well as structural geometry of brain have recently drawn the NASA attention particularly for an eventual manned mission to Mars. In this NASA IRB-approved, intra-individual comparison study, brain MRI examinations of 12 NASA astronauts (ISS Program) obtained before (median 536.5± 87.2 days) and after spaceflight (median 3.1±1.6 days) were analyzed. The average duration of space mission was 159.3±19.2 days. Analysis was performed using the open access FMRIB Software Library program (http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/), MATLAB, Paraview, ITK-SNAP, and IBM SPSS. The analysis was realized by: 1. brain extraction (BET), 2. segmentation (FAST) and 3. volume extraction. To study the effects of spaceflight, the volumes of ventricles and the brain were computed for both pre- and post-flight scans. The volume of brain included the entire parenchyma and both sulci and ventricular CSF. Invoking the constant intra-cranial volume, the change of peripheral CSF volume was assessed as the reverse of the change in brain volume. Results: There was a significant enlargement of the ventricles post-flight compared to the pre-flight values (14% increase post-flight, p=0.001). In addition, our analysis showed that a global linear change is found in the brain of the astronauts returning to the earth following to a long-duration stay in the international space station. This linear change includes superior shift (+0.66mm) and stretching (+0.66%) along with a laterla compression (-0.3%) as shown in the following figure. Long-term microgravity exposure during spaceflight causes significant enlargement of the ventricles representing an alteration in CSF homeostasis. This may play a role in the development of VIIP. Further research is needed to determine the etiology of the ventricular
enlargement. This study has important implications for designers planning a human mission to Mars.

166 Transdiagnostic Effects of Ventromedial Prefrontal Cortex TMS on Drug Cue Reactivity: Sham-controlled Studies in Cocaine Users and Heavy Alcohol Users, Tonisha E Kearney-Ramos, Logan T Dowdle, Mark S George, Raymond Anton, Colleen A Hanlon; Psychiatry and Behavioral Sciences.

Elevated brain response to drug cues is a transdiagnostic hallmark of substance abuse, and likely contributes to the cycle of relapse that occurs in treatment-seeking individuals. Preclinical research demonstrates that optogenetic dampening of drug cue-related activity in infralimbic (IL) cortex will attenuate drug cue reactivity. Prior data from our lab demonstrate that it is possible to dampen activity in the ventromedial prefrontal cortex (VMPFC), the human equivalent of the IL, through non-invasive continuous theta burst stimulation (cTBS). Here we report two experiments evaluating the efficacy of VMPFC cTBS on drug cue reactivity in cocaine users (Study 1; n=25) and alcohol users (Study 2; n=24). Drug cue reactivity was evaluated before and after real and sham cTBS (110% RMT, 3600 pulses). Generalized psychophysiological interaction (gPPI) revealed cTBS-induced changes in drug cue-associated functional connectivity. Following real but not sham VMPFC cTBS, gPPI revealed reduced drug cue-evoked functional connectivity between (1) the VMPFC, left putamen, left caudate, and left insula in cocaine users; and (2) the VMPFC, left putamen, left caudate, right caudate, left insula, and ACC in alcohol users. These data demonstrate that VMPFC cTBS can attenuate cue reactivity in the VMPFC and dorsal striatum (putamen and caudate). These results provide an empirical foundation for future clinical trials that may evaluate the efficacy, durability, and clinical implications of VMPFC cTBS. NIH R01DA036617; K01DA027756; P50 DA015369; T32DA007288

167 Testing a Novel Nanofiber Scaffold for Utility in Bone Tissue Regeneration, R Nicole Howie 1, Emily Durham 1, Zach Grey 1, Braydon Oakes 1, Reed Houck 1, Amanda LaRue 1, Martin Steed 1, Robin Muise-Helmeriks 1, James Cray 1; Oral Health Sciences, MUSC, Dental Medicine, MUSC, Pathology and Laboratory Medicine, MUSC, Oral and Maxillofacial Surgery, MUSC, Regenerative Medicine, MUSC.

Bone is a highly vascularized and dynamic tissue that has an innate capacity for healing after injury. However, there are many variables that serve to alter the process of bone remodeling that diminish regeneration including the size and nature of the wound bed and chronic medical conditions. To overcome these inhibitory factors, tissue engineered, osteoconductive scaffolds paired with various growth factors have been utilized clinically in orthopedics and craniofacial surgery. However, many limitations still remain with commercially available products (e.g. rhBMP2) which can lead to rampant inflammation associated with injury or clinical intervention, ectopic bone formation, and ultimately graft failure. In this investigation we studied the ability for a nanofiber scaffold (Talymed), currently approved to augment cutaneous wound healing, to accelerate growth factor (rhBMP2) generated bone healing compared to the traditional absorbable collagen sponge (ACS) delivery system. To assess this healing after craniofacial fracture, 155 adult wild-type mice were randomly arranged in 16 groups by time, 4 and 8 week, and treatment, ACS or Talymed, loaded with control, low, medium or high dosages of rhBMP2. At experimental endpoints, skulls were subjected to microCT, biomechanical, and histological analysis to assess bone regeneration. The use of Talymed within the defect site was found to decrease the bone volume, bone formation rate, and alkaline phosphatase positivity compared to ACS/rhBMP2 combinations. Interestingly, the Talymed regenerated bone, although less, was found to have a greater hardness value than that of bone within the ACS groups. However, the difference in bone hardness between scaffolds was not detectable by 8 weeks. Based on these results, we found that the nanofiber scaffold generated a better quality of bone regenerate at 4 weeks but, due to the lack of overall bone formation and the inhibition of normal remodeling processes, was not as efficacious as the current clinical standard ACS/rhBMP2 therapy. Medtronic Inc. and Marine Polymer Technologies; AO Foundation S-16-108C; NIH NIDCR 5T32DE017551; NIH NIGM P30GM103331; SCTR NIH/NCATS UL1TR000062

168 Rising to the Challenge: Developing a Method to Measure and Adjust Challenge in Stroke Rehabilitation, Kelly R Anderson1, Deanna Adkins2, Annie Simpson3, Jill Stewart4, Michelle Woodbury1; 1Health and Science and Research, MUSC, 2Neuroscience, MUSC, 3Healthcare Leadership and Management, MUSC, 4Physical Therapy, USC.

Abstract not available.
169 Fli-1 Modulates Pericyte Loss in Murine Sepsis, Pengfei Li¹, Yue Zhou¹, Andrew J Goodwin², James A Cook³, Perry V Halushka⁴, Xian K Zhang⁵, Lynn M Schnapp⁶, Hongkuan Fan¹; ¹Pathology and Lab Medicine, MUSC, ²Pulmonary, Critical Care, Allergy and Sleep Medicine, MUSC, ³Neurosciences, MUSC, ⁴Medicine and Department of Pharmacology, MUSC, ⁵Rheumatology and Immunology, MUSC.

Disruption of pericyte/endothelial cell (EC) interactions and vascular integrity leads to microvascular hyperpermeability during sepsis. Recent studies highlight the critical role of pericyte loss in LPS-induced microvascular dysfunction and mortality. Friend leukemia virus integration 1 (Fli-1), a member of the ETS transcription factor family, is a key regulator in modulating inflammatory responses and survival in endothelial cells. However, the role of Fli-1 in pericytes and sepsis outcomes has not been investigated. In this study, we examined the hypothesis that Fli-1 regulates lung pericyte loss in cecal ligation and puncture (CLP)-induced sepsis. We showed that CLP-induced sepsis led to lung pericyte loss, as evidenced by decreased protein levels of the pericyte marker NG2 (24 hr post-CLP: 42.5 ± 7.9% reduction, 48 hr post-CLP: 63.4 ± 3.6% reduction; P < 0.05), and reduced pericyte density and pericyte/EC coverage in the lung. Inhibition of pericytes by CP673451, a PDGFR inhibitor, significantly exacerbated lung vascular leak (36.8 ± 20.9% increase; P < 0.05) and decreased survival (70% vs. 10%; P < 0.05) in CLP-induced sepsis. In addition, up-regulated Fli-1 mRNA and protein levels were found in lung pericytes from CLP-induced septic mice in vivo, and in LPS-stimulated lung pericytes in vitro. Importantly, specific knockout of Fli-1 in pericytes prevented CLP-induced lung pericyte loss in association with improved survival (0% vs. 40%; P < 0.05). Furthermore, CLP-induced lung pericyte pyroptosis as evidenced by elevated Caspase-1, Caspase-11, IL-1beta and IL-18 expression, were reversed in pericyte Fli-1 knockout mice. In cultured murine lung pericytes, knockdown of Fli-1 also blocked intracellular LPS-induced pyroptosis. This is the first study to demonstrate that Fli-1 modulates lung pericyte loss in CLP-induced sepsis via regulation of pericyte pyroptosis. Our findings suggest that Fli-1 is an important potential therapeutic target in sepsis. NIH GMS 1R01GM113995

170 Glycosphingolipid Catabolism Mediates Mesangial Cell IL-6 Production, Kamala Sundararaj, Jessalyn Rodgers, Tamara Nowling; MUSC.

The development of nephritis is a leading cause of morbidity and mortality in lupus patients. While the general pathophysiological progression of lupus nephritis is known, the molecular mediators and mechanisms are incompletely understood. Previously, we demonstrated that the glycosphingolipid catabolic pathway is elevated in the kidneys of MRL/lpr lupus mice and human lupus patients with nephritis. Specifically, the activity of neuraminidase (NEU) and expression of Neu1, an enzyme in the GSL catabolic pathway is significantly increased. To better understand the role and mechanisms by which this pathway contributes to the progression of LN, we analyzed the expression and effects of NEU activity on the function of MRL/lpr lupus prone mesangial cells (MCs). We demonstrate that NEU1 and NEU3 promote IL-6 production in MES13 MCs. Neu1 expression, NEU activity and IL-6 production are significantly increased in heat aggregated IgG (HA IgG) stimulated primary MRL/lpr lupus prone MCs and that blocking NEU activity inhibits IL-6 production. NEU1 and NEU3 expression overlaps IgG deposits in MCs in vitro and in renal sections from nephritic MRL/lpr mice. Compared to the lupus prone MCs, C57BL/6-derived MCs produced significantly increased, but several fold lower, levels of IL-6 in response to HA-IgG. Furthermore, our data show that NEU activity and IL-6 production were not significantly increased in MCs derived from C57BL/6 Neu1+/+ mice compared to MCs derived from C57BL/6 Neu1+/- MCs. Together, our results suggest that NEU activity mediates IL-6 production in lupus prone MCs possibly through an IgG-receptor complex signaling pathway.

171 Exosomes Derived From Retinal Pigment Epithelial Cells Mediate Cell-cell Communication Under Oxidative Stress Conditions in Age Related Macular Degeneration., Navjot Shah Saxena¹, Masaaki Ishii¹, Abłonczy Zsolt¹, Yutao Liu², James Chou³, Bärbel Rohrer¹; ¹Ophthalmology, MUSC, ²Cellular Biology & Anatomy, Augusta University, ³Pharmacy, MUSC.

Age-related macular degeneration (AMD) is the leading cause of visual impairment and blindness in the elderly worldwide, and the retinal pigment epithelium (RPE) appears to be a primary site of damage in subjects developing AMD. Persistent oxidative stress is recognized as one of the important underlying risk factors that lead to AMD pathology. There are two types of AMD- dry and wet. Dry AMD pathology occurs in patches that slowly coalesce. In
this study, we are trying to understand if these small areas of damage occur randomly, or whether this phenomenon might involve long-distance communication between a damaged and a healthy part of the RPE? And if so, what would mediate this long-distance communication? Exosomes are small membrane vesicles (30-150 nm) derived from endocytic compartments that are released into the extracellular environment by many cell types. Exosomes are thought to play an important role in cell-to-cell communication and influence both physiological and pathological processes. Exosomes were isolated from ARPE-19 and primary pig RPE grown as monolayers on transwells as highly polarized RPE by exoquick and analyzed by zetaview nanoparticle tracking analysis. Transfer assays between donor (normal and oxidatively stressed exosomes) and recipient cells were performed to study cell-cell communication. Our results showed that exosomes from oxidatively stressed donor cells have damaging effect on the recipient cells. These exosomes from oxidatively stressed donor cell were taken up much faster by the recipient cells as compared to control exosomes. Furthermore, mass spectrometry analysis showed that exosomes derived from control or oxidatively stressed cells exhibit different composition of proteins. One of the protein selected, based on its known function in tight junction stability, was HDAC6. Activity was further confirmed by HDAC6 activity assay and transfer assays using HDAC6 inhibitors. We conclude first, that exosomes may be involved in communicating stress messages to healthy RPE cells, and second, that these exosomes may contain HDAC6 which mediates its effects on naive RPE cells by compromising their ability to form a barrier, thereby contributing to AMD pathogenesis. VA 1101BX003050-01A2

172 Targeting Sphingosine Kinase 2/S1P Axis Decreases Immunosuppressive Potential of Myeloid Derived Suppressor Cells (MDSCs) and Improves Tumor Control, Shilpaket Chatterjee1, Paramita Chakraborty1, Selvam Panee Shanmugam2, Besim Ogretmen2, Shikhar Mehrotra1; 1Surgery, MUSC, 2Biochemistry and Molecular Biology, MUSC.

One of the major hindrances for harnessing therapeutic potential of T cells against tumor is the presence of immunosuppressive cells (MDSC, TAMs etc.) in the tumor microenvironment. Thus, strategies to boost the anti-tumor T cell function in vivo by overcoming immunosuppression holds merit. In the present study, we observed that MDSCs isolated from the tumor site have high expression of both Sphingosine kinase 1 (SphK1) and 2 (SphK2). However, genetic ablation of SphK2, but not SphK1, completely diminished the suppressive potential of MDSCs as evident by the increased proliferation and IFN-gamma secretion by T cells co-cultured with SphK2/- MDSCs. Similar dysfunction in suppressive potential was observed when MDSCs from ABC294640 (SphK2 specific inhibitor) treated tumor bearing mice was compared with vehicle control treated mice. The functional impairment of SphK2/- MDSCs also contributed to the better tumor control when melanoma epitope gp100 reactive CD8+ T cells were adoptively transferred to treat subcutaneously established B16 melanoma tumor bearing SphK2/- mice, as compared to those transferred in WT tumor bearing host. Studies delineating the underlying mechanisms revealed that SphK2/- MDSCs exhibit reduced expression of various suppressive molecules like arginase 1, TGF-beta and STAT3. Additionally, SphK2/- MDSCs also displayed reduced expression of HIF-1alpha - that in turn regulates MDSC suppressive function and metabolic commitment. Thus, intracellular level of S1P acts as an important signaling mediator regulating the suppressive potential of MDSCs. Our study unveils an important therapeutic potential of inhibiting SphK2/S1P axis in regulating MDSCs functionality to improve T cell mediated tumor control. Department of Surgery, MUSC, NIHR21CA198646, NIHPO1CA203628, NIHPO1CA154778
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