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 support boards will be available by 7:30 am on Friday, November 8th, with numbers corresponding to the abstract numbers in this program. Posters should be in place by 8:30 am and should remain in place until 12:00 noon. The times indicated for your session in the program are the times we expect that the judges will be in attendance. Do not remove your poster before 12:00 noon in case the judges need to make a return visit to your poster. If you have a scheduling conflict and can only be in attendance at your poster for a specific time, please let the Research Day 2013 Chairman, Dr Steven Kubalak, know immediately. You will have 10 minutes to present the information on your poster to the judges – the judges will also ask you questions. The judges will tell you when they have completed evaluating your poster: Please note, if your session is large, more than one team of judges will be operating and a second team of judges may need to visit your poster. Do not leave the area until the judges have indicated that judging of your poster is complete - if in doubt, ask them.

Oral Presentation Sessions:

Most of the oral sessions will be in the College of Health Professions (CHP) Building A at 151-A Rutledge Avenue. There is one session that will be held in Room 112 of the new Bioengineering Building (BE) and one session will be held in the Education Library Building, Room 107. The CHP building is accessible from Rutledge Avenue and also at the 2nd floor level from the Children’s Hospital-Rutledge Tower crosswalk over Ashley Avenue. Sessions will take place in the 2nd floor lecture rooms: 201, 202, 205, 206, and 207 and two sessions will be in rooms 105 and 106 on the first floor. Computer projection using a PC platform will be available. You can either save your presentation on a CD, to your homeroom or on a memory stick. Ensure that your presentation loads and runs correctly before you save it. Download your presentation into the SRD2013 file for your session on 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 8th. 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 and again at minus 1 minute. 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 covering the areas a) scientific approach to the subject of the research, b) clarity and quality of delivery, and c) handling of questions. 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. If, however, there is a conflict, then the judge affected will not score that presentation. Scores and evaluation sheets will be available to presenters after 4:00 pm on Friday, November 15th in the Graduate Studies office on the 1st floor of the Bioengineering Building. Any evaluation sheets not collected after two weeks will not be kept. The exception to this is for those who are not located on campus in Charleston. In those cases, please let the CGS office know and score sheets will be mailed to the address you gave when submitting your abstract. Please note, there will also be a team of judges selecting presentations for prizes in the following categories: Sigma Xi, Inter-Professional Research, VA Research, Health Disparities, Innovation, and Ethics 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 – 12:00 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. Coffee, soft drinks and cookies will also be available in the CHP Building Atrium from 12:00 pm.

Awards Ceremony:

The Awards Ceremony will begin at 4:30 pm in the Drug Discovery Auditorium. 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.

Door prizes, as part of the Vendor Show in the Gym, will also be awarded – for further information and for your door prize ticket, see the individual exhibitors tables at the Vendor Show. The door prize drawing will occur prior to the Awards Ceremony at approximately 4:30 pm.
ACKNOWLEDGEMENTS

The Perry V. Halushka Student 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 Student Research Day Endowment. This endowment will help to support the activities of Student Research Day in perpetuity. Specifically, the endowment will enable the University to:

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

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MUSC Research Day 2013 – SCHEDULE

THURSDAY, NOVEMBER 7th – Keynote Address
FRIDAY, NOVEMBER 8th – Research Presentations

POSTERS – Harper Wellness Center Gym, 8:30 am – 12:00 noon

ORALS – CHP Building A, 151-A Rutledge Ave, 1st Flr, Rms 105, 106; 2nd Flr, Rms 201 – 207
Bioengineering Building (BE), 1st Flr, Rm 112
Education Library (EL), 1st Flr, Rm 107

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Schedule of Oral Sessions:

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<th>12:00 pm</th>
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Keynote Address: Thursday, November 7th,
Drug Discovery Auditorium, 4:00 – 5:00pm

"Systems Biology of the Heart:
Devil in Detail, Heaven in Integration"

By:
Dr. Peter Kohl
Professor and Senior Fellow of the British Heart Foundation
Chair in Cardiac Biophysics and Systems Biology
National Heart & Lung Institute
Imperial College of London
LOCATION OF ORAL PRESENTATIONS – SESSIONS 13-21

College of Health Professions, Building-A, 151-A Rutledge Avenue, 1st and 2nd floors
Access either (see map below):
   a). from the Children’s Hospital-Rutledge Tower crosswalk over Ashley Avenue at the 2nd floor level, or
   b). through the Ashley Avenue Parking Garage to Rutledge Avenue to the main entrance on Rutledge.

Bioengineering Building, 1st Floor (Session 19)
Follow signs to Room BE 112, first floor of the new Bioengineering Building
MUSC Research Day 2013 - Program

POSTER PRESENTATIONS

Harper Wellness Center Gym

8:30 am - 12:00 noon
Session 1: Undergraduate – I #001-013
Session 2: Clinical/Prof/Masters – I #014-023
Session 3: Clinical/Prof/Masters – II #024-032
Session 4: Clinical/Prof/Masters – III #033-048
Session 5: Clinical/Prof/Masters – IV #049-064
Session 6: Clinical/Prof/Masters – V #065-080
Session 7: Clinical/Prof/Masters – VI #081-089
Session 8: PhD – I #090-099
Session 9: PhD – II #100-110
Session 10: PhD – III #111-121
Session 11: Postdocs/Residents/Fellows – I #122-129
Session 12: Postdocs/Residents/Fellows – II #130-142

ORAL PRESENTATIONS

CHP – College of Health Professions, Building-A – 1st and 2nd Floors
BE – Bioengineering Building, 1st Floor

Session 12: Undergraduate – II EL 105 12:00-2:45 #143-152
Session 13: Clinical/Prof/Masters – VII CHP 105 12:00-3:00 #153-163
Session 14: Clinical/Prof/Masters – VIII CHP 106 12:00-3:00 #164-174
Session 15: Clinical/Prof/Masters – IX CHP 205 12:00-2:45 #175-184
Session 16: PhD – IV CHP 206 12:00-2:30 #185-193
Session 17: PhD – V CHP 207 12:00-3:00 #194-204
Session 18: PhD – VI BE 112 12:00-3:00 #205-215
Session 19: Postdocs/Residents/Fellows – III CHP 201 12:00-2:30 #216-224
Session 20: Postdocs/Residents/Fellows – IV CHP 202 12:00-2:30 #225-233
SESSION 1: Undergraduate I

001 The Association of Stroke Risks By Population Density and REACH Telestroke Sites, Kelby Killoy, Daniel Lackland; Chemistry and Biochemistry, USC.

002 Effects of Fingolimoid Administration in a Genetic Model of Schizophrenia, Darius Becker-Krail1, Antonieta Lavin2; 1College of Charleston, 2COM, MUSC.

003 Dysfunctional Frontal-Striatal Connectivity in Tourette Syndrome, Logan T Dowdle1, William Devries2, Melanie Canterberry2, Nolan R Williams3, Colleen A Hanlon2; 1Biology/Neuroscience, CofC, 2Psychiatry & Behavioral Sciences, MUSC, 3Psychiatry & Neurology, MUSC.

004 REACH Telestroke and the Racial Disparity of Stroke Mortality Risk in South Carolina, Breanna L Grant; Health Promotion, Education, and Behavior, USC.

005 Hollywood Smiles Intervention + Handbook: A Post Program Analysis, George P Stamatiades1, Renata S Leite2; 1Biological Sciences, Clemson University, 2College of Dental Medicine, MUSC.

006 Telomere Attrition and the Effects of Environmental Quality on Aging in Alligator Mississippiensis, Eric M Benfield, Ben Parrott; MBES, MUSC.

007 Effects of Antimicrobial Exposures on Grass Shrimp, Palaemonetes Pugio, and Associated Vibrio Bacterial Density and Development of Antibiotic Resistance, John W Brooker1, Juita Martinez2, Jan Moore3, Marie Delorenzo4; 1College of Charleston, 2College of Charleston REU, 3National Oceanic and Atmospheric Administration.

SESSION 1B

008 Protein Disulfide Isomerase and Estrogen Receptor Alpha Interaction in MCF7 Cells Under Oxidative Stress, Chelsea A Snipes1, Tiffany Ancrum2, Steven Hutchens2, Danyelle M Townsend2; 1CofC, 2MUSC.

009 Alternative De-acylation of Lysine Residues, Bastien H Bacro-Duverger1, Brad Lees2, Elizabeth Inks2, Kalyan Chundru2, Ben Josey2, James Chou2; 1Clemson University, 2Drug Discovery and Biomedical Science, MUSC.

010 A Novel Technique for Rapid Oxygen Measurement Reveals the Suppression of Calcium Current Within Two Seconds of Hypoxia, John A Scaringi1, Angelo O Rosa2, Lars Cleemann2, Martin Morad4; 1Chemistry and Biochemistry, CofC, 2Regenerative Medicine, MUSC.

011 A Potentially Novel Role For Small Leucine Rich Proteoglycans In The Mature Collagen-Rich Extracellular Matrix Of Cardiac Valves, Olivia M Coco1, Loren E Dupuis2, Christine B Kern2; 1Honors College, CofC, 2Regenerative Medicine and Cell Biology, MUSC.

012 Evaluation of Scaffold-free Cell Aggregates for Vascular Construct Bioprinting, Cassandra P Awgulewitsch1, Agnes Nagy-Mehesz2, Zoltan Hajdu2, Richard P Visconti2; 1Biology, CofC, 2Regenerative Medicine and Cell Biology, MUSC.
013 Regulation of the Nkx2.5 Second Heart Field Enhancer Region By Ets Transcription Factors Pea3 and Erm, Meaghan E Flessa¹, Christopher D Clark¹, Anthony J Horton¹, Ann C Foley²; ¹Pediatrics, MUSC, ²Bioengineering, Clemson.

SESSION 2: Clinical-Professional-Masters I Social/Behavioral Sciences

014 Hollywood Smiles: An Oral Health Community Based Multi-Level Intervention, Krista Koch¹, Jabrenta Hubbard¹, George Stamatiades², Martina Mueller³, Renata Leite⁴; ¹Dental Medicine, MUSC, ²Biology, Clemson, ³Nursing, MUSC, ⁴Stomatology, MUSC.

015 The Importance of Older Driver Safety Education in the Tri-County Area, K E Wright, J Zamiela, D Lynch, H Glupker, E Camby, S Kelderhouse, L Price, C Walker, H Breland; Occupational Therapy, MUSC.

016 A Case Presentation of the Effects of Early Power Mobility on Overall Development of a Child Born with a Rare Genetic Neuromuscular Disorder, Emily G Cook¹, Brittany E Ambur¹, Michelle L Morse¹, Chad R Sanders², Megan M Stokes², Sara Kraft³, Patty Coker-Bolt¹; ¹Occupational Therapy, MUSC, ²Physical Therapy, MUSC.

017 Comparison of Blood Pressure and Cardiovascular Risk Factors in Children with and Without ADHD, Kimberly D Lewis¹, Doaa Al-Qaoud², Ibrahim Shatat³; ¹MUSC College of Medicine, ²MUSC, ³Pediatric Nephrology, MUSC.

018 In Utero Exposure to Tobacco Smoke, Subsequent Cardiometabolic Risks, and Metabolic Syndrome in Adolescents, Caroline M West¹, Kelly Hunt²; ¹COM, MUSC, ²Public Health Sciences, MUSC.

019 Can We Screen At-Risk Preterm Infants Quickly and Accurately? Clinical Utility of the Specific Test of Early Infant Motor Performance (STEP), Markey Y Haselden¹, Catherine A Syretz¹, Jessica A Thompson¹, Kathryn Hope², Patty Coker-Bolt¹, Jennifer Poon³, Dorothea Jenkins⁴; ¹Occupational Therapy, College of Health Professions, MUSC, ²Pediatrics, MUSC, ³Developmental Pediatrics, MUSC.

020 Competency-Based Patient Care Provider Disaster Training: The Center for Health Professional Training and Emergency Response, Jamal R Jones¹, Lancer A Scott², Judith Staub¹, Andrew C Seymore¹, Simon Watson², Wade Manaker²; ¹Medicine, MUSC, ²Emergency Medicine, MUSC.

021 The Influence of Race, Gender, and Socioeconomic Status on Self-Care Behaviors in Patients with Type 2 Diabetes, David M Cykert¹, Joni L Strom Williams¹, Leonard E Egede²; ¹Medicine, MUSC, ²Medicine, VAMC.

022 Multiple Risk Factor Management in Depressed Patients with Type 2 Diabetes Mellitus, Jugal M Dalal¹, Leonard E Egede²; ¹Medicine, MUSC, ²Medicine, Ralph H Johnson VA Medical Center.

023 Impact of Socioeconomic Status on Type 2 Diabetes Control in Non-Hispanic Blacks and Non-Hispanic Whites, Laven E Keitt Jr¹, Clara E Dismuke², Leonard E Egede²; ¹Medicine, MUSC, ²Medicine, VAMC.

SESSION 3: Clinical-Professional-Masters II Social/Behavioral Sciences

024 Seeking Care and Antibiotic Expectations with Cough Related Illness in Primary Care, Shannon A Looney¹, Susannah Brown¹, Kevin Floyd¹, Brittany Watson¹, William J Hueston²; ¹COM, MUSC, ²Family Medicine, MUSC.

025 Prevalence of Antenatal Depression and Anxiety, Cameron T Bell, Maddie Caballero, Constance Guille; Psychiatry, MUSC.
Sensory Modulation Strategies Employed By Community-Dwelling Adults with Severe Mental Illness, Pamela L Vesely, Rachel A Boyd, Ella H Hyatt, Sara E Jensen, Kelley M Knoebel, Jessica A Martin, Elizabeth F Stuber, Nancy E Carson; Occupational Therapy, MUSC.

Relationship Between Efficiency of Arm Movement and Patient-Perceived Recovery After Stroke, Blair H Stec¹, Patricia M Pierson¹, Michelle L Woodbury²; ¹Occupational Therapy, MUSC, ²Rehabilitation Research, Ralph Johnson VAMC.

The Effects of a Custom Virtual Reality Gaming System on the Movement of the Paretic Upper Extremity in Stroke Patients, Elaina A Gaither¹, Rebecca M Patten¹, Alison B Gilchrist¹, Michelle L Woodbury²; ¹Occupational Therapy, MUSC, ²Rehabilitation Research, Ralph Johnson VAMC.

Perceived Recovery of Stroke As It Relates to Activity Participation, Whitney N Weigold¹, Anna Blair Price¹, Michelle L Woodbury²; ¹Occupational Therapy, MUSC, ²Rehabilitation Research, Ralph Johnson VAMC.

Pre and Post Injury Alcohol Consumption and Smoking Status Among Acute Spinal Cord Injury (SCI) Participants, Janice F Davis¹, James S Krause²; ¹Medicine, MUSC, ²Health Professions, MUSC.

The Impact of Amount of Cannabis Use on Cognitive Function in Adolescents, Jessica B Lydiard¹, Kevin M Gray²; ¹Psychiatry and Behavioral Science, MUSC, ²Clinical Neuroscience, MUSC.

Plasma Homocysteine Levels As a Putative Marker of N-Acetylcysteine Compliance in Cocaine-Dependent Patients, Camilo F Mateus, Steven D LaRowe, Robert J Malcolm; Psychiatry and Behavioral Science, MUSC.

Effect of SPARC/Exon-2 Deletion on Murine Myocardial Collagen Processing, Ruth E Salas¹, Yuhua Zhang², Bradshaw Amy²; ¹Medicine, MUSC, ²Gazes Cardiac Research Institute, MUSC.

The Role of C3a and C3aR in Acute Cardiac Rejection, Gabriel C Segarra, Carl Atkinson; Microbiology and Immunology, MUSC.

Does Over Reliance on Automated Cardiac Function Analysis Have an Impact on Function Reporting in Patients with Acute Chest Pain?, Nicholas S Honko, Nelson Seabrook, Pal Suranyi; Radiology, MUSC.

Developing a Normal Standard Left Ventricular Wall Motion Assessment with Cardiac MRI Using a Novel Thresholding-Based Post-Processing Algorithm, Rodman L Singleton¹, Matt Duffin¹, Pal Suranyi²; ¹COM, MUSC, ²Radiology, MUSC.

Impact of Maternal Vitamin D Status on Mineralized Tissue, Ann G Kelly, Judy Shary, Myra Ebeling, Carol Wagner, Susan Reed; Pediatrics, MUSC.

Circulating Fibroblast Precursors and Their Role in Metastatic Sarcoma, Dayvia A Laws¹, Andrew S Kraft², Lee R Leddy³, Amanda C LaRue¹; ¹Pathology, MUSC, ²Medicine, MUSC, ³Orthopaedic Surgery, MUSC.

The Analysis of Transforming Growth Factor Beta Signaling in Mouse Thoracic Aortic Fibroblasts, Lee C Morris, Adam W Akerman, Robert E Stroud, Risha Patel, Jeffrey A Jones; COM, MUSC.
040 Exploring Pim Kinases As a Biomarker for Treatment Response and Overall Outcome in Multiple Myeloma, Logan N Roof, John Lazarchick, Margaret Romano, Boding Zhang, Jagadish Kummetha, Tricia Bentz, Terri Matson, Yubin Kang; 1COM, MUSC, 2Pathology, MUSC, 3Hematology/Oncology, MUSC, 4Hollings Cancer Center Clinical Trials Office.

SESSION 4B:

041 Functional Analysis of the Woronin Body Protein in Aspergillus Fumigatus, Sarah Mushtaq, Christopher Gehrke, Shannon K Esher, Praveen R Juvvadi, William J Steinbach; 1COM, MUSC, 2Pediatrics, Pediatric Infectious Diseases, Duke, 3Molecular Genetics and Microbiology, Duke, 4Pediatrics, Pediatric Infectious Diseases, Molecular Genetics and Microbiology, Duke.

042 Anthropometric Variables and Body Composition Data As Predictors for Adiponectin Levels in an Overweight or Obese Youth Population, Callie S Osborne, Sarah Stein, Janet Carter, Melissa Henshaw; Pediatric Cardiology, MUSC.

043 Secondhand Tobacco Smoke Exposure and Exacerbation Severity Among Children Hospitalized for Asthma, Nils Shirley, Annie L Andrews, Karen Wilson, Michelle Robinson, Elizabeth Ojukwu; 1COM, MUSC, 2Pediatrics, MUSC.

044 The Effects of Maternal Phthalate and Bisphenol A Exposure on Fetal Genital Development, Rebecca R Fulmer, Lori Cruze, Louis J Guillette, Roger B Newman; 1COM, MUSC, 2OB/Gyn, MUSC.

045 CELF1 Controls ADAM19 mRNA Expression in Oral Squamous Cell Carcinoma, Mehul Z Patel, Reniqua House, Viswanathan Palanisamy; Craniofacial Biology, MUSC.

046 Increased Degradation of Amyloid-beta Via Uncharacterized Acidic Proteolytic Pathway, Robert J Baranello, Trenton Large, Vasudevaraju Padmaraju, Debomoy K Lahiri, Nigel H Greig, Kumar Sambamurti; 1Neurosciences, MUSC, 2SC Governer's School for Science and Math, 3Psychiatry, Indiana University School of Medicine, 4Drug Design & Development, National Institute on Aging.

047 Effects of the ACT-1 Peptide in Models of Age-related Macular Degeneration, Elisabeth C Obert, Beth Coughlin, Kannan Kunchithapautham, Gautam Ghatnekar, Baerbel Rohrer; 1Neurosciences, MUSC, 2Microbiology and Immunology, MUSC, 3Ophthalmology, MUSC, 4First String Research, Inc.

048 Correlation of ACT1 Administration to Post Surgery Macrophage Phenotype in Skeletal Muscle, Jason A Kopp, Michael J Yost; Surgery, MUSC.

SESSION 5: Clinical-Professional-Masters IV Basic/Clinical Sciences

SESSION 5A:

049 Does a Short Infant Motor Test, The STEP, Correlate with Evidence of Brain Injury By MRS and Later Outcome At 12 Months?, Allison Johnson, Jamie Beckett, Patty Coker-Bolt, Kathryn Hope, Truman Brown, Denise Mulvihill, Dorothea Jenkins; 1Occupation Therapy, MUSC, 2Pediatrics, MUSC, 3Radiology and Radiological Sciences, MUSC.

050 Effects of Social Determinants on Home Blood Pressure Monitoring After Stroke, Kandace A Joye, Daniel T Lackland; 1COM, MUSC, 2Neuroscience, MUSC.

051 The Effect of Home Blood Pressure Monitoring on Recurrent Stroke, Gregory R Franklin, Andrea Boan, Daniel Lackland; 1MUSC, 2Neurosciences, MUSC.
Comparing Ipsilesional and Contralesional Upper Extremity Motor Deficits in Patients with Left or Right Hemisphere Stroke During Reaching Tasks, Danielle C Cardell\(^1\), Lyndsay J Berger\(^1\), Kalyn L Cogswell\(^1\), Michelle L Woodbury\(^2\); \(^1\)Occupational Therapy, MUSC, \(^2\)Rehabilitation Research, Ralph Johnson VAMC.

DKI Patterns of Brain Plasticity in Normal Older Adults Before and After Cognitive Training, Lara Hewett, Fatima Falangola, Rachael Deardorff, Cliff Chan; Center for Biomedical Imaging, MUSC.

Effects of Cocaine Dependence and Childhood Trauma on the Noradrenergic System, Jenna L Hislop\(^1\), Megan M Moran-Santa Maria\(^2\); \(^1\)College of Medicine, MUSC, \(^2\)Psychiatry, MUSC.

High Impulsivity Predicts Non-Abstinence in Marijuana-Dependent Adolescents, Jessica Bentzley, Kevin M Gray; Clinical Neurosciences, MUSC.

The Specific Test of Early Infant Motor Performance (STEP): Psychometric Testing and Factor Analysis, Christine E Ochsner\(^1\), Kristin M Olbrich\(^1\), Patricia Coker-Bolt\(^1\), Dorothea D Jenkins\(^2\), Kathryn E Hope\(^2\), Viswanathan Ramakrishnan\(^3\); \(^1\)Occupational Therapy, MUSC, \(^2\)Pediatrics, MUSC, \(^3\)Public Health Sciences, MUSC.

SESSION 5B:

Blood Pressure Guideline Adherence In Patients With Severe Cerebrovascular Disease, Guilherme B F Porto\(^1\), Alejandro M Spiotta\(^2\), Edward C Jauch\(^3\); \(^1\)COM, MUSC, \(^2\)Neurosurgery, MUSC, \(^3\)Emergency Medicine, MUSC.

Noncontrast Brain CT Detection of Subdural Hematomas: Do Orthogonal Reconstructions Improve Sensitivity?, William C Mostertz\(^1\), Timothy J Amrhein\(^2\), Zoran Rumboldt\(^2\); \(^1\)Medicine, MUSC, \(^2\)Radiology, MUSC.

Total Knee Arthroplasty with Exparel\(^\text{®}\) Provided Improved Pain Control, Shorter Length of Hospital Stay As Compared to Total Knee Arthroplasty with Femoral Nerve Catheter, Ashley B Anderson\(^1\), Brian Burnikel\(^2\), Brandon Broome\(^2\); \(^1\)Orthopaedics, Hawkins Foundation, \(^2\)Orthopaedics, Steadman Hawkins Clinic of the Carolinas.

High Dose RTMS Treatment of the Prefrontal Cortex: Tapping Into the Pain Modulation Pathway, Eliza L Barnwell\(^1\), Jeffrey Borckhardt\(^2\), Matthew Schmidt\(^2\), Kathryn Beaver\(^2\), Mark George\(^2\), Christopher Pelic\(^3\); \(^1\)COM, MUSC, \(^2\)Brain Stimulation Laboratory, MUSC, \(^3\)Ralph H. Johnson VA Medical Center.

Effects of Transcranial Alternating Current Stimulation on Pain Perception, Christian D Baker\(^1\), Jeffrey J Borckardt\(^2\); \(^1\)COM, MUSC, \(^2\)Psychiatry, MUSC.

Variance in White Matter Diffusion in Cocaine Users, Bradley G Sieckman\(^1\), Colleen A Hanlon\(^2\); \(^1\)COM, MUSC, \(^2\)Psychiatry, MUSC.

Lower Cortical Excitability and Cortical Atrophy in Cocaine Users: Does a Correlation Exist?, Julia S West\(^1\), Colleen A Hanlon\(^2\), Mark S George\(^3\); \(^1\)Medicine, MUSC, \(^2\)Neurosciences, MUSC, \(^3\)Psychiatry, MUSC.

Correlation Between Regional Grey Matter Loss and the Extended Disability Status Scale in Multiple Sclerosis Patients Using Voxel-Based Morphometry, Alexandra Parashos, Maria V Spampinato; Radiology, MUSC.
SESSION 6A:

065 Characteristics of Pediatric Patients Enrolled in Diabetes Transition Program, Michelle Khawaja\textsuperscript{1}, Katherine Lewis\textsuperscript{2}, Remberto Paolo\textsuperscript{2}, Deborah Bowby\textsuperscript{2}; \textsuperscript{1}COM, MUSC, \textsuperscript{2}Pediatric Endocrinology, MUSC.

066 Prevalence of Chronic Kidney Disease By Race in Type 2 Diabetes Mellitus, Vandene T Miller\textsuperscript{1}, Joni L Strom Williams\textsuperscript{1}, Leonard E Egede\textsuperscript{2}; \textsuperscript{1}Medicine, MUSC, \textsuperscript{2}Medicine, VAMC.

067 The Role of Patient-Centered Care and Health Literacy in Patients with Type 2 Diabetes, Bradley C Ketner\textsuperscript{1}, Cheryl P Lynch\textsuperscript{2}, Leonard E Egede\textsuperscript{2}; \textsuperscript{1}Medicine, MUSC, \textsuperscript{2}Medicine, VAMC.

068 The Effects of Generalized Anxiety and Stress on Cardiovascular Disease and Self-Care Behaviors in Patients with Type II Diabetes, Amartha N Ogburu-Obonnaya\textsuperscript{3}, Cheryl P Lynch\textsuperscript{2}, Joni L Strom Williams\textsuperscript{2}, Leonard E Egede\textsuperscript{2}; \textsuperscript{1}Medicine, MUSC, \textsuperscript{2}Medicine, VAMC.

069 Pediatric Metabolic Syndrome Study: Is Waist Circumference a Better Indicator of Pre-Diabetes Than BMI?, Brielle Weinstein\textsuperscript{1}, Janet Carter\textsuperscript{2}, Melissa Henshaw\textsuperscript{2}, Sarah Stein\textsuperscript{2}; \textsuperscript{1}COM, MUSC, \textsuperscript{2}Pediatric Cardiology, MUSC.

070 Liver Estrogen Signaling and the Metabolic Response to Dietary Fats and Carbohydrates, Eric K Singhi\textsuperscript{1}, Melissa Martinez\textsuperscript{2}, John Stafford\textsuperscript{2}; \textsuperscript{1}COM, MUSC, \textsuperscript{2}Vanderbilt University Medical Center.

071 G-Protein Signalling Regulator 2 and Role in Islet Cell Proliferation and Insulin Secretion, Rachel L Jester, Hongjun Wang, Zhang Yong; COM, MUSC.

072 Racial Differences in the Risks Associated with Early Graft Loss in Adult Kidney Transplant Recipients, Kevin Douglass\textsuperscript{1}, David J Taber\textsuperscript{2}; \textsuperscript{1}COM, MUSC, \textsuperscript{2}Surgery, MUSC.

SESSION 6B:

073 NEDD:MICAL Interactions Lead to Posttranslational Modification of MICAL in HNSCC Cells, Philip T Sobash, Casey O Holmes, Jessica A Tiedeken, Steven A Rosenzweig; Molecular and Cellular Pharmacology & Experimental Therapeutics, MUSC.

074 Phosphorylation Dynamics in Osteoblasts Stimulated with Parathyroid Hormone (PTH 1-34), Sukhi K Guram, Lauren Ball, Grace R Williams; Pharmacology, MUSC.

075 Hematopoietic Contribution to the Periodontal Fibroblast Population, James P Wilson\textsuperscript{1}, Richard P Visconti\textsuperscript{2}, Zoltan Hajdu\textsuperscript{2}; \textsuperscript{1}Dental Medicine, MUSC, \textsuperscript{2}Regenerative Medicine and Cell Biology, MUSC.

076 The Hematopoietic Origin of Resident Progenitor Cells in the Periodontal Ligament, Zakery R James, Richard P Visconti, Zoltan Hadju; Dental Medicine, MUSC.

077 The Impact of Body Mass Index and Kidney Donor Risk Index on Clinical Outcomes in Renal Transplant Patients, Elizabeth C B Myers\textsuperscript{1}, Dave Taber\textsuperscript{2}, Charles Bratton\textsuperscript{2}, John W McGillicuddy\textsuperscript{2}, Kenneth D Chavin\textsuperscript{2}, Prabhakar Baliga\textsuperscript{2}; \textsuperscript{1}Transplant Surgery, MUSC, \textsuperscript{2}Surgery, MUSC.

078 Can the Optimal Immunosuppression Regimen Be Determined in Aged Kidney Transplant Recipients?, Kristen M Brown\textsuperscript{1}, David Taber\textsuperscript{2}, Kenneth Chavin\textsuperscript{2}, Prabhakar Baliga\textsuperscript{2}; \textsuperscript{1}COM, MUSC, \textsuperscript{2}Surgery, MUSC.
### SESSION 7: Clinical-Professional-Masters VI Basic/Clinical Sciences

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<td>Clark D Sealy&lt;sup&gt;1&lt;/sup&gt;, Will Hand&lt;sup&gt;2&lt;/sup&gt;; &lt;sup&gt;1&lt;/sup&gt;COM, MUSC, &lt;sup&gt;2&lt;/sup&gt;Anesthesiology, MUSC.</td>
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### SESSION 7: Clinical-Professional-Masters VI Basic/Clinical Sciences

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<td>Robert A Sharpe&lt;sup&gt;1&lt;/sup&gt;, Elizabeth D Sharpe&lt;sup&gt;2&lt;/sup&gt;; &lt;sup&gt;1&lt;/sup&gt;Ophthalmology, MUSC, &lt;sup&gt;2&lt;/sup&gt;Ophthalmology, Ralph H Johnson VAMC.</td>
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### SESSION 8: PhD I: Years 1-2

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092 Recovery From Forward Masking of Vowels and Consonants: Effects of Age and Hearing Loss. William J Bologna, Daniel Fogerty, Jayne B Ahlstrom, Judy R Dubno; Otolaryngology - Head and Neck Surgery, MUSC, Communication Sciences and Disorders, USC.

093 Microglial Refinement of the Auditory Nerve in the Postnatal Mouse Inner Ear. LaShardai N Conaway, Yazhi Xing, Juhong Ju, Nancy Smythe, Jeremy Barth, Hainan Lang; Pathology and Laboratory Medicine, MUSC, Regenerative Medicine and Cell Biology, MUSC.

094 Lymphodepletion-induced IL-12 Enhances Tc17 Cell Plasticity and Antitumor Activity. Jacob S Bowers, Sreenath Kundimi, Michelle H Nelson, Logan W Huff, Stefanie R Bailey, Carolyn E Rogers, Kristina Schwartz, Chrystal M Paulos; Microbiology & Immunology, MUSC.

095 Using Novel Small Molecule LSD1 Inhibitors to Understand Mechanisms of Obesity-related Breast Cancer Pathogenesis. Steven L Holshouser, Craig J Kutz, Boobalan Pachiayappan, Patrick Woster; Drug Discovery, MUSC.

096 (Bis)biguanidine Oligoamine Sustain Myocardial Function Following Ischemia-reperfusion Injury in Isolated Perfused Rat Hearts. Craig J Kutz, Sverre E Aune, Patrick Woster, Donald R Menick; Drug Discovery, MUSC, Gazes Cardiac Research Institute, MUSC, South Carolina Clinical and Translational Research Institute, MUSC.

097 Can We Focally Excite Discrete Brain Circuits Non-invasively?: A Pilot Study Using Interleaved Transcranial Magnetic Stimulation (TMS)/fMRI to Assess the FMRI BOLD Response Before and After High Frequ. Bashir W Badran, Joseph J Taylor, William Devries, Xingbao Li, Colleen A Hanlon, Mark S George; Psychiatry & Behavioral Sciences, MUSC.

098 Reduced Actin Polymerization in Lungs of IQGAP1-Knockout Mice: Implication for Scleroderma Interstitial Lung Disease. Tanjina Akter, Sybil L Nelson, Ilia Atanelishvili, Alvaro Martos, Richard M Silver, Galina S Bogatkevich; Rheumatology & Immunology, MUSC, Hospital Universitario 12 de Octubre, Madrid, Spain.

099 Using Stem Cell Fate to Determine Potential Adverse Effects of Oil/Dispersant Exposure: Crude Oil Obesogenicity. Alexis Temkin, Debra Ellisor, John Baatz, Satomi Kohno, Lou Guillette, Demetri Spyropoulos; MBES, MUSC, MBES, Pathology, MUSC, Biochemistry and Molecular Biology, MUSC, Obstetrics and Gynecology, MUSC, Pathology, MUSC.

SESSION 9: PhD II: Years 3+


101 Effects of Prolonged CB1 Receptor Activation During Adolescence in the Prefrontal Cortex of Dysbindin-1 Null Mutant Mice. Jose I Pena Bravo, Antonieta Lavin; Neurosciences, MUSC.

102 Statistical Methods for Dealing with Overdispersion in Modeling Count Responses. Elizabeth H Payne, Mulugeta Gebregziabher; Biostatistics, MUSC.


104 Environmental Determinants of Systemic Lupus Erythematosus (SLE). Delia C Voronca, Rachel Carroll, Andrew Lawson, Diane Kamen, John Vena; Biostatistics, MUSC.
Assessing the Prevalence and Effect of Phthalate Exposure During Gestation, Abby M Goodson1, John W Brock2, Lori Cruze3, John R Kucklick4, Louis J Guillette5; Marine Biomedicine and Environmental Science, MUSC, 2Chemistry/Environmental Studies, Warren Wilson College, 3Obstetrics and Gynecology, MUSC, 4Chemical Sciences Division, NIST.

Longitudinal Impact of Mental Health Outpatient Care on Healthcare Cost For Individuals with Type 2 Diabetes, Rebekah J Walker1, Mulugeta Gebregziabher2, Yumin Zhao3, Clara E Dismuke4, Kelly J Hunt2, R. Neal Axon5, Leonard E Egede6; 1Health Professions, MUSC, 2Medicine, MUSC, 3VAMC, 4Medicine, VAMC.

The Role of Health Literacy in African Americans with Type 2 Diabetes, Brittany L Smalls1, Delia C Voronca2, Leonard E Egede3; 1MUSC, 2Statistics, MUSC, 3Medicine, VAMC.

Developmental Mechanisms of Mitral Valve Prolapse, Kimberly Sauls1, Annemarieke de Vlaming1, Katherine Williams1, Robert Levine2, David Milan3, David Peal3, Sue Slaugenhaupt4, Roger Markwald1, Russell Norris1; 1Regenerative Medicine, MUSC, 2Cardiology, Harvard Medical School, 3Medicine, Harvard Medical School, 4Neurology, Harvard Medical School.

Effect of the Premalignant and Tumor Microenvironment on Immune Cell Cytokine Production in HNSCC, Sara D Johnson1, Corinne Levingston2, Rita Young2; 1Microbiology and Immunology MUSC, 2Medical Research Service, VAMC.

The Effect of α-connexin Terminal Peptide 1 (ACT1) in a Model of Acute Lung Injury (ALI), Kristoffer N Rodriguez, Carl Atkinson; Microbiology & Immunology, MUSC.

SESSION 10: PhD III: Years 3+

From Parkinson’s Disease To Addiction: Preclinically Evaluating Subthalamic Nucleus Inactivation As a Cocaine Addiction Treatment, Brandon S Bentzley, Gary Aston-Jones; Neuroscience, MUSC.

Oxytocin Reduces the Motivation to Self-administer Methamphetamine in a Novel Within-session Behavioral-economic Paradigm: Male-female Comparisons, Brittny M Cox, Brandon S Bentzley, Carmela M Reichel, Ronald E See, Gary Aston-Jones; Neurosciences, MUSC.

Alternative Complement Pathway Deficiency Ameliorates Chronic Smoke-Induced Functional and Morphological Ocular Injury, Alex S Woodell1, Beth Coughlin2, Kannan Kunchithapautham2, Sarah Casey3, Tucker Williamson3, Carl Atkinson3, Bryan Jones4, Barbel Rohrer1; 1Neurosciences, MUSC, 2Ophthalmology, MUSC, 3Microbiology and Immunology, MUSC, 4Moran Eye Center, University of Utah.

The Effect of Soluble MICB on NKG2D-Mediated Regulation of NK Cell Anti-Tumor Immunity, Fahmin Basher, Shengjun Lu, Gang Xiao, Jennifer D Wu; Microbiology & Immunology, MUSC.

NAC and Vit D Treatment Alters Immunologic Sequelae in Neonatal Hypoxic Ischemic Rats, Danielle W Lowe1, Laura G Rollins2, Jamie L Fraser3, Xingju Nie4, Jessica Perkel5, Bruce Hollis4, Inderjit Singh4, Dorothea Jenkins4; 1MBIM, MUSC, 2Clinical Psychology, UMASS, 3Pediatrics, National Medical Center, 4Pediatrics, MUSC, 5COM, MUSC.

Determining the Role of Sphingosine-1-Phosphate in Gemcitabine Resistant Pancreatic Cancer, Clayton S Lewis, Charles D Smith; Drug Discovery and Pharmaceutical Sciences, MUSC.

Scaffold-free Tissue Engineering: Organization of the Tissue Cytoskeleton and Its Effects on Tissue Shape, Caitlin A Czajka1, Agnes Nagy Mehesz2, Thomas C Trusk1, Michael J Yost2, Christopher J Drake1; 1Regenerative Medicine & Cell Biology, MUSC, 2Surgery, MUSC.
SESSION 11: Postdocs-Residents-Fellows I

122 Patterns Of Physical Activity in African Americans With Type II Diabetes Mellitus, Mukoso N Ozieh¹, Clara E Dismuke², Delia C Voronca³, Leonard E Egede¹; ¹Medicine, MUSC, ²Research, VA, ³Public Health Sciences, MUSC.

123 The RNA Binding Protein Tristetraprolin Plays a Protective Role During Periodontal Bone Loss, Heidi M Steinkamp, Mary Gray, Hong Yu, Keith Kirkwood; Craniofacial Biology, MUSC.

124 Gender Differences in Neural Response to Mesolimbic Stimulation: An Interleaved TMS-BOLD Imaging Study, Melanie Canterberry, William DeVries, Joseph J Taylor, Mark S George, Colleen A Hanlon; Psychiatry, MUSC.

125 ROCK-dependent Ezrin-Radixin-Moesin Phosphorylation Modulates Actin Cytoskeleton in Noise-induced Hair Cell Death, Yu Han, Jun Chen, Su-Hua Sha; Pathology and Laboratory Medicine, MUSC.

126 Elucidation on the Non-Canonical Role of Class Ila Histone Deacetylases, Lillianne G Harris, Sabina Wang, Santhosh K Mani, Donald R Menick; Cardiology, MUSC.

127 Discovery of a Novel Cyclic Peptide Based Inhibitor for LSD1 Enzyme, Isuru R Kumarasinghe, Patrick M Woster; Pharmacy, MUSC.

128 Transcrptome and Proteome Discovery of the RNA-binding Protein CELF1 Regulon in Oral Squamous Cell Carcinoma, Reniqua P House¹, Sudha Talwar¹, Jennifer Bethard², Lauren Ball², Viswanathan Palanisamy¹; ¹Craniofacial Biology, MUSC, ²Cell and Molecular Pharmacology, MUSC.

129 Streamlining MRI Liver Reports for Hepatocellular Carcinoma By Using LI-RADS, Matthew R Gillott, Munazza Anis; Radiology, MUSC.

SESSION 12: Postdocs-Residents-Fellows II

SESSION 12A

130 Out of Hospital Cardiac Arrest: A Single Center Experience, Nathaniel Richards¹, Thomas Todoran², Robert Yoe³; ¹Internal Medicine, MUSC, ²Cardiology, Internal Medicine, ³Cardiology, MUSC.
131 Evaluation of Hospitalized Patients on a Family Medicine Inpatient Service Based on Insurance Status, Maribeth Porter1, Peter J Carek1, Vanessa A Diaz1, Lori M Dickerson1, Jennifer Gavin1, William J Hueston1, Ashleigh E Zacarias2; 1Family Medicine, MUSC, 2Family Medicine, Trident Medical Center.

132 Ketamine's Effect on Cravings for Alcohol in a Population of Veterans with Depression and Alcohol Dependence, Erin B Seery1, Robert Glenn1, Dennis Orwat1, Christopher Pelic2, Tamas Szabo3, Paul Everman2, Mark Hamner2, Robert Malcom1; 1Psychiatry, MUSC, 2Psychiatry, VAMC, 3Anesthesia, VAMC.

133 Predictors of Self-Care Behaviors and Medication Adherence in African Americans with Type 2 Diabetes, Joni S Williams, Cheryl P Lynch, Delia C Voronca, Leonard E Egede; Medicine, MUSC.

134 Peroxiredoxin 1 (Prdx1) Inhibits Activated Stroma-Associated Fibroblasts Phenotype Preventing Breast Cancer Progression, Agnieszka Jezierska-Drutel1, Carola A Neumann2; 1Biochemistry & Molecular Biology, MUSC, 2Pharmacology and Chemical Biology, University of Pittsburgh Cancer Institute.

135 Fli-1 Transcription Factor Impacts Lupus Nephritis Development By Regulating Expression of IL-6 in Kidney Endothelial Cells, Shuzo Sato, Mara Lennard Richard, Danielle Brandon, Eva Karam, Zhang John; Rheumatology and Immunology, MUSC.

136 Liver Injury Following Hemorrhagic Shock/Resuscitation: Mechanisms and Targeted Therapy with Minocycline, Andaleb Kholmukhamedov1, Christoph Czerny2, John J Lemasters1; 1Drug Discovery, MUSC, 2Trauma Surgery, J.W. Goethe University.

SESSION 12B

137 Effect of Coronary Rotational Atherectomy in Dominant Vessels Without Use of Temporary Pacemaker After Preemptive Treatment with Theophylline, Navin Nikam, Monique Sandhu, James Hadstate, Arasi Maran, Valerian Fernandes; Cardiology, MUSC.

138 Radial Versus Femoral Access in Rotational Atherectomy of the Diseased Coronary Artery, Monique K Sandhu, Abukarasi Maran, Navin Nikam, Valerian Fernandes, James Hadstate, Frederick Funke; Cardiology, MUSC.

139 Alterations of Sensory Hair Cells Following AAV-miR96 Application to Postnatal Mouse Cochleae, Yazhi Xing1, Michelle Stoller2, LaShardai Conaway1, Jianning Zhang1, Donna Fekete2, Hainan Lang1; 1Pathology and Laboratory Medicine, MUSC, 2Biological Sciences, Purdue University.

140 Intracellular Amyloid Degradation Mechanisms That Paradoxically Increase Amyloid Beta Protein Production Upon Gamma-secretase Inhibition, Padmaraju R Vasudeva1, Baranello Robert3, Barnwell Elisa1, Pacheco-Quinto Javier2, Eckman Elizabeth2, Sambamurti Kumar1; 1Neuroscience, MUSC, 2Atlantic Health System, Morristown, NJ.

141 MTOR and PKCδ Regulate Agonist Stimulated Expression of Connective Tissue Growth Factor in Adult Cardiac Muscle Cells, Kamala p Sundararaj1, Dorea L Pleasant2, Sundaravadivel Balasubramanian2, Dhandapani Kuppuswamy2; 1Medicine, MUSC, 2Cardiology, MUSC.

142 Interaction of Caspases and RIP Kinases Modulates Noise-induced Apoptotic and Necrotic Outer Hair Cell Death Pathways, Jun Chen, Hong-Wei Zheng, Su-Hua Sha; Pathology and Laboratory Medicine, MUSC.
ORAL PRESENTATIONS

College of Health Professions (CHP) Building A: 12:00 – 3:00 pm
Bioengineering Building (BE) Room 112: 12:00 – 3:00 pm
Education Library Building (EL) Room 107 12:00 – 2:45 pm

SESSION 13: Undergraduate II: 12:00 – 2:45 pm: EL 107

12:00 - 12:15
143 Investigating the Interaction Between TBX1 and PRRX1a, Kamryn J Kant¹, Michael J Kern²; ¹College of Charleston, ²Regenerative Medicine and Cell Biology, MUSC.

12:15 - 12:30
144 Small Leucine Rich Proteoglycans (SLRPs) Play a Critical Role in the Development of the Mature Extracellular Matrix of the Murine Heart, Elizabeth Y Brown¹, Loren E Dupuis², Christine B Kern³; ¹Hampton University, ²Regenerative Medicine and Cell Biology, MUSC.

12:30 - 12:45
145 Transforming Growth Factor Alpha and Hypoxia Modulate Neurosphere Formation in Vitro of Auditory Nerve Cells, Luke T Havens¹, Hainan Lang², Yazhi Xing²; ¹Biology, USC, ²Pathology, MUSC.

12:45 - 1:00
146 Age Specific Patterns of Stroke Mortality with Geographic Location of REACH Telestroke Sites, Stacey S Dallas¹, Daniel T Lackland²; ¹Claflin University, ²MUSC.

1:00 - 1:15
147 The Effect of Static Strain Conditioning on Biochemical and Biomechanical Properties in Living Tissue Engineered Toroid Constructs, Moreira M Alexandra¹, Klatt Sandra¹, Shazly Tarek², Zou Boran², Miller Ian², Argraves W Scott¹; ¹Regenerative Medicine & Cell Biology, MUSC, ²USC.

1:15 – 1:30 BREAK

1:30 - 1:45
148 Tissue Engineering with Tri-Culture Spheroids, Katherine I Driscoll¹, Michael J Yost²; ¹Chemistry and Biochemistry, USC, ²Surgery, MUSC.

1:45 - 2:00
149 The Role of Sphingosine 1-phosphate in Polymorphonuclear Leukocyte Functions, Haley A Woodward¹, Titus A Reaves², Samar Hammad²; ¹Biology, UNCW, ²Regenerative Medicine and Cell Biology, MUSC.

2:00 - 2:15
150 Importance of Glutathione S-transferase P1-1 on Bone Marrow Regulation, JennaMarie G Baker¹, Jie Zhang², Zhiwei Ye³, Kenneth D Tew¹; ¹SCGSSM, ²Pharmacology, MUSC.

2:15 - 2:30
151 Molecular Mechanisms of Etiology in Pre-eclampsia, Katherine Sen¹, Elena Rivers², Anthony Horton³, Angela F Hawk⁴, Christopher Robinson⁵, Ann C Foley⁴, Kyu-Ho Lee⁶; ¹Clemson University, ²College of Charleston, ³USC Greenville, ⁴Obstetrics and Gynecology, MUSC, ⁵Bioengineering, Clemson, ⁶Pediatrics, MUSC.
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<td>Angelynn F Glover, Sambandam Yuvaraj, Sakamuri Reddy</td>
<td>1South Carolina Governor's School for Science and Mathematics, Hartsville, SC, 2Pediatrics, MUSC.</td>
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<td>1CODM, MUSC, 2Craniofacial Biology, MUSC.</td>
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<td>Caitlin J Moore, Ee Wern Su, Samantha J Suriano, Neizel E Songalia, Mark P Rubinstein</td>
<td>Surgery, MUSC.</td>
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<td>161</td>
<td>The Role of LIN28B in Neuroblastoma</td>
<td>Azza E Abdalla</td>
<td>COM, MUSC.</td>
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<td>162</td>
<td>Screening of Inhibitors for β-Arrestin2</td>
<td>Sherwin A Soltani, Kathryn M Appleton, Richard E Trager, Yuri K Peterson</td>
<td>1COM, MUSC, 2Drug Discovery and Biomedical Sciences, MUSC.</td>
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2:45 - 3:00  
163 Differentiation of Induced Pluripotent Stem Cells to Retinal Pigment Epithelium in Vitro, Michelle Crouse¹, Jie Gong², Ernesto Moreira², Mark Fields²; ¹COM, MUSC, ²Storm Eye Institute, MUSC.

SESSION 15: Clinical-Professional-Masters VIII: 12:00 – 3:00  
CHP 106

12:00 - 12:15  
164 Incidence of Aneurysmal Subarachnoid Hemorrhage - a Risk Factor and Geodemographic Assessment of Outcome, Thomas W Larrew¹, Will Pryor², Aquilla Turk, Raymond Turner¹; ¹Neurosciences, MUSC, ²Interventional Radiology, MUSC.

12:15 - 12:30  
165 Advanced Glycation End-products Contribute to the Development of Diabetic Macular Edema By Disrupting Retinal Pigment Epithelium Function, Mohammad Dahrouj, Yueying Liu, Zsolt Ablonczy, Craig Crosson; Ophthalmology, MUSC.

12:30 - 12:45  
166 The Role of Kidney Disease in Southeastern Strokes, Mallory N Roberts¹, Andrea D Boan², Daniel T Lackland²; ¹COM, MUSC, ²Neurosciences, MUSC.

12:45 - 1:00  
167 Renal Cell Cancer: Attenuation Values on Unenhanced CT, Ashley N Smith¹, Heather Collins², Nancy Curry³, Munazza Anis³; ¹COM, MUSC, ²Biomedical Imaging, MUSC, ³Radiology, MUSC.

1:00 - 1:15  
168 Donor, But Not Recipient Age, is a Risk Factor for the Development of Post-Operative Surgical Complications in Kidney Transplant Recipients, Jordan A Shealy, David J Taber, Charles F Bratton, John W McGillicuddy, Kenneth Chavin, Prabhakar Baliga; Transplant Surgery, MUSC.

1:15 - 1:30  
169 The Effects of Erratic Peri-operative Blood Pressures and Glucoses on Readmissions and Clinical Outcomes in Kidney Transplant Recipients, John Kalu Odeghe¹, David Taber², Kenneth Chavin², Prabhakar Baliga²; ¹COM, MUSC, ²Transplant Surgery, MUSC.

1:30 – 1:45 BREAK

1:45 - 2:00  
170 Protocol Based Induction Therapy Improves Rejection Rates, Complications, and Transplant Event Costs in Adult Kidney Transplant Recipients, Chris S Vandivort¹, David J Taber², John W McGillicuddy¹, Charles F Bratton², Kenneth D Chavin², Prabhakar Baliga²; ¹COM, MUSC, ²Transplant Surgery, MUSC.

2:00 - 2:15  
171 The Impact of Antihypertensives and Dosing on Blood Pressure Control in Renal Transplant Recipients, Balvir Singh¹, David Taber², Kenneth Chavin², Charles Bratton², Prabhakar Baliga²; ¹COM, MUSC, ²Surgery, MUSC.

2:15 - 2:30  
172 A Comparative Analysis of Outcomes and Resource Utilization in Kidney Transplantation in Standard Criteria Donors Vs. Expanded Criteria Donors, Keith J Orland¹, David J Taber², Prabhakar K Baliga²; ¹COM, MUSC, ²Transplant Surgery, MUSC.
2:30 - 2:45
173 Bougienage: A Safe and Cost Effective Treatment for Coins Lodged in the Esophagus, Aaron M Blackshaw\textsuperscript{1}, Evan Allie\textsuperscript{2}, Rachel Tuuri\textsuperscript{3}; \textsuperscript{1}COM, MUSC, \textsuperscript{2}Pediatrics Residency Program, The Children's Hospital of South Carolina, \textsuperscript{3}Pediatric Emergency Medicine, The Children's Hospital of South Carolina.

2:45 - 3:00
174 Characteristics of Consecutive Esophageal Motility Diagnoses After a Decade of Change, Katherine E Boland, Radu Tutuian, Donald O Castell; Gastroenterology, MUSC.

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SESSION 16: Clinical-Professional-Masters IX: 12:00 – 2:45: CHP 205

12:00 - 12:15
175 A Pilot Study to Investigate the Induction and Manipulation of Learned Helplessness in Healthy Adults, Joseph J Taylor\textsuperscript{1}, Daniel Neitzske\textsuperscript{2}, George Khouri\textsuperscript{1}, Jeffrey Borckardt\textsuperscript{2}, Ron Acerno\textsuperscript{3}, Peter Tuerk\textsuperscript{3}, Matthew Schmidt\textsuperscript{4}, Mark George\textsuperscript{5}; \textsuperscript{1}Neurosciences, MUSC, \textsuperscript{2}Psychiatry, MUSC, \textsuperscript{3}Mental Health, VAMC.

12:15 - 12:30
176 Prescribing Patterns of Mycophenolate in Patients with Systemic Lupus Erythematosus, Roopa Varadarajan\textsuperscript{1}, Kristen Morella\textsuperscript{2}, Gary S Gilkeson\textsuperscript{1}, James C Oates\textsuperscript{1}, Diane L Kamen\textsuperscript{1}; \textsuperscript{1}Rheumatology, MUSC, \textsuperscript{2}Pediatric Epidemiology, MUSC.

12:30 - 12:45
177 Presenting Symptoms As Predictors of Stage in HPV Positive Oropharyngeal Squamous Cell Carcinoma Patients, Amit J Sood, Wesley McIlwain, Shaun A Nguyen, Terry A Day; Otolaryngology-Head and Neck Surgery, MUSC.

12:45 - 1:00
178 Presenting Symptoms in HPV-positive and HPV-negative Oropharyngeal Cancer Patients, Wesley R McIlwain, Amit Sood, Shaun Nguyen, Terry Day; Otolaryngology, MUSC.

1:00 - 1:15
179 Is Very Low Birth Weight Infant First Postnatal Week Energy and Protein Intake Associated with Growth Parameters At Term Age Equivalent?, Jacqueline L Razzaghy\textsuperscript{1}, Carolyn Finch\textsuperscript{2}, Myla Ebling\textsuperscript{3}, Sarah Taylor\textsuperscript{2}; \textsuperscript{1}COM, MUSC, \textsuperscript{2}Neonatology, MUSC, \textsuperscript{3}MUSC.

1:15 – 1:30 BREAK

1:30 - 1:45
180 Plasma Cathelicidin Concentrations in Preterm Infants At Birth and Its Association with Vitamin D Status, Juliana M Sobczyk\textsuperscript{1}, Frank Shary\textsuperscript{1}, Myla Ebling\textsuperscript{2}, Renee Washington\textsuperscript{2}, Carol Wagner\textsuperscript{3}, Bruce Hollis\textsuperscript{2}, Sarah Taylor\textsuperscript{2}; \textsuperscript{1}COM, MUSC, \textsuperscript{2}MUSC, \textsuperscript{3}Pediatrics, MUSC.

1:45 - 2:00

2:00 - 2:15
182 Quantitative Evaluation of Novel Beam Hardening Artifact Correction Technique in Dual-Energy CT Perfusion Imaging of the Myocardium, Christopher D Wolla, Andreas M Bucher, Aleksander W Krazinski, Carlo N Dececco, Felix G Meinel, Lucas L Geyer, U J Schoepf, Andrew D Mcquiston; Radiology, MUSC.
183 Quantitative Analysis of Dynamic CT Myocardial Perfusion Imaging in a Large, Multi-center Patient Population, Jordan A Maivelett¹, Felix G Meinel¹, Ullrich Ebersberger¹, Roy P Marcus², Fabian Bamberg², Carlo N De Cecco¹, Uwe J Schoepff¹; ¹Radiology and Radiological Science, MUSC, ²Institute for Clinical Radiology, Ludwig-Maximilians-University Hospital, Munich, Germany.

184 Examining the Role of Type-I Membrane-associated Matrix Metalloproteinase in Thoracic Aortic Aneurysms, S Russ Richardson¹, Risha K Patel², Robert E Stroud², Jeffery A Jones², John S Ikonomidis²; ¹COM, MUSC, ²Cardiothoracic Surgery, MUSC.

SESSION 17: PhD IV: Years 1-2: 12:00 – 2:30 pm: CHP 206

12:00 - 12:15
185 Trichostatin A Abrogates Advanced Glycation End-product-induced Retinal Pigment Epithelium Dysfunction in an in Vivo Model of Diabetic Eye Disease, Danielle M Desjardins, Mohammad Dahrouj, Yueying Liu, Craig Crosson, Zsolt Ablonczy; Ophthalmology, MUSC.

12:15 - 12:30
186 Phosphorylation Dynamics of Type 1 Parathyroid Hormone Receptor (PTH1R) Signaling in Osteoblasts As Explored By SILAC Mass Spectrometry, Grace R Williams¹, Mary N Berkaw¹, Jennifer Bethard¹, Michael Schilling¹, Louis M Luttrell², Lauren E Ball¹; ¹Pharmacology, MUSC, ²Endocrinology, MUSC.

12:30 - 12:45
187 Identification of Biogenic Residues in the Beta-2 Adrenergic Receptor Via Molecular Modeling, Robert B Cameron, Lauren P Wills, Richard E Trager, Rick G Schnellmann, Yuri K Peterson; Drug Discovery and Biomedical Sciences, MUSC.

12:45 - 1:00
188 MicroRNA-133a Mediated Regulation of Membrane Type-1 Matrix Metalloproteinase in Myocardial Fibroblasts: Differential Effects in Dilated Cardiomyopathy, Adam W Akerman¹, Robert E Stroud¹, Risha K Patel¹, Paul J McDermitt¹, Fancis G Spinale², Rupak Mukherjee¹, John S Ikonomidis¹, Jeffrey A Jones¹; ¹MUSC, ²USC.

1:00 - 1:15
189 Defining the Role of the Novel CD4+CD26high T Cell Subset in Adoptive Cancer Immunotherapy, Stefanie R Bailey, Michelle H Nelson, Kristina M Schwartz, Jacob S Bowers, Shikhar Mehrotra, Chrystal M Paulos; Microbiology and Immunology, MUSC.

1:15 – 1:30 BREAK

1:30 - 1:45
190 The Roles of TGF-beta in B Cell Activation and Function, Caroline H Wallace, Zihai Li; Microbiology & Immunology, MUSC.

1:45 - 2:00
191 Discharge Disposition After Bariatric Surgery, Emily E Johnson, Kit N Simpson; Health Sciences and Research, MUSC.

2:00 - 2:15
192 Using Rasch Analysis to Convert ICF Activity Measure of Gross Upper Extremity to CMS G-codes Modifiers, Ickpyo Hong¹, Craig A Velozo²; ¹Health and Rehabilitation Science, MUSC, ²Occupational Therapy, MUSC.
Random Forest Procedure for Classification of Etiologies of Acute Liver Failure in Patients, Jaime L Speiser¹, Valerie L Durkalski¹, William M Lee²; ¹Public Health Sciences, MUSC, ²Internal Medicine, University of Texas Southwestern.

SESSION 18: PhD V: Years 3+: 12:00 – 3:00 pm: CHP 207

12:00 - 12:15
194 A New Statistical Algorithm for Classifying and Predicting Disease Outcome From Binary and Continuous Predictors and Their Interactions, Sybil Nelson; Public Health Sciences, MUSC.

12:15 - 12:30
195 Acetylation As a Predictor of Glaucomaticous Injury, Oday Alsarraf, Jie Fan, Phillip W Yates, Craig E Crosson; Ophthalmology, MUSC.

12:30 - 12:45
196 Good Things in a Small Package: Estrogen Nanoparticles in Spinal Cord Injury, April A Cox¹, Abhay K Varma¹, John Barry¹, Colleen Bauza¹, Narendra L Banik¹; ¹MUSC, ²Clemson.

12:45 - 1:00
197 Predictive Performance of DRAGON Score: a Pooled Analysis, Liqiong Fan, Sharon D Yeatts; Public Health Science, MUSC.

1:00 - 1:15
198 The Hippocampus and Lateral Septum: an Important Circuit in Context, But Not Cue-induced Reinstatement of Cocaine Seeking, Ellen M McGlinchey, Gary Aston-Jones; Neurosciences, MUSC.

1:15 - 1:30
199 VTA Dopamine Terminals Regulate Neuronal Excitability in the PFC Via Inhibition of the Slow After-hyperpolarization, William Buchta, Benjamin Harlan, Peter Kalivas, Arthur Riegel; Neurosciences, MUSC.

1:30 – 1:45 BREAK

1:45 - 2:00
200 The Role of P53 and the DNA Damage Response Pathway in Activation-Induced Cell Death of Adoptively Transferred T Cells Used in the Immunotherapy of Metastatic Melanoma, Matt Scheffel¹, Shikhar Mehrotra², Christina Voelkel-Johnson¹; ¹Microbiology & Immunology, MUSC, ²Surgery, MUSC.

2:00 - 2:15
201 The Role of 2,4-Dihydroxyquinoline (DHQ) in Pseudomonas Aeruginosa Quorum Sensing and Virulence, Jordon D Gruber¹, Wei Chen¹, Patrick Flume², Yong-Mei Zhang¹; ¹Biochemistry and Molecular Biology, ²Pulmonology and Critical Care Medicine.

2:15 - 2:30
202 Noise-induced Necrotic Outer Hair Cell Death is Modulated By Receptor-interacting Protein Kinases, Kayla R Hill, Hong-Wei Zheng, Jun Chen, Su-Hua Sha; Pathology and Laboratory Medicine, MUSC.

2:30 - 2:45
203 Effects of Aging and Gender on Murine Thoracic Aortic Structure and Mechanical Properties, Jason B Wheeler¹, Rupak Mukherjee², Allison D Rice³, Jeffrey A Jones², John S Ikonomidis²; ¹MCBP, MUSC, ²Surgery, MUSC, ³Medicine, MUSC.
### SESSION 19: PhD VI: Years 3+: 12:00 – 3:00 pm: BE 112

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<th>Time</th>
<th>Presentation</th>
<th>Authors</th>
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<td>12:00</td>
<td><strong>204</strong> GILT Reduces PAX-3 Expression in Human Melanoma Cells, Jessica D Hathaway¹, Bently P Doonan², Azim Hossain³, Duncan Norton³, Lixia Zhang¹, Azizul Haque¹; ¹Microbiology &amp; Immunology, MUSC, ²Medicine, MUSC, ³Medicine, USC.</td>
<td>Jessica D Hathaway¹, Bently P Doonan², Azim Hossain³, Duncan Norton³, Lixia Zhang¹, Azizul Haque¹; ¹Microbiology &amp; Immunology, MUSC, ²Medicine, MUSC, ³Medicine, USC.</td>
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<td>12:00</td>
<td><strong>205</strong> The Role of MK2 in Aggregatibacter Actinomycetemcomitans Mediated Chemokine Receptor Expression in Macrophages, Bethany A Herbert, Michael Valerio, Keith L Kirkwood; Craniofacial Biology, MUSC.</td>
<td>Bethany A Herbert, Michael Valerio, Keith L Kirkwood; Craniofacial Biology, MUSC.</td>
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<td>12:15</td>
<td><strong>206</strong> Using ICF Attention Measure to Develop a Treatment Framework for Individuals with Traumatic Brain Injury, Chih-Ying Li, Craig A Velozo; Occupational Therapy, MUSC.</td>
<td>Chih-Ying Li, Craig A Velozo; Occupational Therapy, MUSC.</td>
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<td>12:30</td>
<td><strong>207</strong> Laterality of Mammary Stem and Progenitor Cell Populations During Normal Development, Jacqulyne P Robichaux¹, Brian W Booth², John W Fuseler³, Ann F Ramsdell¹; ¹Hollings Cancer Center, MUSC, ²Institute for Biological Interfaces of Engineering, Clemson University, ³Cell Biology and Anatomy, School of Medicine USC.</td>
<td>Jacqulyne P Robichaux¹, Brian W Booth², John W Fuseler³, Ann F Ramsdell¹; ¹Hollings Cancer Center, MUSC, ²Institute for Biological Interfaces of Engineering, Clemson University, ³Cell Biology and Anatomy, School of Medicine USC.</td>
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<td>12:45</td>
<td><strong>208</strong> S1P Receptor Signaling in Mesenchymal Stem Cells, Sarah Tucke Marrison, Thomas Beckham, Joseph Cheng, Ping Lu, Xiang Liu, James S Norris; Microbiology and Immunology, MUSC.</td>
<td>Sarah Tucke Marrison, Thomas Beckham, Joseph Cheng, Ping Lu, Xiang Liu, James S Norris; Microbiology and Immunology, MUSC.</td>
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<td>1:00</td>
<td><strong>209</strong> The 1,25(OH)2D3 Response in MKP-1-deficient Mice That Have Primary Hyperparathyroidism, Alfred C Griffin¹, Erica Nelson², Louis Luttrell³, Keith L Kirkwood²; ¹DSTP, MUSC, ²Craniofacial Biology, MUSC, ³Endocrinology, MUSC.</td>
<td>Alfred C Griffin¹, Erica Nelson², Louis Luttrell³, Keith L Kirkwood²; ¹DSTP, MUSC, ²Craniofacial Biology, MUSC, ³Endocrinology, MUSC.</td>
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<td><strong>210</strong> Inhibition Of Histone Deacetylase (HDAC) Activity Promotes M2 Macrophage Polarization Post Myocardial Infarction Reducing Matrix Metalloproteinase-9 (MMP-9) Expression and Improving Left Ventricular F, Denise M Kimbrough, Santhosh K Mani, Harinath Kasiganesan, Donald R Menick; MUSC.</td>
<td>Denise M Kimbrough, Santhosh K Mani, Harinath Kasiganesan, Donald R Menick; MUSC.</td>
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<td><strong>BREAK</strong></td>
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<td>1:45</td>
<td><strong>211</strong> BMP Signaling and Epicardial Contribution to the Atrioventricular Junction, Marie M Lockhart¹, Aimee L Phelps¹, Christina M Brown², Rupak D Mukherjee³, Maurice J van den Hoff⁴, John B Burch⁵, Andy Wessels¹; ¹Regenerative Medicine and Cell Biology, MUSC, ²Biology, USC, ³Surgery, MUSC, ⁴Anatomy, Embryology, and Physiology, Academic Medical Center, Amsterdam, The Netherlands, ⁵Fox Chase Cancer Center, Philadelphia, PA.</td>
<td>Marie M Lockhart¹, Aimee L Phelps¹, Christina M Brown², Rupak D Mukherjee³, Maurice J van den Hoff⁴, John B Burch⁵, Andy Wessels¹; ¹Regenerative Medicine and Cell Biology, MUSC, ²Biology, USC, ³Surgery, MUSC, ⁴Anatomy, Embryology, and Physiology, Academic Medical Center, Amsterdam, The Netherlands, ⁵Fox Chase Cancer Center, Philadelphia, PA.</td>
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<td><strong>212</strong> β3 Integrin Promotes Protein Ubiquitination and Prosurvival Signaling in Cardiomyocytes, Dorea L Pleasant, Kamala Sundararaj, Rebecca Harston, Sundaravadival Balasubramanian, Dhandapani Kuppuswamy; Medicine, MUSC.</td>
<td>Dorea L Pleasant, Kamala Sundararaj, Rebecca Harston, Sundaravadival Balasubramanian, Dhandapani Kuppuswamy; Medicine, MUSC.</td>
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Interferon Alpha Reduces Nitric Oxide Production in Endothelial Cells By Altering Endothelial Nitric Oxide Synthase Transcription and Phosphorylation, Joy N J Buie, Robin Muise-Helmericks, Jim C Oates, Microbiology and Immunology, MUSC, Regenerative Medicine and Cell Biology, MUSC, Rheumatology and Immunology, MUSC.

Understanding the Role of Estrogen Receptor Alpha in Plasmacytoid Dendritic Cell Development and Function in Systemic Lupus Erythematosus, Jennifer L Scott, Melissa Cunningham, Osama Naga, Jackie EuDaly, Jena Wirth, Gary Gilkeson, Microbiology and Immunology, MUSC, Rheumatology, MUSC.

Collagen Homeostasis in the PDL is Dependent on the Regulation of Transglutaminase Activity By SPARC, Jessica Trombetta-eSilva, Greg Wright, Glenn Hepfer, Catalin Baicu, Cui Cui, Mari Kaartinen, Hai Yao, Amy D Bradshaw, Craniofacial Biology, MUSC, Bioengineering, Clemson, Cardiology, MUSC, McGill University, Clemson, MUSC, Cardiology and Craniofacial Biology, MUSC.

Are Specific Residency Program Characteristics Associated with the Pass Rate of Graduates on the ABFM Certification Examination?, Lisa D Mims, Peter J Carek; Family Medicine, MUSC.

A Double-blind, Randomized, Placebo-controlled Clinical Trial Evaluating Fibrin Sealant in Thyroidectomy Closure, Colin W Fuller, Shaun A Nguyen, Marion B Gillespie, Joshua D Hornig; MUSC.

Computational Model Predictions of Age and Hearing Loss Effects on Concurrent Vowel Identification, Ananthakrishna Chintanpalli, Jayne B Ahlstrom, Judy R Dubno; Otolaryngology - Head and Neck Surgery, MUSC.

Multifunctional CD26hi Th17 Cells Eradicate Large Human Tumors, Michelle H Nelson, Stefanie Bailey, Logan Huff, Sreenath Kundimi, Chrystal Paulos; Microbiology & Immunology, MUSC.

Oligoamines Containing 3-5-3 Carbon Backbone Architecture Are Endowed with Both Anticancer and Antibacterial Activity, Boobalan Pachaiyappan, Shannon Nowotarski, Wang Bo, Melissa Sokolosky, Steven Holshouser, Robert Casero, Yong-Mei Zhang, Patrick Woster; Drug Discovery and Biomedical Sciences, MUSC, Sidney Kimmel Comprehensive Cancer Center, John Hopkins University, Biochemistry and Molecular Biology, MUSC.
SESSION 21: Postdocs-Residents-Fellows IV: 12:00 – 2:30 pm: CHP 202

12:00 - 12:15
225 Maximizing Intratumoral Drug Accumulation During Combination Therapy of Radiofrequency Ablation with Thermosensitive Liposomal Doxorubicin: A Computational Study and In-vivo Evaluation, Christian Rossmann, Dieter Haemmerich; Pediatrics, MUSC.

12:15 - 12:30
226 ER Chaperone Gp96: Essential Regulator for Melanoma Growth and Melanogenesis, Yongliang Zhang1, Kristi L Helke2, Saleh Moha Rachidi1, Sergio G Coelho3, Vincent J Hearing4, Shaoli Sun5, Bei Liu1, Zhihai Li1; 1Microbiology & Immunology, MUSC, 2Comparative Medicine, MUSC, 3Laboratory of Cell Biology, NCI, 4Pathology & Laboratory Medicine, MUSC.

12:30 - 12:45
223 MKP-1 Regulates Early NFATc1-Dependent Osteoclastogenesis in RANKL-Induced Defined Progenitor Populations, Michael S Valerio1, Bethany A Herbert1, Alfred C Griffin1, Keith L Kirkwood2; 1Craniofacial Biology, MUSC, 2Craniofacial Biology and Microbiology/Immunology, MUSC.

12:45 - 1:00
228 Heptanol Application to the Mouse Round Window: A Model for Studying Cochlear Lateral Wall Regeneration, Shawn M Stevens1, Yazhi Xing2, Christopher Hensley2, Juhong Zhu2, Judith R Dubno1, Hainan Lang2; 1Otolaryngology-Head and Neck Surgery, MUSC, 2Pathology and Laboratory Medicine, MUSC.

1:00 - 1:15
229 A Quantitative Increase in Regulatory T Cells (Treg) Controls Development of Vitiligo, Shilpak Chatterjee1, Jonathan Eby2, Hee-Kap Kang2, Amir A Al-Khami1, Navtej Kaur1, Osama Naga1, Caroline I Le Poole2, Shikhar Mehrotra1; 1Surgery, MUSC, 2Pathology, Loyola University.

1:15 – 1:30 BREAK

1:30 - 1:45
230 Fli-1 is a Novel Regulator of the Proinflammatory Chemokines MCP-1 and RANTES, Mara L Lennard Richard, Tamara K Nowling, Xian K Zhang; Rheumatology, MUSC.

1:45 - 2:00
231 Higher Antioxidant Level with Decreased Mitochondrial Respiration and Glycolysis Correlates to Persistence of Human CD62Lhi T Cell, Pravin Kesawani1, Amir A Al-Khami1, Gina Scurti2, Christina Voelkel-Johnson3, Elizabeth Garrett-Mayer4, Craig C Beeson5, Michael I Nishimura5, Shikhar Mehrotra1; 1Surgery, MUSC, 2Surgery, Loyola University, 3Microbiology & Immunology, MUSC, 4Biostatistics & Epidemiology, MUSC, 5Pharmacy, Drug Discovery and Biomedical Sciences, MUSC.
2:00 - 2:15

**232  Sphingosine Kinase 1 and Its Role in Modulation of Anti-tumor T-cell Responses**, Krishnamurthy Thyagarajan¹, Amir Al-khami³, Beichu Guo², Besim Ogretmen³, Shikhar Mehrotra¹; ¹Surgery, MUSC, ²Microbiology and Immunology, MUSC, ³Biochemistry and Molecular Biology, MUSC.

2:15 - 2:30

**227  The Role of MicroRNA in Cochlear Lateral Wall Degeneration of Age-related Hearing Loss**, Michael W Moore¹, Yazhi Xing², Christopher T Hensley², Victoria J Findlay², Jeremy L Barth³, Hainan Lang²; ¹Otolaryngology, MUSC, ²Pathology, MUSC, ³Regenerative Medicine, MUSC.
A critical correlation exists between population density and stroke occurrence. REACH telestroke locations have been established throughout South Carolina to reduce stroke mortality rates. The population density specific stroke mortality risks were assessed through geographical proximity to REACH telestroke sites. Stroke mortality rates were mapped based on population density from 2005 to 2007 (before REACH) and 2008 to 2010 (after REACH). The telestroke sites were plotted on maps according to the counties in which they were located. The level of risk for the population density specific stroke rates were then quantified according to their age-adjusted crude rates. This approach assists in the process of evaluating the impact of current REACH sites based on the population density specific stroke mortality rates. There is an insufficient amount of REACH sites located in South Carolina's rural areas. From this study, future REACH sites can be prioritized geographically so that they will be implemented in areas that will have the most significant impact.

Estimated to affect 24 million individuals worldwide, schizophrenia is a heritable neuro-psychiatric disorder characterized by a range of symptoms from hallucinations and delusions to social withdrawal and cognitive deficits. Of particular interest, recent studies have linked deficits in cognition with diminished expression of the dystrobrevin-binding protein 1 (dybindin-1) by mutations in the DTNBP1 gene. Through prior experiments, we have shown that a lack of dybindin-1 reduces glutamate release in the prefrontal cortex (PFC) through decreases in the ready releasable pool of synaptic vesicles, decreased rate of exo- and endocytosis, and diminished expression of the L- and N-type Ca\(^{2+}\) channels. To explore a potential means of restoring glutamate release, and perhaps improving the cognitive deficits, we test the effects of fingolimoid using a dybindin-1 null mutant mouse. Fingolimoid is known to increase endogenous levels of BDNF, and in turn, it has been shown that BDNF increases N-type Ca\(^{2+}\) channels. We test three genotypes (WT, HET and MUT) using a social interaction task. The mice were divided into two groups: one group was treated with saline ip for 7 days and the second group was treated with fingolimoid ip for 7 days. We then analyze levels of intracellular [Ca\(^{2+}\)] in a crude synaptosome preparation from the PFC using both Fluo-3 and Fluo-4 fluorescent calcium assays. Relative to WT mice, nontreated dybindin-1 MUT mice demonstrated impairments in social interaction, decreased working memory, and lower levels of presynaptic intracellular [Ca\(^{2+}\)] in the PFC. However, fingolimoid treated MUT mice showed increased social interaction with novel mice, improved working memory, and higher presynaptic intracellular [Ca\(^{2+}\)] in the PFC. These results show promise for countering social and cognitive impairments associated with schizophrenia and shed light on the role of dybindin-1 in symptom pathology. NARSAD

001 The Association of Stoke Risks By Population Density and REACH Telestroke Sites. Kelby Killoy, Daniel Lackland; Chemistry and Biochemistry, USC.

002 Effects of Fingolimoid Administration in a Genetic Model of Schizophrenia. Darius Becker-Kralj1, Antonieta Lavin2, College of Charleston, 2COM, MUSC.

003 Dysfunctional Frontal-Striatal Connectivity in Tourette Syndrome. Logan T Dowdle1, William Devries2, Melanie Canterberry3, Nolan R Williams3, Colleen A Hanlon1, 1Biology/Neuroscience, CoC, 2Psychiatry & Behavioral Sciences, MUSC, 3Psychiatry & Neurology, MUSC.

Tourette syndrome (TS) is a neuropsychiatric disorder that begins in childhood and can be characterized by multiple motor and phonic tics, which often occur more frequently when an individual becomes agitated or nervous. Although the neurobiological basis of TS is not well understood, it likely involves dysregulation of frontal-striatal systems involved in both limbic (emotional) and motor control. The purpose of this study was to test the hypothesis that there is incomplete segregation of these neural circuits in TS patients compared to their non-TS peers. The integrity of the limbic and motor circuits was assessed through non-invasive transcranial magnetic brain stimulation (TMS) of the medial prefrontal cortex (mPFC) and primary motor cortex (pMC) in the MRI environment. This interleaved TMS/mMRI procedure was performed on TS patients (n=6) and age-matched peers (n=6) recruited from the local community and MUSC neurology clinics. The data were preprocessed according to established methods and significant clusters of BOLD signal change were compared between groups. Among all participants, pMC and mPFC stimulation reliably activated neural circuitry at the targeted location and monosynaptically connected regions. With pMC stimulation TS participants, compared to healthy controls, showed higher brain activity overall, specifically in multiple cortico-limbic brain regions. Additionally TS participants showed a heightened limbic response contralateral to the site of mPFC stimulation. These preliminary results suggest that TS participants have hyperactive limbic circuitry with an additional blending of emotional and motor activity when compared to their peers. Beyond expanding our basic understanding of the disorder, these data may be useful for future studies, which use repetitive TMS as a treatment tool to enhance the functional segregation of these circuits. Further studies will be required to determine if abnormal connectivity changes over time and differentiates those patients whose symptoms erode after adolescence versus those that persist into adulthood. NIH NIDA DA033680

004 REACH Telestroke and the Racial Disparity of Stroke Mortality Risk in South Carolina. Breanna L Grant; Health Promotion, Education, and Behavior, USC.

Abstract: Stroke risks are high in SC compared with other states in the US with highest disease burden among African Americans. Tele-medicine has been proposed as a means to reduce adverse stroke outcomes. The Medical University of South Carolina developed a telemedicine network to address the issue of stroke in South Carolina. However, it is unclear its benefits and accessibility for addressing the racial disparity of stroke among high-risk African Americans. The purpose of this project is to assess stroke risk by race based on location of telemedicine sites in SC. Age-adjusted stroke mortality data was obtained for two time periods, before and after REACH implementation, by county and by race. The counties were grouped into tertiles based on their stroke mortality risk and this information was mapped against the REACH sites. Results show that placing REACH sites high-risk areas could possibly help address the racial disparity in stroke risk in South Carolina.
005 Hollywood Smiles Intervention + Handbook: A Post Program Analysis, George P Stamatides1, Renata S Leite2; Biological Sciences, Clemson University, 2College of Dental Medicine, MUSC.

The primary objective of this project was to evaluate the Hollywood Smiles (HS) intervention and HS Handbook. These projects sought to better understand the causes of poor oral health disparities in the African American Gullah population and to empower communities to improve their oral health. Data was collected through mixed methods (surveys and focus groups). Post-project evaluation was conducted to guide the effective dissemination of the intervention. Qualitative and quantitative data analysis showed a notably positive response to the program, with participants consistently praising the program for having a positive influence on their oral health knowledge and general dentistry perceptions. NIDCR R25 DE022677; IDCR R21 DE021979; UL1 RR029882 and TR000062; SCTR

006 Telomere Attrition and the Effects of Environmental Quality on Aging in Alligator Mississippiensis, Eric M Benfield, Ben Parrott; MBES, MUSC.

Telomere attrition is positively associated with the aging process, and is associated with increased risk of several diseases and complications. In previous studies, our lab has utilized the long-lived American Alligator to examine the effects of environmental factors on reproductive health. The current study has been designed to investigate the relationship between the length of alligators and telomeres, and to examine the effects of environmental quality on the aging process. Telomere length was quantified utilizing standard curves for a single copy gene and an artificial telomere repeat sequence. We measured telomere length in alligators over a wide range of lengths and detected an inverse relationship between animal length and telomere length. In addition, we examined telomere length in juvenile alligators of similar length from three different sites with varying environmental quality. We were unable to detect differences in mean telomere length across sites. However, we did observe significant difference in the amount of variation across individuals from different sites. Further studies are needed to determine if environmental factors contribute to telomere length in adult animals. South Carolina Centers of Economic Excellence Marine Genomics Endowment.

007 Effects of Antimicrobial Exposures on Grass Shrimp, Palaemonetes Pugio, and Associated Vibrio Bacterial Density and Development of Antibiotic Resistance, John W Brooker1, Juita Martinez2, Jan Moore2, Marie Delorenzo2; 1College of Charleston, 2College of Charleston REU, 2National Oceanic and Atmospheric Administration.

Abstract not available.

008 Protein Disulfide Isomerase and Estrogen Receptor Alpha Interaction in MCF7 Cells Under Oxidative Stress, Chelsea A Snipes1, Tiffany Ancrum2, Steven Hutchens2, Danyelle M Townsend2; 1CoC, 2MUSC.

Protein disulfide isomerase (PDI) is a chaperone protein in the endoplasmic reticulum that facilitates folding and disulfide bond formation in its protein substrate. ERalpha, a hormone receptor and transcription factor, is found to make a complex with PDI. The post translational modification prompted by oxidative stress, S-gluthathionylation has been shown to inhibit PDI-ERalpha interaction leading to the conclusion that redox regulation of PDI mediates ERa stability. When an MCF7 breast cancer cell line was treated in vitro with S-gluthationylation inducing anti-cancer agents PABA/NO and Tamoxifen the levels of PDI and ERalpha expression were shown to be statistically decreased after western blot analysis. This PDI-ERalpha interaction has a clinical application by increasing the time span of effective drug use in ERalpha positive breast cancer. The Abney Foundation

009 Alternative De-acylation of Lysine Residues, Bastien H Bacro1, Brad Lees2, Elizabeth Inks2, Kalyan Chundru2, Ben Josey2; 1Clemson University, 2Drug Discovery and Biomedical Science, MUSC.

Abstract not available.

010 A Novel Technique for Rapid Oxygen Measurement Reveals the Suppression of Calcium Current Within Two Seconds of Hypoxia, John A Scarringi1, Angelo O Rosa2, Lars Cleemann1, Martin Morad1; 1Chemistry and Biochemistry, CofC, 2Regenerative Medicine, MUSC.

Cardiac hypoxia, caused by conditions such as ischemic heart disease and cardiac hypertrophy, may rapidly overwhelm cellular capacity to resist injury and lead to pathophysiological function in the heart. It has been theorized that individual myocytes are able to detect acute changes in oxygen levels and rapidly trigger protective responses. We have previously suggested that the L-type calcium channel (Cav1.2) functions as an acute oxygen sensor for the heart through the rapid suppression of calcium current under hypoxic conditions. Others have indicated that the detection of hypoxia is mediated through changes in ROS levels produced in the mitochondria. These opposing views represent a kinetic argument, as it would take far longer for altered ROS levels in the mitochondria to affect calcium channel function than a mechanism that directly acts on the channel protein. Therefore, to evaluate this argument we measured oxygen dependent fluorescence in the immediate vicinity of voltage-clamped cardiac cells subjected to acute hypoxia to ascertain the minimal duration of hypoxia that produced significant modulation of calcium channel current. Oxygen tension was measured by plating cells on ORMOSIL coated coverslips that were embedded with an oxygen sensitive ruthenium compound. Performing simultaneous voltage-clamp and oxygen measurements, we found that acute hypoxia rapidly suppressed calcium channel current, and was significant after 1.5s, reached ~10% after 2.5s and was nearly completely reversible in 5s. The described technique provides a novel way so simultaneously measure calcium current and oxygen tension around cells. Further, the rapid and reversible suppression of calcium channel current under hypoxia is consistent with the notion that the cardiac calcium channel is directly modulated by oxygen. NIH R01 HL107600
011 A Potentially Novel Role For Small Leucine Rich Proteoglycans In The Mature Collagen-Rich Extracellular Matrix Of Cardiac Valves, Olivia M Coco1, Loren E Dupuis2, Christine B Kern; 1Honors College, CoFC, 2Regenerative Medicine and Cell Biology, MUSC.

Abstract not available.

012 Evaluation of Scaffold-free Cell Aggregates for Vascular Construct Bioprinting, Cassandra P Awgulewitsch, Agnes Nagy-Mehesz, Zoltan Hajdu, Richard P Visconti; 1Biology, CoFC, 2Regenerative Medicine and Cell Biology, MUSC.

Organ printing involves computer-aided robotic biofabrication and rapid maturation of three-dimensional living tissue constructs using scaffold-free tissue cell spheroids as modular building blocks. A fundamental principal of organ or tissue bioprinting is that dispensed cell aggregates will self-assemble and undergo homotypic cell segregation to form a functional tissue that can be rapidly matured to exhibit both functional and structural properties that approach those of native organs or tissues. While our ultimate goal is to use this approach for biofabrication of macro-scale blood vessel constructs employing patient specific cells, our current focus is on evaluation of the cell biological behaviors of human vascular cells in micro scale vascular "test bed" modules. As maturation of scaffold-free living micro constructs requires deposition and remodeling of extracellular matrix, we have first focused on analyses of matrix deposition in our modules. To accomplish this, we combined human vascular smooth muscle cells (that we induced to differentiate from adipose progenitor cells) with human endothelial cells and fibroblasts in order to determine how heterotypic vascular cell interactions in our micro scale constructs impact the elaboration and remodeling of the extracellular matrix. We fabricated three groups of cellular aggregates: adipose progenitor cell-derived smooth muscle cells (APC-SMCs), APC-SMCs with HUVECs (human umbilical vein endothelial cells), and APC-SMCs with HUVECs and fibroblasts. These aggregates were analyzed by immunofluorescence micro-scopy and immunoblotting to quantify differences in ECM proteins within them. Mixed cell aggregates showed an increase in ECM protein production compared to the aggregates made of only APC-SMCs. Our current focus is on identification of relative proportions of these cell types to feed to achieve rapid assembly, remodeling and maturation of these vascular modules. NSF RII EPS-0903795

013 Regulation of the Nhx2.5 Second Heart Field Enhancer Region By Ets Transcription Factors Pea3 and Erm, Meaghan E Flessa, Christopher D Clark, Anthony J Horton, Ann C Foley, Kyu-Ho Lee; 1Pediatrics, MUSC, 2Bioengineering, Clemson.

Background. The transcription factor Nhx2.5 is known to play a key role in right heart and outflow tract development and many congenital heart defects found in humans are caused by mutations in the gene itself. Regulation of Nhx2.5 is also important for heart development, as reduced expression in right heart and outflow tract precursors of the second heart field (SHF) leads to heart malformations that increase in severity as Nhx2.5 levels decrease. In the current study we examined the evolutionarily conserved regulation of Nhx2.5 in the SHF by FGF signaling acting through the downstream Ets transcription factors Pea3 and Erm. Methods. Transient transgenic assay, gel shift, and in vitro reporter assay. Results. We found that evolutionarily conserved consensus binding sites for Pea3 and Erm Ets transcription factors are necessary for SHF expression of Nhx2.5 transgenes. We found repression of SHF-enhancer expression in the presence of Pea3, but activation of SHF-enhancer expression in the presence of Erm, consistent with animal studies that have shown that FGF can first activate and then limit Nhx2.5 expression at different stages of heart field development. Pea3 and Erm activity also work in conjunction with other reinforcing transcript-tional complexes potentially by mediating histone acetylation and methylation events. Conclusions. Understanding the detailed regulation of the Nhx2.5 gene in cardiac progenitors by extracellular signaling, intracellular factors, and epigenetic modification may provide overall insight into the complex gene expression relationships governing heart development. American Heart Association

014 Hollywood Smiles: An Oral Health Community Based Multi-Level Intervention, Krista Koch, Jabraenta Hubbard, George Stamatides, Martina Mueller, Renata Leite; 1Dental Medicine, MUSC, 2Biology, Clemson, 3Nursing, MUSC, 4Stomatology, MUSC.

The effectiveness of a community based multi-level intervention on oral health disparities was analyzed within the Hollywood, SC Gullah community. The hypothesis predicted the intervention group to show an improvement during the study period (baseline-3 months). Two churches were randomized into intervention and control groups, with 30 participants each. The intervention received: (1) baseline- three- and six-month examinations and oral cancer screenings; (2) standard of care dental therapy in a community clinic; (3) transportation passes / gas cards; (4) group / church level intervention; (5) peer-level behavioral / educational intervention with accompanying written material; and (6) individual-level behavioral / educational intervention with a Community Oral Health Promoter. The control group received items #1-3. At baseline, three-, and six-month, the participants received surveys about their oral health behavior (OHB) index, OHB attitude, OHB social norms, revised dental anxiety scale (DAS-R), self-efficacy scale for self-care, and revised rapid estimate of adult literacy in dentistry (REALD-30). Using SPSS for statistical analysis, a statistically significant increase occurred in the OHB attitude for the intervention group, whereas a statistically significant decrease was found for the DAS-R. The OHB index resulted in statistically significant increases between each testing period. Compared to the control group, the SESS scores did not achieve statistical significance. However, both experimental and control groups clinically increased their self-efficacy scores. Mean scores of the two groups did not drastically fluctuate in the REALD-30. Other than the intervention’s 3- to 6-month testing period, when a statistically significant difference was observed. The OHB social norms indicated the dentist is the greatest motivator in this Gullah community. The OHB index indicated improvements for frequency of teeth brushing. Overall, participants receiving the intervention tended to have a significantly improved oral health score at their first testing period. A community based multi-level inter-vention can positively impact the Gullah community oral health,
was 18 months at the start of the intervention.

The purposes of this study were: 1) to investigate the effects of early power mobility on the motor, cognitive, and language skills of a child born with a rare neuromuscular disorder 2) to explore the use of a manualized protocol to teach purposeful mobility with a power mobility device. Children with neuromuscular impairments have significantly decreased early mobility which greatly affects their opportunities to explore their physical and social environment. Commercially available ride-on-toys could be used in the clinic, home, community, or school settings to improve purposeful mobility and are a low cost alternative to other mobility devices. This case presentation used a single-subject ABAA design to measure the effects of a manualized early power mobility protocol using an adapted commercially available ride-on-toy. The protocol consisted of 14 training sessions completed over 6 weeks. Child A, who is diagnosed with Pierre Robin syndrome, was 18 months at the start of the intervention.
the mother, but rather continue to affect the fetus at birth, into adolescence, and subsequently carry on into adulthood. Summer Health Professions; NIDDK; National Institute on Minority Health and Health Disparities R01-MD004251

019 Can We Screen At-Risk Preterm Infants Quickly and Accurately? Clinical Utility of the Specific Test of Early Infant Motor Performance (STEP), Markey Y Haselden1, Catherine A Syretz2, Jessica A Thompson1, Kathryn Hope2, Patty Coker-Bolt3, Jennifer Poon3, Dorothea Jenkins5, 1Occupational Therapy, College of Health Professions, MUSC, 2Pediatrics, MUSC, 3Developmental Pediatrics, MUSC.

Although preterm infants are at risk for developmental delays, few get early developmental screening with a validated tool at clinic visits, and a critical period of neuroplasticity passes without therapeutic intervention. Even with an Early Intervention referral, an infant must fail developmental milestones before therapy services are delivered. Through earlier research, a new 10 item test motor assessment, the Specific Test of Early Infant Motor Performance (STEP) was developed by applying Rasch partial credit modeling to choose 10 motor items with the strongest correlation to overall motor ability of high and low risk infants. The aims of our research were to refine this short, new infant motor assessment and determine the clinical utility in using the STEP to detect developmental delays in preterm infants up to three months corrected age (CA). We developed new 4 point rating scales for each of the 10 items of the STEP, which do not require special expertise to score. To test the clinical utility of our 10 item assessments, we tested the scale during routine visits for preterm infants at the MUSC Neonatal High Risk Clinic (no identifiers were recorded). We scored the following quantitative and qualitative markers of clinical utility during the visit: time efficiency, ease of interpretation of the scales and scoring, flow and ordering of test items, and directed feedback from clinic personnel using the STEP. To get preliminary comparative data we recorded the time to administer the STEP and compared to other clinical assessments that were used during these routine clinic visits. The STEP required minimal training of healthcare professionals, and was easy to score. Pictorial representations of written motor descriptions were deemed helpful and quick. This valuable feedback from busy clinicians will be used to refine the STEP instrument and insure its acceptance as a developmental screening tool that could be used in today's newborn nurseries. 

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020 Competency-Based Patient Care Provider Disaster Training: The Center for Health Professional Training and Emergency Response, Jalmar R Jones1, Lancer A Scott2, Judith Staub1, Andrew C Seymore1, Simon Watson2, Wade Manaker2; 1Medicine, MUSC, 2Emergency Medicine, MUSC.

Background: Few patient care provider emergency preparedness training (EPT) pro-grans possess both competency-driven goals and metrics to measure performance during a multi-actor simulated disaster. Methods: We developed a 1-day (8 hour) EPT course for patient care providers to enhance provider knowledge, skill, and comfort necessary to save lives. Nine learning objectives, 18 competencies, and 34 performance objectives were developed. Ten 4th year medical students and 17 Veterans Hospital Administration (VHA) providers volunteered to take the course. During the scenario, trainees working in teams were confronted with 3 human simulators and 10 actor patients at one time. Unless appropriate performance objectives were met, the simulators “died” and the team was exposed to “anthrax”.

Results: Trainees (n=27) included 40% medical students, 28% physicians, 28% nurses, 4% emergency managers, and 4% mental health providers. 47% of the VHA providers reported greater than 17 hours of disaster training per year while 50% of the medical students reported no disaster training per year. The mean (SD) score for the pre-test was 12.7(4.0), or 53% correct, and after the training, the mean (SD) score was 18.8(2.2), or 78% (p<0.01). The overall course rating for the course was 96/100. Trainee self assessment of Overall Skill increased from 63.3/100 to 83.4/100 and Overall Knowledge increased from 60.3/100 to 81.8/100 (p<0.01). 23 of 34 performance objectives were completed by at least half of the teams during their first attempt. All teams (6/6) were able to resuscitate two simulators and nearly all teams (5/6) prevented anthrax exposure to the hospital during their second scenario attempt. Conclusions: Our 1-day EPT course for novice and experienced patient care providers recreated a multi-actor clinical disaster and enhanced provider knowledge, comfort level and EPT skill. A larger scale study, or multi-center trial, is needed to further study the impact of this curriculum.

021 The Influence of Race, Gender, and Socioeconomic Status on Self-Care Behaviors in Patients with Type 2 Diabetes, David M Cykert1, Joni L Strom Williams2, Leonard E Egede2; 1Medicine, MUSC, 2Medicine, VAMC.

Background: Diabetes mellitus is characterized by high blood glucose levels. While the incidence of diabetes has increased throughout the last decade, ethnic minorities experience a disproportionately higher disease burden and mortality rate from diabetes compared to their White counterparts. This research seeks to examine whether race, gender, and socio-economic status influence self-care behaviors. Methods: 361 patients were recruited from two primary care clinics. Participants completed validated surveys to capture demographics, SES, diabetes self-care activities, and medication adherence. The primary predictors were race, gender, and SES. The primary outcomes were self-care behaviors measured by the Summary of Diabetes Self-Care Activities (SDSCA) and the 8-Item Morisky Medication Adherence Scale (MMAS-8). Results: The results show that there is a significant mean difference in the number of days of exercise by race (p=0.05). Additionally, there is a significant mean difference in the number of days of foot care by race (p=0.004), education (p=0.05), and annual income (p=0.03). Adjusted multiple linear regression showed: (1) males did not comply with a special diet (beta=-0.58, 95% CI -1.06 -0.10), (2) non-Hispanic Whites (beta=-1.7, 95% CI -3.07 -0.39) and non-Hispanic Blacks (beta=-1.7, 95% CI -3.08 -0.39) did not exercise as much, (3) those in the $15,000-$19,999 and $25,000-$34,999 income brackets did not exercise as much (beta=-0.96, 95% CI -1.92, -0.003 and beta=-1.3, 95% CI -2.24, 0.41), and (4) those in the $10,000-$14,999 and ≥$75,000 income brackets did not practice foot care as much (beta=-1.01, 95% CI 2.0, 0.02 and beta=-2.11, 95% CI -3.40, 0.82). Conclusion: This study shows that there are significant race, gender,
education, and income differences in adherence to special diet, routine exercise regimen, and foot care regimen. Other self-care behaviors were not significantly associated with race, gender, education, and annual income. When adjusting for covariates, the differences in special diet, exercise, and foot care persisted. NIDDK 5T35DK007431

022 Multiple Risk Factor Management in Depressed Patients with Type 2 Diabetes Mellitus, Jugal M Dalal1, Leonard E Egede2, 1Medicine, MUSC, 2Medicine, Ralph H Johnson VA Medical Center.

Background: Type 2 diabetes (T2DM) is a disease that affects more than 25 million people in the US, which is about 8% of the population. Comorbid depression in individuals with diabetes has a significant impact on patients’ increased health care costs and increased health risks. It is unclear how depressed individuals with diabetes manage risk factors. The purpose of this study is to measure risk factor control in depressed patients with type 2 diabetes and compare it to risk factor management in patients with T2DM who are not depressed. Methods: This cross-sectional study was conducted by administering surveys to 361 individuals at two primary care sites in Southeastern United States. The validated questionnaire included the PHQ-8 to assess depression, a validated instrument to assess self-care behaviors and patients’ lab values including LDL, hemoglobin A1c, and blood pressure levels. Results: The results show that patients with major depression had decreased medication adherence (r=-0.22, p=0.000), general diet (r=-0.14, p=0.009), special diet (r=-0.18, p=0.0005), and exercise (r=-0.18, p=0.0005). The data showed significant differences in general diet (4.5 days vs 5.01 days, p=0.04), special diet (4 days vs 4.6 days, p=0.002), and exercise (1.7 days vs 2.5 days, p=0.004) by depression status. Adjusted multiple linear regression showed that medication adherence (beta=-0.677, 95% CI -0.176, -0.179, p=0.008) and adherence to a special diet (beta=-0.741, 95% CI -1.15, -0.33, p=0.000) were significantly associated with major depression. Conclusion: This study showed that major depression was correlated with a decrease in adherence to pertinent self-care behaviors for managing T2DM. Even after adjusting for covariates, those with major depression had a significant decrease in medication adherence and eating a general diet. However, major depression did not have a significant impact on health outcomes, such as hemoglobin A1c, blood pressure, and LDL. NIDDK 5T35DK007431

023 Impact of Socioeconomic Status on Type 2 Diabetes Control in Non-Hispanic Blacks and Non-Hispanic Whites, Laven E Keitt Jr1, Clara E Dismuke2, Leonard E Egede2, 1Medicine, MUSC, 2Medicine, VAMC.

Background: Type 2 diabetes (T2DM) causes many health complications due to the body’s inability to produce or use insulin. Research supports that those in lower socioeconomic groups and ethnic minorities have poorer diabetes related health outcomes. The purpose of this study is to determine the impact of socioeconomic status on diabetes related health outcomes, such as hemoglobin A1C (HbA1C), LDL, and blood pressure. Methods: A sample of 361 patients with type 2 diabetes was recruited from two primary care sites in Southeastern United States: an academic Internal Medicine clinic and a primary care clinic at a Veteran Affairs (VA) medical center. These patients completed a structured survey containing socioeconomic variables such as: ethnicity, race, years of education, income, and insurance plan. Lab values including HbA1C, LDL, and blood pressure values were obtained from electronic medical records. Results: The results show that non-Hispanic Whites have significantly lower HbA1C, blood pressure and LDL than non-Hispanic Blacks and Hispanic/Asian/American Indian groups. Insurance status is also significantly associated with systolic blood pressure (p=0.003) and LDL (p=0.0005). After accounting for covariates, compared to non-Hispanic Whites, non-Hispanic Blacks had higher systolic BP (beta=6.17, 95% CI 1.77, 10.6, p=0.006) and diastolic BP (beta=7.01, 95% CI 4.13, 9.88, p=0.000). When compared to non-Hispanic Whites, the Hispanic/Asian/American Indian group was associated with having higher HbA1C (beta=1.2, 95% CI 0.04, 2.35, p=0.04) and LDL (beta=44.8, 95% CI 16.0, 73.5, p=0.002). Overall, there was no indication that education or annual income had a significant impact on diabetes related health outcomes. Conclusion: The data indicates a stronger relationship between race and insurance status and diabetes outcomes than the other socio-economic factors assessed. This is an interesting finding because it suggests that race is more strongly associated with diabetes outcomes than education or income. NIDDK 5T35DK007431

024 Seeking Care and Antibiotic Expectations with Cough Related Illness in Primary Care, Shannon A Looney1, Susannah Brown1, Kevin Floyd1, Brittany Watson1, William J Hueston2, 1COM, MUSC, 2Family Medicine, MUSC.

Patients with cough related illnesses are common in primary care practices. The goal of this study was to evaluate what symptoms are associated with seeking care or antibiotic expectations in primary care patients with a cough. We performed a survey of healthy adult patients between the ages of 21 and 65 who came to their physician without a cough related illness. The survey consisted of three scenarios that described a cough related illness but varied in the duration of symptoms and presence of fever. Surveys also differed among patients based on the color of the sputum. 270 patients completed surveys during the summer of 2013. Sputum color was a poor predictor of seeking care or antibiotic expectations, while length of illness and presence of a fever were better predictors of both seeking care and antibiotic expectations. When the duration of illness was changed from 7 to 14 days, patients were 1.47 times more likely to say they would seek care and 1.70 times more likely to expect an antibiotic. When a low grade fever was present, patients were 1.55 times more likely to say would come to the doctor and 1.96 times more likely to expect an antibiotic. These findings were true even though most patients diagnosed themselves as having a viral illness. The duration of symptoms for more than 7 days and the presence of a low-grade fever are predictive of patients’ likelihood to seek care and expectations for antibiotics when they have a cough related illness. Sputum color is not a good predictor of these behaviors.

025 Prevalence of Antenatal Depression and Anxiety, Cameron T Bell, Maddie Caballero, Constance Guille; Psychiatry, MUSC.
Prevalence rates of depression in pregnancy range from 8.5-14.5%. Depression in pregnancy has negative consequences for women and their children, including risk for childhood behavioral problems. Anxiety disorders often co-occur with major depression; however, most studies examine only depressive or anxiety symptoms in pregnancy. In this study we aim to determine the prevalence of depression with comorbid anxiety symptoms in pregnancy and factors that associate with this symptom profile. A cross-sectional survey including demographics, reproductive status, mental health history and current depressive and anxiety symptoms were collected from women receiving outpatient care at an obstetrics clinic at MUSC. Depressive and anxiety symptoms were measured via the Patient Health Questionnaire (PHQ) and Generalized Anxiety Disorder (GAD) Scale. 231 women were enrolled in the survey. From surveys facilitated by summer interns, 74.7% (83/111) of women agreed to participate. Among completed surveys, 107 women were pregnant. 6 of these women failed to finish the depression survey and 7 did not complete the anxiety survey. 9.9% (10/101) of pregnant women met our clinical cut off for depression and 13% (13/100) met the cut off score for GAD. In women that were depressed, 90% (9/10) had a comorbid diagnosis of GAD. After controlling for potentially confounding variables, including age, ethnicity, race, parity, employment, income, education, past and current mental health history, we found that women with lower incomes (OR 0.78; 95% CI: 0.64-0.93) and prior diagnosis of depression (OR 2.33; 95% CI: 1.35-4.42) associated with an increase in depression with comorbidity anxiety. Women with a prior diagnosis of depression and lower income are at higher risk for depression with comorbidity anxiety in pregnancy, compared to women without this history or higher income. Universal screening of all pregnant women for depression with comorbidity anxiety is impracticable. Identifying those at higher risk may help facilitate identification and appropriate treatment referral. 

DART Fellowship Grant Number NIDA R25DA020537

026 Sensory Modulation Strategies Employed By Community-Dwelling Adults with Severe Mental Illness, Pamela L Vesely, Rachel A Boyd, Ella H Hyatt, Sara E Jensen, Kelley M Knoebel, Jessica A Martin, Elizabeth F Stuber, Nancy E Carson; Occupational Therapy, MUSC.

Sensory processing is the way by which a person’s nervous system receives, organizes, and uses sensory information from the body and environment in order to move and function effectively in the environment. Sensory processing disorder occurs when sensory signals are not efficiently organized by the body in order to produce an appropriate response. (Brown et al., 2001). Brown et al. (2002) used the Adult Sensory Profile to study adults with schizophrenia and bipolar disorder. They found that both had higher scores on sensation avoiding and that individuals with schizophrenia had higher scores on low registration and lower scores on sensation seeking as compared to individuals without mental illness. In the United States 1 in 17 adults, or about six percent of the adult population suffers from a severe mental illness (National Alliance on Mental Illness [NAMI], 2011). Addressing sensory modulation strategies to increase occupational performance is one approach to assist individuals with severe mental illness to live in the community independently. The addition of sensory modulation strategies to an individual’s daily routine can be helpful and supportive of functional performance (Champagne, 2010). Using both quantitative data and qualitative data to assess sensory functioning can provide a thorough understanding of the individual’s ability to modulate sensory input. The Adult Sensory Profile and a qualitative questionnaire were used to assess sensory modulation in a cohort of community-dwelling individuals with severe mental illness who attend a community drop-in center. The impact of impaired sensory modulation on their occupational performance is considered and common sensory modulation strategies that they employ are identified. Scores on the Adult Sensory Profile are compared with earlier studies to identify common patterns in sensory tendencies. The information obtained will be used to complete a needs assessment to develop a sensory modulation program for a community mental health drop-in center.

027 Relationship Between Efficiency of Arm Movement and Patient-Perceived Recovery After Stroke, Blair H Stec1, Patricia M Pierson1, Michelle L Woodbury1, 2; 1Occupational Therapy, MUSC, 2Rehabilitation Research, Ralph Johnson VAMC.

Background: Stroke reduces efficiency of reaching movement, which may limit the ability to do tasks of daily living, from reaching for a glass to caring for a child. The inability to successfully complete these tasks negatively affects the patient’s perceived level of recovery after a stroke. Stroke rehabilitation programs aim to improve quality of life and therefore should focus on improving factors contributing to perceived recovery. One important factor of perceived recovery could be movement efficiency. However, the relationship between movement efficiency and perceived recovery is relatively unstudied.

Objective: To explore the relationship between the efficiency of arm movement and patient-perceived recovery. Methods: This was a prospective correlational study of 15 subjects of which 9 were male, between the ages of 20 and 71, at least 3 months post mild to moderate stroke. Patient-perceived recovery was measured by the Stroke Impact Scale. Efficiency of movement was measured during a forward reach-to-grasp task using motion capture kinematic analyses. Efficiency of movement was defined as a smooth, direct reach (kinematic variables: peaks in the velocity profile and index of curvature). Spearman’s rho correlation coefficients were used to determine the relationships between patient-perceived recovery and the kinematic variables (p<0.05). Results: There was a moderately strong inverse relationship (-0.57, p=0.03) between peaks in the velocity profile and perceived recovery. There was a moderate inverse relationship (-0.42, p=0.12) between index of curvature and perceived recovery... Conclusion: Efficiency of movement has a significant impact on how a person perceives their level of recovery after stroke. This implies that it is not only the ability to perform the task, but also the ability to perform the task efficiently, that increases patient-perceived recovery. This makes the argument that stroke rehabilitation should emphasize both performing a task and performing it efficiently. Veterans Affairs Rehabilitation Research & Development, #01RX000799

028 The Effects of a Custom Virtual Reality Gaming System on the Movement of the Paretic Upper Extremity in Stroke Patients, Elaina A Gaither1, Rebecca M Patten1, Alison B Gilchrist1, Michelle L Woodbury1;
Background: Observing a behavior while engaging in a similar movement activates the mirror neuron system, thus promoting neural reorganization during post-stroke rehabilitation. Virtual reality (VR) is a feasible (price, accessibility) and safe addition to traditional rehabilitation. Evidence has suggested the positive effects of VR rehabilitation; however the precise movements of the paretic upper extremity (UE) following VR rehabilitation have yet to be determined. Objective: Determine whether using a custom VR gaming system that encourages repetition of elbow extension enables patients to increase normalized movement. Methods: Nine patients (7 men, aged 24-62 years, 3-144 months post-stroke) underwent 5 consecutive days of rehabilitation, consisting of 60-minute sessions of playing the gaming system. Each session involved an average of 156 repetitions of elbow extension. Pre- and post-intervention, kinematic motion analyses of the paretic UE were measured to determine trunk displacement, elbow extension and velocity of movement. Results: Considering the results on an individual basis, increased normalized movement was noted. Post-intervention, 66.6% of the sample decreased trunk displacement by an average of 52mm, while 3 of 9 patients decreased by over 66mm. In addition, 66.6% of the sample increased elbow extension by an average of 8.2%, while 2 of 9 patients increased by over 15%. Lastly, 56% of patients increased velocity of the paretic UE by an average of 0.14m/s. Considering the wide range of abilities represented, the patients with more severe movement deficits demon-strated greater improvements. Conclusion: The trends in the data show that VR gaming may be an effective intervention for increasing move-ment in stroke patients. Despite the wide range of abilities and the short duration of the trial, the majority of patients showed measurable improvements in just 5 days. A larger trial should be conducted over a longer period of time to determine the maximum effects of the VR gaming system.

029 Perceived Recovery of Stroke As It Relates to Activity Participation, Whitney N Weigold1, Anna Blair Price1, Michelle L Woodbury2, 3, Occupational Therapy, MUSC, 2Rehabilitation Research, Ralph Johnson VAMC.

Introduction: The majority of stroke survivors report limitations participating in meaningful daily activities (activity-participation) following stroke. These activities include self-care, household tasks, vocation and community involvement that bring meaning and purpose to participants’ lives. It is important to know what factors affect activity-participation in order to plan and implement effective rehabilitation. Decreased activity-participation lowers life satisfaction. However, it is unknown how activity-participation affects self-perceived recovery. Objective: To examine the relationship between activity-participation and self-perceived recovery. Methods: Twelve participants (7 males, average age 54 years) with stroke (average 31-months post) completed the Activity Card Sort (ACS) to measure activity-participation and the Stroke Impact Scale (SIS) to measure self-perceived recovery and use of paretic hand to accomplish meaningful and purposeful daily activities. Results: Spearman’s rho correlational analyses indicated the percentage of meaningful activities participated in is strongly correlated to self-perceived recovery (r=0.61, p=0.04), and paretic hand function is strongly correlated to self-perceived recovery (r=0.80, p=0.00). Regression analysis indicated that together paretic hand function and activity-participation account for 66% of perceived recovery (adjusted R2=0.66). Conclusions: The results indicate that activity-participation and self-perceived recovery are strongly related. In addition, use of the paretic hand for completion of meaningful tasks is also related to self-perceived recovery. These findings suggest that restoring participants’ ability to accomplish meaningful and purposeful activities is important for life satisfaction and it is equally important that participants gain the ability to use paretic hand for meaningful activity-participation. It is possible these results could guide treatment planning in stroke rehabilitation. Veterans Affairs Rehabilitation Research and Development, #101RX000799

030 Pre and Post Injury Alcohol Consumption and Smoking Status Among Acute Spinal Cord Injury (SCI) Participants, Janice F Davis1, James S Krause2; 1Medicine, MUSC, 2Health Professions, MUSC.

Objective: To identify patterns of smoking and alcohol use at the time of spinal cord injury onset, how these behaviors change approximately one year after hospital discharge, and how these changes compare to the general population. Methods and Participants: 566 subjects were recruited from a large specialty hospital in the southeastern United States. All participants had sustained a traumatic spinal cord injury, were currently hospitalized for initial rehabilitation at enrollment, and are at least 16 years of age. Participants were asked to complete a health questionnaire at baseline and average of 49.8 days post injury and again at follow-up an average of 17 months post injury. Results: Whereas 37% of respondents were smokers before their injury; 18% smoked after injury. This compares with 23% in the general population. Sixty six percent reported having at least one drink within the past 30 days prior to their injury, compared with 50% had at least one drink within 30 days of completing the questionnaire (51% of the general population had at least one drink within the past 30 days). Forty three percent of respondents engaged binge drinking prior to injury; 18% continued to binge drink post-injury, whereas only 13 % of the general population engaged in binge drinking. Conclusions: Pre-injury binge drinking, alcohol consumption, and smoking rates are higher than the general population. Alcohol consumption and smoking behaviors decrease after injury. When stratified by race, African Americans continue to binge drink more than the general population post injury. Summer Health Professions Research; MUSC Longevity After Injury Project

031 The Impact of Amount of Cannabis Use on Cognitive Function in Adolescents, Jessica B Lydiard1, Kevin M Gray2; 1Psychiatry and Behavioral Science, MUSC, 2Clinical Neuroscience, MUSC.

Background: Cannabis is the most frequently used illicit substance during adolescence, a critical stage of neurodevelopment. The impact of cannabis use during this vulnerable period is underexplored. In this study, we investigate the impact of cannabis use in the past 30 days on cognitive performance in adolescents with the hypothesis that heavier use will be associated with poorer performance. Methods: Participants were 116 cannabis-
dependent adolescents (ages 15-21) entering a pharmacotherapeutic treatment trial. Timeline follow back, confirmed by urine cannabinoid testing, was used to measure days of use at baseline and throughout the 8-week trial. Subjects were categorized as heavy (N=89) or light (N=27) users based on use in the 30 days prior to baseline (≤20/30 vs. >20/30 days). A computerized cognitive assessment was administered at baseline and 4 weeks after study entry. An Independent samples Mann Whitney U-test was used to assess differences between cognitive function scores in heavy and light users at baseline. Change in cognitive performance from baseline to 4 weeks was compared for abstinent vs. non-abstinent subjects. Results: At baseline, heavy users scored significantly higher than light users in executive function (p<.05), sustained attention (p<.05), working memory (p<.05), cognitive flexibility (p<.01), and psychomotor speed (p<.01). Among participants retained in the trial, those who were abstinent at 4 weeks (N=44) demonstrated greater improvement in cognitive testing from baseline as compared to those who were not abstinent (N=34). Discussion: The finding that heavy cannabis users had better cognitive performance at baseline contradicted our hypothesis and is inconsistent with existing literature. Baseline differences in educational status, although not statistically significant, may have influenced this finding, as heavy users were more likely to have some college education. The finding of improvement in all domains of cognitive function with abstinence is consistent with our hypothesis and the literature. NIDA R25 DA020537; R01 DA026377; NCRR UL1 RR029882

032 Plasma Homocysteine Levels As a Putative Marker of N-Acetylcysteine Compliance in Cocaine-Dependent Patients. Camilo F Mateus, Steven D LaRowe, Robert J Malcolm; Psychiatry and Behavioral Science, MUSC.

Cocaine is used by approximately 14 million people in the world and cocaine addiction is difficult to treat, as treatment is limited to talk-therapy with no FDA approved medications. N-acetylcysteine (NAC) has been shown to decrease both cocaine use and reactivity to cocaine-cues. NAC is under investigation as a possible treatment for cocaine dependence, however there is no direct measure of NAC compliance. Homocysteine levels are believed to decrease with NAC administration, suggesting that homocysteine may be used as a proxy measure of NAC treatment adherence. This study examined homocysteine levels in 66 treatment-seeking cocaine-dependent subjects receiving placebo (n=24), 1200mg (n=23) or 2400 mg (n=19) of NAC daily during an 8-week double-blind trial. Riboflavin levels were collected at each study week and were used as a comparison measure of compliance. Individuals with riboflavin levels greater than 1500 ng/mL were considered compliant for the week. Percent compliance was calculated by number of riboflavin levels greater than 1500 ng/mL divided by total number of riboflavin levels. An ANOVA revealed a significant difference between the 2400mg and the 1200mg group at week 4 (p<05) and week 8 (p<05) and a significant difference between the 2400mg group and the placebo group at week 8 (p<01). Regression analysis at week 4 showed a significant group effect, B = 2.7, t= 2.9, p <01, group by %compliance interaction, B = -.04, t= -3.7, p <001 and an overall R-square of26, F (3,65)= 7.1, p<001. Regression at week 8 had an overall R-square of27, F (3,45)= 5.0, p<01 with no significant group or %compliance effect or group by %compliance interaction (p=0.55, 0.63, respectively). There appears to be a threshold dose between 1200mg and 2400mg of N-acetylcysteine to enact a change in homocysteine levels occurring after 4 weeks. Future parametric studies are needed with additional dosage increments between 1200mg and 2400mg NAC. DART Fellowship (NIDA R25 DA020537)

033 Effects of SPARC/Exon-2 Deletion on Murine Myocardial Collagen Processing. Ruth E Salas1, Yuhua Zhang2, Bradshaw Amy2, 3Medicine, MUSC, 2Gazes Cardiac Research Institute, MUSC.

The cardiac ECM contains a fibrillar collagen network composed of collagen fibers made up of type I and III collagen. Collagen type I is known to be the most abundant. Circumstances in which the ECM accumulates during cardiac remodeling is frequently associated with changes in myocardial passive stiffness, and this can in turn affect diastolic function. Chronic pressure overload (PO), as is observed in hypertensive subjects, results in fibrosis, i.e. collagenous ECM deposition. In order to treat, reverse, or prevent fibrotic changes observed following PO, we must first understand the processes and pathways that regulate collagen deposition. Both, SPARC and the N-propeptide of collagen I are believed to have some involvement in collagen processing or deposition, and therefore studying the effects on collagen synthesis, processing, and deposition following the targeted deletion of the genes responsible for encoding these polypeptides has been a focus of our studies. Immunoblot analyses with Col I antibodies showed significantly more procollagen intermediate species were produced by SPARC-null/Exon2Δ murine cardiac fibroblasts when compared to WT. Collagenase digestion of cell extracts of SPARC-null/Exon2Δ and WT cardiac fibroblasts showed that there is significantly more intracellular collagen species in the cardiac tissue of double transgenic mice than in WT. This suggests the possibility that the intermediate collagen species are being retained in the cell, possibly for destruction or further processing and/or transport. Our studies therefore support a role for SPARC as an important regulator of procollagen processing and suggest a role for the N-propeptide as a regulator of deposition and stabilization of fibrillar collagen into the ECM. NIH Grant 5R25HL096316-05

034 The Role of C3a and C3aR in Acute Cardiac Rejection, Gabriel C Segarra, Carl Atkinson; Microbiology and Immunology, MUSC.

Complement activation plays a role in acute rejection (AR) of transplanted cardiac tissue. Previous studies show that inhibition of the C3 activation product C3a and its receptor C3aR improves post-transplant survival time in mice by protecting against onset of AR and graft loss. Here we investigate the role of C3a/C3aR in cardiac AR using C57Bl/6 and Balb/c mice. Tissue allografting resulted in four combinations: B6-Balb/c, Balb/c-B6, B6-Balb/c C3aR-/-, and Balb/c C3aR-/- to B6. To test for potential therapies, an additional group of B6-Balb/c mice were treated with C3aR antagonists. Survival studies showed a peak in AR outcomes at 7 days post-transplant and a survival increase from C3aR antagonist treatment, suggesting a survival benefit from suppression of C3a/C3aR. Day-7 cardiac tissues were analyzed to elucidate C3a/C3aR's role in transplantation and to search for therapeutic opportunities. To determine whether a
specific inflammatory cell subset provides protection from AR, changes in immune infiltrate profiles in grafts from each experimental group were observed immunohistochemically. Formalin-fixed and paraffin-embedded cardiac tissues were IHC-stained for macrophages [MAC-3, M1, M2], neutrophils [Gr-1], T-cells [CD3], B-cells [B220], and the c3d and c4d complement fragments using Anti-Rat and Anti-Goat Ig. Stains were digitized and analyzed to quantify immune cell infiltration. *SURP: NHLBI RO1 94766*

**035 Does Over Reliance on Automated Cardiac Function Analysis Have an Impact on Function Reporting in Patients with Acute Chest Pain?** Nicholas S Honko, Nelson Seabrook, Pal Suranyi; Radiology, MUSC.

The purpose of the study was to evaluate the performance of an automated software tool for left ventricular (LV) functional analysis and the accuracy of radiological reports when compared with manually corrected functional analysis of triple rule-out chest CT data. CT datasets from 168 patients (50.5 +/- 12.0 years, 77 men) with acute chest pain were retrospectively analyzed using post-processing software that was manually adjusted to obtain functional data for the left ventricle (end-systolic volume, end-diastolic volume, stroke volume, ejection fraction, cardiac output). These data were compared with the patients' reported values (from the radiological reports), as well as with the same values as given by the software if no manual adjustments were made. Ejection fraction values from both the fully automated and the reported data were found to be underestimated, mostly due to over-estimation of patient end-systolic volumes. For the fully automated ejection fraction: mean error = -9.14 (R=0.71, p<0.001), and for the radiological reports' ejection fraction: mean error = -5.81 (R=0.75, p<0.001). The errors led to situations where automated and/or reported values yielded a false positive or false negative result for LV function when compared with the manually corrected values. When using the fully automated post-processing tool, 52 normal patients were erroneously identified as having abnormally low ejection fractions. Similarly, when using the radiological reports, 27 patients with normal ejection fractions (per manually adjusted calculations) were identified as having abnormally low ejection fractions. Over-reliance on automated function analysis will lead to systematic underestimation of LV ejection fraction, mainly due to over-estimation of end-systolic volumes, which could lead to possible misdiagnoses (predominantly false-positives). Careful physician input is necessary to correct/override software errors and to avoid erroneous reporting of function data. *Summer Health Profession Program*

**036 Developing a Normal Standard Left Ventricular Wall Motion Assessment with Cardiac MRI Using a Novel Thresholding-Based Post-Processing Algorithm.** Rodman L Singleton1, Matt Duffin1, Pal Suranyi2; 1COM, MUSC, 2Radiology, MUSC.

Abstract not available.

**037 Impact of Maternal Vitamin D Status on Mineralized Tissue.** Ann G Kelly, Judy Shary, Myra Ebeling, Carol Wagner, Susan Reed; Pediatrics, MUSC.

The active form of vitamin D is essential for maintaining adequate levels of calcium and phosphorus, which constitutes nearly 70% of bone and 96% of enamel in the form of hydroxyapatite. Amelogenin is shown to be positively regulated by vitamin D in rat incisors, and ameloblasts contain vitamin D receptors. Deficiency during pregnancy has been linked to maternal hypocalcemia, and it is the fetal environment in which bone and teeth develop. We hypothesize that the maternal sufficiency of vitamin D during pregnancy will promote enamel mineralization, and that it will be related to infant total body bone mineral content (BMC). A cohort of 116 children (22 African American, 57 Hispanic, 37 Caucasian) from the 400 women who participated in one of the two original RCTs, treated with 400 IU, 2000 IU, or 4000 IU of vitamin D daily during pregnancy, were analyzed during the first year of life and then yearly between ages 3 and 6. We compared maternal vitamin D status during pregnancy to presence of enamel hypoplasia (EHP) of the two frontal incisors using a scoring method, and to presence of salivary Streptococcus mutans (SM), the primary caries-causing bacteria which is associated with degree of hypoplasia. We analyzed EHP and SM against several variables, including treatment, race, gender, age, mother's education, insurance status, breastfeeding history, marital status, infant 25(OH)D at delivery, and infant total body BMC. Groups were equally divided by gender and maternal vitamin D treatment. There was a positive correlation between breastfeeding at discharge and 4-6 weeks of age and presence of hypoplasia, a relationship which persisted after controlling for race. Children of mothers who did not breastfeed were 2.3 times more likely to have EHP. Additionally, mother’s race, insurance, education, and whether she was breastfeeding at discharge were correlated with presence of SM. After controlling for race, only level of education was significant, with children of mothers who had high school or less education being twice as likely to have SM. Mother’s vitamin D status throughout pregnancy, and infant 25(OH)D were also correlated to presence of SM, a trend which did not persist after controlling for race. Maternal vitamin D status and infant BMC were not related to presence of EHP or SM, as predicted. Although comparison of mineralized tissues in this initial cohort did not show any statistical significance, further studies should be conducted to confirm these findings, as there is a possible misclassification bias in enamel scoring, in addition to a lack of understanding infant BMC normalization. Furthermore, breastfeeding proved to be protective against EHP using the scoring method, but not against SM. Socioeconomic factors play a large role in the likelihood of children to have salivary SM, likely leading to higher incidence of caries among African Americans, Hispanics, and children of less educated mothers, regardless of maternal vitamin D status during pregnancy.

**038 Circulating Fibroblast Precursors and Their Role in Metastatic Sarcoma.** Dayvia A Laws1, Andrew S Kraft2, Lee R Leddy3, Amanda C LaRue1; 1Pathology, MUSC, 2Medicine, MUSC, 3Orthopaedic Surgery, MUSC.

Approximately half of all patients with soft tissue sarcoma experience disease recurrence and die of metastatic cancer. Gaining a better understanding of the metastatic...
environment is essential to developing new therapies. The tumor microenvironment plays a pivotal role in promoting tumor metastasis. One of the most prominent cell types of the tumor microenvironment is the carcinoma associated fibroblast (CAF). Our studies, based upon a murine single hematopoietic stem cell (HSC) transplantation model, have demonstrated that HSCs are a novel source of CAFs and their circulating fibroblast precursors (CFPs). We have shown that murine CFPs are present in peripheral blood, increase with tumor burden and contribute to tumor growth. However, the role of human CFPs in metastasis of soft tissue sarcoma has yet to be determined. We hypothesize that HSC-derived CFPs promote sarcoma cell proliferation, migration, and invasion. To determine the role of CFPs in sarcoma metastasis, we established a method for culturing fibroblasts from peripheral blood obtained from patients diagnosed with metastatic sarcoma. Cultured cells were then characterized by immunohistochemistry to profile fibroblast and hematopoietic markers. Findings demonstrate that fibroblasts can be isolated from the circulation of patients with metastatic sarcoma. To next address the functional role of CFPs during sarcoma metastasis, we examined the ability of conditioned media from patient-derived CFPs to influence the proliferation, migration, and invasion of HT-1080 cells, a human sarcoma line. Results indicate that cultured CFPs from patients with metastatic sarcoma promote the proliferation, migration and invasion of HT-1080 cells. Given that proliferation, migration, and invasion of tumor cells are essential steps in the metastatic cascade, these findings suggest that CFPs promote tumor progression. Ongoing studies involve analysis of CFPs at various time points based upon chemotherapeutic treatment to evaluate differences in numbers of CFPs, marker expression, growth factor production, and ability to promote metastasis. Biomedical Laboratory Research and Development Program of the Dept. of Veterans Affairs; NIH/NCI RO1 CA148772; P30 CA138313

039 The Analysis of Transforming Growth Factor Beta Signaling in Mouse Thoracic Aortic Fibroblasts, Lee C Morris, Adam W Akerman, Robert E Stroud, Risha Patel, Jeffrey A Jones; COM, MUSC.

Abstract not available.

040 Exploring Pim Kinases As a Biomarker for Treatment Response and Overall Outcome in Multiple Myeloma, Logan N Roof, John Lazarchick, Margaret Romano, Boding Zhang, Jagadish Kummetha, Tricia Bentz, Terri Matson, Yubin Kang; COM, MUSC, Pathology, MUSC, Hematology/Oncology, MUSC, Hollings Cancer Center Clinical Trials Office.

Multiple myeloma is the second most common hematological malignancy in the U.S. where it accounts for ~11,000 deaths each year. Multiple myeloma is a disease with heterogeneous progression and mixed responses to treatment. Some patients relapse even with autologous hematopoietic stem cell transplantation and become resistant to available chemotherapeutics, whereas others respond to treatment and remain in remission years after diagnosis. Identification of molecules and/or genes correlating with treatment response and overall outcome will have important implications in patient care and in our development of novel therapeutic agents. Pim kinase is a family of serine/threonine kinases with 3 members (Pim1, Pim2 and Pim3). We previously found that Pim kinases are highly expressed in myeloma cell lines and are important for myeloma cell survival. We have shown that targeting Pim kinases with Pim inhibitors decreased myeloma cell growth and induced apoptotic cell death. We thus hypothesized that Pim kinases could be used as a biomarker predicting treatment response and outcome in multiple myeloma. We performed a retrospective study of 102 patients to determine the utility of Pim kinase expression as a biomarker and to dissect out the individual contribution of these 3 Pim kinases in myeloma. The paraffin-blocked bone marrow biopsy samples at the time of initial diagnosis were obtained and sectioned. The sections were stained with CD138, Pim1, Pim2 and Pim3 antibody and the expression of Pim1, Pim2 and Pim3 in CD138+ myeloma cells was scored. Patients’ medical records were reviewed and the following information was extracted: age, gender, cytogenetics, FISH, monoclonal M protein level, bone marrow plasma cell number, international stage index, treatment regimen, autologous hematopoietic stem cell transplant, treatment response, and survival. We are currently completing immunohistochemical staining of patient slides and will perform univariate and multivariate analyses. Successful accomplishment of our study will have significant implications in the care of multiple myeloma patients. College of Medicine Dean’s Office; Summer Health Professionals

041 Functional Analysis of the Woronin Body Protein in Aspergillus Fumigatus, Sarah Mushtaq, Christopher Gehrike, Shannon K Esher, Praveen R Juvvadi, William J Steinbach; COM, MUSC, Pediatrics, Pediatric Infectious Diseases, Duke, Molecular Genetics and Microbiology, Duke, Pediatrics, Pediatric Infectious Diseases, Molecular Genetics and Microbiology, Duke.

Aspergillus fumigatus is a fungus that causes invasive Aspergillosis in immunocompromised patients and is of considerable health concern due to increasing mortality rate and drug resistance. The fungus grows as elongated hyphae with septa separating each hyphal compartment. Each septum has a septal pore that aids in communication between the hyphal compartments. Located within the hyphae of this fungus are proteinaceous organelles, Woronin bodies, whose main function is to plug the septal pore and protect the fungus during hyphal injury. HexA is a protein that is a major component of the Woronin body, and is related to the core structure of this organelle. Previous work in the lab focused on generation of a hexA knockout strain, which was compared to wild-type and showed a decrease in hyphal growth under cell wall stress conditions. It was noted that there was hypersensitivity to β-glucan synthase inhibitor, caspofungin. Localization experiments of HexA revealed that caspofungin treatment resulted in the plugging of the Woronin body indicative of cell wall stress. To further investigate the role of the Woronin body, I cloned the hexA CDNA into a pGEX6P-1 vector in order to prepare the recombinant protein to study protein interactions in vitro. I also constructed a plasmid pBHPMCHHT, which was used for transformation into the Aspergillus fumigatus (Af293 strain) for visualization of the Woronin body. This strain will be used to study Woronin body protein interactions in vivo. Because Woronin body is a filamentous fungal specific organelle, research on its function and interactions will lead to identification of better antifungal targets for future therapies against invasive Aspergillosis. Duke University Medical Center.
042 Anthropometric Variables and Body Composition Data As Predictors for Adiponectin Levels in an Overweight or Obese Youth Population, Callie S Osborne, Sarah Stein, Janet Carter, Melissa Henshaw; Pediatric Cardiology, MUSC.

Introduction: Nearly 17% of children and adolescents ages 2-19 years are obese. Childhood obesity is a major risk factor for developing premature cardiovascular disease (CVD) including coronary artery disease (CAD). Novel serum biomarkers, such as adiponectin, are emerging as screening markers of CAD risk. Adiponectin levels are lowered in the obese state and decreased adiponectin levels are associated with CAD. The purpose of this study was to analyze the relationship between adiponectin concentrations, anthropometric variables, and body composition variables in an overweight or obese South Carolina pediatric population. Methods: The data collected for this study was extracted from a 2009-present study conducted at the Medical University of South Carolina. The subjects included 101 overweight or obese youths aged 4-21. Overweight and obese were defined by CDC BMI percentile definitions. Anthropometric covariates included relative BMI percentiles, waist circumference percentiles, waist to hip ratio, and average daily exercise, age, race, and gender. Body composition data as determined by DEXA scans were body fat and net average percent fat of the abdomen. Univariate and multivariate regressions were used to assess the associations between serum adiponectin and the various anthropometric and body composition variables. Results: In the univariate models, negative significant correlations existed with age, weight, waist circumference percentile, waist to hip ratio, and relative BMI. Significant correlations were also found among males and whites. Body fat was moderately correlated. No significant correlations were found regarding net average percent fat or daily exercise. In the multivariate model, adiponectin remained significantly correlated with all measurements significantly correlated in the univariate models. Conclusions: This study found strong correlations between adiponectin and waist circumference percentile, relative BMI, and waist to hip ratio. Evaluations of anthropometric measurements are non-invasive and quick assessments to perform in order to assess adiponectin serum levels and thus risk of CAD. SCTR; NIH/NCRR ULI RR029882 and ULI TR000062

043 Secondhand Tobacco Smoke Exposure and Exacerbation Severity Among Children Hospitalized for Asthma, Nils Shirley1, Annie L Andrews2, Karen Wilson3, Michelle Robinson, Elizabeth Ojukuwic4, LCOM, MUSC, Pediatrics, MUSC

Introduction: Secondhand tobacco smoke (SHS) is of major concern in the pediatric population due to its negative effects on the respiratory system. The objective of this study was to assess if there is an association between SHS exposure and exacerbation severity among children hospitalized for asthma. Methods: MUSC, in conjunction with Children’s Hospital of Colorado, conducted a retrospective chart review of all patients age 2-18 admitted to either institution in 2012 with a primary discharge diagnosis of asthma according to ICD-9 codes. 689 charts are being reviewed. Demographic variables included age, gender, race, and primary payer. The study assessed asthma exacerbation severity using: length of stay (LOS), PICU admission, oxygen requirement, IV steroids, and IV magnesium. The primary independent variable was reported SHS exposure. All information was entered into REDCap. Statistical analysis software program (SAS 9.3) abstracted the data from RedCap. Once Children’s Hospital of Colorado has completed their data collection, we will run bivariate analysis (chi-square, t-test, Mann-Whitney U test) to assess for an association between SHS exposure and exacerbation severity. Logistic regression models will be built to identify any independent association between SHS exposure and the exacerbation severity variables. Results: This project is ongoing and the final analysis is yet to be done. The results described below represent preliminary analysis of MUSC data only. Of the 251 patients admitted to MUSC for asthma during the study period, the mean age was 6.3 years and 59% of the patients were male. Race: 57% AA, 29% Caucasian, 9% Hispanic, and 5% other. 67% of the population was on Medicaid, and 32% were privately insured. 42% of patients reported exposure to SHS on a regular basis. Of note, no information regarding SHS was provided in 7% of the population. 20% of patients received IV magnesium and 30% received IV steroids. Conclusion: A large proportion of children admitted to MUSC for asthma report SHS exposure. We anticipate that children with SHS exposure will have more severe exacerbations.

044 The Effects of Maternal Phthalate and Bisphenol A Exposure on Fetal Genital Development, Rebecca R Fulmer1, Lori Cruze2, Louis J Guillette2, Roger B Newman2, COM, MUSC, OB/Gyn, MUSC.

Endocrine disrupting chemicals (EDCs) are products that interrupt normal endocrine signaling in the human body. BPA and Phthalates are the two endocrine disrupting chemicals that the human population is most exposed to. BPA is found in receipts and canned foods, and phthalates are found in personal care products. BPA exerts estrogenic effects by activating endogenous estrogen receptors (Maffini et al. 2006). A variety of widely used phthalates produce anti-androgenic effects. The effects of BPA and phthalates may be a concern for pregnant women. Both BPA and phthalates cross the placenta and can disrupt reproductive tract development in animal models. In male mice, BPA exposure in utero was shown to shorten anogenital distance, a validated marker of decreased androgen exposure (Gupta, 2000). Swan et. al. (2005) showed maternal urine phthalate levels correlated with a shorter anogenital distance in male infants. The present study sought to examine the effects of BPA and phthalates on fetal genital development. Maternal BPA and phthalate exposure, along with health and lifestyle, was assessed through a self-report questionnaire. BPA and phthalate exposure as well as health and lifestyle indices were created from survey responses and compared to genital measurements in males in utero and both males and females at birth. Mean male penile length (PL) and penile width (PW) in utero were 6.76mm (+ 1.37 n=144) and 5.17mm (+ 0.76 n=144) respectively. In males at birth, mean anoscrotal distance was 21.33mm (+4.73 n=95), mean anogenital distance was 42.99mm (+4.78 n=95), mean PW was 10.50 (+1.43 n=94), and mean PL was 25.91mm (+5.94 n=95). In females, the mean anofourcette distance was 12.70mm (+2.65 n=69) and anocitoral distance was 32.29mm (+4.22 n=69). Correlation data between genital measurements and the questionnaire indices are currently under way. Summer Health Professional Program
045 CELF1 Controls ADAM19 mRNA Expression in Oral Squamous Cell Carcinoma, Mehul Z Patel, Reniqua House, Viswanathan Palanisamy; Craniofacial Biology, MUSC.

Post-transcriptional gene regulation plays an important role in modulating and diversifying protein expression CELF1, also referred to as CUGBP1, is a RNA-binding protein which controls nuclear (alternative splicing) and cytoplasmic (mRNA turnover and translation) mRNA processing events. Although, CELF1 is widely studied for its contribution to the development of myotonic dystrophy (DM1), recent studies support CELF1 playing a role in cancer. Published observations from our laboratory determined that CELF1 protein is overexpressed in head and neck squamous cell carcinoma cell lines as well as human tumor samples in comparison to normal specimens. Unpublished work from our laboratory utilizing next generation sequencing (RNA-seq), identified 731 mRNAs controlled by CELF1 in the UM-SCC-74B oral cancer cell line. The data revealed that the mRNA expression of ADAM19 (a disintegrin and metalloproteinase domain 19) is significantly elevated upon CELF1 knockdown in comparison to control UM-SCC-74B cells. ADAM19 is a member of the ADAM family of membrane-anchored metallo-proteinasome implicated cytokine and growth factor shedding, proliferation, migration, degradation of extracellular matrix and neurogenesis. In addition to CELF1 controlling ADAM19 mRNA turnover, reduction of CELF1 also increased ADAM19 protein expression. Preliminary studies to determine the underlying mechanism of CELF1 regulation of ADAM19 revealed that after two hours of Epidermal Growth Factor (EGF) stimulation both CELF1 and ADAM19 protein levels were increased. Furthermore, ADAM 19 protein expression remained constant in EGF stimulated CELF1 knockdown UM-SCC-74B cells, suggesting that CELF1 is a major regulator of ADAM19 expression in oral cancer cells. Experiments to determine the biological role of ADAM19 in oral squamous cell carcinoma are currently under way.

046 Increased Degradation of Amyloid-beta Via Uncharacterized Acidic Proteolytic Pathway, Robert J Baranello1, Trenton Large1, Vasudevaraju Padmaraju1, Debomoy K Lahiri1, Nigel H Greig1, Kumar Sambamurthy1, 1Neurosciences, MUSC, 2SC Governer's School for Science and Math, 3Psychiatry, Indiana University School of Medicine, 4Drug Design & Development, National Institute on Aging.

Accumulation of the β-amyloid (Aβ) protein in the brain as senile plaques is a signature lesion of Alzheimer’s disease (AD). Multiple findings suggest that the fundamental role for Aβ in AD is that the Aβ precursor protein (APP) is primarily processed by alternate pathways and Aβ is a minor metabolite. Although Aβ accumulation can be mediated by either an increase in its production or a decline in its turnover, the degradation of Aβ is not well understood. Endothelin converting enzyme (ECE) is an Aβ-degrading enzyme with a nearly neutral pH optimum and when inhibited increases intracellular Aβ. SH-SYSY cells were cultured in MEM and harvested in cold PBS. Cells were counted with a hemocytometer and lysed in a lysis buffer containing 1% Triton X-100. Mouse brain samples were homogenized in 10 volumes of homogenization buffer (50mM HEPES, 150mM NaCl, pH 7.4) and centrifuged to separate subcellular fractions and pellets were lysed in lysis buffer. Degradation reaction mixes were prepared with: lysates at various concentrations, pH-corrected buffer, 1.5M NaCl, and 100 ng/ml Aβ40, and were incubated at 37°C for one hour and assayed immediately for Aβ utilizing a sensitive double-sandwich ELISA assay. Our studies show that two pools of proteases are active at acid and neutral pH values and rapidly degrade Aβ in cell lysates. We also see strong degradation at acid pH in mouse brain homogenates in the 10k and 100k pellets, however not as significant in the 100k supernatant. Inhibitor sensitivity profiles suggests that metalloproteinases(s) are major contributors to the turnover process at neutral pH, but multiple acid proteases appear to be responsible for degradation at acid pH in both cell and brain lysates. A combination of protease inhibitors failed to significantly inhibit the degradation of Aβ occurring at acid pH, suggesting that other unidentified activities play a key role in Aβ clearance. Alzheimer's Association IIRG 10-173180; NIH AG022103, AG046200, AG042804.

047 Effects of the ACT-1 Peptide in Models of Age-related Macular Degeneration, Elisabeth C Obert1, Beth Coughlin1, Kannan Kunchithapatham2, Gautam Ghatnekar2, Baerbel Rohrer3, 1Neurosciences, MUSC, 2Microbiology and Immunology, MUSC, 3Ophthalmology, MUSC, 4First String Research, Inc.

Age-related macular degeneration (AMD) is a multifactorial disease and is regarded as the most common cause of central vision loss in industrialized countries. The main target tissue affected by AMD is the retinal pigment epithelium (RPE), which together with Bruch’s membrane forms the blood retina barrier. Zonula Occludens-1 (ZO-1) interacts with various cell junction proteins, contributing to cell junction function in the RPE. RPE-barrier dysfunction and blood vessel leakage associated with AMD might result from altered ZO-1 function. Designed to decrease ZO-1’s interactions with its respective binding partners, a synthetic peptide ACT-1 (Alpha connexin carboxy terminus) was developed that competes for the binding of ZO-1. We examined the effects of the ACT-1 peptide in a murine model of laser-induced choroidal neovascularization (CNV). Optical coherence tomography images were taken to measure the cross-sectional area of the individual lesions. Murine RPE flatmounts were stained for markers of cell junction proteins to examine the structure of the RPE surrounding the lesions. The effects of the ACT-1 peptide were determined in vitro in ARPE-19 cells, an established RPE monolayer system. ACT-1 applied via eye drops significantly reduced CNV lesion sizes (26%; P=0.015) when compared to controls. In control animals, ZO-1 staining revealed a large halo of unhealthy RPE cells around the lesion; the diameter of which was greatly reduced by ACT-1 (P<0.001). In vitro data revealed that RPE barrier function was maintained when cells were pretreated with ACT-1 before exposing cells to Vascular Endothelial Growth Factor. We have shown that the ACT-1 peptide is effective in models of RPE cell dysfunction both in an in vivo mouse model, as well as in an in vitro RPE monolayer system. Future research will be conducted to further understand the effects of ACT-1 on the different cell junction types and their relationships to retinopathies like AMD. Stanley and Theodora Feldberg Research Fund.
048 Correlation of ACT1 Administration to Post Surgery Macrophage Phenotype in Skeletal Muscle, Jason A Kopp, Michael J Yost; Surgery, MUSC.

ACT1 is a novel peptide shown to reduce fibrous scarring in skeletal muscle following surgery. The present study examines the effect of administration of ACT1 on macrophage phenotype distribution following creation of an abdominal wall defect in a rat model. Based on separate correlations linking ACT1 and a high M2:M1 macrophage ratio to scar reduction, it was postulated that ACT1 administration would result in an increase in M2:M1 ratio. This study made use of Western blotting to determine macrophage marker concentrations in tissue samples undergoing varying ACT1 treatment. While the present study has not yet produced sufficient data to determine the validity of the hypothesis, it has shown that there is a modification of immune response following administration of ACT1, with a resulting reduction in overall macrophage levels. Future work will focus on correlating the results of this study with neutrophil levels in tissue samples undergoing the same treatment regimen. Summer Health Professional Program; NIH R01 DE019355-01 A2

049 Does a Short Infant Motor Test, The STEP, Correlate with Evidence of Brain Injury By MRS and Later Outcome At 12 Months?, Allison Johnson1, Jamie Beckett1, Patty Coker-Bolt1, Kathryn Hope1, Truman Brown2, Denise Mulvihill2, Dorothea Jenkins3; 1Occupation Therapy, MUSC, 2Pediatrics, MUSC, 3Radiology and Radiological Sciences, MUSC.

Premature infants with normal cranial ultrasounds remain at risk for later motor delays, which go undetected in early infancy. Early magnetic resonance spectroscopy (MRS) is able to detect acute brain injury in infants and correlates with long term outcome in infants with HIE, but has not been related to early infant motor milestones. The aim of this study was to determine the relationship of premature infants performance on a new 10-item motor test, the STEP (Specific Test of Early Infant Motor Performance) scores to MRS measures of brain biochemistry, the Test of Infant Motor Performance (TIMP), and Bayley III Scales. We used existing data from a cohort of preterm infants (n=22), who had MRS scans at term corrected gestational age (CA), using single voxel placement in the basal ganglia (BG) and frontal white matter (WM) (n=11), video recordings of TIMP at 12 weeks (n=22), and Bayley tests (n=19) at 12 months CA. Videos were reviewed and scored using 2 different types of STEP scales, a linear (0 to 3 scale) and matrix version (more defined motor components). TIMP at 12 weeks correlated with both linear (p=0.03) and matrix STEP scoring versions (p=0.004). Bayley motor scores correlated with only the matrix STEP scale (p=0.05). The matrix and linear STEP scales correlated with MRS metabolite Glutamate/Creatine in BG (p=0.055 both). However, TIMP at 12 wks correlated with some brain metabolites that the STEP did not, indicating that further refinement of the STEP scales is required to better relate overall score to this new assessment to key brain metabolites. The correlations between the STEP, TIMP, Bayley, and MRS data provide pilot data for proof of concept for the STEP test. Early motor skills tested in the STEP reflect biochemical evidence of subtle brain injury that may be representative of later development. SCTR Discovery & Early Career Grant; Grant Number: SCTR FY13 UL1 TR000062

050 Effects of Social Determinants on Home Blood Pressure Monitoring After Stroke, Kandace A Joye1, Daniel T Lackland2; 1COM, MUSC, 2Neuroscience, MUSC.

Stroke is a leading cause of death in the United States with over 800,000 people in United States dying each year from strokes and other cardiovascular complications. Hypertension is a major risk factor for stroke. The generation of anti-hypertensive therapies has become imperative especially in preventing recurrent stroke. As such, self-monitoring of hypertension has been proposed as a method for reducing blood pressure. The American Heart Association’s Heart 360 Program is an at home blood pressure monitoring system. Many factors may impact one’s ability to successfully enroll in Heart 360. Such factors can be social determinants. This study sought to examine how health literacy, access to care, and compliance with therapy impacts ones ability to participate in home blood pressure monitoring. It was hypothesized that social determinants impact the patient’s ability to participate in the Heart 360 Program and thus success in at home management of blood pressure. Results showed that a significant amount (59.2%) of stroke patients were eligible to enroll and could benefit from receiving a home blood pressure monitor. Worth noting, of the eligible patients, 65.2% of Black Americans had a diagnosis of hypertension, which was greater than the percentage for White Americans. In summary, it was found that based on race, there is a difference in the number of patients that were eligible to enroll in Heart 360 showing that racial disparities could impact enrollment in home blood pressure monitoring programs. R25 Summer Health Professionals Research

051 The Effect of Home Blood Pressure Monitoring on Recurrent Stroke, Gregory R Franklin1, Andrea Boan2, Daniel Lackland2; 1COM, 2Neurosciences, MUSC.

Hypertension has long been known to be the primary risk factor for stroke, especially in preventing recurrent strokes in post-ischemic patients. Studies have shown that home blood pressure monitoring is an inexpensive way to provide a clear representation of patients’ hypertension and helps to overcome many of the limitations of clinic (in-office) blood pressure readings. The Heart 360 program, sponsored by the American Heart Association, gives patients the ability to record blood pressure readings onto an online database so that clinicians can better treat hypertension, thereby reducing the incidence of recurrent strokes. This study intends to show that home blood pressure monitoring is effective in reducing recurrent strokes in post-ischemic patients by: 1) making post-ischemic patients feel more comfortable about their health 2) giving clinicians more data to be more accurate in treating hypertension in post-ischemic patients 3) assessing the feasibility of using the Heart 360 program 4) using the results from this study to make home blood pressure monitoring a more widespread prophylactic treatment for post-ischemic patients. Summer Health Professional Program; Short Term Research Training for Minority Medical Students in Cardiovascular Research
052 Comparing Ipsilesional and Contralesional Upper Extremity Motor Deficits in Patients with Left or Right Hemisphere Stroke During Reaching Tasks, Danielle C Cardell, Lyndsay J Berger, Kalyn L Cogswell, Michelle L Woodbury, Occupational Therapy, MUSC, Rehabilitation Research, Ralph Johnson VAMC.

Introduction: Brain hemispheres are lateralized for arm movement control; left (L) hemispheric stroke impairs coordination and right (R) hemispheric stroke impairs accuracy. Lateralization studies only examined upper extremity (UE) movements with the arm supported on a horizontal, frictionless surface, and have not examined both ipsilesional and contralesional UE deficits during functional 3D-reach. Objective: Document hemisphere lateralization of both UEs during 3D-reaching. We hypothesize that participants with R-hemisphere damage will exhibit deficits in spatial aspects of reaching; participants with L-hemisphere damage will exhibit deficits in planning reaching movement paths in both UEs.

Methods: Secondary analysis of existing kinematic data obtained during 3D-reaching tasks; 24 subjects (12 males, 11 subjects with L-hemisphere stroke), average 4.75 years post-moderately severe stroke (Fugl-Meyer UE score 23-45), 50-88 years of age. Reaching outcomes included measures of the spatial aspects (e.g., compensatory trunk displacement, error in end-point accuracy) and planning (e.g., curvature, segmentation). Means were compared, and the numbers of accurate/inaccurate reaches counted. Results: Participants with R-hemisphere damage exhibited greater deficits in end-point accuracy in contralesional UE vs. subjects with L-hemisphere damage. Preliminary ipsilesional UE data analysis is ongoing. After comparing the means between trunk displacement, segmentation, and curvature in the contralesional UE; L-hemisphere damage showed greater trunk displacement (L: 121.97 ± 41.48 mm, vs. R: 113.97 ± 40.26 mm) and segmentation (L: 1.36 ± 0.49 vs. R: 1.16 ± 0.34), whereas R-hemisphere damage showed greater curvature (R: 1.26 ± 0.16 vs. L: 1.23 ± 0.13). However, group differences were not statistically significant. Ipsilesional UE data were similar. Conclusions: Consistent with our hypothesis, R-hemispheric damage impaired accuracy. Contrarily, there were no statistically significant differences in other variables. Possible explanations for our results include sample variability and reaching-context differences; ours was an uncontrolled 3D-environment. More difficult reaching contexts magnify overall stroke deficits and mask lateralization. To optimize functional outcomes, evaluation/treatment of rehabilitation patients should consider reaching context and hemisphere lesioned. Veterans Affairs Rehabilitation Research & Development, Merit Review Award #I01RX000799

053 DKI Patterns of Brain Plasticity in Normal Older Adults Before and After Cognitive Training, Lara Hewett, Fatima Falangola, Rachael Deardorff, Cliff Chan; Center for Biomedical Imaging, MUSC.

Abstract not available.

054 Effects of Cocaine Dependence and Childhood Trauma on the Noradrenergic System, Jenna L Hislop, Megan M Moran-Santa Maria, College of Medicine, MUSC, Psychiatry, MUSC.

Exposure to childhood trauma is a risk factor for the development of psychiatric disorders including cocaine dependence. Recent studies have also linked childhood trauma to long-term changes in the hypothalamic-pituitary-adrenal (HPA) axis. However, the response of the noradrenergic system to childhood trauma and its relationship to cocaine dependence are still unknown. The present study examined heart rate and subjective responses to yohimbine, an α2-noradrenergic receptor antagonist which increases noradrenaline release, and cocaine-paired cues in cocaine-dependent subjects with low (n=19) and high (n=35) levels of childhood trauma, and non-cocaine-dependent subjects with low (n=28) and high (n=26) levels of childhood trauma. Subjects were divided into low and high trauma categories based on a median split of their total score on the Adverse Childhood Experiences (ACE) Questionnaire. Cocaine-dependent subjects with high levels of childhood trauma demonstrated a higher level of anxiety than non-dependent subjects with low levels of trauma following the administration of placebo (p<0.01). A similar trend level relationship was found for stress levels between the same two groups following the administration of placebo (p=0.051). There were no significant differences in craving levels and heart rate following the administration of placebo between the four groups (p>0.05). A between-subjects effect of cocaine status on anxiety levels was found demonstrating that cocaine-dependent subjects had higher levels of anxiety than non-dependent subjects in response to yohimbine and yohimbine combined with cocaine-paired cue (p<0.01). A within-subjects effect of time on heart rate was found demonstrating that all subjects had an increased heart rate following yohimbine administration and cocaine-paired cue (p<0.05). There were no significant differences in craving and stress levels following yohimbine administration and cocaine-paired cues (p>0.05). These preliminary data suggest that cocaine-dependent individuals experience higher levels of anxiety following treatment with yohimbine than non-dependent individuals. High levels of childhood trauma may also exacerbate basal levels of anxiety in cocaine-dependent individuals. NIH R25DA020537, NIH P50DA016511, NIH UL1TR000062

055 High Impulsivity Predicts Non-Abstinence in Marijuana-Dependent Adolescents, Jessica Bentzley, Kevin M Gray; Clinical Neurosciences, MUSC.

Background: Marijuana (MJ) accounts for most adolescent drug treatment admissions. Although N-acetylcysteine (NAC) improves abstinence outcomes in MJ-dependent adolescents, further work is needed to identify neurobehavioral factors that predict treatment response. Impulsivity is one such factor that has been repeatedly linked to drug abuse and dependence. This study presents secondary analyses involving impulsivity and outcomes from a parent randomized controlled trial of NAC in MJ-dependent adolescents. We hypothesized that baseline impulsivity would predict abstinence. Methods: Participants were 71 treatment-seeking MJ-dependent ado-lescents who completed treatment in the parent trial. Participants received 1200 mg NAC or placebo orally twice daily, added to contingency management...
intervention and brief cessation counseling. Qualitative urine cannabinoid testing was conducted at the end of treatment. Baseline impulsivity was assessed with the 30-item Barratt Impulsiveness Scale (BIS-11); median split was used to derive baseline high (HI) and low impulsivity (LI) groups (Median=65). Baseline marijuana craving was assessed with the Marijuana Craving Questionnaire (MCQ). Medication adherence was calculated as number of capsules taken divided by number of capsules that should have been taken to obtain ratios (0.0–1.0). Results: Baseline HI was associated with non-adherence (x2=4.25, p=0.039, n=71), particularly in the NAC group (x2=4.86, p=0.028, n=37). Baseline impulsivity, baseline craving, and medication non-adherence during treatment were independent predictors of non-adherence after adjusting for gender, treatment group (NAC versus placebo), and years of marijuana use. The HI group was 5.5 times as likely to be non-abstinent as compared to the LI group (p=.05). Discussion: Baseline HI adolescents had worse treatment outcomes than LI adolescents. This finding is consistent with other reports that high impulsivity predicts worse treatment outcomes for drug-dependent adolescents. HI individuals may benefit from individualized treatment approaches that target impulsivity. Future studies should assess why HI adolescents are at increased risk for worse outcomes.

056 The Specific Test of Early Infant Motor Performance (STEP): Psychometric Testing and Factor Analysis. Christine E Ochsner1, Kristin M Olbrich1, Patricia Coker-Bolt1, Dorothea D Jenkins2, Kathryn E Hope3, Viswanathan Ramakrishnan3, 3Occupational Therapy, MUSC, 1Pediatrics, MUSC, 2Public Health Sciences, MUSC.

An infant’s first year of life is critical for brain growth and overall development. Infants that exhibit developmental deficits are eligible to receive state-funded therapy, but unfortunately, developmental delays often go undiagnosed, missing a critical window of brain plasticity. The Test of Infant Motor Performance (TIMP) is the current gold standard for infant motor assessments; however, the 42-item TIMP is rarely used by busy pediatricians during well-child surveillance visits. A short, standardized screening is desperately needed to uniformly screen all infants. A new 10-item assessment, the Specific Test of Early infant motor Performance (STEP), was developed in consultation with experts on infant motor development and through Rasch analysis of preterm infant performance on items from the TIMP. The aims of our study were to evaluate the STEP’s robustness through factor analysis of the 10 motor items with new theoretical system, and test these factors against known, validated outcome measures of development. We performed a secondary analysis of existing data from a cohort of preterm infants (n=22) who underwent videotaped motor assessment at term corrected gestational age (CA), 12 weeks CA and one year follow-up testing with the Bayley Scales of Infant and Toddler Development- III (Bayley). Early videotaped motor assessments were viewed and scored using a new linear scaling of the 10 motor items of the STEP assessment. An exploratory factor analysis (EFA) of motor item scores was used to identify latent constructs. The matrix scaled STEP correlated with Gross motor Bayley outcomes (p=0.05, n=19). Using EFA, 8-9 scorable motor items were grouped into latent constructs. Strength of factor loading determined principal components in each factor, which were different for matrix and linear scoring systems of the STEP. Further analysis will allow for item refinement, prior to validation of the STEP as a clinically useful infant motor assessment.

057 Blood Pressure Guideline Adherence In Patients With Severe Cerebrovascular Disease, Guilherme B F Porto1, Alejandro M Spiotta2, Edward C Jauch3, COM, MUSC, 4Neurosurgery, MUSC, 5Emergency Medicine, MUSC.

Background and Purpose: Patients with acute brain injuries (stroke, traumatic brain injury, hemorrhage) require strict physiologic control, especially within the first hours of injury, to minimize clinical deterioration, morbidity, and death. This study aimed to assess in-hospital compliance to strict blood pressure parameters in current practice in these patient populations. Methods: In this IRB approved observational cohort study, patients with severe cerebrovascular disease were admitted to the neurocritical care unit and several channels of real-time physiologic data were continuously recorded using the BedMasterEX (Excel Medical Electronics Inc, FL) system. This platform collected hemodynamic data (blood pressures (BP) and heart rate) via an arterial catheter continuously in 5-second intervals as well as data from other physiologic monitors. Raw data were analyzed initially using descriptive statistics. Results: Fifty patients, 48% male, mean age 59.7 ± 13.9 years (15 subarachnoid hemorrhages, 9 unruptured aneurysms, 6 ischemic strokes, 6 subdural hematomas, 4 intracerebral hemorrhages, 3 ischemic strokes, 1 arteriovenous malformation, 1 intraventricular hemorrhage and 5 miscellaneous injuries) were enrolled. Data acquired represented 2259 total hours of continuous BP monitoring. Systolic BP were compared to current BP guideline parameters and were on average outside of recommended ranges 29.4 ± 30.19% of the patient’s monitoring period. We have found specifically for systolic BP management 6%, 28%, 18%, 12% and 36% of our patients were 99%, 90%, 80%, 70%, and <70% of the time within the specified SBP goal. Conclusion: Hemodynamic management of patients with cerebrovascular injuries, based on current guidelines, yielded optimal control of SBP in only 34% of our patients (within parameters ≥90% of time). More detailed analyses of the data are underway and additional physiologic variables concurrently collected with those presented here are also being studied. Future analyses will evaluate these data for the potential correlation with clinical outcomes (worsening neurological conditions, hemotoma growth, re-rupture of aneurysm, hemorrhagic conversion of stroke).

058 Noncontrast Brain CT Detection of Subdural Hematomas: Do Orthogonal Reconstructions Improve Sensitivity?2, William C Mostertz1, Timothy J Amrhein2, Zoran Rumboldt2, 1Medicine, MUSC, 2Radiology, MUSC.

With an estimated 1.7 million affected in the United States each year, traumatic brain injury is a major clinical concern as a leading cause of disability and mortality. The acquisition and review of axial noncontrast brain computed tomography (CT) images remains the current standard for the initial evaluation of acute head trauma. Early detection of acute intracranial pathology, specifically subdural hematoma, is of clinical importance due to the intensive
monitoring and surgical intervention often required for the prevention of severe negative sequelae. With multi-detector CT technology and isotropic voxel acquisition, modern CT scanners are capable of rapidly creating image reconstructions in orthogonal planes in order to provide greater anatomic detail. This has provided proven increases in sensitivity and specificity for the detection of pathology in multiple areas (i.e. cervical spine fractures, bowel obstruction). Such improvement is in large part due to the decreased conspicuity of pathologic processes that develop within the same plane as the provided image. The addition of orthogonal CT reconstructions are likely to facilitate significant improvements in the current detection of subdural hematomas and other clinically significant intracranial pathology. Such findings could benefit patients by providing evidence for early clinical intervention and thus preventing complications and reducing costs associated with undetected pathology. A retrospective patient screening identified noncontrast brain CT images of 100 subdural hematomas plus 100 controls without intracranial hemorrhage in the setting of trauma. Patient images were anonymized and randomly divided into 5 reading sessions. Three readers, two board-certified neuroradiology attendings and a radiology resident, were asked to provide their diagnostic impressions. Readers were presented with a randomized patient order and each session reading was performed twice, once with axial images only and the other with the addition of orthogonal CT reconstructions. Sessions were timed while diagnostic impressions were collected. Final impressions for each patient will be compared with the initial findings in order to confirm pathology detection and location. This study will evaluate the advantages of CT reconstructions for detecting subdural hematomas in comparison to standard axial images alone. Furthermore, this research could potentially result in an alteration to the current standard-of-care imaging method for routine brain CT, including the inclusion of orthogonal CT reconstructions as part of standard brain CT protocols.

**059 Total Knee Arthroplasty with Exparel® Provided Improved Pain Control, Shorter Length of Hospital Stay As Compared to Total Knee Arthroplasty with Femoral Nerve Catheter.** Ashley B Anderson,1 Brian Burnikel2, Brandon Broome2; 1Orthopaedics, Hawkins Foundation, 2Orthopaedics, Steadman Hawkins Clinic of the Carolinas.

Background: Conventional TKA utilizes femoral nerve catheterization post-operative pain control. This method results in decreased quad function, which delays rehab and increases fall risk. Local anesthetics provide additions mediums for pain control at surgical sites. It was hypothesized that increased analgesic time with local anesthetics will result in comparable or better opioid usage and visual analog scale scores, but shorter length of hospital stay, better inpatient PT evaluations, improved range of motion after 3-weeks, and less PT assistance after the TKA with Exparel® soft tissue infiltration as compared to the TKA with femoral nerve catheter. Methods: 23 Patients with subsequent bilateral TKA (one knee with the standard femoral catheter and the contralateral knee with Exparel®) were evaluated for the following post-operative parameters: length of stay, surgical anesthesia type, opioid usage range of motion, visual analog scale score, and physical therapy evaluations. A paired samples t-test was used to calculate differences between the outcomes measures of length of stay, and discharge for extension and flexion and 3-weeks extension and flexion. Results: There was a statistically significance difference in favor of Exparel® between the two groups for length of stay (p<0.01), total degrees of range of motion after 3-weeks (p<0.02), and gate (p<0.05). Conclusions: TKA with Exparel® provided better outcome as compare to TKA with femoral catheter alone. Future developments will use Exparel® with nerve blocks as a part of surgical protocol. This is currently undergoing clinical trials. Hawinons Foundation

**060 High Dose RTMS Treatment of the Prefrontal Cortex: Tapping Into the Pain Modulation Pathway.** Eliza L Barnwell,1 Jeffrey Borckardt2, Matthew Schmidt2, Kathryn Beaver,1 Mark George,2 Christopher Pellegrini3. 1COM, MUSC, 2Brain Stimulation Laboratory, MUSC, 3Ralph H. Johnson VA Medical Center.

Introduction: Repetitive transcranial magnetic stimulation (rTMS), a treatment approved for major depression, sends magnetic pulses to stimulate the prefrontal cortex of the brain. Previous research shows that painfulness associated with rTMS, often high at first, decreases steadily over a course of three weeks, suggesting that rTMS may have analgesic effects. To investigate the treatment of suicidal ideation, inpatient veterans at the Ralph H. Johnson VA Medical Center were treated with high-dose rTMS for 3 days in a row, as apposed to standard treatment over the course of several weeks. Data regarding pain was collected in order to assess safety and tolerability of high-dose rTMS and to better understand the role of rTMS in pain modulation. We hypothesized that participants receiving active rTMS, compared to sham, would have a rapid reduction in their ratings of the painfulness of TMS over three days, in a manner seen previously over three weeks. Methods: Treatment consisted of 9 rTMS sessions delivered over 3 days. The treatment group (n=18) received 6000 pulses per session (10 Hz, 120% motor threshold). Sham rTMS was used as placebo (n=20). Participants rated pain levels associated with the treatment on computerized visual analog scales after each session. Results: Though high at the beginning, painfulness levels from high-dose rTMS rapidly and significantly dropped over the three days, with no change in painfulness in those receiving sham a nearly identical pattern shown previously from standard rTMS treatment over 3 weeks. Conclusions: High-dose rTMS may be painful at first, yet tolerable after only a few treatments. As patients become quickly adjusted to high doses, future studies using aggressive TMS strategies may be feasible. The similar, yet more rapid, effect from high-dose rTMS vs. standard dose suggests that the pain-relieving action of TMS is dependent on number of doses, rather than duration of treatment. VA INTRUST Study; DoD PT071968 / V81XWH-08-2-0159; NIDA R25 DA020537

**061 Effects of Transcranial Alternating Current Stimulation on Pain Perception.** Christian D Baker,1 Jeffrey J Borckardt2; 1COM, MUSC, 2Psychiatry, MUSC.

Nearly 100 million Americans suffer from chronic pain to the cost of around 635 billion dollars per year. Many treatments attempt to combat this public health concern, but few provide adequate relief for numerous patients. Recently, low amplitude transcranial direct current stimulation (tDCS) of the human cortex has been investigated for its pain-relieving effects. By changing the
excitability of cortical neurons beneath the electrodes, activity in certain brain areas associated with pain perception and tolerance can be manipulated. Much of the research with tDCS thus far has focused on increasing pain tolerance and thresholds. Preliminary studies have returned positive results, prompting an expansion toward investigating alternating current. Claims have been made that this lesser-investigated modality, transcranial alternating current stimulation (tACS), administered via the Fisher Wallace Stimulator, has similar analgesic effects. This method delivers a 2.0mA alternating current electrical stimulus through two sponge electrodes to specific areas of the brain. The present study aims to assess the efficacy of tACS as a method of altering pain perception in healthy volunteers. Subjects were 26 healthy individuals from Charleston, South Carolina, ages 20-38. Participants reported for three separate randomized visits to receive 20 minutes of tACS with electrodes in configuration 1 (left prefrontal cortex and right motor strip for the hand area) at one visit, configuration 2 (bilaterally 3 cm anterior and 2 cm dorsal to the tragus as per Fisher Wallace manual) at another visit, and sham stimulation in configuration 2 at the third. Sensory thresholds, pain thresholds, and pain tolerance were assessed in the laboratory setting using a thermode on the subject’s left volar forearm. Subjects underwent pain testing prior to and after the 20 minutes of stimulation. After stimulation, subjects were found to have significant increases in sensory and pain thresholds in both real configurations and significant tolerance increases with configuration 1. Drug Abuse Research Training (DART) program funding through the National Institute on Drug Abuse R25DA020537

062 Variance in White Matter Diffusion in Cocaine Users, Bradley G Sieckman1, Colleen A Hanlon2, 1COM, MUSC, 2Psychiatry, MUSC.

Chronic cocaine use is associated with well-established deficits in both limbic and executive function and control. Recent functional imaging literature has linked these behavioral traits to alterations in functional connectivity from the ventromedial (VMPFC) and dorsolateral (DLPFC) prefrontal cortices, respectively. The biological basis for this lower functional connectivity is unclear. The purpose of this experiment was to test the hypothesis that cocaine users have lower structural connectivity and tissue density in the same areas that have been implicated in lower functional connectivity as well as several regions with well-defined white matter tracts. Non-treatment-seeking cocaine users (n=20) and healthy controls (n=14) were recruited from the local community. Diffusion tensor imaging (DTI) data was collected (30 directions, b=1000) and preprocessed with FSL to generate fractional anisotropy (FA) and mean diffusivity (MD) maps. The following regions of interest (ROIs) were drawn in the native space for each participant (MriCron): corpus callosum rostrum, internal capsule, VMPFC, DLPFC, and cerebellum. Fiber tracts were created from these seed ROIs in the VMPFC and DLPFC (MedInria). Although cocaine users showed no significant difference in mean values, they showed significantly higher variance in both fractional anisotropy in the corpus callosum (splenium: p<0.05; rostrum: p<0.03, df = 32) and mean diffusivity in the VMPFC (p<0.009, df=32) compared to controls. Variance in the left and right VMPFC was correlated both with age and alcohol use behavior, respectively (correlation =545, p<.02; correlation = -.448, p<.05). Increased variability in these regions suggests that cocaine use may be related to altered structural connectivity that correlates to previously demonstrated regions of altered functional connectivity. Preliminary tractography data suggests that cocaine users have lower structural connectivity from seeds in the VMPFC and DLPFC. Advances in tractography techniques may help bridge the gap between functional and structural connectivity to explain these variations and trends.

063 Lower Cortical Excitability and Cortical Atrophy in Cocaine Users: Does a Correlation Exist?, Julia S West1, Colleen A Hanlon2, Mark S George3, 1Medicine, MUSC, 2Neurosciences, MUSC, 3Psychiatry, MUSC.

Background. Prior studies have demonstrated that cocaine users have lower cortical excitability than controls. While this observation may be associated with changes in cortical glutamate, it may also be related to decreased grey matter density or to a larger skull-cortex distance resulting from brain atrophy. The purpose of this study was to determine whether baseline cortical excitability in cocaine users is related to brain atrophy or loss of tissue density. Methods. We collected excitability data using TMS and neurostructural data via MRI from 13 controls and 15 users. We used voxel-based morphometry (VBM) to calculate grey matter density and medlinia image processing software to calculate skull-cortex distance. Finally, we correlated these data with motor threshold as well as other demographic variables such as age, years of cocaine use, and alcohol use. Results. Consistent with prior studies, cocaine users have higher motor thresholds than controls. This cohort of cocaine users does not show lower grey matter density than controls in the motor cortex. While cocaine users do tend to have a larger brain to skull distance on average, this did not correlate with cortical excitability. Conclusions. Taken together these data suggest that lower cortical excitability in cocaine users is not directly related to cortical atrophy, and may in fact reflect an alteration in cortical glutamate or GABA in cocaine users an observation that extends current basic science research. NIDA R25DA020537; K01DA027756

064 Correlation Between Regional Grey Matter Loss and the Extended Disability Status Scale in Multiple Sclerosis Patients Using Voxel-Based Morphometry, Alexandra Parashos, Maria V Spampinato; Radiology, MUSC.

Multiple Sclerosis is a chronic, disabling, neurological disease that destroys white and grey matter. Because progress, severity, and symptoms of the disease are unpredictable, better imaging techniques are needed to better assess disease damage extent and help plan for a more efficient treatment. We used voxel-based morphometry to investigate a correlation between increasing EDSS (disability) scores and a decrease in volume in a specific grey matter region of the brain in 40 MS patients. We found that there was a significant cluster of grey matter atrophy that negatively correlated with EDSS scores in the Medial Superior Frontal Lobe, Brodmann Area 10, an area associated with information processing, memory recall, and concentration functions. Our findings suggest that voxel-based morphometry can be used to distinguish damaged anatomical areas that may correspond to the disability symptoms of MS patients. Summer Health Professionals Research Program, MUSC
Medical care for adolescents with diabetes mellitus (DM) as they transition from pediatric to adult care is important. Studies have shown poor glycemic control, higher rates of diabetic ketoacidosis (DKA) admissions and lower clinic attendance in adolescents. Several factors contribute to poor management of DM during this transition period. The multidisciplinary Diabetes Transition Program at the Medical University of South Carolina (MUSC) will improve patient care. The purpose of this study is to characterize the initial cohort enrolled in the Diabetes Transition Program at MUSC. A retrospective chart review collected data (N=133) from May 31st 2012 to June 1st 2013. The average age was 17.05 ± 1.08 yrs with 51% males and 71% were non-Hispanic white. 88% of patients were type 1 DM, and 71% were using multiple daily insulin injections. The average A1C was 9.17 ± 1.92%, with only 19% of patients reaching their A1C goal. 6% of patients had a DKA admission. 9% had nephropathy, 8% had hyperlipidemia, 7% had thyroid disease, and 5% celiac. 15% had ADHD and 9% had depression. 67% of patients lived in a 2-parent household; however Department of Social Services involvement was present in 7% of patients. Only 70% of patients received annual screening evaluation. Only 32% of patients had at least 4 annual clinic visits. 27% had Medicaid. This study supports previous data that has shown adolescents are poorly managing their DM. The goal of the Diabetes Transition Program at MUSC is to improve DM care including attaining A1C goal, decreasing DKA admissions and increasing annual clinic visits. This initial cohort data will be used to monitor outcomes as patients transition from pediatric to adult care in the Diabetes Transition Program.

Background: Type 2 diabetes (T2DM) currently affects more than 23 million people in the US. Recent literature has shown that diabetes education and improved health literacy can significantly improve self-management behaviors and diabetes related health outcomes. The purpose of this study is to determine if health literacy and patient-centered care is associated with diabetes related health outcomes and self-care behaviors. Methods: A sample of 361 patients was recruited from two primary care sites in Southeastern United States. Patients completed a survey to collect demographic information and different aspects of patient centered care and health literacy. Clinical measures including weight, height, blood pressure, hemoglobin A1c, and cholesterol were taken to assess diabetes related health outcomes. Health literacy was specifically measured by the Chew Health Literacy Screening questionnaire and a 9-item questionnaire that focused on patient centered care. Diabetic outcomes were measured using lab values taken during the patients’ clinic visit including hemoglobin A1c, low density lipoprotein (LDL), and blood pressure. Results: The results showed that inadequate health literacy was significantly correlated with lower patient-centered care (r=-0.16, p=0.002) and decreased exercise (r=-0.11, p=0.03). Additionally, patient-centered care was significantly correlated with medication adherence (r=0.2, p=0.0001). There was a significant difference in mean days of exercise in those with adequate health literacy (2.5 days vs 1.8 days, p=0.03) compared to those with inadequate health literacy. In the adjusted multiple linear regression, medication adherence was associated with patient-centered care (beta= 0.093, 95% CI 0.04, 0.14, p= 0.001). Conclusion: Overall, health literacy and patient-centered care had effects on diabetes self-care behaviors, but not health outcomes. There were modest correlations between health literacy and patient-centered care with self-care behaviors but not with hemoglobin A1c, LDL, or blood pressure. In the adjusted multiple linear regression models there was a significant association between patient-centered care and medication adherence. NIDDKD 5T35DK007431

Background: Type 2 diabetes (T2DM) is a well-known chronic disease that affects approximately 26 million people in the United States. One of the notable complications that result from diabetes is kidney disease, defined as having an estimated glomerular filtration rate (eGFR) of <60mL/min. The purpose of this study is to assess the prevalence of chronic kidney disease in patients with T2DM. Methods: A sample of 361 patients with diabetes was recruited from two primary care sites in Southeastern United States. Study participants completed a survey assessing socioeconomic and health status, medication adherence, access to care and belief system. Kidney function was assessed by extracting participants’ eGFR from their medical records. Descriptive statistics and logistic regression were used to determine the prevalence of chronic kidney disease (defined as eGFR <60) in patients with type 2 diabetes. Results: The results showed that in the sample population 38.8% of non-Hispanic Whites, 26.8% of non-Hispanic Blacks, and 16.7% of Hispanic/Asian/American Indians (p=0.04) had chronic kidney disease. Prevalence of chronic kidney disease did not differ significantly by education level, annual income, or insurance status. Non-Hispanic Blacks and Hispanic/Asian/American Indians were less likely to have chronic kidney disease (OR 0.69, 95% CI 0.38, 1.24, p=0.21; OR 0.37, 95% CI 0.07, 2.08, p=0.26). Though these findings are not statistically significant, it does indicate a disproportionate prevalence of chronic kidney disease in this sample population. Conclusion: This study revealed that non-Hispanic Whites in this sample population had increased prevalence of chronic kidney disease, contrary to what has been found in other studies. However, almost one-third of the study population had chronic kidney disease indicating a need for more aggressive management of diabetes and hypertension in order to prevent further progression of CKD in this population. NIDDK 5T35DK007431

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067 The Role of Patient-Centered Care and Health Literacy in Patients with Type 2 Diabetes, Bradley C Ketner1, Cheryl P Lynch2, Leonard E Egede2, 1Medicine, MUSC, 2Medicine, VAMC.

Background: Type 2 diabetes (T2DM) currently affects more than 23 million people in the US. Recent literature has shown that diabetes education and improved health literacy can significantly improve self-management behaviors and diabetes related health outcomes. The purpose of this study is to determine if health literacy and patient-centered care is associated with diabetes related health outcomes and self-care behaviors. Methods: A sample of 361 patients was recruited from two primary care sites in Southeastern United States. Patients completed a survey to collect demographic information and different aspects of patient centered care and health literacy. Clinical measures including weight, height, blood pressure, hemoglobin A1c, and cholesterol were taken to assess diabetes related health outcomes. Health literacy was specifically measured by the Chew Health Literacy Screening questionnaire and a 9-item questionnaire that focused on patient centered care. Diabetic outcomes were measured using lab values taken during the patients’ clinic visit including hemoglobin A1c, low density lipoprotein (LDL), and blood pressure. Results: The results showed that inadequate health literacy was significantly correlated with lower patient-centered care (r=-0.16, p=0.002) and decreased exercise (r=-0.11, p=0.03). Additionally, patient-centered care was significantly correlated with medication adherence (r=0.2, p=0.0001). There was a significant difference in mean days of exercise in those with adequate health literacy (2.5 days vs 1.8 days, p=0.03) compared to those with inadequate health literacy. In the adjusted multiple linear regression, medication adherence was associated with patient-centered care (beta= 0.093, 95% CI 0.04, 0.14, p= 0.001). Conclusion: Overall, health literacy and patient-centered care had effects on diabetes self-care behaviors, but not health outcomes. There were modest correlations between health literacy and patient-centered care with self-care behaviors but not with hemoglobin A1c, LDL, or blood pressure. In the adjusted multiple linear regression models there was a significant association between patient-centered care and medication adherence. NIDDK 5T35DK007431

068 The Effects of Generalized Anxiety and Stress on Cardiovascular Disease and Self-Care Behaviors in Patients with Type II Diabetes, Amartha N Ogbaru-Obonnaya1, Cheryl P Lynch2, Joni L Strom Williams3, Leonard E Egede2, 1Medicine, MUSC, 2Medicine, VAMC.
Background: Type 2 diabetes (T2DM) is a chronic disease that increases the risk of cardiovascular disease (CVD) in patients. Studies show that anxiety and stress can lead to the development of metabolic risk factors for CVD. The purpose of this study is to determine whether a relationship exists between stress and anxiety and pertinent CVD risk factors and self-care behaviors in patients with T2DM. Methods: 361 participants were recruited from two primary care clinics in Southeastern United States. Each participant completed a set of previously validated surveys including a 16-question Chronic Health Conditions questionnaire, the Generalized Anxiety Disorder 8-item (GAD-8) questionnaire, the Diabetes Distress Scale and the Serious Psychological Distress questionnaire. The primary outcomes were HbA1c, LDL levels, and blood pressure that were obtained from patient medical records. Results: The results showed that in this sample of individuals with T2DM, generalized anxiety was significantly correlated with poorer medication adherence (r= -0.29, p=0.000), general diet (r= -0.15, p=0.006) and higher LDL levels (r=0.13, p=0.02). Psychological distress was correlated with poorer medication adherence (r=-0.21, p=0.0001) and special diet (r= -0.12, p=0.02). The difference in the mean LDL levels for those with generalized anxiety and those without (107.3 mg/dL, SD 54.8 vs 93.4 mg/dL, SD=44.8) were slightly statistically significant (p=0.056). Lastly, the multiple linear regression, when adjusting for covariates, showed that generalized anxiety was associated with poor medication adherence (beta=1.2, 95% CI -1.69, -0.61, p=0.000) and increased LDL levels (beta=15.3, 95% CI 0.95, 29.7, p=0.03). Conclusion: In this group of individuals with T2DM, data shows that generalized anxiety has the most impact on self-care behaviors and CVD risk factors than psychological distress when adjusting for covariates. More specifically, anxiety seems to influence medication adherence and LDL levels. However, data analysis showed that there is a correlation between psychological distress and medication adherence.

NIDDK 5T35 DK007431

069 Pediatric Metabolic Syndrome Study: Is Waist Circumference a Better Indicator of Pre-Diabetes Than BMI?, Brielle Weinstein¹, Janet Carter⁴, Melissa Henschaw², Sarah Stein⁴, COM, MUSC, ²Pediatric Cardiology, MUSC.

Metabolic syndrome is becoming an increasingly prevalent disease in the pediatric population in South Carolina and is strongly associated with early hypertension and type II diabetes. Elevated fasting glucose (>100mg/dL) and elevated fasting insulin (>20 mcU/mL) are markers for glucose intolerance that may lead to type II diabetes. In this cross sectional study we analyzed the relationships between easily measured anthropometric data and fasting glucose and insulin levels. The anthropometric measurements used were waist circumference (cm) and body mass index percentile as calculated by an algorithm using CDC data. Our population was an obese pediatric cohort (n=269) aged 4 to 21 from the Pediatric Metabolic Syndrome Study at MUSC. To analyze the relationships we used Pearson correlation coefficients in SPSS. Our results showed that waist circumference had a significantly stronger correlation with fasting glucose and insulin than body mass index percentile. Specifically, the correlation value of 0.482 between fasting insulin and waist circumference was significant at the 0.01 level, and the correlation value of 0.145 between fasting glucose and waist circumference was significant at the 0.05 level. In comparison, the correlation value of 0.140 between fasting insulin and body mass index percentile was significant at the 0.05 level, and the correlation value of 0.035 between fasting glucose and body mass index percentile was not significant. The difference in correlation values between the relationships of body mass index percentile and waist circumference demonstrates that waist circumference may be a better indicator of glucose intolerance in an obese pediatric population. With further research this information can be used as a clinical indicator and as an important educational tool as we work to make children healthier.

NIDDK; Summer Health Professionals Research Program; SCTR; NIH UL1 RR029882 and UL1 TR000062

070 Liver Estrogen Signaling and the Metabolic Response to Dietary Fats and Carbohydrates, Eric K Singh1, Melissa Martinez2, John Stafford2, COM, MUSC, ³Vanderbilt University Medical Center.

Coronary Heart Disease (CHD) is an important health issue in developed countries. Although there are many risk factors for CHD, the consequences of overconsumption are important to understand as an excess intake of dietary fats and carbohydrates has been shown to have an impact on glucose tolerance, insulin sensitivity, and lipid metabolism. Although many diet strategies aim to improve the complications of obesity and prevent CHD, identifying which diet is most appropriate for an individual remains challenging. Previous research has demonstrated that women are better protected from CHD than men. By contrast, some studies suggest that high-carbohydrate diets may be more harmful for women than men. With this in mind, we asked if there is a differential effect of estrogen signaling on glucose vs. lipids. Because the liver integrates glucose and lipid metabolism, we decided to explore the role that hepatic estrogen signaling plays in the metabolic response to different macronutrient compositions. In order to determine the impact of a high-fat diet (HFD) vs. a high-sucrose diet (HSD) in the presence or absence of hepatic estrogen signaling, we studied 12-week-old female C57BL/6 mice lacking hepatic estrogen receptor alpha (ERalpha) compared to their wild-type littermates. We fed them either a HFD or HSD for 8 weeks. After performing intraperitoneal glucose tolerance tests and examining differences in lipid profiles, we determined that a knockout model of hepatic ERalpha (LKO-ERalpha) worsened glucose tolerance on HFD feeding. Interestingly, mice with LKO-ERalpha showed improved glucose tolerance on HSD feeding, but their lipid profile was worse than that of the wild-type controls. Thus, we believe that liver estrogen signaling is beneficial for glucose metabolism with HFD feeding, but is harmful with HSD feeding. These findings may have important health benefits in helping pre- or postmenopausal women choose the most appropriate diet to minimize complications of obesity. NIH T35DK007383

071 G-Protein Signalling Regulator 2 and Role in Islet Cell Proliferation and Insulin Secretion, Rachel L Jester, Hongjun Wang, Zhang Yong; COM, MUSC.

G-protein signaling regulator 2 (RGS2) is a GTPase activating molecule that regulates signaling through Gs protein coupled receptors by hydrolyzing GTP in the G-alpha subunit and inhibiting cAMP production. Gs receptors mediate the signaling of incretin hormone glucagon-like peptide 1(GLP1) in pancreatic beta cells.
RGS2 has been implicated as an important regulator of cell survival and insulin release and is upregulated by GLP1. This study aims to understand the role of RGS2 in beta cells. We transfected beta cell model βTC3 cells with RGS2 shRNA to create RGS2 knock-down cell lines for experimentation along with control shRNA cells. Western immunoblotting was performed to confirm the knockdown status of the shRGS2 cells. XTT cell proliferation assays of the knockdown cells revealed that they (clones 3 and 4) grew more slowly than control or wild type βTC3 cells. Flow cytometry with Propidium Iodide staining revealed that at least one of the knockdown clones (clone 3) remained in the G1/G0 phase of the cell cycle for a longer time and the S phase for a shorter time that the control and wild type cells. Insulin secretion measurements of control shRNA and shRGS2 clone 4 cells cultured in zero, 16.7 mmol/L glucose, and 16.7 mmol/L glucose supplemented with 50 nM of GLP1 agonist Exendin 4 revealed that knock-down and control cells had similar levels of insulin secretion in zero glucose and showed an increase in secretion in 16.7 mmol/L glucose. However shRGS2-clone 4 secretion increased less than the control. Upon addition of Exendin 4, shRGS2 clone 4 showed greater increase in insulin secretion than controls. These results suggest that RGS2 acts as a negative regulator of insulin secretion through the GLP1 pathway. This may have some protective effect on islet cells during islet cell transplantation by limiting insulin exhaustion, however GLP-1 induced insulin secretion and islet cell proliferation may be enhanced by silencing negative regulators of GPCR such as RGS2 in order to treat diabetes in general. Manipulating the expression of beta cell specific RGS2 could be revolutionary to diabetes treatment in the future. *Summer Healthcare Professionals Program; NIH 5T35DK007431*

072 Racial Differences in the Risks Associated with Early Graft Loss in Adult Kidney Transplant Recipients, Kevin Douglass1; David J Taber2; 1COM, MUSC; 2Surgery, MUSC.

African-Americans (AAs) exhibit a complex health disparity with regards to outcomes following kidney transplant (KTX). AAs have a higher propensity to develop end-stage renal disease and require KTX at higher rates compared with other races. Furthermore, AA KTX recipients fare significantly worse in long-term graft survival. Many studies have attempted to elucidate the salient etiologies surrounding this disparity, with conflicting results. The aim of this study was to investigate and compare the potential risks associated with early graft loss in AAs vs non-AA KTX recipients. The results of this study demonstrate that AA KTX recipients have a number of unique risk factors for early graft loss compared to non-AA patients, most importantly public health insurance and elevated post-transplant systolic BPs or serum gluoses. This information may be useful to design future interventional trials aimed at reducing racial disparities for graft outcomes in KTX recipients. *MUSC College of Medicine Dean’s Office*

073 NEDD:MICAL Interactions Lead to Posttranslational Modification of MICAL in HNSCC Cells, Philip T Sobash, Casey O Holmes, Jessica A Tiedeken, Steven A Rosenzweig; Molecular and Cellular Pharmacology & Experimental Therapeutics, MUSC.

Abstract not available.

074 Phosphorylation Dynamics in Osteoblasts Stimulated with Parathyroid Hormone (PTH 1-34), Sukhi K Gurum, Lauren Ball, Grace R Williams; Pharmacology, MUSC.

Recombinant human PTH, residues 1-34, also known as Forteo, is an anabolic drug used for treatment of osteoporosis. The anabolic actions elicited by intermittent stimulation of the G coupled PTH receptor in osteoblasts are mediated, in part, through the activation of IGF-1 receptor signaling. Immunoblot analyses indicated that pretreatment of MC3T3-E1 osteoblasts with PTH1-34 blunted IGF-1/insulin-induced phosphorylation of insulin receptor substrate (IRS1) at known inhibitory sites. This is consistent with observations indicating that PTH1-34 activates the phosphatase MKP1 (J Endocrinol. 2011; 211:145-56). In an unbiased approach to identify proteins that undergo a change in phosphorylation status with receptor stimulation, a phosphoproteomic approach was applied to differentiating murine MC3T3-E1 osteoblasts. SILAC labeled cells were induced to differentiate for 10 days and treated rhPTH 1-34 for 5 min. Cells were lysed in urea buffer and trypsin digested phosphopeptides were enriched using TiO2 and fractionated by SCX chromatography. Peptides were analyzed by nLC-CID MS/MS and ETD MS/MS using a decision tree approach (Orbitrap Elite). Data were searched and quantified using Proteome Discoverer (Thermo). Ongoing analyses are being performed to elucidate the phosphorylation dynamics following acute PTHR stimulation. Initial observations confirmed elevated phosphorylation within the C-terminus of PTH R1 at sites responsive to receptor stimulation. The goals of these studies are to provide novel information regarding PTH receptor signaling in osteoblasts and to serve as a control for future studies aimed at identifying signaling components employed by functionally selective (biased) agonists of the PTH receptor. *Department of Craniofacial Biology*

075 Hematopoietic Contribution to the Periodontal Fibroblast Population, James P Wilson1, Richard P Visconti2, Zoltan Hajdu3; 1Dental Medicine, MUSC, 2Regenerative Medicine and Cell Biology, MUSC.

Historically, tissue fibroblasts are thought to be derived from mesenchymal progenitors during embryonic development. However, previous studies by our group and others have identified contribution of post-natal bone marrow hematopoietic stem cell (HSC)-derived cells to interstitial cell populations in mesenchymally-derived tissues during both homeostatic conditions and during repair of injury. The purpose of this study was to investigate whether there is hematopoietic contribution to the fibroblast population in the periodontal ligament. To accomplish this, periodontal tissues surrounding the second and third maxillary molars from mice subjected to luxation injury and contralateral control PDL were analyzed by immunofluorescence for the expression of hematopoietic antigens and fibroblast markers. Using laser scanning confocal microscopy, we identified cells in the PDL that were immunopositive for both CD45, a hematopoietic stem cell marker, and HSP47 or Periostin, which are proteins produced and used during Collagen Type I synthesis, in the unmanipulated PDL. Further, luxation injury resulted in a marked increase in these HSC-derived fibroblast populations. These findings suggest that there is HSC contribution to the PDL fibroblast population and that these cells actively
076 The Hematopoietic Origin of Resident Progenitor Cells in the Periodontal Ligament, Zakery R James, Richard P Visconti, Zoltan Hadju; Dental Medicine, MUSC.

The cellular populations of the periodontal ligament (PDL) arise from the dental follicle, a developmental structure originating from neural crest ectomesenchyme. However, the precise origin of PDL cells and progenitors that participate in maintenance and repair of the PDL throughout postnatal life is largely unknown. Previous studies by our group and others have identified contribution of post-natal bone marrow hematopoietic stem cell (HSC)-derived cells to cell populations in other mesenchymally-derived organs and tissues. The purpose of this study was to investigate whether there is hematopoietic contribution to similar populations in the post-natal PDL. To accomplish this, periodontal tissues surrounding the second and third maxillary molars from mice subjected to luxation injury, and contralateral control PDL, were analyzed by immunofluorescence for the expression of hematopoietic antigens and progenitor markers. We specifically focused on cells that were clustered in the paravascular niche, as this is where periodontal progenitor cell are known to reside. Using laser scanning confocal microscopy, CD45+/Stro-1+ and CD45+/CD133+ double-positive paravascular cell clusters were detected in the unmanipulated PDL, as well as increased numbers of these cell populations in the injured PDL. These findings support the hypothesis that, in addition to contribution to the fibroblastic population, cells of HSC origin contribute to a tissue-resident mesenchymal progenitor cell population in the PDL and that these cells are responsive to periodontal injury.

077 The Impact of Body Mass Index and Kidney Donor Risk Index on Clinical Outcomes in Renal Transplant Patients, Elizabeth C B Myers1, Dave Taber2, Charles Bratton2, John W McGillicuddy2, Kenneth D Chavin2, Prabhakar Baliga2, 1Transplant Surgery, MUSC, 2Surgery, MUSC.

BACKGROUND: The increasing obesity epidemic in the general population has led to corresponding increases in obesity rates for both renal transplant donors and recipients. Studies have shown that increasing BMI in renal transplant recipients can increase the risk of prolonged hospitalization, hospital readmission and graft failure, but there is limited data analyzing the influence of both donor and recipient BMI on outcomes after transplant. The Kidney Donor Risk Index (KDRI) was developed to determine the risk of graft failure following renal transplantation based on donor characteristics. This is an objective measure of donor risk, which includes BMI as a covariate. Therefore, the aim of this study was to determine the influence of recipient BMI and donor KDRI on clinical outcomes in renal transplant patients.

METHODS: This was a retrospective longitudinal cohort study of patients receiving renal transplants between 2007 and 2012. Pediatrics and multi-organ transplant recipients were excluded. Patients were grouped and compared based on their donor KDRI (low, normal, or high) and their pre-transplant BMI (non-obese or obese). RESULTS: 1,177 patients underwent renal transplant during this period, of which, 730 (63%) met inclusion criteria and had BMI and KDRI data available for analysis. Table 1 displays the results, demonstrating that patients with a primary diagnosis of diabetes and history of hyperlipidemia increased within each of the three KDRI groups and within the obese BMI cohort as well; recipient age increased across KDRI groups, regardless of BMI; gender and race were similar across all groups. Clinical outcomes demonstrated that hospital LOS, readmissions, acute rejection and graft survival were not associated with either KDRI or recipient obesity. The rate of delayed graft function increased within each KDRI group and within the obese BMI groups as well. CONCLUSIONS: The results of this study suggest that recipient BMI and donor KDRI independently impact the risk of developing delayed graft function. As both BMI and KDRI increase, the probability of delayed graft function also increases. This data suggest that clinicians need to consider both donor and recipient factors when determining the likelihood for the development of post-transplant delayed graft function. Interestingly, contrary to previous studies, in this cohort of patients, neither BMI nor KDRI were important factors associated with hospital LOS, readmissions, acute rejection or graft survival. Summer Health Professionals

078 Can the Optimal Immunosuppression Regimen Be Determined in Aged Kidney Transplant Recipients?, Kristen M Brown1, David Taber2, Kenneth Chavin2, Prabhakar Baliga2, 1COM, MUSC, 2Surgery, MUSC.

Background: The number of elderly patients receiving kidney transplants has dramatically increased over the past decade; 7.5% of patients receiving a KTX were ≥65 yo in 1998, which increased 2.5-fold to 18.6% in 2009. It is well documented that elderly KTX recipients have lower rates of acute rejection, but are at an increased risk for infection. There is paucity in the literature examining the optimal immunosuppressant doses and goal trough concentrations in this high-risk cohort of patients. The aim was to determine the optimal immunosuppressant target doses and concentrations based on KTX recipient age. Methods: This was a retrospective longitudinal cohort study of adult solitary KTX recipients transplanted between 2005 and 2012 at our center. Patients were divided into cohorts based on age and immunosuppressant doses and trough concentrations were compared between those that developed an acute allograft rejection vs. an infection vs. neither. Results: 1,176 patients were included, 380 (32%) were ≥60 years old. The ≥60 years cohort were more likely to have diabetes and hypertension, and more likely to receive marginal donor kidneys. Younger recipients were more likely to experience an allograft rejection while older recipients were more to experience an infection. In multivariate analyses, after controlling for difference, younger age was found to be a strong risk for acute rejection, while older age was found to be a strong risk for infection of immunosuppression doses and concentrations revealed that only tacrolimus trough concentrations were strongly associated with the risk of rejection or infection. This linear relationship was stronger in elderly, as compared to younger recipients. Induction therapy, mean mycophenolate doses and mean prednisone doses had limited ability to discern differences between those that developed infection, rejection, or neither in both the elderly and younger cohorts. Conclusions: Age is strongly and independently associated with a decreased risk of rejection and an increased risk of infection. Tacrolimus trough concentrations appear to influence the risk of developing rejection and infection, particularly in elderly patients.
patients. Future studies are needed to improve methods to monitor and adjust immunosuppression that can marginalize the strong effects of age on clinical outcomes following KTX.

079 Goal-Directed Therapy Using the FloTrac Device in Patients Receiving Head and Neck Microvasculature Free Tissue Transfer, Clark D Sealy, Will Hand, COM, MUSC, Anesthesiology, MUSC.

Abstract not available.

080 Bladder Outlet Obstruction: Activation of the Inflammasome Cascade, Case M Wood, F Monty Hughes Jr., J Todd Purves; Urology, MUSC.

Abstract Purpose: In many tissues the activation of structures known as inflammasomes results in the production of the pro-inflammatory cytokine IL-1 beta, which subsequently triggers an inflammatory reaction. Bladder outlet obstruction (BOO), which is most commonly found in older men with prostatitis, is well known to elicit an inflammatory reaction although the mechanisms leading to this reaction are unknown. In this study we investigate the involvement of the NLRP3 inflammasome in the bladder dysfunction associated with BOO. Materials and methods: In female Sprague-Dawley rats, BOO was produced by insertion of a 1 mm catheter followed by tying of a silk ligature around the urethra and removal of the catheter. Sham rats had the suture passed around the urethra but not tied. Animals were then given 2.5 mg/kg (p.o.) of the NLRP3 inhibitor glyburide or vehicle daily for 12 days. Urine was collected followed by urodynamics to measure in vivo bladder function. Results: The urine of vehicle-treated rats showed elevations in IL-1 beta, the product of inflammasome activation, compared to untreated rats. Oral glyburide blocked this increase demonstrating the efficacy of this drug to inhibit the NLRP3 inflammasome in this tissue. Cystometry measures important indices of in vivo bladder function such as voiding volumes, voiding pressures, flow rates, voiding frequency and non-voiding contractions. The presence of an obstruction in the outlet physically decreases flow rates and increases voiding pressures and these changes were apparent in both the vehicle and glyburide-treated rats. Inflammation induced by BOO is known to stimulate greater voiding frequency (and the related decrease in voiding volume) as well as more non-voiding contractions. These parameters are thought to reflect the increase in urinary frequency and urgency widely reported by obstructed patients. As expected, BOO rats treated with vehicle displayed these changes, reflecting the expected inflammation in these animals. In contrast, BOO rats treated with glyburide did not show a reduction in voiding volumes, increases in voiding frequency, or increases in non-voiding contractions. Conclusion: BOO is associated with the activation of the NLRP3 inflammasome and production of the pro-inflammatory cytokine IL-1 beta. Glyburide, an FDA-approved NLRP3 inhibitor, alleviated the urinary dysfunction associated BOO suggesting it may be efficacious in protecting against the urinary frequency and urgency experienced by these patients. SURP: T35DK007431-29

081 Influence on Various Dosage Regimens on the Pharmacodynamic Profile of Eravacycline, Caroline J Raho, Roger White; Pharmacy, MUSC.

Monte Carlo analysis (MCA) can be used to assess population pharmacodynamics (PD) profiles. For eravacycline, an investigational antibiotic, the PD parameter associated with efficacy is the AUC/MIC. Thus, percentage target attainment of the PD parameter (TA%) can be used as a surrogate marker for efficacy. We used MCA to identify optimal dosages with four bacterial pathogens. A 10,000 patient MCA was performed using MICs, pharmacokinetic data (volume=3.3L/Kg, clearance=13.5L/hr, and serum protein binding=60%), and PD targets from previous literature. AUC/MIC targets of 7 (static effect on organisms) and 18 (1 log reduction) were used. Steady-state pharmacokinetics were performed for: 1.5 mg/kg q24h and 1.0 mg/kg, 50mg and 100mg q12h using body weights of 60-90 kg. Since there are no data relating eravacycline clearance to physiologic variables, clearance from normal volunteer pharmacokinetic studies was used. The AUC0-24h was calculated and AUC/MIC distributions created for Escherichia coli (EC), MRSA, Klebsiella pneumoniae (KP) and Vancomycin-resistant Enterococci (VRE). TA% was calculated for each organism and dosage regimen. For a 70kg patient, TA% rates were 85% or greater for MRSA and VRE for all four dosing regimens. TA% for EC was 53% or less for AUC/MIC = 18 and reached 93% only at the two highest total daily doses. TA% was low for KP at all targets and dosages. Irrespective of the AUC/MIC target and bacterial pathogen, TA% was reflective of total daily dose. Eravacycline reached high target attainment rates for the resistant Gram-positives evaluated and will likely be effective against infections with these organisms. Against the Gram-negative organisms evaluated, eravacycline is likely to be less efficacious.

082 Monte Carlo Simulation of Plazomicin Against Common Pathogens As Compared to Amikacin, Jordan A Miller, Roger White; Pharmacy, MUSC, SCCP Drug Discovery and Biomedical Sciences.

Plazomicin is an aminoglycoside currently being developed to target pathogens resistant to current antimicrobials. Previous research has demonstrated a good concordance between pharmacokinetic-pharmacodynamic (PK-PD) animal studies and data from infected patients. This allows for the analysis of pre-clinical data to best determine treatment regimens that will optimize clinical outcomes in patients. For plazomicin the PD parameter associated with efficacy is AUC/MIC. Using Monte Carlo Simulation (MCS) we can determine percentage target attainment (TA%) of the AUC/MIC goals and use them as surrogate markers for efficacy. A 10,000 patient MCS was performed using four body weight distributions ranging from 60 to 90 kg, MICs, pharmacokinetic data (volume=0.23L/Kg, clearance=0.0462(CrCl) + 0.12, and serum protein binding=12%), and PD targets from previous literature. Attainment of the MICs for E coli, Pseudomonas aeruginosa, MRSA and Acinetobacter spp. was accomplished through extensive journal searches for antimicrobial activity analysis of plazomicin compared to amikacin and other antimicrobials. Clearance was determined from PK animal studies coupled with data from previously published aminoglycoside PK articles and verified with recent human PK trials. AUC/MIC targets of 80 and 135 were utilized.
based on previous literature. A dosing schedule adjusted for renal function (CrCl) was created as follows: 15mg/kg q 24 hours for CrCl ≥ 60mL/min, 15mg/kg q 48 hours for CrCl 25-59mL/min, 10mg/kg q 72 hours for CrCl 10-24mL/min, and 10mg/kg q 144 hours for CrCl ≤10mL/min.

TA% was calculated for each organism/dosage regimen. For E. coli, MRSA, P. aeruginosa and Acinetobacter spp., plazomicin had a TA% (low goal AUC/MIC 80/high goal AUC/MIC 135) of 99/95, 99/97, 32/17 and 23/12 respectively. For E. coli, MRSA, P. aeruginosa and Acinetobacter spp., amikacin had a TA% of 87/87, 16/6, 44/24 and 98/77 respectively. Plazomicin had higher TA% against E. coli and MRSA whereas amikacin had higher TA% against P. aeruginosa and Acinetobacter spp.

083 Inflammatory Biomarkers in Pregnancy Predict Risk of Postpartum Anxious Depression, Leah D Fryml1, Roger Newman2, C. Neill Epperson3, Laura Goetz2, Constance Guille4,1,COM, MUSC, 2OBGYN, MUSC, 3Psychiatry, University of Pennsylvania, 4Psychiatry, MUSC.

Background: Alterations in Th-1/Th-2 cytokine represent a promising biomarker for risk of major depression but findings have been inconsistent owing to disease heterogeneity. Further, cross-sectional studies preclude inference regarding directionality of cytokines and depression. Depression with comorbid anxiety is common during the postpartum period and likely represents a distinct subclass of depressive symptoms (anxious depression). Moreover, the postpartum period can be anticipated, allowing prospective assessment of cytokine levels. Objective: To determine if cytokines in pregnancy are associated with subsequent postpartum anxious depression (ppAD). Methods: Medical records were reviewed to identify cases of depression and anxiety during pregnancy and the year postpartum in participants in a prospective study of cytokines in pregnancy. Signature Th-1/Th-2 cytokines (7 in total) were measured at 34-42 weeks gestation. Logistic regression methods were used to assess the relationship between individual cytokines and ppAD. Results: 231 women with a complete cytokine profile were included in the analysis. After controlling for potentially confounding variables women were more likely to experience ppAD with lower Interferon-gamma (IFN-γ) (OR 0.78; 95%CI 0.61-0.99), higher Interleukin (IL) 6 (OR 1.6; 95%CI 1.002-2.79) and higher IL-10 (OR 1.2; 95%CI 1.01-2.79). Conclusions: We report a novel temporal relationship between altered Th-1/Th-2 cytokine profile in pregnancy and subsequent risk of ppAD. One therapeutic mechanism of selective-serotonin reuptake inhibitors is upregulation of IFN-γ, therefore our finding of an association between lower IFN-γ and increased ppAD has biologic validity. Higher IL-6/IL-10 levels suggest that maternal inflammatory response to pregnancy may mediate mood and/or anxiety symptoms. Further prospective evaluation of these relationships are needed.

084 Rotational Atherectomy Facilitated Percutaneous Coronary Intervention in Patient with High-Risk Coronary Anatomy, James N Hadstate Jr, Anbukarasi Maran, Monique Sandhu, Navin Nikam, Christopher Nielsen, Eric Powers, Daniel Steinberg, Valerian Fernandes; Cardiology, MUSC.

BACKGROUND: Complex percutaneous interventions are becoming more common in patients with high-risk anatomy that are deemed inappropriate for surgical revascularization. Rotational Atherectomy (RA) is often used in heavily calcified vessels and complex lesions because it facilitates stent delivery and expansion. We sought to evaluate the safety and efficacy of RA prior to stenting of high-risk anatomy (as determined by their SYNTAX score) in patients who were turned down for coronary artery bypass surgery or were poor candidates for it. METHODS: 112 consecutive patients who underwent RA at our medical center from January 2009 through June 2013 were retrospectively analyzed. A SYNTAX score was calculated on all patients and the patients were categorized into low/intermediate (1-32), and high (33 and above) risk groups. Patients with prior CABG were excluded. A two tailed student t-test or chi-squared test were used to determine statistical significance where appropriate. RESULTS: The high SYNTAX group had a higher burden of surgical disease anatomy (58.8%) compared to the low risk group (20%, p<0.01). RA was performed with a 1.25 burr (32%), 1.5 burr (60%) or 1.75 burr (8%) and was uniformly successful in both the groups. There was no evidence of increased peri-procedural complications in patients with a high SYNTAX score. Transient bradycardia was noted intermittently but no patients required the use of a temporary pacemaker. There was no incidence of peri-procedural mortality in either group. The increased fluoroscopy time and contrast volume in the high SYNTAX score group likely reflected the increased complexity of intervention. No significant difference in mortality was noted between the two groups during follow-up. CONCLUSION: Rotational Atherectomy is a safe adjunctive therapy to facilitate PCI in patients with high risk coronary anatomy who are not candidates for coronary artery bypass grafting.

085 A Systematic Review and Meta-analysis of the Immunohistochemical Staining Profile of Anaplastic Thyroid Carcinoma, Kristen N DeYoung1, Amit J Sood1, Laura Spruill2, Jyotika K Fernandes1, Shaun A Nguyen1, Terry A Day1, Otolaryngology, Head and Neck Surgery, MUSC, 2Pathology, Division of Surgical Pathology, MUSC, 3Medicine, Division of Endocrinology, MUSC.

Introduction: Anaplastic thyroid carcinoma (ATC) is a highly aggressive malignancy with a dismal prognosis, making its correct and prompt diagnosis a paramount concern for health care providers. The diagnosis of ATC is often a diagnosis of exclusion, confirmed by histological impression and immuno-histochemical staining. No staining panel or standard protocol exists for diagnostic confirmation of ATC. This study was undertaken to identify the most commonly reported immunohistochemical staining tests performed for ATC and which of these stains were most sensitive or specific for ATC. Methods: A systematic-review and meta-analysis of the literature reporting staining profiles for ATC was conducted in accordance with PRISMA guidelines. Results: The immunohistochemical stains of 544 ATC tumors from 35 publications between 1985 and 2013 are reported as pooled proportions. In our cohort, Vimentin (80%), Galectin-3 (72%), keratin (66.7%), EGFR (78.8%), and P53 overexpression (71%) have the highest relative frequency among the ATC tumors analyzed. Stains that returned with relative frequencies less than 30% include Thyroglobulin (18%), TTF-1 (29%), Calcitonin (4%), HMGB (15.8%), and E-cadherin (22%). Conclusion: The staining profiles presented herein provide a framework for surgical
pathologists and clinicians faced with the urgent need for rapid diagnosis of highly aggressive thyroid malignancies. This study is the first to systematically review reports on staining patterns of anaplastic thyroid carcinoma thus providing a framework for the future diagnosis and staging. Based upon the data provided, we suggest utilizing stains for pankeratin, P53 overexpression, EGFR, TTF-1, Calcitonin, and E-cadherin as confirmatory stains for anaplastic thyroid cancer.

086 Transradial Primary PCI Should Be Routine At US Training Institutions, Ashley A Waring, Rodolfo Machado, Frederick W Funke, Monique Sandhu, Arasia Maran, Thomas M Todoran, Valerian L Fernandes, Christopher D Nielson, Eric R Powers, Daniel H Steinberg; MUSC.

Background: Numerous studies demonstrate reduced bleeding and mortality in STEMI patients undergoing primary PCI (pPCI) via transradial (TR) versus transfemoral (TF) access. However, concerns about increased door-to-device (D2D) time metrics remain a barrier to routine TR pPCI. We hypothesized that routine TR pPCI could be established in a major US teaching hospital without significant differences in procedural time metrics or outcomes. Methods: Over a 34-month period (July 2010-April 2013), 136 STEMI patients were treated via pPCI at our hospital. Of these, 49 had TR access while 87 had TF access. We compared baseline characteristics, procedural times and outcomes between patients undergoing primary PCI via TR or TF access routes. Results: Baseline characteristics and the frequency of cardiogenic shock were similar between groups. As shown in Figure 1, access times (TF 3.00 ± 2.87 vs. TR 2.71 ± 2.39 minutes, p=0.76), cath lab-device times (TF 28.0 ± 13.6 vs. TR 24.6 ± 8.3 minutes, p=0.08) & D2D (TF 49.2 ± 30.8 vs. TR 42.0 ± 20.4 minutes, p=0.11) times were similar between TF and TR. Additionally, there were no significant differences in length of stay (3.2 ± 3.0 days TF vs. 3.4 ± 3.5 days TR, p=0.38), in-hospital (2.3% TF vs. 0.0% TR, p=0.50) or 30-day mortality (3.5% TF vs. 0.0% TR, p=0.35). 5/49 (10.2%) TR cases required conversion, but none of these failed the D2D metric (mean 52.4 minutes, range 24-70). There were no significant vascular complications in either group. Conclusions: In this consecutive series of STEMI patients undergoing pPCI at a major US teaching hospital, TR access is associated with similar procedure time metrics and similar overall outcomes. Given the significant clinical benefit of TR access in STEMI over larger populations, training fellows in TR pPCI should become routine practice. Disclosure: Daniel Steinberg, MD is a consultant for Terumo Interventional Systems.

087 Success of Trabeculectomy Compared to Combined Phacoemulsification-Trabeculectomy By Residents in a Veterans Hospital Setting, Robert A Sharpe1, Elizabeth D Sharpe1, 2, Ophthalmology, MUSC, 2Ophthalmology, Ralph H Johnson VAMC.

Aims: To investigate whether simple trabeculectomy with mitomycin C (trab) for glaucoma has a similar outcome compared to combined phacoemulsification-trabeculectomy (phaco-trab) when performed by residents in a Veterans Hospital center. Methods: Data were collected through a review of the VAMC electronic health records. Patients who underwent trab or phaco-trab performed by a resident at the VAMC between 2005-2012 were included. The primary outcome measured was the rate of complications following each type of surgery: immediately (< 1 week), early (1wk-1mo), intermediate (1mo-3mo), and late (3mo-12mo), as well as intraoperatively. Additionally, intraocular pressure (IOP), cup-to-disc (C:D) ratio, and number of glaucoma medications were compared pre- and post-operatively to evaluate treatment efficacy. Results: Of a total of 272 glaucoma surgeries identified, 106 met inclusion criteria. The trab group (n=56) and phaco-trab group (n=50) had mean age of 62.1 and 71.0 years, respectively (p=<0.01). The majority of patients were male, constituting 96% in the trab group and 100% in the phaco-trab group. For trab versus phaco-trab, the rate of intra-operative complications was 7.1% and 18.0% (p=0.14), respectively. Both groups also showed similar rates of immediate, early, and intermediate post-operative complications (p>0.34). For later complications, the complication rate was 30.4% for the trab group and 18.0% for the phaco-trab group (p=0.07). Pre-operative IOP was 24.4 and 20.8 (p=0.006) for trab and phaco-trab, respectively. The trab group was on more medications pre-operatively, averaging 3.4 versus 3.0 in the phaco-trab group (p=0.04). The C:D ratio was also greater preoperatively for trab group than phaco-trab group at 0.87 and 0.81 (p=0.01), respectively. However, the one year post-operative parameters for both groups were similar regarding IOP, C:D ratio, and number of medications (p>0.17). Conclusion: Both glaucoma procedures have overall similar complication rates and produce significant reductions IOP, requiring fewer medications, when performed by resident physicians at a VAMC.

088 Embracing Past Trauma: A Study Comparing Prolonged Exposure Therapy and a Mindfulness-based PTSD Treatment, Asa P Pharr1, Matthew Yoder2, Aaron Miller1, Kristy Center1, MUSC, 2RHJ VAMC.

Abstract not available.

089 C5a Recruits IL-17 Producing T-cells to the Eye in a Mouse Model of Age-Related Macular Degeneration, Beth Coughlin1, Kannan Kunchithapatham2, Chrystal M Paulos1, Baerbel Rohrer1; 1Microbiology and Immunology, MUSC, 2Ophthalmology, MUSC.

Background: Choroidal neovascularization (CNV) is a hallmark of advanced age-related macular degeneration (AMD). Genome-wide associations and histological studies have provided evidence that the complement system is involved in the pathogenesis of AMD. Relevant for my work is the fact that the anaphylatoxin and complement cascade component C5a is found at higher levels in serum of those subjects with AMD. While the role of inflammatory cytokines in choroidal neovascularization (CNV) and the cells that produce them has been partially investigated, the role of IL-17, a cytokine prevalent in tissue-destructive pathologies, has not yet been established. Interestingly, IL-17 is elevated in serum of patients with AMD when compared with healthy controls, much like C5a. However, unlike C5a, IL-17 is not manufactured locally by the retinal pigment epithelium of the eye. Methods: CNV was induced in control and ICOS-l/- mice and analyzed for size using immunohistochemistry (ICAM-2 staining). Using flow cytometry and QRT-PCR for cell-specific marker-genes, we elucidated what cells are migrating to the eye at what time point after CNV induction (12h, 24h, 48h, 3d, and 6d). Results: We found that IL-17...
was present in the eyes of mice with laser-induced experimental CNV. Inducible T-cell costimulator (ICOS) is a molecule thought to be critical for the differentiation and expansion of one of the IL-17 producing cells, Th17. When compared to control animals (C57BL/6) we found that ICOS KO mice show significantly reduced CNV lesion volumes. Conclusion: Our overarching expectation is that there is a unique cooperative effort among innate immune components, which promotes neovascularization in the eye. In future experiments, we plan to use blocking antibodies for C5a and IL-17 independently and in conjunction. In these conditions we will look at VEGF expression (Western), CNV lesion size (OCT), and cell recruitment on the day or days of interest (flow cytometry).

090 Characterization of mTORPhosphorylation and Basal Forebrain Cholinergic Neuron Loss in the Ts65Dn Mouse Model of Down Syndrome in Response to Various Diets and Inhibitors, Eric D Hamlett, Jason P Lockrow, Lotta Granholm-Bentley; Neuroscience, MUSC.

Trisomy 21 is the most common aneuploidy in the US and is classically associated with a delay in development and cognitive deficits, which are collectively called Down’s Syndrome (DS). Individuals with DS develop Alzheimer's related dementia in their 40s or 50s due to loss of cholinergic neurons of the basal forebrain coupled with other AD-related neuropathology in the hippocampus and entorhinal cortex. Mammalian Target of Rapamycin protein (mTOR) is a key protein for synaptic plasticity, cognitive memory, and potential disease pathologies in the brain. Neuronal survivability is directly linked to mTOR via signaling cascades from neurotropic factors, signal integration from nutrient sensing, control of protein synthesis and autophagy. Further mTOR phosphorylation is significantly increased in patient’s with Alzheimer’s disease. Finally, inhibition of mTOR phosphorylation has been shown to significantly increase cognitive deficits in mice providing justification to more fully characterize this biological signaling cascade. We explore a mouse model of DS, Ts65Dn mice, which mimic the cognitive deficits and neurodegeneration seen in humans with DS and AD. This poster details a proposed study which will quantify mTOR phosphorylation with residue specificity at discrete time points that will be correlated with memory deficits and neuronal loss. A mechanistic experimental design is introduced to measure mTOR phosphorylation levels. A final endpoint will be to correlate findings with behavior and neuronal outcomes. The findings presented herein suggest that the Ts65Dn mouse model can provide insightful knowledge about early signaling pathways that precedes AD-related dementia in individuals with DS. The primary hypothesis for this study is that aberrant mTOR phosphorylation is a post-translational event that precedes and may be at least partially responsible for cognitive deficits and neurodegeneration in the basal forebrain and hippocampus of the Ts65Dn model of DS. NIH NIA 5R01AG044920

091 Phenotypic, Molecular and Functional Characterization of Hematopoietic Stem Cell-Derived Cancer-Associated Fibroblasts, Ryan R Kelly, Lindsay T McDonald, Dayvia A Laws, David P Turner, Victoria J Findlay, Amanda C LaRue; Pathology and Laboratory Medicine, MUSC.

Among the most prominent cell types in the tumor microenvironment are fibroblasts, termed cancer-associated fibroblasts (CAFs). We have developed a unique transplantation model in which the bone marrow of lethally irradiated recipient mice is reconstituted by a clonal population of cells derived from a single EGFP+ hematopoietic stem cell (HSC). Using our single cell transplantation methodology in conjunction with two murine models of solid tumor, Lewis lung carcinoma (LLC-1) and E0771 (breast cancer), we sought to isolate and characterize HSC-derived CAFs based on phenotype, molecular signature and function. CAFs from clonally engrafted animals were first isolated and analyzed based on expression of markers associated with fibroblasts or activated fibroblasts by immunofluorescent staining. These findings show that HSC-derived CAFs express collagen I, alpha-smooth muscle actin and vimentin, all markers of activated fibroblasts. They were found to be negative for expression of F4/80, a marker of macrophages, and cytokeratins, a marker of epithelial cells. Profiling by qRT-PCR confirmed the HSC origin of these cells and revealed a molecular signature indicative of activated fibroblasts, demonstrating these cells were indeed HSC-derived CAFs. Molecular analysis also demonstrated expression of matrix metalloproteinases, known to have a role in extracellular matrix (ECM) remodeling and vascularization, as well as vascular endothelial growth factor (VEGF) and transforming growth factor beta (TGFb), factors known to play a role in tumor vascularization. Functional in vivo studies demonstrate that co-injection of HSC-derived CAFs with tumor cells significantly enhanced tumor growth, in part by increased vascularization. In vitro mechanistic studies showed that this was due to production of VEGF and TGFb. Collectively, our studies suggest that HSC-derived CAFs play a critical role in tumor progression, specifically through their role in ECM remodeling and tumor vascularization, thus representing potential targets for novel therapies in the tumor microenvironment. National Cancer Institute, R01 CA148772; Veterans Affairs Merit Award

092 Recovery From Forward Masking of Vowels and Consonants: Effects of Age and Hearing Loss, William J Bologna,1 Daniel Fogerty,2 Jayne B Ahlstrom,1 Judy R Dubno1,1;1Otolaryngology - Head and Neck Surgery, MUSC, 2Communication Sciences and Disorders, USC.

In everyday listening, fluctuations in the level of background noise and the relative timing of noise and speech improve perception of speech sounds, such as vowels and consonants, during brief moments when the noise level is low. Vowels are longer in duration and higher in level than consonants, which may favor vowel perception when speech and noise occur at the same time (“simultaneous masking”). In addition, the slow periodic fluctuations of vowels contrast with aperiodic noise maskers, which may improve perception of vowels that occur immediately after a masker’s offset (“forward masking”). Older adults with or without hearing loss may be poorer at coding these temporal periodicity cues, which may limit their performance in fluctuating maskers. To test these hypotheses, younger adults with normal hearing and older adults with normal and impaired hearing identified consonants or vowels in the initial or final position of noise-masked syllables. Syllable and masker duration and relative timing assured that the final 10, 40, or 100 ms of the syllable occurred after masker offset. Spectral shaping of syllables for individual subjects minimized confounding
effects of reduced audibility in regions of hearing loss. Preliminary results for initial-position phonemes indicate vowels are less susceptible to simultaneous masking than consonants. Recognition of final-position vowels is facilitated by the 40-ms delay, whereas final consonants require 100-ms delay or longer for similar improvement. Younger adults benefit most from these delays, older adults with normal hearing benefit less, and older adults with hearing loss benefit least of all. These findings support the hypothesis that age and hearing loss contribute to prolonged recovery from forward masking, and vowels have greater resistance to forward masking than consonants. NIH/R25 GM072643

093 Microglial Refinement of the Auditory Nerve in the Postnatal Mouse Inner Ear. LaShardai N Conaway1, Yazhi Xing1, Juhong Ju1, Nancy Smythe1, Jeremy Barth2, Hainan Lang1, 1Pathology and Laboratory Medicine, MUSC, 2Regenerative Medicine and Cell Biology, MUSC.

A fine wiring pattern between the spiral ganglion neurons of the auditory nerve and cochlear hair cells must be established for proper hearing. In the mouse, refinement of these fibers occurs during the first postnatal week, just before the onset of hearing, by unknown mechanisms. Microglia are special-ized immune cells in the nervous system that respond to inflammation in the brain. It has been demonstrated that the microglia-neuron interaction plays a role in nervous system development. Microglia are present in the cochlea during postnatal development, however, their role during this time is unclear. Thus, we hypothesize that microglia are present in the postnatal auditory nerve and play an important role in the refinement of synaptic fibers during inner ear development. To address this hypothesis, we processed immunohistochemical assays and gene microarrays on auditory nerve specimens isolated from postnatal CBA/CaJ mice at postnatal day 0, 3, 7 and 14. Cochlear glia and microglia were identified by immunostaining with specific markers for IBA-1 and CD11b (microglia), ED1 (phagocytosis), and Sox10 (glial cells). Quantitative analysis of IBA-1+ cells was processed in two locations of the peripheral auditory nerve: Rosenthal canal (RC) and osseous spiral lamina (OSL). Immunohistochemistry revealed that at postnatal day 7, microglia are mostly phagocytic and directly interact with cochlear glial cells. IBA-1+ cell counts indicated that the highest expression of microglia appeared around postnatal day 7, concurrent with the initiation of auditory nerve refinement. A decrease in IBA-1+ cell counts was recorded after P14, when the auditory nerve has nearly completed refinement. Gene array analysis revealed a corresponding pattern between putative nerve refinement genes and the peak of IBA1+ cell density. This unique temporal pattern suggests that the presence of microglia in the auditory nerve is associated with spiral ganglion neuron fiber refinement of the mouse cochlea during postnatal development. NIH R01 DC7506; NIH P50 DC0422; NCRR UL1RR029882; NIH R25 GM072643

094 Lymphodepletion-induced IL-12 Enhances Tc17 Cell Plasticity and Antitumor Activity. Jacob S Bowers, Sreenath Kundimi, Michelle H Nelson, Logan W Huff, Stefanie R Bailey, Carolyn E Rogers, Kristina Schwartz, Chrystal M Paulos; Microbiology & Immunology, MUSC.

Increasing the intensity of lymphodepletion enhances the antitumor activity of adoptively transferred CD8+ T cells in melanoma patients. Yet, the role of lymphodepletion on antitumor IL-17-producing CD8+ T cells (Tc17) remains incompletely elucidated. To address this, we polarized murine p-mel CD8+ T cells to secrete IL-17 and infused them into mice bearing melanoma that were either 1) lymphoreplete (0 Gy TBI) or lymphodepleted with 2) a non-myeloablative (5 Gy TBI) or 3) a myeloablative (9 Gy TBI plus HSC transplant) regimen. We found that Tc17 cells mediated superior tumor regression in myeloablated mice compared to lymphoreplete or non-myeloablated mice. Moreover, tumor regression was mediated to a greater extent by Tc17 cells than IL-2-polarized, IFN-gamma-producing CD8+ T cells. Additional studies revealed a strong correlation between the intensity of lymphodepletion and the degree of Tc17 plasticity, as Tc17 cells that mainly secreted IL-17 (>80%) in vitro converted into an array of cells that co-secreted IL-17 and IFN-gamma (25%) secreted IL-17 alone (11%) and IFN-gamma alone (31%) immediately after their infusion into myeloablated mice. These findings correlated with increased dendritic cell activation and heightened levels of systemic IL-12 and IL-23, suggesting that these cytokines promote Tc17 plasticity and antitumor activity. Blockade of endogenous IL-12 (but not IL-23) reduced the antitumor activity of Tc17 cells in myeloablated mice. Conversely, Tc17 cells primed with IL-12 in vitro enhanced tumor regression in non-myeloablated mice. Tc17 cells primed with IL-12 co-expressed RORgammaT and T-bet, co-secreted IFN-gamma and IL-17, expressed heightened ICOS, CD25 and CD127 levels on their cell surface and possessed an early effector memory phenotype. Of clinical significance, administration of IL-12 post-adaptive transfer enhanced the antitumor activity of IL-12-primed Tc17 cells, obviating the requirement for lymphodepletion to elicit T cell-mediated curative responses in mice. Thus, IL-12-induced lymphodepletion accelerates Tc17 plasticity and enhances their antitumor activity.

095 Using Novel Small Molecule LSD1 Inhibitors to Understand Mechanisms of Obesity-related Breast Cancer Pathogenesis. Steven L Holshouser, Craig J Kutz, Boobalan Pachiayappan, Patrick Woster; Drug Discovery, MUSC.

Obesity is currently an epidemic in the United States. The current statistic is that 35% of women in the United States population are currently obese, and these numbers are on the rise. Not only does this condition cause coronary heart disease and type II diabetes, but also recently, there has been an overwhelming amount of data that has shown there is an enhanced risk of breast cancer in patients who are obese or have been diagnosed with obesity. Prominently, these cases have been documented in women more so than men. Previous studies have shown that women who are obese have a 40% higher risk of developing breast cancer than women who is not obese. Since there are around 156 million women in the U.S., around 22 million women are at a severe risk of developing breast cancer. The mechanisms that underlie these risks from increased adipogenesis to breast cancer tumorigenesis are not accurately known. Relevant research of epigenetic regulators such as Lysine Specific Demethylase (LSD1), has been shown to alter the methylation status as well as location of key cell cycle regulation proteins such as p53 while also maintaining complexes with multiple transcription factors such as
estrogen receptor alpha (ERα). This complexing, as well as binding with transcriptional co-repressors such as PELP1, plays a crucial role in breast cancer tumorigenesis development. Upon the onset of adipogenesis, Aromatase activity is increased significantly. Research has shown that this increase in aromatase activity leads to a dramatic increase of estrogen signaling to neighboring cells. Hence, this proposal outlines as series of experiments that will determine the mechanistic role of LSD1 in the regulation of p53/ERα and PELP1 throughout the cell. We hypothesize that LSD1 is a direct modulator for p53 along with ERα complexing and has a direct correlation with increased estrogen production from adipocytes to increase ERα expression as well as H3K4 methylation. Along with inhibiting the formation of this complex, we further hypothesize that inhibiting LSD1 demethylation at H3K4 through specific, small molecule inhibitors will further activate the transcription of tumor suppressor oncogenes by direct demethylation. Through inhibition of LSD1, we will alter the nuclear translocation availability status of p53 to transactivate the cell cycle checkpoint via p21. Changes that are contributing to these links between obesity and cancer can also be linked to epigenetic changes through posttranslational modifications that are marked after high levels of insulin exposure within a cell. These risks may be reversible through these epigenetic changes as literature shows these posttranslational modifications can be altered multiple times. Even if a woman was obese at one point in her life, and now is not, the potential risk of breast cancer development could still be prominent if the epigenetic marks have been altered. Understanding these mechanisms of action could prove to reduce the breast cancer risk with people who are or have been obese. In addition to gaining valuable, cutting edge techniques in the field of synthetic chemistry as well as molecular biology, these studies could also lead to other discoveries in the field of epigenetics that have a regulatory control based on key posttranslational modification changes upon developing certain diseases. NIH

096 (Bis)biguanidine Oligoamine Sustain Myocardial Function Following Ischemia-reperfusion Injury in Isolated Perfused Rat Hearts. Craig J Kutz1, Sverre E Aune2, Patrick Woster3, Donald R Menick4, 5Drug Discovery, MUSC, 2Gazes Cardiac Research Institute, MUSC, 3South Carolina Clinical and Translational Research Institute, MUSC.

Current therapies to assist short- and long-term outcomes after acute myocardial infarction (AMI) are dependent on expeditious restoration of flow to the tissue. However, upon reperfusion, localized oxidative stress and inflammatory signaling can further damage the myocardium - termed Ischemia-Reperfusion (IR) injury. To date, epigenetic modifiers, such as histone deacetylases (HDAC) inhibitors, have been beneficial in maintaining cardiac contractility and reducing infarct area post-IR Injury. Yet, little focus has been placed on the other vast milieu of epigenetic enzymes in cardiopathology. In particular, the histone demethylase, lysine specific demethylase-1 (LSD1), shows a critical interdependency with HDACs and other cofactors. Thus, we hypothesized that a (bis)biguanidine oligoamine inhibitor (IC50 8.5uM) of LSD1, verlindamyocin (formerly known as 2d), would unveil a new target to abrogate IR injury. Male Sprague-Dawley rats were i.p. injected with 10mg/kg of verlindamyocin or vehicle (DMSO) at 18-hrs and 1-hr prior to heart isolation and perfusion by Langendorff model using Krebs-Henseleit buffer bubbled with 95% O2/5% CO2. Ischemia was induced for 30-mins followed by 1-hr reperfusion. A saline-filled balloon fixed to a pressure transducer inflated to 5-10mmHg in the left ventricle (LV) measured contractile function. After reperfusion, 2-mm cross-sections of LV tissue were collected for measurement of infarct area, superoxide production, and protein expression. Verlindamyocin preconditioning of hearts maintained LV end diastolic pressure, LV maximum pressure variation rate ( dp/dtmax), developed pressure, and rate-pressure product after induction of IR injury as compared to vehicle treated rats. Also, increased levels of phosphorylated p38 in verlindamyocin-treated rat hearts corroborate a pro-survival preconditioning event. Therefore, this study provides evidence that a (bis)biguanidine oligoamine preconditioned the heart against IR injury and suggests potential involvement of LSD1. Future studies aim to determine which targets of LSD1 provide cardioprotection and determine whether known off-targets play a role. NIH/NCATS Grant Number TL1 TR 000061 and UL1 TR 000062; NIH RO1 CA149095.
Introductions: Scleroderma interstitial lung disease (SSc-ILD) is an irreversible progressive complication leading to respiratory failure and death. Myofibroblasts, characterized by the expression of α-smooth muscle actin (α-SMA), are principal cells responsible for tissue remodeling in SSc-ILD. The current study was initiated to examine the role of IQGAP1 in regulating α-SMA expression and function. Methods: Protein interaction studies were performed using co-immunoprecipitation, 2D-gel electrophoresis and mass spectrometry. Actin polymerization was studied using FLIPR. Effects of IQGAP1 in vivo were investigated using the bleomycin-induced murine model of pulmonary fibrosis. Results: Lung tissue isolated from bleomycin-treated mice is characterized by extensive peribronchial and interstitial infiltrates of inflammatory cells, thickening of alveolar walls and multiple focal fibrotic lesions. Significantly fewer cellular infiltrates and decreased thickness of alveolar septae are present in IQGAP1-knockout mice, as well when control mice are treated with IQGAP1-siRNA or CTGF-siRNA. Analysis of lung tissue by immunoblotting reveals an increase in both α-SMA and CTGF in bleomycin-treated mice, whereas intranasal administration of IQGAP1-siRNA and CTGF-siRNA together reduces the expression of α-SMA and diminishes severity of pulmonary fibrosis. Studies on lung fibroblasts isolated from patients with SSC-ILD demonstrate that IQGAP1 forms a protein interaction complex with α5β1 integrin and CTGF, regulating α-SMA organization. Immunofluorescent studies reveal that IQGAP1 co-localizes with monomeric and with highly organized α-SMA suggesting that IQGAP1 serves as a scaffold protein in α-SMA polymerization process. Indeed IQGAP1-knockout mice exhibit reduced speed of actin polymerization and lower amount of pulmonary F-actin as compared with wild-type mice. Conclusion: We conclude that IQGAP1 forms a signal transduction complex with CTGF that interact with α5β1 integrin, leading to an increased α-SMA organization generating amplified contractile forces in lung myofibroblasts. Targeting IQGAP1 therefore has the potential to be an effective novel strategy for the treatment of increased lung stiffness associated with SSC-ILD. Scleroderma Foundation; T32GM074934

098 Reduced Actin Polymerization in Lungs of IQGAP1-Knockout Mice: Implication for Scleroderma Interstitial Lung Disease. Tanjina Akter1, Sybil L Nelson1, Ilia Atanelishvili1, Alvaro Martos1, Richard M Silver1, Galina S Bogatkevich1, 2Rheumatology & Immunology, MUSC, 3Hospital Universitario 12 de Octubre, Madrid, Spain.

Obesity has become an increasingly prevalent public health problem in the United States. Recently there has been a shift in understanding obesity and studies are now focused on the psychological factors involved in the development of the disease. Brain-derived neurotrophic factor (BDNF) has an integral role in glucose regulation, satiety, and control of food consumption. There is extensive evidence that altered BDNF signaling plays a role in chronic overconsumption of food to the point of obesity. Selective BDNF knockdowns have further implicated BDNF in selectively enhanced palatable food intake. We used an operant model of animal food self-administration to examine the differences in food self-administration and reinstatement between groups of Sprague Dawley rats lever pressing for either standard chow pellets or palatable chocolate pellets with an enhanced sucrose content. Our results indicate that BDNF protein levels in the dmPFC, an area highly implicated in control of reward seeking behavior, was decreased immediately following 7 weeks of self-administration of palatable chocolate pellets. Furthermore, preliminary evidence indicates a possible down regulation in total mRNA of BDNF’s activity dependent exon IV transcript in dmPFC. In a separate cohort, we found that rats will escalate their lever pressing to receive palatable pellets but not standard chow pellets over the last 5 weeks of self-administration. Following extinction of lever pressing, both groups of rats reinstated with a cue and pellet prime. However rats that self-administered standard chow pellets reinstated to a greater degree than those that self-administered the chocolate pellets. Furthermore, pellet and cue primed reinstatement of palatable food seeking produced greater activation of the prelimbic (PrL) cortex than reinstatement of standard chow seeking. These data provide both a role for BDNF and the PrL in palatable food

097 100 Prefrontal Cortical Neuroadaptations Following Self-administration and Reinstatement of Highly-palatable Food: the Role of Brain-derived Neurotrophic Factor. Sarah M Barry1, Megan N Huizenga*, Ghazaleh Sadri-Vakili2, Jacqueline F McGinty1, 1Neurosciences, MUSC, 2NeuroEpigenetics, MassGeneral Institute for Neurodegenerative Disease.

Obesity is a growing health problem in the United States. Recently there has been a shift in understanding obesity and studies are now focused on the psychological factors involved in the development of the disease. Brain-derived neurotrophic factor (BDNF) has an integral role in glucose regulation, satiety, and control of food consumption. There is extensive evidence that altered BDNF signaling plays a role in chronic overconsumption of food to the point of obesity. Selective BDNF knockdowns have further implicated BDNF in selectively enhanced palatable food intake. We used an operant model of animal food self-administration to examine the differences in food self-administration and reinstatement between groups of Sprague Dawley rats lever pressing for either standard chow pellets or palatable chocolate pellets with an enhanced sucrose content. Our results indicate that BDNF protein levels in the dmPFC, an area highly implicated in control of reward seeking behavior, was decreased immediately following 7 weeks of self-administration of palatable chocolate pellets. Furthermore, preliminary evidence indicates a possible down regulation in total mRNA of BDNF’s activity dependent exon IV transcript in dmPFC. In a separate cohort, we found that rats will escalate their lever pressing to receive palatable pellets but not standard chow pellets over the last 5 weeks of self-administration. Following extinction of lever pressing, both groups of rats reinstated with a cue and pellet prime. However rats that self-administered standard chow pellets reinstated to a greater degree than those that self-administered the chocolate pellets. Furthermore, pellet and cue primed reinstatement of palatable food seeking produced greater activation of the prelimbic (PrL) cortex than reinstatement of standard chow seeking. These data provide both a role for BDNF and the PrL in palatable food
self-administration and seeking, respectively. Klarman Family Foundation

101 Effects of Prolonged CB1 Receptor Activation During Adolescence in the Prefrontal Cortex of Dysbindin-1 Null Mutant Mice. Jose I Pena Bravo, Antonieta Lavin; Neurosciences, MUSC.

Schizophrenia is a complex disease characterized by cognitive, social and perceptual deficits generally present in early adulthood. We are interested in how a deletion in the DTNTP1 gene, a schizophrenia susceptibility gene, can produce cognitive deficits by reducing dysbindin protein levels. Post-mortem human studies show reductions in dysbindin in the prefrontal cortex (PFC) of schizophrenics. Our studies report deficits in excitatory neurotransmission and NMDA receptor function in the PFC of dysbindin deficient (sandy) mice. Currently, we will focus on gene-environment interactions and their influence on schizophrenia susceptibility. We believe the endocannabinoid system is sensitive to changes by the environment during adolescent brain development. In order to test our hypothesis we examined the state of the endocannabinoid neurotransmission between wild type (wt/wt), sandy heterozygous mutants (wt/dys-) and homozygous mutants (dys/-dys-) mice (PND 35-60) using whole-cell patch clamp. To determine any changes in suppression of excitatory and inhibitory inputs into pyramidal cells of the PFC, we tested a protocol of endocannabinoid mediated depolarization induced suppression of excitation and inhibition (DSE and DSI respectively). The magnitude of DSE shows a trend towards a decrease in wt/dys- and dys/-dys- compared to wt/wt mice. These results suggest a reduction of endocannabinoid production in sandy mice. Changes in DSI magnitude were variable. Direct activation of CB1 receptor by WIN 522,212-2 (3uM) on excitatory inputs showed similar decreases in amplitude between the different genotypes, suggesting no difference in CB1 receptor function. Recordings of inhibitory inputs before and after bath application of WIN, showed a trend towards a reduction in inhibition of wt/dys- mice compared to wt/wt and a large amount of variability in the amplitude of IPSCs in dys/-dys- mice. These results suggest a possible alteration in the function of CB1 receptors in sandy mice that will be further tested using different protocols of endocannabinoid induction. *NIDA T32DA007288-21*

102 Statistical Methods for Dealing with Overdispersion in Modeling Count Responses. Elizabeth H Payne, Mulugeta Gebregziabher; Biostatistics, MUSC.

Abstract not available.

103 Joint Bayesian Spatial Modeling for Studies Combining Longitudinal and Cross-sectional Data. Rachel M Carroll¹, Andrew B Lawson¹, Marcia Castro²; ¹Biostatistics, MUSC, ²Global Health and Population, Harvard.

Design for intervention studies may combine longitudinal data collected from sampled locations over several survey rounds, and cross-sectional data from other locations in the study area. In this case, modeling the impact of the intervention requires an approach that can accommodate both types of data, accounting for the dependence between individuals followed up over time. In this paper we use data from a larval intervention for malaria control implemented in Dar es Salaam, Tanzania, collected over a period of almost 5 years. In this case, inadequate modeling can mask the intervention effects, with serious implications for policy making. We apply a joint spatial Bayesian model to the Dar es Salaam data, combining follow-up and cross-sectional data, treating the correlation in longitudinal observations separately, and controlling for potential confounders. We contrast the results with other Bayesian modeling formulations, including cross-sectional approaches that consider individual-level random effects to account for subjects followed-up in two or more surveys. All modeling approaches indicate that the intervention significantly reduced the prevalence of malaria infection in Dar es Salaam, but the magnitude of the reduction (in the odds scale) varied between 36.6%-49.4%, with the largest reduction observed in the joint model. *NIAID R03AI094401-01*

104 Environmental Determinants of Systemic Lupus Erythematosus (SLE). Delia C Voronca, Rachel Carroll, Andrew Lawson, Diane Kamen, John Vena; Biostatistics, MUSC.

Abstract not available.

105 Assessing the Prevalence and Effect of Phthalate Exposure During Gestation. Abby M Goodson¹, John W Brock², Lori Cruz³, John R Kucklick⁴, Louis J Guillette⁵; ¹Marine Biomedicine and Environmental Science, MUSC, ²Chemistry/Environmental Studies, Warren Wilson College, ³Obstetrics and Gynecology, MUSC, ⁴Chemical Sciences Division, NIST.

Endocrine disrupting compounds (EDCs) are substances that disrupt endogenous endocrine signaling, and phthalates are one of the most commonly encountered EDCs by humans. Phthalates are commonly used as stabilizers in personal care products and solubilizers in flexible plastics. Human exposure occurs mainly through contact with personal care products such as cosmetics and perfumes, but exposure can also occur through contact with plastics routinely used in medical and household products. Phthalates interfere with steroid signaling pathways and have been found to exert anti-androgenic effects. In rodent and human males, increased phthalate exposure has been linked with decreased anogenital distance (AGD), a marker of the androgenic signaling pathways and have been found to exert anti-androgenic effects. In rodent and human males, increased phthalate exposure has been linked with decreased anogenital distance (AGD), a marker of the androgenic environment experienced in utero. My goals are to determine: 1) the extent to which pregnant women in the Charleston area are exposed to phthalates, 2) whether phthalate levels differ between pregnant women from different racial ethnicities or socioeconomic statuses, and 3) whether higher maternal phthalate exposure is associated with reduced AGD in male neonates. Urine samples are being collected from 450 expectant mothers at three time points across the pregnancy (18-20 weeks, 24-32 weeks, and delivery). In the first phase, we are currently developing a method for analyzing a suite of eight commonly encountered phthalate metabolites in maternal urine using liquid chromatography coupled with tandem mass spectroscopy. Phthalate metabolites currently being measured are monobutyl phthalate, mono-isobutyl phthalate, monobenzyl phthalate, mono-(2-ethylhexyl) phthalate, mono (2-ethyl-5-hydroxyhexyl) phthalate, mono-(2-ethyl-5-oxoheptyl) phthalate, monoethyl phthalate, and monomethyl phthalate. In the second
phase, we will add more phthalate metabolites to this list, as well as prominent phthalate replacement chemicals. NIST

106 Longitudinal Impact of Mental Health Outpatient Care on Healthcare Cost For Individuals with Type 2 Diabetes. Rebekah J Walker, 1 Mulugeta Gebregziabher 2, Yumin Zhao, 3 Clara E Dismuke 4, Kelly J Hunt 5, R. Neal Axon 6, Leonard E Egede 7, Health Professions, MUSC, 8 Medicine, MUSC, 9 VAMC, Medicine, VAMC.

Diabetes affects over 285 million adults worldwide. Patients with diabetes and comorbid psychiatric disorders tend to have worse health outcomes and higher healthcare costs than other diabetes patients. A national cohort of 120,852 Veterans with diabetes and at least one mental health diagnosis in 2002 was followed through 2008. Type 2 diabetes was identified by two or more ICD-9 codes and receipt of prescriptions for insulin or oral hypoglycemic agents. Mental health conditions (MHC) examined included depression, substance abuse, and psychoses. Number of mental health visits (MHV) was defined as referral to a mental health provider other than primary care and categorized as 0, 1, 2 and 3+. The primary outcome was total inpatient, outpatient, and pharmacy costs measured in 2006 U.S. dollars with the perspective of the federal payer. 81% had one MHC, 15.2% had two MHC, and 3.1% had all three MHCs. Least-square estimates from the joint model of total VA costs of the number of MHV indicate that relative to those with fewer MHV, those with 3+ MHV had the lowest mean inpatient cost ($21,406), but the highest mean outpatient and pharmacy cost ($9,727 and $2,015, respectively). If all Veterans who received zero MHV actually received 3+ MHV, between $32,272,329 and $181,460,247 in inpatient costs would be saved. However, these savings would be offset by additional expenditures of between $1,166,017,547 and $1,166,224,787 in outpatient costs and between $151,604,683 and $161,439,632 in pharmacy costs. Therefore, among Veterans with diabetes and comorbid MHC, having 3+ MHV is associated with decreased inpatient costs, but these potential savings are offset by increased outpatient and pharmacy costs. Increasing clinic visits alone may not result in significant net cost savings and a more nuanced approach to provision of mental health services may be required. VHA Health Services Research and Development IIR-06-219

107 The Role of Health Literacy in African Americans with Type 2 Diabetes. Brittany L Smalls1, Delia C Voronca2, Leonard E Egede3, MUSC, 4Statistics, MUSC, 5Medicine, VAMC.

Background: Type 2 diabetes mellitus (T2DM) affects more than 25.3 million people in the United States. Major complications and comorbid illnesses result from T2DM, including blindness and vision problems, nervous system disorders, kidney disease, amputations, periodontal disease, heart disease, and stroke. Literature suggests that health literacy maybe associated with health outcomes. Very little is known about the health literacy of African Americans with type 2 diabetes in a primary care setting. The purpose of this study was to evaluate the prevalence of health literacy in African Americans with type 2 diabetes and examine the relationship of health literacy on diabetes related health outcomes. Methods: Baseline survey data on 277 African Americans with type 2 diabetes was obtained from a 2008 four-year clinical trial. Participants were recruited from two primary care clinics: an academic Internal Medicine clinic and a Veterans Affairs (VA) primary care clinic in Southeastern United States. Health literacy was the primary independent variable to evaluate the impact of health literacy on diabetes related health outcomes (e.g., HbA1c, systolic blood pressure, LDL). Health literacy was measured using the short form Test of Functional Health Literacy Assessment (S-TOHFLA). Pearson’s correlation was used to determine if there was a correlation between health literacy and relevant health outcomes. Multiple linear regression was used to determine if there was an independent effect of health literacy, adjusting for appropriate covariates. Means were used to show the distribution of health literacy scores through population demographics. SAS version 9.3 was used for all statistical analyses. Results: The results showed that in this sample of African Americans with type 2 diabetes, 21.3% were 65 years or older, 44.8% were women, 19.1% had less than high school education, and 26.4% had an annual income of $10,000-$25,000. Overall, the mean health literacy scores were comprehension 26.5 ± 9.7, numeracy 8 ± 2.4, and overall literacy 34.5 ± 11.4. Approximately 20% of the sample had inadequate comprehension scores (score 0-16). Health literacy was not shown to have a significant correlation with HbA1c, systolic blood pressure, or LDL. In the adjusted multiple linear regression model, health literacy was not significantly associated with HbA1c, systolic blood pressure, or LDL. Even when adjusted for relevant covariates health literacy was not significantly associated with health outcomes. However, in the adjusted linear regression model, LDL was marginally associated with inadequate comprehension (β =-11.9, 95% CI -25.2, 1.37, p=0.014) and systolic blood pressure was significantly associated with marginal comprehension (β=8.72, 95% CI 0.57, 16.9, p=0.04). Conclusion: Overall, in this sample of African Americans with Type 2 diabetes, approximately 70% had adequate health literacy. Yet, there is no significant association to relevant outcomes. This is consistent with the current literature and questions the impact of health literacy on health outcomes. Further research should be conducted to address the impact of health literacy and diabetes health outcomes. NIDDK R01DK081121

108 Developmental Mechanisms of Mitral Valve Prolapse. Kimberly Sauls1, Annemarieke de Vlaming3, Katherine Williams1, Robert Levine2, David Milan3, David Peal2, Sue Slaugenhaupt1, Roger Markward1, Russell Norris1, Regenerative Medicine, MUSC, 2Cardiology, Harvard Medical School, 3Medicine, Harvard Medical School, 4Neurology, Harvard Medical School.

Affecting 1 in 40 people worldwide, mitral valve prolapse is one of the most common human diseases. Valve-disease manifestation and clinical expression occur gradually over a patient’s life due to progressive weakening of the valve leaflets and can lead to secondary cardiac diseases and death. Because gene mutations that cause mitral valve prolapse (MVP) remain elusive, etiology is poorly understood. Discovering disease genes will facilitate understanding of pathogenetic mechanisms that cause MVP, with potential for future remedial or therapeutic insights. Using a large multigenerational pedigree with inherited MVP, we recently reported genetic, functional, and mechanistic data that implicate the cell polarity gene, DCHS1 (dachsous-1), in the pathogenesis of non-syndromic MVP. This is the first discovery of a gene that
causes the common form of MVP in humans and our studies demonstrate disease inception occurs during fetal development. Additionally, these studies have identified planar cell polarity as a previously unrecognized facet of cardiac development.

109 Effect of the Premalignant and Tumor Microenvironment on Immune Cell Cytokine Production in HNSCC, Sara D Johnson, Corinne Levingston, Rita Young; Microbiology and Immunology MUSC, Medical Research Service, VAMC.

Head and neck squamous cell carcinoma (HNSCC) is an aggressive form of head and neck cancer marked by immunosuppression, a state in which the established tumor escapes immune attack. Previous studies using the carcinogen (4-nitroquinolone)-induced mouse model have shown that the immune response changes during HNSCC carcinogenesis. Though a significant pro-inflammatory response is observed in the tumor-draining lymph nodes of premalignant mice, conventional T cell function is significantly compromised in HNSCC-bearing mice, leading to persistence of the tumor. How the tumor microenvironment contributes to the immune response has yet to be elucidated. The purpose of this study is to characterize the supernatant of pre-malignant and HNSCC tumor cell lines derived from the 4-NQQ mouse model and to determine the effect of this supernatant on immune cell cytokine production. Our hypothesis is that premalignant cells will secrete increased levels of proinflammatory cytokines compared to HNSCC tumor cells, which will lead to a significant increase in the production of proinflammatory cytokines by splenocytes co-cultured with premalignant supernatant compared to HNSCC supernatant. To address this hypothesis, cytokine/prostaglandin levels in premalignant and HNSCC cell line supernatants and splenocyte co-cultures were analyzed by cytokine bead array (CBA) and ELISA. It was found that premalignant cell supernatant contains significantly increased levels of G-CSF, RANTES, MCP-1, and PGE2 compared to HNSCC supernatant. Control splenocytes co-cultured with premalignant supernatant secreted significantly increased levels of Th1-associated IL-2 and IFN-gamma, Th2-associated IL-4, IL-6 and IL-10, macrophage-associated TNF, G-CSF, GM-CSF and MIG, and several other proinflammatory mediators including IL-1 alpha, IL-1 beta, IL-17A, RANTES and PGE2 compared to splenocytes co-cultured with HNSCC supernatant. These studies in the 4-NQQ mouse model suggest that whereas the premalignant microenvironemnt stimulates cytokine production, a robust proinflammatory immune response, the tumor microenvironment is significantly less immune stimulatory and may contribute to immunosuppression in established HNSCC. Medical Research Service of VAMC; NIH/NCI R01 CA128837

110 The Effect of α-connexin Terminal Peptide 1 (ACT1) in a Model of Acute Lung Injury (ALI), Kristoffer N Rodriguez, Carl Atkinson; Microbiology & Immunology, MUSC.

Acute lung injury (ALI) is a syndrome annually affecting ~50 of 100,000 people in the United States. ALI is clinically characterized by low lung compliance, hypoxemia, and eventual pulmonary failure due to the degradation of normal alveolar function. The key pathogenic characteristics of ALI, edema, neutrophil infiltration and cytokine production, result as a consequence of destruction/degradation of the alveolar wall. Central to this destruction and inflammation is the loss of tight and gap junction functions, which are associated with a loss of connexin integrity. Connexin 43 (Cx43) is an abundant respiratory epithelial transmembrane protein. Cx43 has shown to act as a membrane anchor for tight junction ZO-1 and is essential in composition of gap junction hexamers. Alpha Connexin Terminal 1 Peptide (ACT1) is a highly permeable peptide mimetic of Cx43, utilized for maintaining lung epithelial gap junction and tight junction function. Through utilizing of epithelial transwell cell culture system and an in vivo murine ALI survival model, we have begun to evaluate the potential therapeutic utility of ACT-1 for the treatment of ALI by exploring the peptide's impact on cell injury, function of tight and gap junctions, inflammatory cytokine expression, and rodent survival post-ALI induction. Current data analysis demonstrates that the administration of ACT1 in our in-vitro and in vivo models, leads to improved transepithelial electrical resistance (a marker of tight junction function), reduced epithelial cytokine production, and improved animal survival post LPS exposure. Taken together these data support the potential use of ACT1 as a novel therapy for the treatment of acute lung injury. First String Research, Inc

111 From Parkinson’s Disease to Addiction: Preclinically Evaluating Subthalamic Nucleus Inactivation As a Cocaine Addiction Treatment, Brandon S Bentzley, Gary Aston-Jones; Neuroscience, MUSC.

The subthalamic nucleus (STN) is targeted for neurosurgical treatment of Parkinson's disease, obsessive-compulsive disorder and major depression. Recent reports indicate a role of STN in cocaine reward; however, STN has not yet been linked to addiction-like behavior leaving its potential as an addiction treatment mediator unknown. The current study determined the role of rat STN in driving the economic essential value of cocaine. Economic essential value of a drug has been shown to predict several clinical measures of addiction in human and several addiction-like behaviors in rat, including relapse and compulsive drug taking. The essential value of cocaine was determined by measuring consumption of cocaine across 11 ascending cocaine prices (lever responses/mg cocaine) in a single 110-min session. Rats were pretreated with bilateral microinjections (0.3 µL) into STN of either vehicle (artificial cerebrospinal fluid) or the GABAA receptor agonist muscimol (0.2 mM) immediately prior to sessions in a within-subjects crossover design. Muscimol pretreatment significantly attenuated the essential value of cocaine compared to vehicle or injections of muscimol immediately dorsal to STN. In contrast, muscimol pretreatment did not reduce cocaine consumption when the price of cocaine remained low throughout the session (e.g., FR1 schedule), indicating that STN inactivation results in price-dependent changes in cocaine consumption. Further, muscimol treatment did not alter locomotor activity in a novel environment. Given the clinical promise of economic measures of drug use, these results support a possible clinical utility of STN inactivation in treating cocaine abuse. NIDA R37 DA006214, T32 DA007288, and F30 DA035065.
112 Oxytocin Reduces the Motivation to Self-administer Methamphetamine in a Novel Within-session Behavioral-economic Paradigm: Male-female Comparisons, Brittney M Cox, Brandon S Bentzley, Carmela M Reichel, Ronald E See, Gary Aston-Jones; Neurosciences, MUSC.

Human and animal studies indicate that females have greater motivation to use methamphetamine (meth), which may contribute to enhanced relapse vulnerability. Women initiate meth use at a younger age and transition faster to dependence than men. Similarly, female rats acquire meth self-administration at higher rates and exhibit greater meth intake than males. Behavioral-economic (BE) models have been designed to assess changes in consumption as a function of effort and provide separate measures of meth intake (Q0) and motivation normalized to intake (α, a measure of demand elasticity). These measures have been shown to predict relapse in both human and animal studies, indicating that BE models will further our understanding of the relationship between motivation to seek drug and relapse behavior, and facilitate screening novel pharmacotherapies for treatment of addiction. Thus, utilizing a within-session BE paradigm, we used these measures to directly compare males and female rats during meth self-administration. We also tested oxytocin, a potential antirelapse medication, for its ability to attenuate meth seeking in both sexes. Females showed greater motivation to seek meth (lower α) compared to males and higher meth intake (higher Q0). Oxytocin decreased motivation to seek meth in both sexes, but did not alter their intake at null price. Correlations between behavioral-economic and reinstatement measures, and determination of whether oxytocin during the within-session BE paradigm can predict attenuation of subsequent reinstatement, will also be presented. Overall, this novel paradigm will help to delineate sex differences observed in motivation to seek meth and may predict the efficacy of pharmacotherapies to treat meth addiction. NIH R01 DA022658, R37 DA006214, T32 DA007288

113 Alternative Complement Pathway Deficiency Ameliorates Chronic Smoke-Induced Functional and Morphological Ocular Injury, Alex S Woodell1, Beth Coughlin2, Kannan Kunchithapatham2, Sarah Casey3, Tucker Williamson4, Carl Atkinson4, Bryan Jones4, B. J. bel Rohrer5; 1Neurosciences, MUSC, 2Ophthalmology, MUSC, 3Microbiology and Immunology, MUSC, 4Moran Eye Center, University of Utah.

Age-related macular degeneration (AMD), a complex disease involving genetic variants and environmental insults, is among the leading causes of blindness in Western populations. Genetic and histologic evidence implicate the complement system in AMD pathogenesis; and smoking is the major environmental risk factor associated with increased disease risk. Although previous studies have demonstrated that cigarette smoke exposure (CE) causes retinal pigment epithelium (RPE) defects in mice, and smoking leads to complement activation in patients, it is unknown whether complement activation is causative in the development of CE pathology; and if so, which complement pathway is required. Mice were exposed to cigarette smoke or clean, filtered air for 6 months. The effects of CE were analyzed in wildtype (WT) mice or mice without a functional complement alternative pathway (AP; CFB−/−) using molecular, histological, electrophysiological, and behavioral outcomes. CE in WT mice exhibited a significant reduction in function of both rods and cones as determined by electroretinography and contrast sensitivity measurements, concomitant with a thinning of the nuclear layers as measured by SD-OCT imaging and histology. Gene expression analyses suggested that alterations in both photoreceptors and RPE/choroid might contribute to the observed loss of function, and visualization of complement C3d deposition implies the RPE/Bruch’s membrane (BrM) complex as the target of AP activity. RPE/BrM alterations include an increase in mitochondrial size concomitant with an apical shift in mitochondrial distribution within the RPE and a thickening of BrM. CFB−/− mice were protected from developing these CE-mediated alterations. Taken together, these findings provide clear evidence that ocular pathology generated in CE mice is dependent on complement activation and requires the AP. Identifying animal models with RPE/BrM damage and verifying which aspects of pathology are dependent upon complement activation is essential for developing novel complement-based treatment approaches for the treatment of AMD. VA Merit Award RX000444; Research to Prevent Blindness and Foundation Fighting Blindness, NIH NHLBI RO1 091944; NIH C06RR015455

114 The Effect of Soluble MICB on NKG2D-Mediated Regulation of NK Cell Anti-Tumor Immunity, Fahmin Bashir, Shengjun Lu, Gang Xiao, Jennifer D Wu; Microbiology & Immunology, MUSC.

Shedding of the soluble NKG2D ligand MIC is one method by which tumor cells escape immunosurveillance to promote cancer progression. Previous studies in our laboratory using a humanized bi-transgenic prostate adenocarcinoma model showed that tumor progression to metastasis correlated with serum sMICB levels and deficits in NK cell homeostasis. To investigate possible mechanisms by which NK cell homeostasis is affected, in vitro co-cultures were performed that demonstrated a significant increase in NK cell PD-1 expression when exposed to TC2 cell lines expressing soluble but not membrane-bound MICB. An in vivo study in which Rag−/− mice were inoculated with TC2-sMICB cells found that treatment with IL-15/IL-15Ra, antibody against MICB, or the combination significantly decreased splenic apoptotic (total annexin V+ and Annexin V+/PD-1+) frequency as well as decreased the frequency of micrometastases in the lung. Further in vitro mouse NK cell co-cultures demonstrated a rescue from apoptosis induced by TC2-sMICB in the presence of IL-15/IL-15Ra alone or in combination with anti-MICB and a similar rescue by IL-15 from apoptosis in the human cell line NK92 induced by sMICB. Current studies involve determining the mechanisms by which IL-15, PD-1 blocking, and anti-MICB affect NK cell survival and function in the presence of soluble and membrane MICB both in vivo and in vitro. NIH R01CA149405
Splenectomy has been observed after severe stroke in adults, and in our work in neonatal rats 6 weeks after HI insult. Leukocyte apoptosis and prolonged immune suppression are mediated in part by glutamate receptors and reactive oxygen species, which could be important factors in splenic depletion. Gender effects have also been reported in peripheral immunosuppression after stroke, with males showing greater reduction in spleen size and peripheral immunosuppression compared with female mice. Previously we have shown that 6 week old male HI rats with severe gross brain pathology scores also showed lower spleen to body weight ratios compared with females with severe HI injury and males with less severe injury. To investigate the mechanism of immunodepletion in our neonatal HI model, we evaluated Vitamin D homeostasis and systemic immune response to treatment at an earlier time point, 11 days post injury. After HI in PND 7 rats, we randomized hypothermia treated animals to saline (HYPO), NAC 50mg/kg/d, or NAC+VitD 0.01mg/kg/d (daily for 7 days ip, then 4 days po) with sacrifice at 18 days of age. HI injury of any severity decreased the number of IL-17+ cells in spleens regardless of treatment. However, in animals with severe HI brain injury, increased IL-17+ cells significantly correlated with greater splenic atrophy, suggesting increased systemic inflammation, which was not affected by treatment. Serum cytokines analysis indicated a significantly decrease in Leptin, an anti-apoptotic marker, in HYPO HI animals, compared with NAC+VitD. NAC+VitD significantly increased the expression of 24-hydroxylase, the enzyme responsible for Vitamin D degradation, and decreased the circulating levels of 25-OH Vitamin D. Our findings confirm the association of significant systemic immune depletion and severe focal brain injury in neonatal rats, in spite of treatment with hypothermia, N-acetylcysteine and 1,25-Vitamin D3, which improve brain injury and functional outcomes.

Pancreatic cancer remains extremely difficult to combat. Last year the disease claimed the lives of over thirty-eight thousand people in the United States making it the third deadliest cancer. The average lifespan following diagnosis is only 3-6 months with a death to incidence ratio of 95. A major reason for this high mortality rate is resistance to the main chemotherapy agent used to treat this disease, gemcitabine, a di-fluorinated nucleoside analog of deoxycytidine. Pancreatic cancer escapes gemcitabine induced death by taking advantage of multiple proliferation pathways such as the MAPK/ERK pathway and the NF-kB pathway as well as tilting the balance of apoptotic mediators such as the Bcl-2 family of proteins and the sphingolipid ceramide:sphingosine-1-phosphate rheostat in favor of anti-apoptotic control. Countering these measures of resistance is of utmost importance. All of these mechanisms of resistance have a single common influencer, sphingosine-1-phosphate (S1P). S1P is known to be a promoter of proliferation, survival, and migration. It has been shown to promote the activation of NF-κB through both intracellular and extracellular means and the induction of Erk phosphorylation through the S1P Receptor 3. Additionally, S1P can cause upregulation of both Bcl-2 and Bcl-xL two of the primary anti-apoptotic mediators of intrinsic apoptosis. With the connection being made between such a powerful molecule as S1P and so many means of chemoresistance, investigation into whether its ablation can potentiate the therapeutic power of the main line chemotherapeutic agent gemcitabine is essential. Here we present the results of in vivo experiments combining gemcitabine and sphingosine kinase inhibitors in three different pancreatic adenocarcinoma cell lines. NIH R01 CA122226

117 Scaffold-free Tissue Engineering: Organization of the Tissue Cytoskeleton and Its Effects on Tissue Shape, Caitlin A Czajka, Agnes Nagy Mehesz, Thomas C Trusk, Michael J Yost, Christopher J Drake; Regenerative Medicine & Cell Biology, MUSC; Surgery, MUSC.

Introduction: Scaffold-free tissue engineering can be traced to Holtfreter and Moscona, who showed that cells isolated from a tissue sort to reform a replica of the original tissue, and Steinberg, whose Differential Adhesion Hypothesis explains cells organization into spheroids due to intercellular adhesion, surface tension, and liquid thermodynamics. Steinberg and others showed that two spheroids “fuse” into a single, larger spheroid. Interested in generating non-spheroidal tissues, we investigated culture systems that controlled the propensity of spheroid fusion to form larger spheres. Our work characterizes tissues generated from scaffold-free, non-adherent culture systems and investigates their utility in modular tissue engineering. Methods: Human umbilical vein and adipose microvascular endothelial cells, human aortic smooth muscle cells, and human dermal fibroblasts were used to generate mixed-cell spheroids (used as modules to generate tissues within non-adherent molds) and/or were seeded directly into non-adherent molds to generate tissues. ROCK inhibitor Y-27632 was used to evaluate cytoskeletal tension during tissue formation. Tissue constructs were assessed via stereo-microscopy, confocal immuno-fluorescence microscopy, and morphometric analysis. Results: Immunofluorescence analysis revealed that all tissues formed using scaffold-free, non-adherent systems organize tissue cortical cytoskeletons under apparent tension. Real-time spheroid fusion analysis illustrated modular (spheroid) motion compatible with alterations in tensions due to cortical cytoskeleton disassembly/reassembly. Tissues generated from linearly-constrained modules (restricted modular motion) deformed upon release from molds. Treatment of forming tissues with Y-27632 reduced tissue deformation but did not disrupt initial spheroid formation. Conclusions: Our results suggest: cytoskeletal machinery is not critical to spheroid formation; spheroids undergo numerous changes while organizing from a group of associated cells into a tissue; culture-induced tension influences tissue morphogenesis; and an active actin-myosin cytoskeleton is used to contract in response to tension. Our studies suggest that tissue deformation due to tensions mediated via the tissue cortical cytoskeleton represents a major challenge to modular tissue engineering. NIH R01 HL080168; NSF
118 Advances in Geospatial Modeling for Small Area Cancer Data. Georgiana Onicescu 1, Andrew B. Lawson 1, Jiajia Zhang 2, Mulugeta Gebregziabher 1, Kristin Wallace 1, Jan M. Eberth 1, 2. Biostatistics, MUSC, 2Epidemiology & Biostatistics, USC. 1 1Epidemiology, MUSC.

Abstract not available.

119 The Impact of Covariate Adjustment At Randomization and Analysis: Understanding Differences Between Superiority and Non-Inferiority Trials. Katherine S. Nicholas, Wenle Zhao, Valerie Durkalski; Biostatistics, MUSC.

It remains unclear whether it is necessary to adjust for important prognostic variables during randomization and analysis, or whether adjustment at randomization alone is sufficient. The current simulation-based research seeks to explore this issue in the non-inferiority setting, as compared to the typical superiority setting, by assessing the differential impact on power, Type-I error, coverage, and bias in the treatment estimate as well as its standard error in the context of logistic regression. In the superiority setting, failure to adjust for covariates in the analysis phase produces results in decreased power and treatment estimates (and standard errors) that are biased downward. When only examining the impact of randomization without adjustment in analysis, Type-I error is decreased and coverage increased. In non-inferiority, unadjusted analyses preserve (with simple randomization) or inflate (with permuted block randomization) power, but Type-I error is increased and coverage decreased dramatically under both simple and covariate adjusted permuted block randomization. Furthermore, treatment estimates are biased upward with associated standard errors that are biased downward. Adjusted analyses, in both settings, are marked by some decrease in power but nominal coverage as well as appropriate Type-I error and some positive bias in the standard error of the treatment estimate regardless of use of the covariate in randomization. Results from this simulation study suggest that it is inappropriate to adjust for important prognostic covariates in analysis, as this yields unbiased estimates of treatment as well as nominal Type-I error and coverage. Furthermore, the results demonstrate that the benefit of including covariates in randomization is small when adjusted analyses are performed, but this lack of impact may be due to a lack of severe covariate imbalance across treatment groups. Finally, simple randomization coupled with unadjusted analysis preserves Type-I error and coverage in the context of superiority, but not in the context of non-inferiority. NETT U01NS059041

120 Receptor Isoform-specific Estrogen Signaling in Müllerian Duct Differentiation of the American Alligator. Brenna M. Doheny, Satomi Kohno, Jessica A. Cloy-McCoy, Louis J. Guillette Jr.; Ob/Gyn, MUSC.

Perturbation of endocrine signaling during critical developmental windows has been implicated in adult reproductive disorders. This developmental origins of disease paradigm is the basis for our investigation of the role of estrogen signaling in embryonic differentiation of female reproductive tract in the American alligator. To this end, we first investigated pathways leading to sex reversal. Alligator eggs incubated at a temperature that produces 100% males (33.5°C) were treated with estradiol-17beta (E2) or 4,4',4''-[(4-Propyl-[1H]-pyrazole-1,3,5 -triyl)trisphenol (PPT), a specific agonist for estrogen receptor alpha (ERα), at a stage just prior to sex determination. E2 induced 100% sex reversal, indicated by Müllerian duct presence and gonadal histology. PPT treatment induced 100% gonadal sex reversal and abnormal enlargement of the Müllerian duct. Histological analysis indicated precocious glandular development in these tissues. Quantitative RT-PCR expression assays for steroid hormone receptors revealed significant downregulation of ESR1 and significant upregulation of progesterone receptor in oviductal tissue from PPT treated embryos. Receptor isoform-specific estrogen signaling was further studied by treating embryos incubated at a temperature that produces 100% females (30.5°C) with E2, PPT and ERβ specific agonist WAY 20070. Only PPT treatment induced the previously characterized oviductal phenotype. Further investigation via immunohistochemistry and RT-QPCR continues to reveal significant differences in PPT-treated oviductal tissue. The results of this study provide insight into the factors critical for healthy reproductive system formation in this sentinel species. South Carolina Centers of Economic Excellence Marine Genomics Endowment

121 Acetylation Regulates MiR-133a Expression in Cardiac Hypertrophy. Ludivine Renaud 1, Michael R. Zile 1, Santhosh K Mani 1, Catalin F. Baicu 1, An Van Laer 1, Robert E. Stroud 2, Jeffrey A. Jones 2, Ronald D. Menick 1; 1Medicine, MUSC, 2Surgery, MUSC.

BACKGROUND: The expression level of several microRNAs (miRNAs) is affected by pressure overload hypertrophy and has an impact on cardiac function. Histone deacetylases (HDACs) regulate the transcription of many genes whose expression is altered in hypertrophy. Therefore, we hypothesize that acetylation regulates the expression of some miRs during cardiac hypertrophy. METHODS: Transverse aortic constriction (TAC) was performed to initiate cardiac hypertrophy induced by pressure overload. Mice were treated with the Class I and IIb HDAC inhibitor via drinking water post-TAC for 2 and 4 weeks. miRNAs expression normalized to RNU6B was determined by qRT-PCR. Echocardiography was performed at baseline and post-TAC endpoints to assess physiological parameters. Chromatin immunoprecipitation (ChIP) was used to identify HDACs and transcription factors associated with miR-133a promoter. RESULTS: Based on previous studies, we selected 8 miRNAs that play major roles in cardiac hypertrophy. The expression of one of the miRNAs, miR-133a was significantly (P < 0.05) downregulated at both 2 weeks (1887 ± 105, n=8) and 4 weeks post-TAC (1651 ± 103, n=9) compared to control group (2972 ± 334, n=11). SAHA treatment significantly de-repressed miR-133a expression 2 weeks post-TAC (3317 ± 560, n=12) and to a lesser extent after 4 weeks post-TAC (2391 ± 455, n=10). ChIP analysis revealed that HDAC2 was present on the miR-133a promoter. CONCLUSION: We show that HDAC2, a Class I HDAC, plays a role in the regulation of miR-133a expression in cardiac hypertrophy. HDACs and miRNAs are key regulators of the events mediating cardiac pathology. Our work demonstrates that HDAC inhibition may be an attractive therapeutic strategy.
for the regulation of some miRNAs in heart disease. NIH R01 HL095696; AHA 09GRNT2020202

122 Patterns of Physical Activity in African Americans With Type II Diabetes Mellitus, Mukoso N Ozieh1, Clara E Dismuke2, Delia Ç Vorona3, Leonard E Egede3; 1Medicine, MUSC, 2Research, VA, 3Public Health Sciences, MUSC.

Diabetes prevalence in the US is 8.3%. Minorities are disproportionately affected with a prevalence of 12.6% and 11.8% amongst non-Hispanic blacks and Hispanics respectively. Lifestyle modification is widely accepted as an initial and ongoing part of diabetes management. Physical activity at least 30 to 45 mins/day at least 3 to 5 days a week is considered adequate as an initial regimen. A cohort of 277 African Americans with type II diabetes were surveyed in 2008, as part of a baseline analysis for a 4-year randomized controlled clinical trial. Eligible participants were those with A1C >=9. Participants were recruited from an academic medical center and a VHA facility in the southeast. At baseline, participants provided blood samples. Pearson pairwise correlations, unadjusted and adjusted multivariate regression analyses of the association of physical activity with A1c, Systolic Blood Pressure and physical (PCS) and mental health (MCS). Physical activity was classified as “sleep”, “light”, “moderate”, “hard” and “very hard” using the seven-day interviewer guided physical activity recall scale. Covariates for adjustment included gender and income. All statistical analyses were done with SAS 9.3. Results of the Pearson correlations between levels of activity and health outcomes showed a significant correlation (0.15) between moderate activity and PCS. The results of the unadjusted models also showed a significant association between moderate activity and PCS (0.21, 95% CI 0.02:0.42) relative to no activity. However, in adjusted models, moderate activity is no longer significant and light activity becomes significantly associated (0.29, 95% CI 0.00-0.58) with PCS. In this African American diabetes population, physical activity levels did not have a significant impact on A1C or blood pressure and had a modest impact on physical health. However, because the physical activity levels were low in this population, it is likely the true benefits were not observed. NIDDK R01 DK081121

123 The RNA Binding Protein Tristetraprolin Plays a Protective Role During Periodontal Bone Loss, Heidi M Steinkamp, Mary Gray, Hong Yu, Keith Kirkwood; Craniofacial Biology, MUSC.

Abstract not available.

124 Gender Differences in Neural Response to Mesolimbic Stimulation: An Interleaved TMS-BOLD Imaging Study, Melanie Canterberry, William DeVries, Joseph J Taylor, Mark S George, Colleen A Hanlon; Psychiatry, MUSC.

The medial prefrontal cortex (MPFC) is the primary cortical hub of mesolimbic circuitry which governs emotional and reward processing. Disruptions in this circuit are associated with disordered affect and substance-dependence. Preliminary evidence suggests women may have a particularly responsive mesolimbic circuit, which may be related to their high levels of stress-induced substance abuse. The current study aimed to determine whether MPFC stimulation has a greater effect on mesolimbic circuit activity in women than men through the use of interleaved transcranial magnetic stimulation (TMS)-BOLD imaging. Functional neuroimaging data (BOLD) were acquired from 20 healthy participants (45% women) and a small cohort of cocaine users (n=12, 58% women). Single TMS pulses were applied to their MPFC while the participants lay still in the scanner. The BOLD response to MPFC stimulation was modeled as events using standard voxel-based analyses and compared between genders within groups. Results showed that among controls, women had significantly more BOLD activity than men in the MPFC and caudate. Men had significantly more activity in the inferior parietal cortex and the lateral frontal cortex (BA 9). As with the controls, female users had significantly more activity in the prefrontal cortex than men. There were no areas in which male users had a larger response to MPFC stimulation than women. These preliminary data suggest that both healthy and substance-dependent women have an elevated baseline mesolimbic response to stimulation compared to men. Understanding these gender differences may be critical to understanding individual differences in acquisition of and treatment of limbic-related disorders, including addiction. NIDA F32DA036329 and K01DA027756

125 ROCK-dependent Ezrin-Radixin-Moesin Phosphorylation Modulates Actin Cytoskeleton in Noise-induced Hair Cell Death, Yu Han, Jun Chen, Su-Hua Sha; Pathology and Laboratory Medicine, MUSC.

Genes are often deregulated in pathologies which perpetuates adverse organ function. Many transcription factors (TFs) which dictate gene expression are reversibly acetylated via histone acetyltransferases (HATs) and histone deacetylases (HDACs) hence, conferring an additional level of regulation. The Sodium Calcium Exchanger (NCX1) and Brain Natriuretic peptide (BNP) are upregulated in cardiac pathologies which contributes to adverse outcomes. Class I and class Ila HDACs are recruited to the proximal promoters of these genes and inhibition of HDACs reduces Ncx1 and Bnp expression while improving cardiac function. TFs such as Nkx2.5 and YY1 regulate Ncx1 and Bnp respectively, can be acetylated and interact with class I, HDAC1/2, and class II, HDAC5. Class Ila HDACs have poor catalytic activity, thus we hypothesized, class Ila HDACs interact with TFs and serve as scaffolds that stabilize class I HDAC-regulatory complexes. To test our hypothesis cardiomyocytes were treated with vehicle, class I or class Ila selective HDAC inhibitor. Class I HDAC inhibition abrogates adrenergic stimulated upregulation of Ncx1 expression in cardiomyocytes to almost control levels (p<0.05) while class Ila HDAC inhibition has no significant effect (p>0.05). In vivo, class I inhibition blunts Ncx1 upregulation post transaortic constriction (TAC), a model of hypertrophy. We assessed the role of class Ila HDAC5 in Ncx1 regulation, by subjecting HDAC5-Knockout mice (HDAC5-KO) to TAC. We saw reduced induction of Ncx1 and Bnp expression post-TAC. Co-IP and ChIP analyses show that interactions between the Sin3a/HDAC1
repressor complex and Nhx2.5 or YY1 are lost in the absence of HDAC5 expression and fail to promote tumors. To conclude, our data suggests HDAC5 is a scaffold that recruits a Sin3a/HDAC1 repressor complex. Our novel findings provide insight into the non-canonical role of class IIa HDACs in regulation of gene expression which may be relevant for efficacious therapeutic intervention for pathologies.

127 Discovery of a Novel Cyclic Peptide Based Inhibitor for LSD1 Enzyme, Isuru R Kumaraasinghe, Patrick M Woster; Pharmacy, MUSC.

Abstract not available.

128 Transcriptome and Proteome Discovery of the RNA-binding Protein CELF1 Regulon in Oral Squamous Cell Carcinoma, Reniqua P House1, Sudha Talwar2, Jennifer Bethard1, Lauren Ball1, Viswanathan Palanisamy1, 1Craniofacial Biology, MUSC, 2Cell and Molecular Pharmacology, MUSC.

Oral cancer is the 6th leading cause of death worldwide. To facilitate disease progression oral cancer cells will exploit post-transcriptional regulatory pathways to promote their proliferation and cell death. RNA binding protein CELF1 (otherwise called CUGBP1), associates with GUU- and U-rich element (GRE/U-rich) containing mRNAs and post transcriptionally regulates mRNA alternative splicing, stability and translation. Although there is emerging evidence that supports CELF1 playing a role in cancer, the underlying mechanism of action is still poorly understood. Observations from our laboratory suggest that CELF1 overexpression alters the balance between cell proliferation and apoptosis in oral squamous cell carcinoma. Specifically, inhibition of CELF1 induced apoptosis and inhibited proliferation of oral cancer cells. Therefore, to further understand CELF1’s role in cancer pathogenesis, we performed next generation sequencing (RNA-seq) of wild type and CELF1 knockdown UM74B oral carcinoma cells. Following RNA-seq, gene enrichment analysis of our data sets revealed that the 731 genes differentially regulated by CELF1 are significantly involved in biological processes such as cell communication, cell adhesion and cell proliferation. In addition, secondary analysis utilizing splice junction array identified 601 alternatively spliced transcripts in UM74B cells controlled by CELF1 expression. In conjunction with our transcriptome analysis, Pulsed-Stable Isotope Labeling by Amino acids in Cell culture (pSILAC) experiments identified 251 proteins that displayed altered synthesis in CELF1 depleted UM74B cells. Lastly, utilizing a mouse model of oral carcinogenesis, we determined that upon transitioning from normal to hyperplastic and from hyperplastic to oral squamous cell carcinoma the expression level and the number of CELF1 positive cells increases along with its RNA regulons. Altogether, these observations illuminate the potential of CELF1 and/or its associated mRNA regulons as therapeutic targets or diagnostic markers for cancer.

129 Streamlining MRI Liver Reports for Hepatocellular Carcinoma By Using LI-RADS, Matthew R Gillott, Munazza Anis; Radiology, MUSC.

The criteria for liver transplantation are quite stringent for cirrhotic patients. A hepatocellular cancer of 2 cm qualifies a cirrhotic patient for an exception and moves them up on the transplant list. In cirrhotic patients with larger hepatocellular cancers, Milan and USCF criteria are used to determine candidacy for liver transplantation. The Milan criteria allow a solitary lesion less than 5 cm or three or fewer lesions, each less than 3 cm, with no extra-hepatic or vascular involvement. The UCSF criteria is more inclusive, allowing a solitary lesion less than 6.5 cm or three or fewer lesions, each less than 4.5 cm with the total tumor diameter less than 8.5 cm. With these precise criteria, accurate hepatocellular cancer measurement is very important for liver transplant consideration and should be kept in mind while reporting these tumors on Computed tomography (CT) or magnetic resonance imaging (MRI). BI-RADS (Breast Imaging-Reporting and Data System) has been in use for several years to adequately describe and report breast lesions. In this model, LI-RADS (Liver Imaging- Reporting and Data System) has recently been devised to standardize the reporting and data collection of CT and MR imaging for hepatocellular carcinoma (HCC). This method of categorizing liver findings for patients with cirrhosis or other risk factors for developing HCC allows the radiology community to apply consistent terminology, reduce imaging interpretation variability and errors, enhance communication with referring clinicians, and facilitate quality assurance and research. We will show examples of LI-RADS reporting so as to familiarize the medical community with this system.

130 Out of Hospital Cardiac Arrest: A Single Center Experience, Nathaniel Richards1, Thomas Todoran2, Robert Yoe3, 1Internal Medicine, MUSC, 2Cardiology, Internal Medicine, 3Cardiology, MUSC.

Abstract not available.

131 Evaluation of Hospitalized Patients on a Family Medicine Inpatient Service Based on Insurance Status, Marieth Porter1, Peter J Carek1, Vanessa A Diaz1, Lori M Dickerson1, Jennifer Gavin1, William J Hueston1, Ashleigh Zacarias2, 1Family Medicine, MUSC, 2Family Medicine, Trident Medical Center.

It is unclear whether insurance status impacts cost of care. As the number of uninsured patients in South Carolina is increasing, gauging their impact on health care costs is relevant to resource allocation. The objective of this study is to compare costs and utilization data by insurance status (Unfunded-Medicaid-Commercial) for adult patients admitted to a family medicine residency inpatient service. A retrospective review of billing data from 1102 admissions to the Family Medicine service at Trident Medical Center from July 1, 2010 to June 30, 2012 considers patients aged > 18 years old (N=899) admitted to a family medicine residency inpatient service. The primary outcomes considered are variable and total charges obtained from billing data. Utilization data (length of stay, emergency department (ED) visits and readmission status) are secondary outcomes. Of 899 patients, 40.04% had Medicaid, 25.14% were commercially insured and 34.82% were unfunded. The average total cost per admission was $6750.87+11994 for the Medicaid population, $4618.46+5923 for the commercially funded population, and $4955.87+7429 for the uninsured population (p<0.05). The average length of stay in days was 5.17+ 11.28 for Medicaid patients, 3.10+3.23 for commercially insured patients, and 3.29+3.94 for uninsured patients (p<0.05). Readmission rates were
higher for the Medicaid group (26.55%), vs the commercial (6.6%) and uninsured group (2.87%) (p<0.05). Medicaid patients accounted for 39.25% of ED visits, while commercially insured (28.41%) and uninsured (32.34%) were seen in the ER less frequently (p<0.05). Uninsured patients were less likely to be readmitted than Medicaid or commercially insured patients. Overall the Medicaid population had more ER visits, higher hospital costs, longer hospital stays, and a higher readmission rate, suggesting the need to further evaluate costs for this population.

132 Ketamine’s Effect on Cravings for Alcohol in a Population of Veterans with Depression and Alcohol Dependence. Erin B Seery1, Robert Glenn1, Dennis Orwat1, Christopher Pelic2, Tamas Szabo3, Paul Everman2, Mark Hamner1, Robert Malcom1, 1Psychiatry, MUSC, 2Psychiatry, VAMC, 3Anesthesiology, VAMC.

Altered NMDA receptor function has been implicated in the development of alcohol dependence (Petrukis et al., 2004). These alterations have even been found in subjects with only a family history of alcohol dependence. Using Ketamine, an NMDA antagonist, those with a family history of alcohol dependence demonstrated an attenuated response to perceptual alterations and dysphoric mood as compared to those without such family history (Petrukis et al., 2004). In a different study, subjects having a family history of alcohol dependence and personal history of treatment resistant depression, reported a robust antidepressant response to Ketamine infusion (Phelps et al., 2009). Krystal et al. found that in detoxified alcoholics, Ketamine did not cause an increase in cravings for alcohol despite its similarity to alcohol in discrimination tests (Krystal et al., 1998). There has been limited investigation into ketamine’s effects both on the acutely depressed population with comorbid alcohol dependence. Given the response found in previous studies, subjects may have significant improvement in depression and have attenuated cravings for alcohol.

Methods: Participants were treatment seeking male inpatients meeting criteria for alcohol dependence and major depressive disorder (n=4). Subjects were abstinent from alcohol for at least 5 days prior to infusion. Participants completed a clinical interview and responded to standardized questions that assessed cravings, depression, risk for suicide anxiety, and dissociative symptoms. Following baseline assessment, subjects received a one-time infusion of Ketamine hydrochloride IV at 0.5mg/kg over 40 minutes. Participants then rated alcohol cravings using a visual analog scale (scale of 1 to 10) for alcohol cravings and for perceived ability to resist alcohol following infusion of Ketamine. There was a significant decrease in craving scores over time from baseline (p=0.00). At baseline the mean craving score was 4.5 (95% CI 1.21, 7.79). At 240 minutes post-infusion, there was a decrease to 2.5 (-1.74, 6.74). By Day 1 post-infusion the mean craving score had decreased to 0 (0,0). There was a significant decrease in resisting scores over time from baseline (p=0.018). At baseline the mean resisting score was 5.75 (95% CI 1.57, 9.93). At 240 minutes post-infusion, there was a decrease to 3.25 (-7.75, 7.25). By Day 1 post-infusion the mean resisting score had decreased to 0 (0,0). Conclusions: These preliminary findings help identify ketamine’s impact on cravings for alcohol use and may have important clinical implications in the treatment of comorbid depression and alcohol dependence. NIDA R25DA020537; MUSC DART Residency Track; Ralph H. Johnson VAMC.

133 Predictors of Self-Care Behaviors and Medication Adherence in African Americans with Type 2 Diabetes, Joni S Williams, Cheryl P Lynch, Delia C Voronca, Leonard E Egede; Medicine, MUSC.

Background: African Americans (AA) have a higher prevalence of type 2 diabetes (T2DM) compared to White Americans. Self-care behaviors (SCB), including medication adherence (MA), have been shown to impact outcomes. This study examines the relationship between SCBs and MA in AA patients with T2DM. Methods: Baseline data of 277 AA participants with T2DM recruited from an academic internal medicine clinic and a primary care veteran’s affairs medical center in the southeastern US was analyzed. Participants completed surveys to assess sociodemographic characteristics, MA, and diabetes SCB. T-tests determined mean scores of independent SCBs. Pearson correlation tested the association between MA and SCBs. Multiple linear regression models explored the covariates associated with individual self-care behaviors. Statistical analyses were done using SAS v9.3. Results: Medication adherence was positively and moderately correlated with general diet (r = 0.23; p=0.0001), special diet (r = 0.26; p=0.0001), exercise (r = 0.12; p=0.0389), blood sugar testing (r = 0.36; p<0.0001), and foot care (r = 0.20; p=0.0011). In regression models, age of 65+ (beta = -2.41; 95% CI -4.23,-0.58), income of $10,000-$25,000 (beta = 0.70; 95% CI -0.02, 1.38) and some college (beta = 0.79; 95% CI 0.13, 1.45) were significantly associated with MA. Eating a specific diet was statistically associated with being 65+ years (beta = 1.54; 95% CI -0.03, 3.11) and female (beta = 0.57; 95% CI 0.16, 0.98). Blood sugar testing was associated with income levels ranging between $10,000 - $25,000 (beta = -0.79; 95% CI -1.55, -0.03) and $25,000 - $50,000 (beta = -1.12; 95% CI -2.06,-0.17). Conclusions: MA was associated with different SCBs. Different factors, such as being elderly and having a specific annual income, were associated with several SCBs. Behaviors such as exercising, eating a healthy diet, and performing foot care, are potential targets for education, counseling, and skills building in AA patients with T2DM. NIDDK R01 DK081121-01A1.

134 Peroxiredoxin 1 (Prdx1) Inhibits Activated Stroma-Associated Fibroblasts Phenotype Preventing Breast Cancer Progression, Agnieszka Jezierska-Drutel1, Carola A Neumann2; 1Biochemistry & Molecular Biology, MUSC, 2Pharmacology and Chemical Biology, University of Pittsburgh Cancer Institute.

Continuous communication between cancer cells and their surrounding microenvironment evokes numerous signaling pathways influencing cancer cell malignancy. After acquiring an activated phenotype, almost 80% of stroma-associated fibroblasts (SAF) become cancer associated fibroblasts (CAFs) in breast carcinomas. Activated fibroblasts are highly mobile, contractile, express numerous mesenchymal markers and have the ability to secrete elevated levels of growth factors, cytokines, matrix metalloproteinases (MMPs) and reactive oxygen species (ROS). ROS, often a byproduct of growth factor-induced
activation of cell membrane localized NADPH, have been linked specifically to SAF activation-induced tumor spreading. We have shown that mice lacking the H202 scavenger peroxiredoxin 1 (Prdx1), die prematurely due to hemolytic anemia and different types of cancer, including breast cancer. We have demonstrated that murine embryonic fibroblasts (MEFs) Prdx1-/- expressing a catalytically inactive Prdx1 show intra- and extracellular increased levels of H202 when compared with MEFs Prdx1+/-+. Stimulated with various growth factors or H202, mouse mammary gland fibroblasts (SFAFs)Prdx1-/- exhibit increased activity levels of Akt and JNK kinases compared to (SAFs)Prdx1-/-/. Our lab described that Prdx1 is a safeguard for the lipid phosphatase activity of PTEN. Prdx1 binding to PTEN is essential for protecting PTEN from oxidation-induced inactivation and could prevent fibroblasts from initiation, progression and malignant transformation of mammary epithelial tumors. Our data show that the lack of Prdx1 in fibroblasts isolated from mammary glands causes elevated secretion of MMP9 and increased expression of activated fibroblasts markers including alpha-SMA, procollagen and vimentin. Cultivation experiments have shown that SAFPrdx1-/- increases breast cancer cell migration and invasion, whereas SAFPrdx1+/-/+ did not. Our data strongly suggest that Prdx1 may be a key player in preventing breast tumor development through controlling the cancer promoting effects of the tumor micro-environment.

135 Fli-1 Transcription Factor Impacts Lupus Nephritis Development By Regulating Expression of IL-6 in Kidney Endothelial Cells, Shuzo Sato, Mara Lennard Richard, Danielle Brandon, Eva Karam, Zhang John; Rheumatology and Immunology, MUSC.

Introduction: Fli-1, an Ets family transcription factor, regulates the development of nephritis in murine models of systemic lupus erythematosus. We have reported that the Fli-1 heterozygote (Fli-1+/-) MRL/lpr mice, a murine lupus mouse model, has significantly prolonged survival and reduced glomerulonephritis compared with Wild-type (WT) littersmates. Cytokine IL-6 is deeply associated with lupus disease progression in humans and mice. We hypothesized that Fli-1 affects IL-6 expression and regulates lupus nephritis development in MRL/lpr mice. To investigate this hypothesis, we performed following experiments. Materials and Methods: We investigated the serum IL-6 concentrations and relative mRNA expression in the kidney from Fli-1+/- MRL/lpr mouse and WT littersmates. Next, we examined expression of IL-6 in the kidney sections from WT and Fli-1+/- MRL/lpr mice by immunohistochemical staining. Following Fli-1 specific siRNA transfection in murine endothelial MS1 cells were stimulated using LPS. After stimulation, the supernatants were collected and analyzed by ELISA to measure IL-6 concentrations. To examine if Fli-1 directly regulates the expression of IL-6, we performed Chromatin Immunoprecipitation assay (ChIP) using MS1 cell to study if Fli-1 directly binds to the IL-6 promoter region. Results: The serum IL-6 concentration was significantly decreased in Fli-1+/- MRL/lpr mouse compared to WT MRL/lpr mice. Relative expression of IL-6 in the kidney from Fli-1+/- MRL/lpr mouse was lower than WT littersmates. In immunohistochemistry, IL-6 deposition was mainly seen in WT glomerulus but rarely seen in Fli-1+/- mice. MS1 cells transfected with Fli-1 siRNA showed significantly decreased production of IL-6 compared to cells transfected with non-specific siRNA. We also demonstrated that Fli-1 directly binds to the IL-6 promoter region in MS1 cells by ChIP assay. Conclusion: Fli-1 directly regulates IL-6 production and affects lupus nephritis development in MRL/lpr mice. NIH AR056670; Medical Research Service, Department of Veterans Affairs

136 Liver Injury Following Hemorrhagic Shock/Resuscitation: Mechanisms and Targeted Therapy with Minocycline, Andaleb Khomukhamedov¹, Christoph Czerny², John J Lemasters³; ‘Drug Discovery, MUSC; ‘Trauma Surgery, J.W. Goethe University.

Abstract not available.

137 Effect of Coronary Rotational Atherectomy in Dominant Vessels Without Use of Temporary Pacemaker After Preemptive Treatment with Theophylline, Navin Nikam, Monique Sandhu, James Hadstate, Arasi Maran, Valerian Fernandes; Cardiology, MUSC.

Prophylactic temporary pacemakers are recommended for coronary rotational atherectomy (RA) in dominant vessels due to complications of bradycardia and high grade AV block. Since this bradyarrhythmia is thought to be Adenosine-mediated, Theophylline can be used preemptively and need for temporary venous pacing can be averted. This is the standard practice at our medical center. We undertook this study to assess the effectiveness of this approach. From 2009-2013 all RA patients performed at the Ralph H. Johnson VA Medical Center were analyzed and separated into 2 groups: dominant vessels (n=28) and non-dominant vessels (n=109). Dominant vessels received 100 mg Theophylline IV before starting RA. All RA was done with infusing cocktail (NTG, Heparin, Verapamil). If bradycardia developed the patient was treated with additional theophylline or atropine. There was a total of 137 coronary lesions treated in 28 in dominant vessels and 109 in non-dominant vessels. There was a total of 14 bradycardia events (OR 3.47 [CI 1.09 to 11.0], p = 0.0344). All bradycardia events were transient and successfully treated with medications. No temporary pacing wires were placed. Despite bigger vessel size in dominant vessels a smaller burr size (1.37 vs 1.47 p = 0.001) was used. Dominant vessels received larger stents (3.22mm vs 3.0mm p = 0.09), more stents (1.6 vs 1.3 p = 0.04) and longer total stent length (34.4mm vs 29.2mm, p = 0.09), more stents (1.6 vs 1.3 p = 0.04) and longer total stent length (34.4mm vs 29.2mm, p = 0.016) compared to non-dominant vessels. There were no other acute procedural complications. TIMI 3 flow was achieved in all dominant vessels. Coronary RA is safe without prophylactic temporary pacing in dominant vessels after preemptive Theophylline. Transient breakthrough bradycardia is more likely to occur in dominant vessels but is easily treated medically.

138 Radial Versus Femoral Access in Rotational Atherectomy of the Diseased Coronary Artery, Monique K Sandhu, Anbukarasi Maran, Navin Nikam, Valerian Fernandes, James Hadstate, Frederick Funke; Cardiology, MUSC.

Calcified coronary lesions make for difficult stent delivery in percutaneous coronary intervention (PCI). The use of Rotational Atherectomy (RA) serves as a useful adjunct for stent delivery in these lesions. Radial access for PCI has
improved patient satisfaction and improved morbidity. Use of RA from a radial approach versus traditional femoral approach raises several technical concerns. We reviewed our RA cases over 4 years at the VA in order to describe the feasibility and safety of using RA via radial access. Single-center, retrospective observational study. Consecutive patients who received RA via femoral and radial access from 2009 to 2013 were collected and analyzed. Student T test was used to compare continuous variables and Chi Square test was used to compare categorical variables. A total of 137 patients received RA. 107 received RA via femoral access while 30 patients received RA via radial access. Baseline characteristics were similar between the two cohorts. The Syntax score between the 2 groups did not vary, nor did ACS indications, suggesting similar lesion populations. Larger 7F sheaths routinely used for femoral cases to allow for larger catheters and larger burrs. Vast majority of radial cases utilized 6F systems and smaller burr sizes. Outcomes were similar to include fluoroscopy time, complications, use of vasodilators, and bradycardia requiring additional treatment. Trend toward less contrast being used in the radial group (p=0.045). No significant difference between lengths of stents delivered. Trend toward longer stent length in the femoral cases. Stent diameters were statistically different with a mean stent diameter in the femoral of 3.1 mm vs 2.8 mm from radial approach. Routine use of smaller sheaths and smaller burrs in the Veteran population with radial access, showed fluoroscopy time and complication rates to include bleeding and bradycardia were similar. Average contrast use less in radial population and no statistically significant difference in stent length. Our review shows RA via radial access can safely be accomplished and is non-inferior to RA via femoral access.

139 Alterations of Sensory Hair Cells Following AAV-miR96 Application to Postnatal Mouse Cochlea, Yazhi Xing1, Michelle Stoller1, LaShardai Conaway1, Jiannin Zhang2, Donna Fekete2, Hainan Lang1. 1Pathology and Laboratory Medicine, MUSC; 2Biological Sciences, Purdue University.

MicroRNAs are a group of small non-coding RNAs essential for the determination and maintenance of sensory hair cells in the mammalian inner ear. In human DFNA50 hearing loss families and ENU-induced Diminuendo (Dmdo) mice, mutations in the seed region of miR-96 were identified as the genomic basis for sensory hair cell degeneration. We hypothesize that the supplementation of miR-96wt and/or miR-96Dmdo sponges to Dmdo mice prevents degeneration of sensory hair cells and progressive hearing loss caused by the miR-96 mutation. To test this hypothesis, AAV8 (a subgroup of adeno-associated virus vectors)-GFP-miR96wt, AAV8-mCherry-miR96Dmdo sponges or both were delivered into the scala media of CBA, wild type (+/+), heterozygous (Dmdo/+), and homozygous (Dmdo/Dmdo) mouse ears at postnatal day 3 (P3). Auditory function was evaluated by auditory brainstem response (ABR) measurements. Cochleae were collected at 5, 7, 11, and 25 days after virus inoculation and sensory hair cells were observed with confocal microscopy by staining with phalloidin and other hair cell markers. Over 60% of the AAV8-GFP-miR96wt treated animals showed moderate to robust GFP expression in sensory hair cells. Some inner hair cells (IHCs) infected with GFP-miR96wt showed unusual stereocilia bundles that resembled outer hair cells (OHCs), which may imply that relative miR-96 levels are responsible for maintaining the differential morphology of stereocilia bundles between these two cell types. The mCherry-miR96Dmdo sponges treated group showed robust mCherry expression in auditory nerve and other cochlear locations. More sensory cells and supporting cells were transfected with AAV8-mCherry-miR96Dmdo sponges in animals delivered with both viruses simultaneously than those of individual virus inoculation. In addition, small size IHCs were seen after GFP-miR96wt or dual virus inoculation, suggesting miR-96wt overexpression and/or miR96Dmdo suppression may induce phenotypic alterations of sensory cells or hair cell regeneration. NOHR 206048; NIH R01 DC7506; NIH P50 DC0422; NOHR 206048

140 Intracellular Amyloid Degradation Mechanisms That Paradoxically Increase Amyloid Beta Protein Production Upon Gamma-secretase Inhibition, Padmaraju R Vasudeva1, Baranello Robert2, Barnwell Elisa1, Pacheco-Quinto Javier2, Eckman Elizabeth2, Sambamurti Kumar1; 1Neuroscience, MUSC; 2Atlantic Health System, Morristown, NJ.

Introduction: The presence of the 42 aa Amyloid-beta peptide (Abeta42) in senile plaques is a defining feature of Alzheimer’s disease (AD). Genetic and toxicity studies show that Abeta is involved in AD-associated neurodegeneration. Abeta is reported to be formed through the sequential proteolytic processing of a larger precursor (APP) by beta-secretase (BACE1) to a C-terminal fragment (CTF) of 99 amino acids (C99) and the subsequent action of gamma-secretase. To date, the most successful attempts to reduce Abeta in cellular and animal models are to use gamma-secretase inhibitors (GSI). Methods: SH-SYSY (human neuroblastoma) and CHO (2B7) cell lines are used for the study. Both cell lines are treated with gamma-secretase inhibitor, DAPT with varying concentrations for 8h. The cells are chased for another 16h after the DAPT treatment. The medium is analyzed for the Abeta40 and Abeta42 using sandwich ELISA. The cell lysates are analyzed for C99, C83, APP using western blot. The same experiment was performed using Phosphoramidon (Inhibitor for the amyloid beta protein degrading enzyme, endothelial converting enzyme). Result: Paradoxically, low doses of GSI robustly increase levels of both Abeta40 and Abeta42 in human neuroblastoma cells. With phosphoramidon the GSI induced stimulation at low doses vanish and show dose dependent decrease in Abeta40 levels. We identify two mechanisms for GSI-mediated Abeta increase. The first is a rebound effect caused by GSI-induced substrate accumulation and acts during an extended washout period. The intracellular abeta decreased at low doses of inhibition in the presence of phosphoramidon compared to phosphoramidon alone. Conclusion: We therefore conclude that partial gamma-secretase inhibition should accelerate AD pathology by fostering amyloidosis, which can also provide an explanation for the large number of familial AD (FAD) mutations in the active subunit of Gamma-secretase that may actually be hypomorphic.
141 **MTOR and PKC5 Regulate Agonist Stimulated Expression of Connective Tissue Growth Factor in Adult Cardiac Muscle Cells**, Kamala p Sundararaj, Dorea L Pleasant, Sundaravadivel Balasubramanian, Dhandapani Kuppuswamy, Medicine, MUSC, Cardiology, MUSC.

Connective tissue growth factor (CTGF), a potent fibrogenic cytokine, has been shown to promote fibrosis in various organs. In the hypertrophying myocardium, since cardiomyocytes (CM) have been reported as a source of CTGF expression, and since mTOR (mammalian target of rapamycin) that forms two distinct complexes, mTORC1 and mTORC2, plays a central role in integrating biochemical signal for protein expression, we explored the role of mTOR on the agonist-stimulated CTGF expression in isolated adult feline CM following their stimulation with phenylephrine (PE). Our results show that treatment of CM with 10 µM PE for 24 h causes a substantial increase in CTGF mRNA expression, which could be further augmented by treatment with torin1, a specific inhibitor mTOR. However, inhibition of mTORC1 using rapamycin or activation of its downstream target S6K1 using rapamycin-resistant S6K1 adenovirus had no impact on the PE-stimulated CTGF expression. On the other hand, loss of mTORC2 by silencing Rictor, a specific component of mTORC2, with shRNA enhanced the PE-induced CTGF expression similar to torin1. Our additional work shows that the expression of dominant negative PKC delta isoform (DN-PKCδ) also blocks CTGF expression, although mTORC2 activation was also affected under these conditions. These results demonstrate that mTORC2 which requires PKCδ for its activation, plays a repressive role in CTGF expression in adult CMs, indicating the loss of mTORC2-mediated repression of CTGF expression in PO myocardium might be a potential mechanism for the onset of cardiac fibrosis in hypertrophying myocardium. NIH T32; NIH R01 RHL092124A

142 **Interaction of Caspases and RIP Kinases Modulates Noise-induced Apoptotic and Necrotic Outer Hair Cell Death Pathways**, Jun Chen, Hong-Wei Zheng, Su-Hua Sha; Pathology and Laboratory Medicine, MUSC.

Background: Inhibition of caspase activation has prevented noise-induced hearing loss (NIHL) and hair cell death. However, inhibition of caspase 8 promotes the activation of receptor-interacting protein (RIP) kinases. Our recent studies have revealed that RIP kinases promote noise-induced necrotic outer hair cell (OHC) death pathways. Here, we investigated the interaction of caspases activation and RIP kinases in noise-induced apoptotic and necrotic OHC death pathways using adult CBA/J mice. Methods: Broadband noise from 2 - 20 kHz at 106 dB SPL for 2 hours to induce permanent threshold shifts (PTS). Propidium iodide labeling of OHC nuclei to identify apoptosis and necrosis via morphological criteria. Auditory brainstem responses as measurement of auditory function. Western blot assay to evaluate the levels of RIP1 and RIP3 in whole cochlear homogenates. Anti-cleaved caspase-8, caspase-9 immunolabeling of cochlear surface preparations to detect cleaved caspase-8, caspase-9, and endonuclease G (EndoG) in OHCs. Delivery of caspase inhibitor or RIP3 siRNA to the round window via intratympanic application to observe the inhibition of apoptotic and necrotic OHC death. Combination treatment of caspase inhibitor via intra-peritoneal (IP) injection and RIP3 siRNA to observe the synergic effect on NIHL. Results: Both apoptotic and necrotic OHC nuclei were observed in the basal region of the cochlea 1 hour after noise exposure. Treatment with pan-caspase inhibitor ZVAD blocked noise induced activation of caspase-8 and reduced the number of apoptotic nuclei, while increasing levels of RIP1 and RIP3 and necrotic OHCs. Conversely, blocking noise-induced over expression of RIP1 and RIP3 by treatment with necrosis inhibitor necrostatin-1 (Nec-1) or RIP3 siRNA (siRIP3) decreased necrotic OHC nuclei, but increased the number of apoptotic nuclei without increasing activation of caspase-8. In addition, ZVAD treatment also resulted in the elevation of noise-induced p-AMPKα levels. Furthermore, pretreatment with siRIP3 did not alter the activation of caspase-8, but instead increased activation of caspase-9 and promoted EndoG translocation into OHC nuclei. Finally, ABR functional measurements and morphological assessment of OHCs showed that ZVAD treatment reduces noise-induced deficits. This protective function is potentiated when combined with siRIP3 treatment. Conclusions: Noise-induced OHC apoptosis and necrosis are modulated by caspase-8 and RIP kinases, respectively. Inhibition of either pathway shifts the prevalence of OHC death to the alternative pathway. NIH R01 DC009222

143 **Investigating the Interaction Between TBX1 and PRRX1a**, Kamryn J Kant, Michael J Kern; College of Charleston, Regenerative Medicine and Cell Biology, MUSC.

Abstract not available.

144 **Small Leucine Rich Proteoglycans (SLRPs) Play a Critical Role in the Development of the Mature Extracellular Matrix of the Murine Heart**, Elizabeth Y Brown, Loren E Dupuis, Christine B Kern; Hampton University, Regenerative Medicine and Cell Biology, MUSC.

Abstract not available.

145 **Transforming Growth Factor Alpha and Hypoxia Modulate Neurosphere Formation in Vitro of Auditory Nerve Cells**, Luke T Havens, Hainan Lang, Yazhi Xing; Biology, USC, Pathology, MUSC.

Hearing loss affects approximately 36 million Americans and as such is a major problem in our society. Though hearing aids and cochlear implants greatly help a large subset of this population, they do not approach native hearing in quality nor do they help those with auditory nerve damage. For this reason, cell regeneration therapies are a possible future avenue for hearing repair. Ideally, endogenous cells in the damaged area would be stimulated to replace injured cells, avoiding the need for overly invasive procedures or the possibility of donor cell rejection. Our recent study has shown that adult cells from the auditory nerve have neural stem cell (NSC) properties in neuropsen culture conditions. Hypoxic conditions are beneficial to NSCs derived from human embryos, and transforming growth factor alpha (TGFα) promotes the formation of cochlear stem cells derived from the sensory epithelium of postnatal rodent cochleae. We hypothesized that both TGFαs and hypoxia increase the number of neurospheres formed from cells from the auditory nerve of...
adult mice. Using the neurosphere assay, we tested the effect of both hypoxia and TGFα on cells isolated from the auditory nerves of adult CBA/CaJ mice. Neurosphere formation increased in hypoxic environments, whereas TGFα decreased the number of neurospheres formed. Hypoxic conditions could be a signal of the NSC niche, while TGFα could block the action of other growth factors, decreasing growth. Unfortunately, this does not seem to make the use of TGFα to induce sensory hair cell regeneration a less viable option as it could also inhibit auditory nerve regrowth. NIH RO1 DC7506; NIH P50 DC0422

146 Age Specific Patterns of Stroke Mortality with Geographic Location of REACH Telestroke Sites, Stacey S Dallas1, Daniel T Lackland2; 1Claiﬁn University, 2MUSC.

Stroke and stroke risks vary signiﬁcantly by age. REACH Telestroke sites have been implanted to reduce stroke mortality associated with an event. This assessment considers the geographic location of the REACH sites with age-speciﬁc mortality. The aim of this is to assess age-speciﬁc stroke mortality risk proximal to REACH Telestroke sites. Maps of age-speciﬁc mortality will be constructed and stroke mortality identiﬁed from South Carolina death records from 2005-2007 and 2008-2010. Mortality rate is then categorized into tertiles. Telestroke sites are located by county and age-speciﬁc stroke mortality is quantified by levels of risk. The location of current REACH sites will be evaluated based on age-speciﬁc stroke mortality. Future REACH sites can be prioritized based on age-speciﬁc geographic location. The purpose of this study is to determine the ideal location for a new REACH (Remote Evaluation of Acute isCHemic stroke) site in South Carolina. This is based on the counties with a high stroke mortality rate in people under the age of 65. The crude rate from the years 2005-2007 and 2008-2010 is determined and each county is mapped by color using a tertile method. The counties with higher crude rates are colored black, counties with a moderate crude rate are colored blue, and counties with a lower crude rate are colored grey. After creating a map for 2005-2007, before REACH MUSC began, and 2008-2010, after REACH MUSC began, it is determined that

147 The Effect of Static Strain Conditioning on Biochemical and Biomechanical Properties in Living Tissue Engineered Toroid Constructs, Moreira M Alexandra1, Sandra Klatt1, Tarek Shazly2, Zou Boran3, Ian Miller4, W Scott Argraves5; 1Regenerative Medicine & Cell Biology, MUSC, 2Surgery, MUSC.

We have developed an approach to fabricate living toroid constructs using microcarrier beads seeded with human umbilical vein endothelial cells and vascular smooth muscle cells. Toroids having an outer diameter of 4mm, an inner diameter of 2mm and a wall thickness of 1mm are cultured in a tubular agarose mold for 12 days during which they elaborate an extracellular matrix containing collagen and elastin. Tensile testing showed that these constructs display biomechanical properties consistent with their collagen and elastin composition. We hypothesized that the mechanical conditioning of the toroids would increase their stiffness and elasticity. Our initial efforts to test this hypothesis involved removing the toroid constructs from agarose molds and apply static mechanical strain, by placing them onto posts of varying diameter i.e., 2mm diameter (un-stretched conditions) and 3mm diameter (stretched conditions). After 7 days of culture on these posts, uniaxial mechanical testing was performed to measure the biomechanical properties of the toroids. The results showed that static strain did not significantly alter the elastic moduli. Future experiments will evaluate the effects of dynamic strain conditioning on the elastic moduli of the toroid constructs. This data will provide valuable insights for future work in optimizing the fabrication of biocompatible tissue engineered blood vessel replacement. SC EPSCoR/IDeA NSF EPS-0903795

148 Tissue Engineering with Tri-Culture Spheroids, Katherine I Driscoll1, Michael J Yost2; 1Chemistry and Biochemistry, USC, 2Surgery, MUSC.

The tissue engineering field strives to develop living tissue replacements that are biologically compatible and viable when implanted into a host. These two characteristics will be maximized when the materials and the ensuing structures can mimic in vivo tissues as closely as possible. Our research has focused on the development of skeletal muscle implants that can be used to treat patients with defects and involved the observations of interactions between various cell types when placed in tissue spheroids and when bioprinted using the Palmetto Printer. Successful co-cultures have been observed when human endothelial cells have been paired with human dermal ﬁbroblasts and also with human skeletal muscle myoblasts. Recently, we found that tri-culture spheroids composed of all three cell types previously listed could be cultured successfully. These spheroids were observed and analyzed via immunohistochemical procedures after various amounts of time. Then, all three cell types were cultured to a quantity sufﬁcient enough to be bioprinted via the Palmetto Printer. The capability to culture these tri-culture spheroids and then to bioprint ring-like structures with a complex composition demonstrates the advances being made in the tissue engineering and biofabrication ﬁeld and the potential of surgically successful skeletal muscle tissue implants.

NIH DE019355

149 The Role of Sphingosine 1-phosphate in Polymorphonuclear Leukocyte Functions, Haley A Woodward1, Titus A Reaves2; Samar Hammad1; 1Biology, UNCW, 2Regenerative Medicine and Cell Biology, MUSC.

Inflammatory bowel disease (IBD) consists of Crohn’s disease (CD) and Ulcerative colitis (UC). Both are characterized by dysregulated intestinal inﬂammation resulting in epithelial destruction, over-activation of intestinal ﬁbroblasts, aberrant cytokine production, and leukocyte migration. UC can be localized in the large intestine and the rectum, while CD is commonly localized in the terminal ileum. Sphingolipids are structural components of cell membranes that also function as signaling molecules. Studies have shown that the sphingolipid derivative sphingosine 1-phosphate (S1P) affects migration, proliferation, and apoptosis in monocytes. S1P has been shown to mediate Ca2+ influx during polymorphonuclear leukocyte (PMN) activation. Despite this information, little is known about the signaling events that modulate S1P in PMN. Therefore, to characterize the role of S1P in PMN function, we performed immunofluorescence, cell adhesion, and trans-migration experiments. Data using immunofluorescence show that treatment with bacterial formylated peptides,
which activate PMN, did not increase PMN expression of sphingosine kinase (SK), the enzyme that phosphorylates sphingosine to S1P. Inhibition of SK revealed minimal effects on PMN adhesion to fibrinogen, a CD11b ligand. Interestingly, results show that SIP may play a role in PMN migration toward bacterial formylated peptides, but such migration appeared to be delayed and uncoupled to PMN adhesion. These results expose a possible mechanism mediating PMN activation and migration in the intestinal epithelium during disease flares.

150 Importance of Glutathione S-transferase P1-1 on Bone Marrow Regulation. JennaMarie G Baker, Jie Zhang, Zhiwei Ye, Kenneth D Tew; 1SCGSSM, 2Pharmacology, MUSC.

Abstract not available.

151 Molecular Mechanisms of Etiology in Pre-eclampsia. Katherine Senf, Elena Rivers, Anthony Horton, Angela F Hawk, Christopher Robinson, Ann C Foley, Kyu-Ho Lee; 1Clemson University, 2College of Charleston, USC Greenville, 3Obstetrics and Gynecology, MUSC, 4Bioengineering, Clemson, 5Pediatrics, MUSC.

Background. Preeclampsia complicates 2-8% of pregnancies worldwide, and causes half a million deaths annually. It is not well understood, although much progress has been made in recent years towards understanding the process of the disease. One factor which is involved in preeclampsia is soluble fms-like tyrosine kinase 1, or sFlt1, an alternatively spliced variant of vascular endothelial growth factor receptor 1 (VEGFR1), and an important transducer of proangiogenic signaling that is expressed during normal pregnancy at varying levels. It is known that sFlt1 is expressed at abnormally high levels in patients with preeclampsia, however, the mechanisms regulating its splicing from VEGFR1 mRNA and, as a consequence, its expression levels, are unknown. We previously observed high levels of Nkx2.5 and a downstream target gene, Sam68, in placental samples from women with early onset and severe preeclampsia (EOSPE) that correlate with sFlt-1 expression levels. Because Sam68 regulates the same type of splicing that produces sFlt-1, we hypothesized that Sam68 (likely due to increased Nkx2.5 expression), may mediate the alternative splicing of VEGFR1 into sFlt-1, thereby inducing the elevated levels of sFlt-1 evident in our EOSPE patients placental samples. To test this we have begun studies to knock down Sam68 in HEK 293T cells to determine if loss of this gene results in changes of sFlt expression. Methods. Lentiviral knockdown of Sam68 and qPCR Results. It was preliminarily shown that three separate anti-Sam68 shRNAs, each targeting a different region of the Sam 68 transcript, were able to knock down Sam68 expression to varying degrees in transient transfections. Lentiviral knockdown of target genes in model cell lines will be useful for testing molecular hypotheses regarding the pathogenesis of pre-eclampsia.

152 TRAIL and RANKL Expression in Oral Cancer Cells. Angelynn F Glover, Sambandam Yuvaraj; Sakamuri Reddy; 2South Carolina Governor’s School for Science and Mathematics, Hartsville, SC, 2Pediatrics, MUSC.

Osteoclasts are cells that remove bone matrix through the process of bone resorption. Osteoclasts are formed by interaction with cytokines, proteins used to carry signals between cells, specifically the receptor activator of nuclear factor kappa-B ligand (RANKL) and TNF-related apoptosis inducing ligand (TRAIL). TRAIL is a cytokine that induces apoptosis in tumor cells. However, it has also been shown to increase the formation of osteoclasts. Cancer cells are also known to promote the formation of osteoclasts. Forty percent of head and neck cancers are found in the oral cavity. The oral cancer cells tend to cause jaw bone destruction. Tumor cells have been shown to enhance osteoclast activity in the tumor-bone environment. We hypothesized that RANKL and TRAIL expression in oral cancer cells modulates osteoclastogenesis and bone destruction at the tumor microenvironment. Oral Squamous Cell Carcinoma line SCC14A (OSCC14A) were cultured and analyzed using Western Blot Analysis and real-time PCR. Various concentrations of RANKL were treated with TRAIL samples to test the effects of RANKL on TRAIL. Western blot analysis showed that the presence of RANKL increases TRAIL expression. Real-time PCR results also showed that RANKL increases TRAIL and therefore increases osteoclastogenesis. These results show that RANKL increases TRAIL expression in tumor cells. Therefore, RANKL directly and indirectly through TRAIL expression increases osteoclast formation, resulting in bone destruction at the tumor-bone environment.

153 MKP-1 Controls Chemokine-Mediated Osteoclast Formation in RANKL-Primed, LPS-Stimulated Defined Progenitors. Dimitrios S Basilikiou, Michael S Valerio, Keith L Kirkwood; 1CODM, MUSC, 2Craniofacial Biology, MUSC.

Periodontitis is a local inflammatory disease derived from a host response to gram-negative pathogens of the periodontium, resulting in alveolar bone loss directed by bone-resorbing osteoclasts (OCs), specialized cells of hematopoietic origin. Pathologically, OCs become overactive due to increased inflammatory cytokine and chemokine production, resulting in net bone resorption. Control over the MAPK inflammatory pathway by periopathogenic LPS is crucial in regulating the fusion of hematopoietic stem cells to form multinucleated OCs. MAPK phosphatase-1 (MKP-1), which is expressed by the Dusp1 gene, has been shown to control cytokine and chemokine production in response to inflammatory stimuli. Based on its role in MAPK activity, we hypothesize that MKP-1 deficient cells will have excessive OC formation due to chemokine dysregulation. Primary BM cells were isolated from WT and Dusp1-/- female mice and sorted based on expression of CD11b. Cells were primed with M-CSF and RANKL for 48 hours then stimulated with LPS (100ng/ml) for up to 4 days. OC formation was determined by TRAP assay and gene expression was determined by qPCR. Results from these experiments indicate MKP-1 deficiency yields significantly more numerous and larger osteoclasts compared to WT. Dusp1 deficiency shows a 1.5- to 3.5-fold greater expression of CXCL1 and a 2- to 3-fold greater expression of CXCL2 compared to WT across
154 Role of Intestinal Fibroblasts in Inflammation Across the Intestinal Epithelium. Meghan K Anderson¹, Anita Smalls², Titus A Reaves³; ¹COM, MUSC, ²Regenerative Medicine and Cellular Biology, MUSC.

Fibroblasts are mesenchymal cells known to produce extracellular matrix (ECM) proteins such as collagens, laminins, and proteoglycans, which allow them to play a major role in tissue repair and the resolution of inflammation. However, fibroblasts may also contribute to inflammation in the local environment through the release of cytokines, growth factors and differentiation factors. Activated fibroblasts can be referred to as myofibroblasts, which are fibroblasts that display characteristics of muscle cells (e.g. contraction during wound healing). CD36 is a membrane bound and scavenger receptor that is an indicator of inflammation and interacts with TLR-2, 4, and 6. Using gene silencing, we investigated the role of CD36 in intestinal inflammation. Intestinal fibroblasts were cultured in 24-well plates and treated with a series of cytokines for several time periods and the supernatants were examined. The cells were treated with interleukin-6 (IL-6, inflammatory cytokine), adiponectin (APN, pleotropic adipokine released by adipocytes), tumor necrosis factor-α (TNF-α, inflammatory cytokine) and interleukin-10 (IL-10, anti-inflammatory cytokine). While Flow Cytometry analysis of CD36-deficient fibroblasts for expression of immune receptors revealed minimal differences, analysis of supernatants revealed the presence of interleukin-8 (IL-8) (potent chemoattractant for polymorphonuclear leucocytes, (PMN)) in IL-6 treated cells from both normal and CD36-deficient. Interestingly, previous studies indicate that fibroblasts following exposure to IL-8 display a phenotype closer to a myofibroblast. PMN migration experiments were also performed and show a statistically significant reduction in migration using CD36-deficient cells compared to cells that normally express CD36. There were also differences in attachment of fibroblasts to collagen type I. Using kinase inhibitors, IL-8 signaling was examined in fibroblasts from other mucosal surfaces; skin and lung. Results reveal that PI3 kinase may be involved in the release of IL-8 from fibroblasts treated with IL-6. Taken together, results show that fibroblasts can play a major role in inflammation in the intestine and at other mucosal surfaces, PI3 kinase may be involved in IL-6-mediated IL-8 release, and highlight CD36 as a potential molecule that can reduce such inflammatory responses.

155 Activation of NLRP3 Stimulates Inflammase-mediated Cystitis. Melissa N Youssef¹, Francis M Hughes², J Todd Purves³; ¹COM, MUSC, ²Urology, MUSC.

Cystitis, or inflammation of the urinary bladder, is a painful condition associated with increased urinary frequency and urgency. The most common cause of cystitis is bacteria, leading to a urinary tract infection (UTI). Indeed, UTIs are the second most common infection in the body (after respiratory), accounting for 8.1 million healthcare visits per year. Previous studies in our lab have identified the presence of the inflammation-initiating NLRP3 Inflammasome in bladder urothelial cells and its activation (measured as activation of caspase-1) in other models of cystitis. Since NLRP3 acts as a receptor for the bacterial endotoxin lipopolysaccharide (LPS), this study aimed to develop a rat model of cystitis following direct injection of LPS into the wall of the bladder (intradetrusor injection). Caspase-1 activity demonstrated a dose-dependent activation of the NLRP3 inflammasome following injection of LPS. In addition, bladder dysfunction was measured in vivo by urodynamics and LPS-injected rats were found to have a decrease in voiding pressure with an increase in voiding volume compared to saline-injected controls. Overall, the results demonstrate the efficacy of intradetrusor injection of LPS at activation of NLRP3 and the induction of cystitis.

156 Targeting Cell Surface Nucleolin As a Tumor Antigen in Breast Cancer Cells. Craig D Millar, Natalie Sutkowski², Wei Sun²; ¹COM, MUSC, ²Immunology, MUSC.

Breast cancer is the most common malignant type of cancer in women, and targeted therapeutics are of special interest because they do not harm normal breast tissue. Herceptin is a well-known example of a targeted therapeutic for breast cancer, but it can only be used for a minority of breast cancer patients due to its specificity for HER2 positive cancer cells. Nucleolin is a protein that is found to be overexpressed in several breast cancer cell types and because of this, nucleolin is a candidate for a targeted therapeutic drug. Dr. Sutkowski’s lab has developed a fully humanized anti-nucleolin antibody that kills MCF-7 and BT-20 cancer cells. This antibody is especially significant because evidence shows that can work independently of complement and cell-mediated cytotoxicity. With this project, we plan to confirm the presence of nucleolin in the cytoplasmic and cell surface of MCF-7 and BT-20 cells using mouse anti-nucleolin and the fully humanized anti-nucleolin. Results correlate with cytotoxic findings from the Sutkowski lab. Some results, especially the western blots for HumAbs were inconclusive and need further investigating. Future studying by the Sutkowski lab should provide conclusive evidence of overexpression of nucleolin in the cytoplasm of MCF-7 and BT-20 cells and reactivity with the fully humanized anti-nucleolin antibody. This antibody, once fully investigated, can be used to kill breast cancer cells with overexpression of nucleolin and has the potential to be used for other cancer types. College of Graduate Studies SHP Program; DOD W81XWH-12-1-0241
Breast cancer is a heterogeneous disease with multiple subtypes, which are clinically classified based on the expression of estrogen receptor (ER), progesterone receptor (PR) and HER2. Triple negative breast cancer (TNBC) is defined as ER-/PR-/HER2- and without these molecular targets, these cancers are insensitive to highly effective targeted therapies and systemic chemotherapy. It remains the mainstay of treatment for these women. A recent study has shown single agent cisplatin induces a response in a subset of patients with TNBC and suggests a need for the identification of biomarkers to predict response. This will allow identification of patients most likely to benefit from this agent and avoidance of toxicity from treatment in those most likely to be resistant. We have published studies examining the role of miR-510 in breast cancer and observed that miR-510 expression is elevated in tumors when compared to matched non-tumor samples. We have also shown peroxiredoxin 1 (Prdx1) as a direct target of miR-510. Drug cytotoxicity assays indicate miR-510 mediates sensitivity to platinum agents in vitro. Furthermore, miR-510 expression restores sensitivity to cisplatin in resistant breast cancer cell lines both in vitro and in vivo. TNBCs have a high percentage of mutant p53 (~60%), in which case mechanistic studies have shown the activation of the DeltaNp63/Tap73 apoptotic pathway in response to DNA damaging agents. Studies have also demonstrated Prdx1 mediates resistance to cisplatin through the negative regulation of the DeltaNp63/Tap73 pathway suggesting that miR-510 may mediate sensitivity to cisplatin through the negative regulation of Prdx1. We demonstrate an increase in the activation of this pathway in p53 mutant breast cancer cells expressing miR-510 in response to cisplatin treatment. Based on these data we propose that elevated levels of miR-510 mediates cisplatin sensitivity and that it may serve as a non-invasive biomarker to predict response to cisplatin in TNBC patients. American Cancer Society

Investigating the Effects of PRRX1a OAR Mutation on Protein Binding Partners and Disease, Mallory A Ulmer, Mary Ann Baybo, Michael Kern, Dental Medicine, MUSC; 2Regenerative Medicine and Cell Biology, MUSC.
Recent research has uncovered a recessive missense mutation (A231P) in the OAR domain of PRRX1a linked to the Agnathia-Otosephaly Complex. This complex is normally a fatal congenital malformation characterized by mandibular hypoplasia. The PRRX1a is in the class of highly conserved homeoproteins which bind DNA and are transcription factors. It also contains a phylogenetically conserved C-terminal domain called the OAR domain. This OAR domain is likely involved in protein-protein interactions and is found in 16 different human proteins that are known to be important for craniofacial morphogenesis. PITX2 is one such protein whose interactions with TBX1 and DLX2 have been documented to control tooth patterning and amelogenesis respectively. Because DLX2 interacts with PITX2 at the OAR, and TBX1 interacts with PITX2 at the C-terminus (likely at the OAR), DLX2 and TBX1 were chosen as experimental binding partners for PRRX1a. Additionally, all of the proteins named thus far are transcription factors and located in the 1st pharyngeal arch suggesting the possibility of intracellular encounters between the proteins. We employed the HaloTag pull down system to interrogate the potential protein binding interactions between PRRX1a wildtype/mutant and TBX1-FLAG as well as between PITX2 and TBX1-FLAG. Our analysis revealed that TBX1 protein binding is occurring specifically at the OAR domain of PITX2. Western blot analysis suggested PITX2 bound TBX1-FLAG with high affinity, while PRRX1a-A231P binds TBX1 just as well, if not better, than PRRX1a wildtype. It is possible that the molecular mechanism behind Agnathia-Otosephaly is an affinity modification of PRRX1a allowing for interactions with improper proteins and the competitive sequestering of binding partners. SHP CDM

MicroRNA 510 As a Predictive Marker for Response to Platinum-Based Chemotherapy in Triple Negative Breast Cancer Patients, Qi J Guo, Jamie N Mills, Natalie Mason, Tihana Rumboldt, Lourdes Nogueira, Rita Kramer, David P Turner, Victoria J Findlay, 1Pathology, MUSC, 2Hematology and Oncology, MUSC.

Neuroblastoma is a cancer that involves the abnormal growth of developing nerve cells, called neuroblasts, that are destined to form parts of the human nervous system. This cancer mostly affects children ages 5 and under and is the most common cancer affecting infants in the US. LIN28B has been found to be overexpressed in neuroblastoma and other advanced malignancies, inhibit the tumor suppressor let-7 miRNA family, and increase MYCN levels, leading to tumor formation. The goal of this project was to use the CRISPR system to assess the role of LIN28B in two neuroblastoma cell lines, BE2C and SKNAS by overexpressing LIN28B, conducting a LIN28B 3' UTR knockout, and a LIN28B knockout. Here, it is shown, based on immunoassays, that overexpression of LIN28B in these cell lines indeed can lead to increased expression of MYCN (an oncogene). Further growth assays and study will need to be conducted to determine the effect of loss of LIN28B and the LIN28B 3'UTR on BE2C and SKNAS cells.

Screening of Inhibitors for β-Arrestin2, Sherwin A Soltani, Kathryn M Appleton, Richard E Trager, Yuri K Peterson, COM, MUSC, 2Drug Discovery and Biomedical Sciences, MUSC.

-β-arrestin2 is a protein which regulates internalization of activated, phosphorylated GPCRs from the cell membrane in human cells. It has been implicated not only as one of the main regulators of receptor desensitization and internalization, but also as an independent signaling pathway. β-arrestin2 is implicated in asthma pathogenesis, bladder cancer, and many inflammatory diseases.
Previously we have used high performance docking on the NICS Kraken supercomputer to identify an optimal site for selectively inhibiting β-arrestin2, and following virtual screening of a 1.4 million compound library we had identified 61 compounds as candidates for β-arrestin2 inhibitors. In this study we screened these candidate inhibitors using a dually-transfected β2AR/β-arrestin2 live-cell assay with a novel fluorescent microscopy and analysis method to quantify receptor internalization and arrestin mobilization. We then identified 9 compounds from the initial screen for further testing with PTH1R/β-arrestin2 transfected systems and analyzed them in the same manner. We identified five candidate compounds which showed inhibitory effects on the cells in both screens for further analysis and development.

163 Differentiation of Induced Pluripotent Stem Cells to Retinal Pigment Epithelium in Vitro. Michelle Crouse1, Jie Gong2, Ernesto Moreira3, Mark Fields2; 1COM, MUSC, 2Storm Eye Institute, MUSC.

Abstract not available.

164 Incidence of Aneurysmal Subarachnoid Hemorrhage - a Risk Factor and Geodemographic Assessment of Outcome. Thomas W Larrew1, Will Pryor2, Aquilla Turk3, Raymond Turner1; 1Neurosciences, MUSC, 2Interventional Radiology, MUSC.

Objective: Aneurysmal subarachnoid hemorrhage (aSAH) is a devastating illness with nation-wide mortality rates reaching almost 50% within the first 30 days. Our objective is to evaluate how treatment modality, physical presentation, and geodemography contribute to the outcome of these patients, including complications and disposition status. Methods: The authors reviewed all of the cases of subarachnoid hemorrhage in fiscal year 2011 (July 2011-2012) treated at the Medical University of South Carolina. Ninety-nine patients were identified and information including aneurysm properties, Hunt-Hess grade, Fisher grade, and symptoms occurring at and after admission were analyzed. Results: Seventy-two females and twenty-seven males were treated for aneurysmal subarachnoid hemorrhage. Fifty-five of the patients self-identified as white, thirty-nine as black, and five as other. Ninety-two patients were treated with endovascular coiling, fifty-eight of which also required transulminal balloon deployment. Four patients had their aneurysms clipped and two had stents placed and were put under direct observation. Hypertension, tobacco use, and hyperlipidemia were the most prevalent comorbidities, 72.7%, 56.6%, and 29.3% respectively. Presentation varied but largely included headache as well as hydrocephalus, motor disturbance, and nausea/vomiting (92.9%, 51.5%, 32.3%, and 28.3% respectively). The most common post-admission symptom was urinary tract infection followed by hydrocephalus and vasospasm (28.3%, 17.2%, and 13.1% respectively). Conclusion: Previously established risk factors were identified as well as novel factors that may contribute to the incidence of aSAH. The disparity between incidence rates in subgroups, particularly females and blacks, reveal that preventative measures must be taken for these high-risk groups.
a significantly increased 30 day case fatality (p <0.001) even after adjusting for age. To assess whether these same high-risk stroke patients could be identified through traditional risk factors, the prevalence of hypertension (HTN) and diabetes mellitus type 2 (DMT2) was compared by kidney disease status. Surprisingly, HTN-only and HTN-and-DMT2 were more often observed in those without kidney disease. However, DMT2 alone was significantly more common in kidney disease patients (p = 0.02). These findings suggest that kidney disease does not simply indicate a confluence of traditional vascular risk factors, but provides additional information towards a stroke patient’s prognosis. This study validates the need for future research to clarify the role of kidney disease in poor recovery from stroke, and specifically, whether diabetes-related kidney disease may help explain the racial disparities observed in southeastern strokes. *NIH 5T35DK007431-29*

### 167 Renal Cell Cancer: Attenuation Values on Unenhanced CT

**Ashley N Smith, Jordan A. Shealy, David J. Taber, Charles F. Bratton, John Kalu Odeghe, Munazza Anis, COM, MUSC, Radiological Imaging, MUSC, Biomedical Imaging, MUSC.**

Determination of renal cell cancer using unenhanced computed tomography (CT) is a necessary, albeit complex diagnostic strategy. Historically, differentiation of lesions has been made using the attenuation value window of 20-70 Hounsfield Units (HU). The rule of thumb holds that masses within this range should be considered cancerous, while masses falling outside this range require no further work up as they are likely benign. Based on their experience in diagnosing renal cell carcinomas (RCCs), the authors of this study suspect that such a diagnostic criterion for tumors is too simplistic. One reader reviewed unenhanced CT images of 97 malignant lesions in 91 patients. Average attenuation value of the tumors was 26 plus or minus 10 HU, with 29% falling outside the 20-70 HU window. Our data show that the lower range of the 20-70 HU window for determination of renal cell tumors should be lowered to at least 15 so as not to miss a significant number of renal cell cancers. *NIH 5T35DK007431-29*

### 168 Donor, But Not Recipient Age, is a Risk Factor for the Development of Post-Operative Surgical Complications in Kidney Transplant Recipients

**Jordan A Shealy, David J Taber, Charles F Bratton, John W McGillicuddy, Kenneth Chavin, Prabhakar Baliga; Transplant Surgery, MUSC.**

**BACKGROUND:** There has been a dramatic increase in the number of aged patients developing end stage renal disease (ESRD) and requiring kidney transplant (KTX). Studies conducted in Europe demonstrate older KTX recipients have higher risks for complications; however, European organ allocation and post-transplant care are significantly different compared to the U.S. Therefore, the aim of this study was to quantify the impact of donor and recipient factors on the risk, severity and outcomes of surgical complications in aged (≥60 years) KTX.

**METHODS:** This was a longitudinal, retrospective cohort study of consecutive adult solitary KTX who underwent transplant at our center between 2005 and 2012. Patients were initially grouped and compared based upon age (<60 and ≥60 yo), with a secondary objective of analyzing risk factors and outcomes in those that develop post-operative surgical complications. The cohorts were compared using recipient and donor sociodemographics, transplant characteristics, and clinical outcomes. **RESULT:** A total of 1,176 patients were included, 796 (68%) were <60 yo and 380 (32%) were ≥60 yo. Aged KTX were more likely to have private insurance (58% vs. 77%, p<0.001), a history of diabetes (26% vs. 51%, p<0.001), hyperlipidemia (39% vs. 59%, p<0.001), CAD (13 vs. 29% p<0.001), and receive kidneys from older (34 ± 14 vs. 41 ± 16 yo, p<0.001) and marginal donors. Despite these disadvantages, univariate analysis demonstrated similar rates of hospitalization for surgical complications (11% vs. 8%, p=0.226) in aged KTX patients, which was confirmed using multivariate analysis controlling for differences between groups (HR 1.1, 95% CI 0.98-1.01, p=0.09). The secondary analysis demonstrated that donor age (36 ± 15 vs 40 ± 14 yo, p=0.005), donor history of diabetes >10 yrs (1% vs. 3%, p=0.012) and donor history of hypertension >10 yrs (3% vs. 7%, p=0.007) were all significant risk factors for the development of a surgical complication. The multivariate model for development of a surgical complication is displayed in Table 1, demonstrating that donor age (HR 1.03, 95% CI 1.01-1.04) and the development of an opportunistic infection (HR 1.79, 95% CI 1.05-3.04) were strong independent risk factors for the development of a post-KTX surgical complication. Patients that developed surgical complications had lower rates of graft survival at 3-years post-transplant (p=0.048, Figure 1).

**CONCLUSIONS:** Contrary to previous studies, this large-scale analysis demonstrated that recipient age was not a risk factor for the development of post-KTX surgical complications. It appears that donor characteristics, most importantly age, and post-operative opportunistic infections are the strongest risk factors for developing this complication. *Summer Health Professionals Program*

### 169 The Effects of Erratic Peri-operative Blood Pressures and Glucoses on Readmissions and Clinical Outcomes in Kidney Transplant Recipients

**John Kalu Odeghe, David Taber, Kenneth Chavin, Prabhakar Baliga; COM, MUSC, Transplant Surgery, MUSC.**

**Introduction:** Readmission rates have emerged as a strong clinical indicator for kidney transplant (KTX) outcomes; being linked to increased cost of care and morbidity. Because of this, clinicians have sought methods to identify patients at risk for readmission and intervene to reduce these occurrences. Previous studies have identified sociodemographic risk factors for readmission following KTX, but these studies have not included peri-operative clinical variables, such as in-hospital laboratory values and vital signs. Thus, the aim of this study was to utilize baseline sociodemographics coupled with post-operative clinical data to identify patients at high-risk of hospital readmission. **Methods:** This was a retrospective longitudinal cohort study of all adult solitary KTX recipients that were transplanted between 2005 and 2012. Data collection included all baseline donor and recipient sociodemographics, medical histories and transplant characteristics, along with post-operative clinical laboratory values, vital signs, and outcomes. Patients were grouped based on being readmitted to the hospital within one year of transplant and compared using univariate and multivariate analyses. **Results:** 1,176 patients were included, of which 500 (43%) were readmitted within one-year. Baseline risk factors associated with being readmitted included history of diabetes (38% vs. 32%, p=0.03), history of CAGB (6.8%
vs. 4%, p=0.03), history of CHF (7% vs. 4%, p=0.02), need for pre-transplant dialysis (82.4% vs. 25.7%, p<0.01), and marginal donors, using the mean kidney donor risk index between groups (KDR). Transplant risk factors included warm ischemic time (min), (37 vs. 35, p=0.04) and delayed graft function (DGF), (20% vs. 8.9%, p<0.001). Peri-operative clinical data revealed that a lower median diastolic BP (77 vs. 79, p=0.009) and higher median blood glucose (60 vs. 63, p=0.008) were factors significantly associated with readmission. The final multivariate model for readmission is summarized demonstrating that median in-hospital glucose, even after controlling for pre-existing diabetes, was an independent risk factor for readmission. Other risks included cycloytic induction therapy, DGF and KDR. Patients with elevated in-hospital glucose levels were more likely to be readmitted for infection (Odds-ratio 1.7, p<0.001) and cardiovascular events (Odds-ratio 1.9, p=0.007), with readmissions for other etiologies being similar between groups. Patients that were readmitted within one year of transplant had significantly lower graft survival rates. Conclusions: There are important sociodemographic and peri-operative factors that can predict risk of readmission following KTX. Elevated in-hospital blood glucose levels are a strong risk for readmission, regardless of the presence of diabetes. This data can aid clinicians in determining patient risk and future prospective studies should determine if interventions can reduce this risk. Summer Health Professions


Background: Induction therapy is the cornerstone of early immunosuppression in renal transplantation. The choice of induction agent based on donor/recipient characteristics is controversial. The aim of this study was to assess the safety and efficacy of protocols designed to optimally prescribe induction therapy based on donor/recipient risk compared to random therapy. Methods: This was a longitudinal cohort study that analyzed the safety and efficacy of induction therapy in patients that received protocol-guided therapy delineating use based on donor/recipient risks (>20% PRA, cold ischemic time >24 hrs, or re-transplant status were considered high immunologic risk and received T-cell depleting agents [rATG]; all others received IL-2 receptor blockers) compared to patients that received induction randomly as part of a RCT. Adult solitary kidney transplant recipients transplanted between 2005 and 2012 were included in this study. Outcomes included acute rejection, infections (BK, CMV, and composite), mean eGFR, and transplant event costs. Results: 1,176 patients were included, 978 received induction based on protocols, compared to 198 that received random induction. Baseline characteristics were similar between groups, except for hypertension, re-transplant, HLA mismatches, and warm ischemic time. Univariate analysis demonstrated acute rejection rates between the protocol and random groups were 14% vs. 17%, (p=0.22), infection rates were 40% vs. 47%, (p=0.06), mean eGFRs were 58 ± 18 vs. 58 ± 19 mL/min, (p=0.45) and transplant event costs were $70.5k vs. $79.5k, respectively (p<0.001). After adjusting for baseline differences between groups, the use of random induction increased the risk of rejection by 50% (HR 1.5, 95% CI 1.02-2.22, p=0.04), increased the risk of infection more than two-fold (HR 2.3, 95% CI 1.81-3.00, p<0.001) and increased transplant event costs by $5,900 (95% CI: $3,400-8,300, p<0.001). Conclusion: Protocols delineating the prescription of induction based on donor/recipient immunologic risk appear to improve the efficient use of this therapy in adult kidney transplant recipients.

171 The Impact of Antihypertensives and Dosing on Blood Pressure Control in Renal Transplant Recipients. Balvir Singh1, David Taber2, Kenneth Chavin2, Charles Bratton2, Prabhakar Baliga2, 1COM, MUSC, 2Surgery, MUSC.

Purpose: Hypertension (HTN) is a ubiquitous complication post renal transplant, affecting 60%-90% of recipients. Uncontrolled HTN results in significantly reduced rates of graft and patient survival. The effect of antihypertensive agents (AHAs) and dosing on BP control has not been studied in the renal transplant population. Thus, this study aimed to evaluate the relationship between AHAs, dosing of AHAs and BP control. Methods: This was a single center retrospective longitudinal cohort study of adult solitary renal recipients transplanted from 2005 to 2012 at our institution. Patient demographics, comorbidities, transplant characteristics, laboratory values, vital signs, medication history and other relevant data were collected and compared between groups. Uncontrolled HTN was defined as mean SBP >130 mmHg or mean DBP >80 mmHg throughout follow-up. Results: 1,078 patients were included in this analysis, of which 307 (28%) had controlled HTN and 771 (72%) were uncontrolled. Baseline socio-demographic and transplant characteristics comparisons demonstrated patients with uncontrolled HTN were, on average, older at time of transplant (52 years vs 50 years; P = 0.003) more likely to be African-American (68% vs 45%; P = 0.040), have a higher BMI (29.3 kg/m2 vs 27.7 kg/m2; P <0.001) and a history of HTN (94% vs 88%; P = 0.002), develop delayed graft function (16% vs 9%; P = 0.002), and receive a transplant with a higher kidney donor risk index (1.29 vs 1.19; P = 0.002) On follow-up, patients with uncontrolled HTN were more likely to receive multiple AHAs at higher mean doses throughout the study period. After multivariate logistic regression to control for baseline differences between cohorts, use of Beta Blockers was associated with reduced BP control (HR = 0.57, 95% CI = 0.33,1.00, P = 0.050) while the use of other AHAs did not appreciably influence BP control. High pre-transplant BMI (HR = 0.95, 95% CI = 0.92,0.98, P = 0.002) and unfavorable kidney donor risk index (HR = 0.57, 95% CI = 0.35,0.93, P = 0.024) were strongly associated with lack of BP control. Conclusions: This analysis suggests that despite use of multiple AHAs and higher doses, the majority of kidney transplant patients have uncontrolled HTN. Focusing efforts on modifying other risk factors, especially educating patients on weight loss, may be an important mechanism to improve BP control in this high risk cohort of patients.


Background: The use of expanded criteria (ECD) and deceased after cardiac death (DCD) donors has been an
additional source of kidneys for transplantation into patients with end stage renal disease. Studies have demonstrated these donors require more resources and can be financially infeasible. The aim of this study was to analyze the differences in resource utilization and associated outcomes between standard criteria donor (SCD) and ECD/DCD recipients. Methods: This was a retrospective longitudinal cohort analysis of adult solitary renal transplant recipients who received deceased donor kidney transplants between 2005 and 2012. Patients were grouped based on receiving a SCD kidney (control cohort) vs. an ECD or DCD kidney (risk cohort). Outcomes compared were initial hospital length of stay, readmissions, and initial transplant event costs, which were adjusted for inflation. Results: 949 patients were included, 141 in the ECD/DCD cohort (15%) and 808 in the SCD control group (85%). Rates of initial length of stay greater than 3 days were not significantly different between the marginal and SCD groups (30% vs 29%, p = 0.792, respectively). The initial transplant event costs for ECD transplant was $96,936, compared to $93,964 in the control group (p = 0.08). The 30 day, 90 day, and 1-year readmission rates of the marginal group was similar to the control group (12% vs 11%, 24% vs 20 %, and 50% vs. 42%, p = 0.07, respectively). Multivariate modeling demonstrated that delayed graft function (DGF) and recipient age > 60 years were the predominant factors associated with increased LOS and transplant cost. DGF, infection, and rejection were the major risks associated with hospital readmission. Conclusion: Contrary to previous studies, these results indicate that the use of marginal donors did not increase resource utilization, when compared to standard donor kidneys. Future studies are warranted to determine transplant center-specific reasons for the variations observed in resource utilization.


Despite several published studies demonstrating the safety and effectiveness of bougienage, it is not widely practiced for the management of lodged esophageal coins in children. This study aimed to report a single tertiary care center’s experience with bougienage in the pediatric emergency department (PED). We also compared the length of stay and hospital charges for esophageal bougienage versus surgical treatments for lodged coins. This was a retrospective observational study of all children presenting to a PED between 2009-12 with ingested coins lodged in the esophagus. Medical record of all children with ICD-9 codes for foreign body ingestion, or procedure charge codes for bougienage were screened for inclusion. A total of 536 charts were examined, and 126 patients were identified as having acutely lodged coins in the esophagus. Of these, 80 patients underwent successful bougienage. Only 4 patients experienced a failed bougienage, and were then successfully managed using endoscopy. There were no readmissions or major complications from any of the bougienage procedures. A total of 42 patients were treated using surgical interventions. Ten of these patients were eligible for bougienage but received endoscopy instead. A patient undergoing bougienage required an average hospital stay of 2.3 hours (± 0.85 hrs) and had average hospital charges of $1,080 (± $380). In comparison, endoscopy patients stayed for an average of 14.8 hours (± 10.7 hrs) and had total average charges of $9,739 (± $2,182). The patients undergoing successful bougienage had significantly shorter hospital length of stay (p < 0.001) and significantly reduced hospital charges (p < 0.001) as compared to the group undergoing endoscopy. Therefore, we conclude that esophageal bougienage is both safe and highly effective. It is also more time and cost efficient than other surgical interventions.

**174 Characteristics of Consecutive Esophageal Motility Diagnoses After a Decade of Change**, Katherine E Boland, Radu Tutuian, Donald O Castell; Gastroenterology, MUSC.

Abstract: Background: Combined multichannel intraluminal impedance and esophageal manometry (MII-EM) measures concomitantly bolus transit and pressure changes allowing determination of the functional impact of esophageal motility abnormalities Ten years ago our laboratory reported MII-EM results in 350 consecutive patients. Since then high-resolution impedance manometry (HRIM) became available and the definitions of ineffective esophageal motility (IEM) and nutcracker esophagus (NE) were revised. The aim of this study was to assess the impact of these new developments on esophageal function testing. Methods: From August 2012 through May 2013, HRIM was performed in 350 patients referred for esophageal function testing. Each patient received 10 liquid and 10 viscous swallowing. While taking advantage of the new technology and revised criteria esophageal motility and bolus transit, HRIM findings were classified, for comparative reasons according to the conventional criteria. Results: Compared to the study performed 10 years ago, the prevalence of normal manometry (36% vs 35%), achalasia (7% vs 8%), scleroderma (1% vs 1%), hypertensive LES (7% vs 7%), and hypotensive LES (1% vs 2%) remained the same while the prevalence of DES (9% vs 5%), nutcracker (9% vs 3%) and poorly relaxing LES (10% vs 3%) decreased and the prevalence of IEM increased (20% vs 31%), significantly. None of the patients with achalasia, scleroderma, or DES had normal bolus transit for liquid swallows. The proportion of patients with normal bolus transit in various motility abnormalities was smaller compared to the values reported 10 years ago. Conclusion: This study brings to light the increased prevalence of IEM to epidemic proportions and identified that hypertensive LES and poorly relaxing LES may affect bolus transit in about half of patients.

**175 A Pilot Study to Investigate the Induction and Manipulation of Learned Helplessness in Healthy Adults**, Joseph J Taylor1, Daniel Neitzske2, George Khouri1, Jeffrey Borckardt1, Ron Aciero2, Peter Tuerk3, Matthew Schmidt4, Mark George5; 1Neurosciences, MUSC, 2Psychiatry, MUSC, 3Mental Health, VAMC.

Abstract not available.
Lupus nephritis (LN) is a major cause of morbidity and mortality among patients with systemic lupus erythematosus (SLE). Several studies have demonstrated favorable efficacy and safety for mycophenolate mofetil (MMF). Use of MMF for extra-renal manifestations of SLE has not been as well-described. The aim of this study is to compare prescribing patterns of MMF with other therapies for SLE. In addition, analyses are underway to test the hypotheses that use of MMF for extra-renal manifestations of SLE protects against development of LN. Retrospective data from 600 patients with SLE enrolled in the longitudinal MUSC Lupus Database were included in this study. Patients with LN were compared to SLE patients without renal involvement. Demographic and medication use categories were compared using Chi-square tests. Two-sided p-values <0.05 were considered significant. Of the 600 patients, 91.3% were female, 76.3% AA and 20.5% Caucasian. 32.67% have ever taken azathioprine, 79.83% have ever taken hydroxychloroquine and 40.67% have ever taken MMF. Although African Americans (AAs) with SLE were more likely to have LN (55.2% AA vs 27.9% non AA), MMF use did not differ between ethnicities. Patients with LN were significantly more likely to have ever taken MMF (p=0.001), yet 60 patients (10%) with no history of LN reported taking MMF. There was no significant difference in the percentage of patients with and without LN that have ever taken azathioprine or hydroxychloroquine (p=0.502, p=0.53). MMF use is growing for both LN and now extra-renal manifestations of SLE. Of interest, we found that MMF is more commonly prescribed than azathioprine, long considered the first-line steroid-sparing immunosuppressant for SLE. This study confirms the trend towards using MMF for extra-renal manifestations of SLE at our institution, and further analyses will examine whether these patients are less likely to develop LN.

177 Presenting Symptoms As Predictors of Stage in HPV Positive Oropharyngeal Squamous Cell Carcinoma Patients, Amit J Sood, Wesley McIlwain, Shaun A Nguyen, Terry A Day; Otolaryngology-Head and Neck Surgery, MUSC.

Background: Our objective was to determine if presenting symptoms are predictors of T Stage and Overall TNM Stage in HPV positive OPSCC patients. Methods: Retrospective review of all untreated oropharyngeal cancer patients with known HPV status over a five year period. Results: A total of 71 patients met inclusion criteria with no symptoms correlating with T1. However, globus sensation (r=0.258, p=0.05) correlated with T2, visible mass (r=0.227, p=0.05) and otalgia (r=0.306, p=0.01) correlated with T3, and otalgia (r=0.273, p=0.02) and weight loss (r=0.214, p=0.07) indicated late T3/T4a stage. For overall stage, globus sensation (r=0.305, p=0.001), sore throat (r=0.541, p=0.07), and visible mass (r=0.310, p=0.006) correlated with Stage I/II while neck mass (r=0.352, p=0.002) correlated with Stage III/IVA. Dysphagia (r=0.332, p=0.004), pain (r=0.292, p=0.01), and altered tongue mobility (r=0.252, p=0.03) correlated with Stage IVb/IVc. Conclusion: This study provides preliminary evidence that certain symptoms may predict T Stage and Overall Stage in HPV positive OPSCC patients.

178 Presenting Symptoms in HPV-positive and HPV-negative Oropharyngeal Cancer Patients, Wesley R McIlwain, Amit Sood, Shaun Nguyen, Terry Day; Otolaryngology, MUSC.

Importance: This study addresses the most common initial symptoms of oropharyngeal squamous cell carcinoma and investigates differences between HPV-positive versus HPV-negative tumors. Objectives: To analyze the most common initial symptoms in patients with oropharyngeal cancer and to determine if any differences in initial symptoms occur between HPV-positive and HPV-negative OPSCC. Design: Retrospective single-institution review of medical records Setting: Tertiary Care Referral Center Participants: We retrospectively reviewed records of previously untreated patients with oropharyngeal squamous cell carcinoma (OPSCC) diagnosed between January 1, 2008 and May 20, 2013 that were evaluated by one physician (senior author) at the Medical University of South Carolina. Main Outcomes and Measures: Determine the most common initial symptoms of oropharyngeal cancer and analyze differences in presentation between HPV-positive and HPV-negative OPSCC. Results: Neck mass (44%, n=39) and sore throat (33%, n=29) comprised the most common initial symptoms in OPSCC. HPV-positive patients were more likely to present with neck mass than HPV-negative patients (51 vs 18%, p = 0.02), whereas HPV-negative patients were more likely to notice sore throat (53% vs 28%, p = 0.09), dysphagia (41% vs 10%, p = 0.05) or odynophagia (24% vs 6%, p = 0.04). Conclusion and Relevance: This study provides preliminary evidence supporting neck mass and sore throat as the initial symptoms of patients with oropharyngeal carcinoma. HPV positive patients more commonly presented with a neck mass as the initial symptom while HPV negative patients more commonly had symptoms related to the primary tumor site, including sore throat, dysphagia and/or odynophagia.

179 Is Very Low Birth Weight Infant First Postnatal Week Energy and Protein Intake Associated with Growth Parameters At Term Age Equivalent?, Jacqueline L Razzaghy1, Carolyn Finch2, Myle Ebling3, Sarah Taylor2, 1COM, MUSC, 2Neonatology, MUSC, 3MUSC.

For very low birth weight (VLBW) infants, aggressive nutritional practices (early, high protein delivery) have been shown to benefit growth during hospitalization, but less emphasis is given to energy intake and growth until term age equivalent (TAE). Therefore, the objective was to assess the role of first week protein and energy delivery in growth at TAE. Parenteral and enteral intake for the first 168 postnatal hours, birth growth parameters, and TAE growth parameters and growth status were collected for a cohort recruited for a lager vitamin D health study. Data was tested for normality and Spearman Correlations and regression models and T tests were performed. First week protein and energy intake were both significantly but weakly correlated with TAE weight (r=0.22 and 0.2 and p= 0.02 and 0.04 respectively). No significant correlation was seen for TAE length, HC, or growth velocity and first week nutritional intake. TAE weight was significantly negatively correlated with birth weight (r=-0.2, p=0.04) and positively with gestational age at TAE visit (r=0.4, p<0.0001).
controlling for birth weight and TAE visit gestational age, protein intake remained significantly associated with TAE weight (p=0.02), but energy intake was no longer significantly associated with TAE weight. Infants <10th%tile for weight at TAE did not have significantly different first week protein or energy intake when compared to infants with appropriate weight for age. First postnatal week protein and energy intake were associated with TAE weight. When controlling for the week of gestational age at the TAE (range 37-41 weeks) visit and weight at birth, the association between early energy intake and TAE was no longer significant, but the significant association for early protein intake and TAE weight persisted. Early protein was not associated with TAE length, the preferred marker for lean mass. No significant association with TAE HC was seen. NIH K23 RR021891; RR01070

180 Plasma Cathelicidin Concentrations in Preterm Infants At Birth and Its Association with Vitamin D Status, Juliana M Sobiczyn1, Frank Shary1, Myla Ebling2, Renee Washington2, Carol Wagner2, Bruce Hollis2, Sarah Taylor3. 1COM, MUSC, 2MUSC, 3Pediatrics, MUSC.

Abstract not available.


Abstract not available.

182 Quantitative Evaluation of Novel Beam Hardening Artifact Correction Technique in Dual-Energy CT Perfusion Imaging of the Myocardium, Christopher D Wolla, Andreas M Bucher, Aleksander W Krazinski, Carlo N DeCocco, Felix G Meinel, Lucas L Geyer, U J Schoepf, Andrew D Mcquiston; Radiology, MUSC.

In cardiac dual energy CT (cDECT) perfusion, contrast medium filling of the left ventricle and descending aorta in combination with the spine are relevant sources of beam hardening artifacts (BHA) impeding diagnostic evaluation of myocardial regions for perfusion defects. The purpose of this study was to quantitatively assess the impact of a novel Kernel (D33f) with implemented beam hardening correction on beam hardening artifacts (BHA) of the myocardium. Rest series of cDECT perfusion examination from 14 patients were retrospectively analysed. All image acquisitions were performed on a second-generation dual-source CT system (Definition Flash; Siemens Healthcare, Forchheim, Germany). DECT studies were acquired using retrospective ECG-gating, ECG-dependent tube current modulation, and the following scan parameters: 2 x 64 x 0.6mm detector collimation with z-flying focal spot technique, 280 msec gantry rotation time. Temporal resolution was 140 milliseconds. Six different data-set reconstructions were performed for each patient with 3.0 mm section thickness a) 100kV b) 140kV and c) mixed image, each with (D33f) and without (D30f) BHA correction kernel. 792 myocardial regions of rest studies were compared. Regions of interest (ROI) traced by a reader equally subdivided the myocardium at height of most visual beam hardening artifact. Three subdivisions were made within areas of BHA. Paired student-T Test was used for statistical evaluation. Myocardium attenuation significantly differed on corrected reconstructions (D30f 85.1 HU ? 82.9-87.3; D33f 89.2 HU ? 87.0-91.4, p<0.001). Relative difference from average myocardial attenuation (RDTM) significantly differed within visually chosen ROIs (D30f 21.9 % ? 18.6-25.2 %; D33f 11.1 % ? 9.3-12.8 % p<0.001). RDTM difference was greatest for BHA occurring in the infero-lateral basal myocardium (D30f 30.7 % ? 26.5-34.9 %; D33f 11.5 % ? 8.7-14.3 % p<0.001). The application of kernel D33f in the post-processing of cDECT perfusion studies can significantly reduce beam hardening artifacts improving myocardial perfusion defects assessment.

183 Quantitative Analysis of Dynamic CT Myocardial Perfusion Imaging in a Large, Multi-center Patient Population, Jordan A Maivelet1, Felix G Meinel1, Ulrich Ebbersberger1, Roy P Marcus2, Fabian Bamberg3, Carlo N De Cocco1, Uwe J Schoepf1. 1Radiology and Radiological Science, MUSC, 2Institute for Clinical Radiology, Ludwig-Maximilians-University Hospital, Munich, Germany.

Abstract not available.

184 Examining the Role of Type-I Membrane-associated Matrix Metalloproteinase in Thoracic Aortic Aneurysms, S Russ Richardson1, Risha K Patel2, Robert E Stroug2, Jeffery A Jones2, John S Ikonomidis2, 1COM, MUSC, 2Cardiothoracic Surgery, MUSC.

Aneurysm of the thoracic aorta affects approximately 6 in 100,000 people each year and it is one of the leading causes of death in the United States. Although advances in the treatment of thoracic aortic aneurysms (TAAAs) have greatly decreased mortality, the pathophysiology behind TAA development is still not completely understood. Matrix metalloproteinases (MMPs) are zinc-dependent enzymes that remodel the extracellular matrix and have been linked to cardiovascular diseases, including TAAAs. Over-expression of MMPs, including type-1 matrix metalloproteinase (MT1-MMP), has been observed in TAAAs of animal models and it may be a key mediator of TAA development in humans. The objective of this study was to determine the relationship between human TAA size and MT1-MMP abundance and activity and also to examine the role of additional MT1-MMP-associated proteins involved in TAA development. Thoracic aorta specimens from patients with tricuspid aortic valves were obtained at the time of surgical TAA repair (n=73) and specimens were classified as normal (diameter<3 cm, n=19) or TAA (diameter>3.0 cm, n=54). Abundance and activity of MT1-MMP was determined using caged fluorescent assay and through a surrogate marker, MMP-2, abundance and activity. Results (mean ± SEM) have been expressed as a percent change from normal aorta. Expression of MT1-MMP was significantly increased in TAA specimens (151 ± 11) versus normal thoracic aorta (101 ± 13) (p=0.02). MMP-2 abundance was also elevated in TAAAs (211 ± 22) versus normal thoracic aorta (100 ± 34) (p<0.05). Interestingly, the activity status of MT1-MMP or MMP2 were not significantly higher in TAA tissues, suggesting a post-translational process alters MT1-MMP activity in TAAAs. The results of this study confirm aberrant MT1-MMP expression in the thoracic aorta of patients with a clinically significant TAA. Determining the processes involved in MT1-MMP expression and signaling are underway and may identify therapeutic targets that can be
185 Trichostatin A Abrogates Advanced Glycation End-product-induced Retinal Pigment Epithelium Dysfunction in an in Vivo Model of Diabetic Eye Disease, Danielle M Desjardins, Mohammad Dahrouj, Yueying Liu, Craig Crosson, Zsolt Ablonczy; Ophthalmology, MUSC.

186 Phosphorylation Dynamics of Type 1 Parathyroid Hormone Receptor (PTH1R) Signaling in Osteoblasts As Explored By SILAC Mass Spectrometry, Grace R Williams, Mary N Berkaw, Jennifer Bethard, Michael Schilling, Louis M Luttrell, Lauren E Ball; 1Pharmacology, MUSC, 2Endocrinology, MUSC.

The PTH1R is a key regulator of calcium homeostasis and bone turnover. We are employing quantitative phosphoproteomic and bioinformatic approaches to understand the contribution of G protein- and arrestin-mediated signaling to PTH1R actions in bone. To characterize conventional PTH1R agonism, 10-day cultures of differentiating SILAC-labeled MC3T3-E1 osteoblasts were stimulated for 5 min with hPTH(1-34), after which trypsin digested phosphopeptides were enriched using TiO2 and fractionated by SCX chromatography. Peptides were analyzed by nLC-CID MS/MS and ETD MS/MS using a decision tree approach (Orbitrap Elite). Data were searched and quantified using Proteome Discoverer (Thermo). We identified 2,210 unique site-localized phosphopeptides, of which 238 peptides increased and 220 decreased by least 1.5 fold, representing a total of 291 proteins whose phosphorylation state changed with agonist treatment (n=4). Kinase motif analysis revealed that the dominant motifs for increased phosphorylation were consensus PKA (RxxS) and CAMK2 (RxxpS) sites, while the dominant motif for decreased phosphorylation was a consensus MAP kinase site (SP). Targeted immunoblotting confirmed activation of PKA and inhibition of ERK1/2 in response to hPTH(1-34) in these cells. Bioinformatic pathways analysis (Ingenuity Systems, Gene Ontology) of the phosphoprotein datasets revealed that Gs, Gq/11 and G12/13 signaling; Rho, Rac and Cdc42 small G protein activation; cytoskeletal rearrangement, and cell motility were the dominant biological processes regulated by hPTH(1-34) after 5 min stimulation. Future work will compare the phosphorylation profiles of hPTH(1-34) and the arrestin pathway-selective agonist [D-Trp12,Tyr34]-bPTH(7-34) to identify arrestin-dependent signaling pathways/processes and determine the degree of overlap between conventional and arrestin-biased PTH1R agonism. NIH RO1 DE020925; S10 D010731; R01 DK055524

Abstract not available.

187 Identification of Biogenic Residues in the Beta-2 Adrenergic Receptor Via Molecular Modeling, Robert B Cameron, Lauren P Wills, Richard E Trager, Rick G Schnellmann, Yuri K Peterson; Drug Discovery and Biomedical Sciences, MUSC.

Abstract not available.

188 MicroRNA-133a Mediated Regulation of Membrane Type-1 Matrix Metalloproteinase in Myocardial Fibroblasts: Differential Effects in Dilated Cardiomyopathy, Adam W Akerman, Robert E Stroud, Risha K Patel, Paul J McDermott, Fancis G Spinale, Rupak Mukherjee, John S Ikonomidis, Jeffrey A Jones; 1MUSC, 2USC.

Background: Increased myocardial abundance of Membrane-Type 1 Matrix Metalloproteinase (MT1-MMP) occurs in patients with dilated cardiomyopathy (DCM). Furthermore, upon isolation of myocardial fibroblasts, MT1-MMP abundance was increased in DCM cells and associated with an aberrant myocardial fibroblast phenotype. MicroRNAs (miRs) fine-tune protein translation by interrupting ribonucleoprotein:mRNA complexes attenuating protein translation. Interestingly, miR-133a expression was found to be significantly reduced in DCM compared to normal fibroblasts. Using a bioinformatic approach and reporter vectors, containing the 3' untranslated region of human MT1-MMP mRNA, MT1-MMP was validated as a direct target for miR-133a. This study tested the hypothesis that modulation of miR-133a would regulate MT1-MMP protein abundance and return cellular phenotype to within defined normal levels. Methods and Results: Primary cultures of left ventricular myocardial fibroblasts were established from explanted DCM hearts (n=5) and a normal cohort without DCM (n=4). Fibroblast proliferation and migration rates were found to be increased with DCM. Using viral transduction, miR-133a over expression reduced MT1-MMP protein abundance (Figure). Conversely, miR-133a knockdown was associated with increased MT1-MMP abundance in both normal and DCM fibroblasts (190 ± 12% and 284 ± 56%, p<0.05). Importantly, neither intervention miR-133a overexpression or knockdown - was associated with any change in MT1-MMP mRNA expression. Preliminary data suggests a reduction in both proliferation and migration rates following miR-133a overexpression in DCM fibroblasts. Conclusion: These unique findings demonstrate that a persistent dysregulation of miR-133a and miR-133a mediated changes in MT1-MMP occur in myocardial fibroblasts in the context of DCM and are associated with an abnormal cellular phenotype. Thus, this study identifies a novel mechanism through which MT1-MMP abundance may be modulated to regulate phenotype in a key cell type responsible for adverse and progressive remodeling with DCM.

CD4+ T cells polarized to secrete IL-17 (termed Th17 cells) mediate tumor regression to a greater extent than IFN-gamma-producing CD4+ T cells following infusion into mice bearing established melanoma. Unfortunately, the polarizing cytokines (such as TGF-beta, IL-6, IL-23, etc.) required to generate Th17 cells are not currently FDA approved for clinical use. To overcome this hurdle, we sought to determine if Th17 cells could be enriched from peripheral blood and more importantly, if these enriched cells could eradicate large murine tumors. Herein, we found that a high frequency of IL-17-producing CD4+ T cells could be enriched from peripheral blood using an extracellular marker called CD26. In contrast to bulk CD4+
T cells, we discovered that polarizing cytokines were not required to induce IL-17 secretion by CD4+CD26high T cells. Along with IL-17, CD4+CD26high T cells displayed enhanced poly-functionality by also secreting IFN-gamma, IL-22 and IL-2. Excitingly, the CD4+CD26high T cell subset displayed enhanced antitumor activity and survival upon transfer into mice bearing established melanoma compared to mice treated with CD4+CD26negative or bulk CD4+ T cells. Interestingly, CD4+CD26high T cells expressed lower levels of exhaustion markers CD39 and CTLA-4 but higher levels of PD-1 compared to bulk CD4+ or CD4+CD26negative T cells. CD4+CD26high T cells also expressed the homeostatic cytokine receptors CD25, CD122 and CD127 on their cell surface to a significantly greater extent than CD4+CD26negative or bulk CD4+ T cells, which may be responsible for supporting their engraftment and long-term persistence in vivo. Collectively, these findings describe a novel T cell subset that has promise in vaccine or cell-based therapies for patients with cancer. Moreover, the ability to enrich CD4+CD26high T cells from the peripheral blood of patients bypasses the need for polarizing cytokines, thereby enhancing the translational potential for Th17 cells in immunotherapy. 

KL2 Start Up; NIH R01 (1R01CA175061)

190 The Roles of TGF-beta in B Cell Activation and Function, Caroline H Wallace, Zihai Li; Microbiology & Immunology, MUSC.

Transforming growth factor beta (TGF-beta) plays a critical role in immune regulation and tolerance, through regulating the homeostasis of both effector and regulatory T cells. In the B cell compartment, TGF-beta plays roles in the negative selection of auto-reactive B cells and class-switching of immunoglobulin to IgA. However, the roles of TGF-beta in regulating mature B cells, particularly during infections and inflammatory conditions are incompletely understood. This question is also confounded by the presence of multiple forms of TGF-beta including the active form, soluble and membrane-bound latent form. The focus of this study is to delineate the roles of various forms of TGF-beta on the function of mature B cells. This includes proliferation, survival and differentiation to plasma cells as well as class-switching, particularly when B cells encounter pathogen-associated molecular patterns such as endotoxin and Toll-like receptor (TLR) 9 ligands. We found that the cell-surface latent TGF-beta can be strongly induced by TLR but not by B cell receptor-ligation alone. While mouse models are beneficial for mechanistic investigation, we are also investigating if the dysregulation of TGF-beta production and signaling could contribute to the severity of patients with systemic lupus erythematosus. The long-term goal of this research is to understand the roles of TGF-beta on B cells mechanistically within a high impact human disease.

191 Discharge Disposition After Bariatric Surgery, Emily E Johnson, Kit N Simpson; Health Sciences and Research, MUSC.

Introduction: Cost of care may be a significant factor associated with access to bariatric surgery as the extent that private insurance reimburses the surgery is unclear. Financial distress due to expensive medical treatments is common and increasingly being examined in medical literature. Patient discharge to home after hospital admission related to bariatric surgery may be expected to decrease the total cost of care to the patient. Being discharged home can also be associated with higher quality of life and faster integration of weight loss protocols into patients routines. However, there is minimal existing literature on discharge destination post-bariatric surgery or on factors that may identify patients at high risk of discharge to the non-home setting. This study will examine the records of bariatric surgery patients from observational databases to identify the factors associated with discharge directly to home post-bariatric surgery. Methods: The Agency for Healthcare Research and Quality (AHRQ) Healthcare Cost and Utilization Project (HCUP) State Inpatient Database from New Jersey 2010 was utilized to identify all adult patients with prior bariatric surgery or bariatric surgery during hospital admission and determine which factors were associated with and predictive of home discharge. Results: Patients that were discharged home were found to be younger, have shorter length of stay, lower total hospital costs, lower number of chronic conditions, and lower readmission rates than patients discharged somewhere else post-surgery. The factors predictive of being discharged home were age, Hispanic race, private insurance, and being married. Conclusion: Being discharged home is associated with shorter length of stay and lower total hospital charges and could also be associated with other characteristics vital to patient’s long-term weight loss post-bariatric surgery. It is imperative to focus on factors predictive of home discharge in order to reap the most beneficial outcomes of the surgery.

192 Using Rasch Analysis to Convert ICF Activity Measure of Gross Upper Extremity to CMS G-codes, Ickpyo Hong, Craig A Velozo; Health and Rehabilitation Science, MUSC, "Occupational Therapy, MUSC.

Introduction/rationale The Centers for Medicare and Medicaid Services (CMS) mandated the use G-Codes and 7 modifiers indicating level of dependence for medical service reimbursement [1]. While websites are available to convert disability scores to G-Code modifiers, the output is flawed. We hypothesized that an item map of the ICF Activity Measure (ICF-AM) of gross upper extremity function can be used to link Rasch derived measures to CMS G-Code modifiers (i.e., percent of impairment). Methods: Participants: Item-level data from a secondary data set of 203 outpatients with upper extremity disability or low back pain was used for analysis. The participant average age was 48.3 ± 17.9 years old (range: 18-89). Sixty-four percent of the sample were females and 36% were males. Design: Rasch analysis (WINSTEPS 3.75.0) was used to determine number of strata and to generate an item map. Instrument: The ICF-AM is a self-report measure that consists of 27 items that reflect upper extremity functional ability. Results: The 27 items showed 4.7 statistically distinct person strata and person reliability of 0.91. The person strata demonstrated five distinct functional disability patterns on an item map that can be conceptually linked to the percent disability. Conclusion: The determination of percent disability from the scores/measures of an instrument is dependent in connecting that score/measure to a meaningful description of disability. By placing person ability measures on the same linear continuum as item difficulty measures, Rasch can directly connect measures on an instrument to meaningful descriptions of disability. References: 1. Centers for Medicare & Medicaid Services (CMS), Physician Fee Schedule Final Rule for CY 2013,
193 Random Forest Procedure for Classification of Etiologies of Acute Liver Failure in Patients, Jaime L Speiser, Valerie L Durkalski, William M Lee. Public Health Sciences, MUSC. *Internal Medicine, University of Texas Southwestern.

Abstract not available.

194 A New Statistical Algorithm for Classifying and Predicting Disease Outcome From Binary and Continuous Predictors and Their Interactions, Sybil Nelson; Public Health Sciences, MUSC.

In the US, prevalence of Systemic Lupus Erythematosus (SLE) is much higher among African Americans (AAs). However, lupus is very rare among people in West Africa, the ancestral home of most AAs. Both genetic and environmental differences exist between West Africans and AAs leading to the hypothesis that a combination of genetic and environmental factors may be responsible for the high prevalence of SLE in AAs. One goal of the Multidisciplinary Clinical Research Center (MCRC) for Rheumatic Diseases in AAs at MUSC is to identify possible gene-gene and gene-environment interactions associated with having SLE in the SC Gullah population. Identifying high order interactions such as those that might describe SLE status can be difficult using traditional statistical methods where interactions must be selected a priori and where a model must contain interactions and all associated main effects. Classification and regression trees (CART), a nonparametric tree-based method, can build classification models that have flexibility to identify relationships among predictor variables. However, CART tends to be biased towards inclusion of continuous variables. Logic regression is an alternative tree-based classification method capable of identifying interactions among binary variables (e.g. SNPs), but it is currently not designed for inclusion of continuous covariates. We develop a new algorithm, CLogic, that allows for incorporation of binary and continuous covariates in a logistic regression framework. The CLogic selects an optimal cut point for each continuous variable by testing 18 different appropriate methods of dichotomization. The optimized cut point is then used to dichotomize the corresponding continuous variables. CLogic then uses the simulated annealing and Boolean Logic of logic regression. We conduct a simulation study to explore the ability of CLogic relative to CART to correctly identify predictors and interactions. Our results show that CLogic is superior to CART in classifying disease outcome from continuous and binary predictors. National Institute of Arthritis and Musculoskeletal and Skin Diseases P60 AR062755; NIGMS T32 GM074934

195 Acetylation As a Predictor of Glaucamomatous Injury. Oday Alsarraf, Jie Fan, Phillip W Yates, Craig E Crosson; Ophthalmology, MUSC.

Purpose: The current studies investigate whether early changes in acetylation following ischemic and ocular hypertensive injury influence retinal cell survival. Methods: Rat eyes were unilaterally subjected to retinal injury, either in the form of acute ischemia or ocular hypertension. Animals were treated with either a histone deacetylase (HDAC) inhibitor or vehicle. Changes in the acetylation state of histone-H3, HDAC activity, and cleaved caspase-3 were measured at several early time points following injury. Retinal degeneration was evaluated by both morphologic and functional changes. Results: In a retinal ischemic injury model, acetyl histone-H3 levels were significantly decreased by 48% after 4 hours and class I HDAC activity was significantly increased by 12% after 2 hours compared to contralateral control eyes. Cleaved caspase-3 levels did not demonstrate significant changes until 24 hours post ischemia by 129.4 51.1% of contralateral control eyes. Eyes that received HDAC inhibitor treatment demonstrated a significant increase in acetyl histone-H3 and decrease in cleaved caspase-3 levels at 24 hours post injury, in addition to a preserved retinal morphology and function, compared to vehicle treated eyes. In ocular hypertensive eyes, acetyl histone-H3 levels were decreased after 3, 7, and 14 days by 4%, 26%, and 38% of contralateral control eye values, respectively. Class I HDAC activity was increased at 3, 7, and 14 days by 5%, 13%, and 18%, compared to contralateral control eyes, respectively. Ocular hypertensive eyes receiving HDAC inhibitor treatment provided structural and functional neuroprotection compared to vehicle treated eyes. Conclusions: These studies provide evidence that changes in acetylation levels are early events after glaucomatous injury, precede elevations in caspase activity, and can be reversed by hyperacetylation, providing a basis for the development of HDAC inhibitors in the treatment of optic neuropathies.


Abstract not available.

197 Predictive Performance of DRAGON Score: a Pooled Analysis, Liqiong Fan, Sharon D Yeatts; Public Health Science, MUSC.

Background and Rationale: Increasing attention has been drawn to intra-arterial therapy (IAT) for patients after acute ischemic stroke. However, for some patients, the risk of complications may overweight any potential benefit. Identifying those who can actually benefit from this therapy is very important. The DRAGON score is a newly developed functional outcome predictive score. The current research aims to evaluate the clinical predictive ability of DRAGON score in patients receiving combined IV/IA therapies and compare its performance with that of two common predictive scores: HIAT2 and THRIVE. Methods: Patients receiving combined IV/IA therapies from the IMS I and II stroke trials were selected into this pooled analysis. Sensitivity and specificity of each score in predicting poor outcome (mRS score ≥ 4) at 3-months were calculated. Areas under the receiver operating characteristic curve (AUC) were compared among DRAGON, HIAT2, and THRIVE scores in order to assess the predictive performance for each score. Results: Totally 98 patients were included in the analysis. 52 out of 98 patients had poor outcome at 3-months follow-up. DRAGON score ranged from 3 to 8. 71.43% of the patients with dragon score of 7 and above and 75% of those with dragon score of 8 had poor outcome. The AUC for DRAGON score was 0.7018 with 95%CI [0.60, 0.80]
compared with HIAT2 score (0.6773, 95%CI [0.57, 0.79]) and THRIVE score (0.6769, 95%CI [0.57, 0.79]). Conclusion: Based on the AUC, the DRAGON score performed slightly better than HIAT2 score and THRIVE score in terms of predicting poor outcome after combined IV/IA therapy in patients with acute ischemic stroke. However, the observed difference may not be clinically relevant. Moreover, DRAGON score may not be appropriate in clinical decision-making regarding add-on rescue approaches like IAT. A large sample is needed for future verification.

198 The Hippocampus and Lateral Septum: an Important Circuit in Context, But Not Cue-induced Reinstatement of Cocaine Seeking. Ellen M McGlinchey, Gary Aston-Jones; Neurosciences, MUSC.

Drug relapse often occurs when addicts are re-exposed to drug-associated contexts or discrete drug cues. In a rodent model of addiction, this is modeled by context- or cue-induced reinstatement of extinguished drug seeking. The dorsal hippocampus has been found to be necessary for context-, but not cue-induced reinstatement, suggesting different circuits may mediate these two modalities. Recent evidence from our lab revealed a functional circuit between the hippocampal CA3 neurons to the ventral tegmental area (VTA), via a relay in the caudal-dorsal lateral septum (cdLS). As the CA3 region is important for contextual processing and the VTA in reward processing, this circuit indicates the cdLS may be important for linking contextual information with reward seeking. It is clear from early self-stimulation studies in both humans and rodents that the lateral septum plays a role in reward-driven motivation; however, this brain region has been largely understudied in drug abuse and relapse. This study aims to understand the role of the hippocampus-lateral septum circuit in the context- vs. cue-induced reinstatement of cocaine seeking. A modified self-administration model of addiction was designed to dissociate between the drug-associated contextual environment and the discrete light/tone cues paired with cocaine infusions during training. Fos expression was used as a marker of neuronal activation in the hippocampus (CA3, CA1, and dentate gyrus) and lateral septum (cdLS, caudal LS, rostral LS) following context or cue reinstatement tests. Fos expression was greater in all lateral septum and dorsal hippocampal sub-regions for context- compared to cue-induced reinstatement. Furthermore, preliminary data indicate that inhibition of LS neurons using Designer Receptors Exclusively Activated by Designer Drug (DREADD) technology may attenuate context-induced, but not cue reinstatement. Together these findings indicate that the hippocampal-LS circuit may be important for drug reward-environment associations that drive addicts to relapse. PHS R37 DA006214

199 VTA Dopamine Terminals Regulate Neuronal Excitability in the PFC Via Inhibition of the Slow After-hyperpolarization. William Buchta, Benjamin Harlan, Peter Kalivas, Arthur Riegel; Neurosciences, MUSC.

Calcium activated K+ channels support a slow after-hyperpolarization (sAHp) that contributes to neuronal excitability and synaptic plasticity in animal models of learning. To better understand how dopamine (DA) regulates these channels in prefrontal cortex, whole cell patch clamp electrophysiological recordings were performed in L5 pyramidal cells in brain slices from naïve rats or rats that underwent operant training for cocaine. In slices from naive animals, neurons displayed a robust spike-frequency adaptation (accommodation) and large sAHp that could be inhibited by bath application of DA (1nM-100uM) or optogenetic (ChR2) activation of VTA DA terminals within the cortical slice from TH-Cre rats during application of cocaine. In both instances, antagonists for DA D1 (but not D2) receptors blocked this inhibition, suggesting VTA release of DA increases neuronal firing via D1 coupled signaling. In animals with a history of chronic cocaine self-administration firing was elevated, and the sAHp and accommodation were absent under basal conditions. However, normal firing patterns (accommodation) could be restored by stabilization of KCNQ ion channels, suggesting that chronic cocaine self-administration reduces KCNQ channel function. To examine the behavioral relevance of these adaptations, KCNQ channel function was enhanced with retigabine injections into the cortex immediately prior to cue-reinstatement testing. Results indicate a significant reduction in drug-seeking behavior. Taken together, this suggests that VTA DA terminals may regulate accommodation in the PFC via D1 receptors to inhibit the sAHp. Following chronic cocaine self-administration, this mechanism is corrupted, and may enhance drug seeking in response to cues. T32 DA007288; R01 DA03342A

200 The Role of P53 and the DNA Damage Response Pathway in Activation-Induced Cell Death of Adoptively Transferred T Cells Used in the Immunotherapy of Metastatic Melanoma. Matt Scheffel1, Shikhar Mehrotra2, Christina Voelkel-Johnson1; 1Microbiology & Immunology, MUSC, 2Surgery, MUSC.

Melanoma is one of the few cancers with an increasing incidence rate in the United States. Stage I melanoma is generally curable via surgery; however once the cancer has metastasized, a favorable prognosis quickly diminishes with a Five Year Survival (FYS) rate of only ~15%. To date, the most effective treatment regimen for metastatic melanoma is the adoptive transfer of melanoma specific T cells with the most optimized clinical trials demonstrating a FYS upwards of ~40%. The persistence of the adoptively transferred T cells as well as their age and activation status all correlate with therapeutic success with younger, less differentiated, and more durable T cells associating with better outcomes. The persistence of activated T cells is regulated by both intrinsic and extrinsic mechanisms to maintain immune-homeostasis which can often be problematic when T cells are manipulated for therapeutic purposes. In vitro, activated T cells that have undergone restimulation of their T cell receptor (TCR) often die by Activation Induced Cell Death (AICD). Hernandez-Chacon, et al. (J. Immunotherapy 2011,34:236-250) has shown that T cells that have gone through the Rapid Expansion Protocol for use in adoptive transfer therapy die by AICD when restimulated with OKT3 in vitro. The overall hypothesis of this project is that AICD limits the persistence, and thereby therapeutic efficacy, of adoptively transferred T cells in vivo; and conversely, blocking AICD via novel intervention points should increase the persistence, memory development, and anti-tumor efficacy of T cells. It has been shown that AICD occurs independent of death receptor signaling but is dependent on JNK and generation of reactive oxygen species. Since p53 plays an important role in both oxidative stress and cell death, we evaluated the role of
this protein in AICD. Our results reveal that while total levels of p53 decline during AICD, the protein is activated via the phosphorylation of its Serine-15 residue early after TCR restimulation. Markers indicative of a DNA damage response (p-ATM, p-SMC1, yH2AX) are upregulated with the same kinetics as p53(p-Ser15) suggesting activation of the DNA damage response pathway occurs early following TCR restimulation. The JNK inhibitor SP600125, which has previously been shown to block AICD, prevents the upregulation of the p-ATM/p53(p-Ser15) pathway. Pharmacological inhibition of ATM and p53 also protects T cells from AICD and unlike inhibition of JNK, do not significantly decrease the ability of cells to secrete interferon-gamma. Additionally, assays with p53-null splenocytes have demonstrated interference of p53 signaling to be protective against AICD. Moreover, emerging data suggests that p53-null T cells have increased anti-melanoma cytotoxic functionality in vitro compared to wild-type controls. Future studies will evaluate the impact of blocking AICD on anti-tumor efficacy in vivo. In summary, our data indicate that TCR restimulation results in activation of the DNA damage response pathway and that blocking this pathway downstream of JNK but at or upstream of p53 provides a novel point of intervention to protect adoptively transferred therapeutic T cells from AICD. NIH P01 CA154778

201 The Role of 2,4-Dihydroxyquinoline (DHQ) in Pseudomonas aeruginosa Quorum Sensing and Virulence. Jordon D Gruber1, Wei Chen1, Patrick Flume2, Yong-Mei Zhang1; 1Biochemistry and Molecular Biology, 2Pulmonology and Critical Care Medicine.

Pseudomonas aeruginosa (Pa) is an increasingly prevalent hospital associated pathogen that forms antibiotic resistant biofilms during colonization of a host. Pa commonly infects wounds, tissues associated with indwelling medical devices, and lungs of more than 90% of patients with the genetic disorder cystic fibrosis (CF). Pa controls virulence factor production and biofilm formation via quorum sensing, a form of bacterial communication through the secretion and detection of small molecules. Of the three quorum-sensing systems in Pa, the Pseudomonas quinoline (Pqs) system produces greater than 50 different quinoline quorum-sensing molecules. Previously studied alkylquinolones HHQ and PQS activate virulence factor production by activating the transcriptional regulator PqsR. DHQ is produced in significantly higher concentrations than HHQ or PQS, but has no known function. Using mutants of the pqs operon for transcriptional analysis, we showed that DHQ activated pqs operon expression in a PqsR-dependent manner, which complemented the results that DHQ-only producing strains were more virulent than a quinolone-null strain. Moreover, DHQ from endogenous production and exogenous supplementation increased transcription of pqsA. The ligand-binding domain of PqsR was expressed and purified for in vitro analysis between the transcriptional regulator and quinolones. Our results showed that DHQ caused a conformational change in PqsR similarly to alkylquinolones HHQ and PQS. Identification of DHQ as another ligand of PqsR demonstrates multiple mechanisms to activate transcription of the pqs operon and will increase the understanding of virulence factor regulation via the pqs operon. DOD/DM090161; CFF-ZHANG1210; SCTR TL1 Fellowship UL1TR000062

202 Noise-induced Necrotic Outer Hair Cell Death is Modulated By Receptor-interacting Protein Kinases, Kayla R Hill, Hong-Wei Zheng, Jun Chen, Su-Hua Sha; Pathology and Laboratory Medicine, MUSC.

Background: Receptor-interacting protein (RIP) kinases promote the induction of necrotic cell death pathways. The interaction of RIP1 and RIP3 through the RIP homotypic interaction motif leads to cellular ATP depletion and necrotic cell death pathways. It is well-known that traumatic noise induces both apoptotic and necrotic outer hair cell (OHC) death. Here, we investigated role of RIP kinases in noise-induced necrotic OHC death pathways using adult CBA/J mice. Methods: Broadband noise from 2 - 20 kHz at 106 dB SPL for 2 hours to induce permanent threshold shifts (PTS). Propidium iodide labeling of OHC nuclei to determine apoptosis and necrosis via morphological criteria. Anti-RIP3, anti-RIP1, and anti-phospho-AMPK-alpha (p-AMPK-alpha) labeling of cochlear surface preparations to determine expression of RIP3, RIP1, and p-AMPK-alpha in OHCs. Delivery of necrosis inhibitor necrostatin-1 (Nec-1) to the round window via intra-tympanic application to determine the number of apoptotic and necrotic OHC nuclei. Intra-tympanic delivery of RIP3 siRNA to reduce the expression of RIP3. Results: One hour after noise exposure, OHCs in the basal region of the cochlea displayed apoptotic and necrotic features, increased RIP1 and RIP3 protein levels and increased formation of RIP1/RIP3 complexes. Treatment with necrosis inhibitor necrostatin-1 or RIP3 siRNA (siRIP3) diminished noise-induced increases in RIP1 and RIP3 and decreased necrotic OHC nuclei. Noise-induced active AMPK-alpha levels, commonly associated with necrotic cell death, decreased with Nec-1 and siRIP3 treatment, consistent with the reduction of levels of RIP1 and RIP3. Finally, morphological assessment of OHCs showed that siRIP3 treatment reduces noise-induced OHC death. Conclusions: Our results suggest that noise-induced OHC necrosis is modulated by RIP kinases. Inhibition of RIP kinase levels by a necrosis inhibitor or silencing RIP3 can reduce noise-induced necrotic OHC death. NIDCD R01 DC009222

203 Effects of Aging and Gender on Murine Thoracic Aortic Structure and Mechanical Properties. Jason B Wheeler1, Rupak Mukherjee2, Allison D Rice3, Jeffrey A Jones2, John S Ikonomidou2, 1MCBP, MUSC, 2Surgery, MUSC, 3Medicine, MUSC.

Introduction: Inherent characteristics of the thoracic aorta, including passive (extracellular matrix composition) and active (smooth muscle cell contraction) tension, provide the mechanical compliance to support the high hemodynamic force generated during the cardiac cycle. Because cardiovascular disease risk is modified by age and gender, it is expected that the structural and cellular composition of the aorta is also modified by age and gender. Accordingly, the goal of this study was to determine the effects of age and gender on thoracic aortic structure, passive and active tension. Methods: Thoracic aortic rings were harvested from young (6 months) and old (21 months) C57BL/6 mice. Aortic wall collagen was measured with PSR staining. To evaluate passive tension, aortic rings denuded of endothelium were stretched by applying sequentially increasing tension within a physiologic bath and calculating the percent recoil at each interval after 3 minutes. Active tension was determined in identically prepared aortic rings over a range of applied
tension by stimulating contraction with potassium chloride. Results were compared by age and gender. Results: Old rings exhibited increased collagen vs. young (66.5 ± 1.3 vs. 55.8 ± 2.5, p<0.05), as did young male vs. young female (60.6 ± 3.1 vs. 51.1 ± 2.6, p<0.05). Surprisingly, passive tension was similar between age and gender groups. Maximum active tension was decreased in old vs. young rings (125.1 ± 35.8 vs. 247.9 ± 83.4, p<0.05), as well as male vs. female rings (155.7 ± 61.0 vs. 201.0 ± 56.9, p<0.05). Interestingly, the applied tension needed to achieve maximum active tension shifted lower in old vs. young aortic rings (0.88 ± 0.02 vs. 0.98 ± 0.05, p<0.05) but was similar between genders. Conclusions: This study demonstrated that significant changes in the structure and mechanical properties of the murine thoracic aorta occur with aging, including increased mural collagen and a decreased, shifted maximum active tension, suggesting decreased aortic compliance with age. Furthermore, these properties appear affected by gender. NIH 5R01AG03695403; NIH HL 007260

204 GILT Reduces PAX-3 Expression in Human Melanoma Cells. Jessica D Hathaway1, Bently P Doonan2, Azim Hossain1, Duncan Norton3, Lixia Zhang1, Azizul Haque1, 1Microbiology & Immunology, MUSC, 2Medicine, MUSC, 3Medicine, USC.

Melanoma is an aggressive skin cancer that has an increasing prevalence in Western populations. Standard treatments such as surgery, high-dose radiation, chemotherapy, and immunotherapy have had some success, but often fail in treating late stage metastatic melanoma. This stresses the need to improve disease targeting for overall survival. Our lab has recently shown that an induction of Gamma-Interferon-inducible Lyosomal Thiol Reductase (GILT) in melanoma cells favors HLA class II antigen processing and CD4+ T cell recognition of tumors. GILT expression in melanoma cells also reduces a tumorigenic molecule, paired box 3 (PAX-3) protein, which has been implicated in the pathogenesis of late stage metastatic melanoma. While PAX-3 is involved in cell survival events in melanocyte development, it remains unknown whether this is true in the development of various stages of melanoma tumors. Data obtained suggest that GILT’s targeting of PAX-3 sensitizes melanoma cells to radiation therapy. These data suggest that GILT expression plays multiple roles in altering melanoma pathology, immune recognition, and radiation sensitivity. Understanding the mechanisms of GILT-mediated reduction of PAX-3 could lead to a new target for devising novel therapeutics for metastatic melanoma. NIH R01 CA129560; R01 CA129560-S1

205 The Role of MK2 in Aggregatibacter Actinomycetemcomitans Mediated Chemokine Receptor Expression in Macrophages. Bethany A Herbert, Michael Valerio, Keith L Kirkwood; Craniofacial Biology, MUSC.

Aggregatibacter actinomycetemcomitans (A.a.), a Gram-negative capphile, is involved in aggressive periodontal disease pathogenesis. Inhibition of mitogen activated protein kinase-activated protein kinase 2 (MK2), a downstream target of p38 MAPK, decreases A.a. LPS driven inflammation. Monocytes are innate inflammatory cells, derived from the hematopoietic lineage, that possess chemotactic receptors critical for migration into the local environment during periodontal disease progression. CXCR4 down regulation enhances hematopoietic cell mobilization from the bone marrow into peripheral sites during infection. Taken together, we hypothesize that A.a. up-regulates monocyte chemotaxis through MK2 inhibition of CXCR4. Bone marrow cells were harvested from 8-12 weeks old aged and sex-matched C57BL/6 (WT) and Mk2/-/- mice. Cells were sorted with CD11b-conjugated magnetic beads into CD11b+ cells, differentiated into macrophages for 6 days with M-CSF, and stimulated with fixed A.a. Immunoblot results show that A.a. induces MK2 phosphorylation in primary-derived macrophages after 30 minutes (n=2). Flow cytometry was used to determine protein surface expression of CXCR4 on CD11b+ bone marrow cells. There was no significant difference in CD11b+CXCR4+ bone marrow cells in Mk2/-/- mice compared to WT mice (n=3). A.a. stimulation decreases expression of Cxcr4, shown by RT-qPCR, in mouse macrophage/monocyte RAW264.7 cells and primary-derived murine macrophages up to 16 hours (n=3, P<0.05). To determine the role of MK2 in Cxcr4 gene regulation, Cxcr4 was quantified by RT-qPCR in WT and Mk2/-/- primary-derived macrophages. Cxcr4, but not Cxcr2, was increased in Mk2/-/- untreated and A.a. treated cells (n=3, P<0.01), supporting that MK2 regulates Cxcr4 gene expression. A.a. treatment significantly decreased Cxcr4 in Mk2/-/- macrophages compared to Mk2/-/- untreated cells (n=3, P<0.001), reducing levels to that of untreated WT macrophages. These data suggest that A.a. and MK2 negatively regulate Cxcr4 gene expression, which may be responsible for modulating monocyte/macrophage mobilization during A.a. - driven perio-dental disease. NIH T32 DE017551; NIH R01 DE02142303; Center for Oral Health Research

206 Using ICF Attention Measure to Develop a Treatment Framework for Individuals with Traumatic Brain Injury. Chih-Ying Li, Craig A Velozo; Occupational Therapy, MUSC.

Introduction: Individuals with Traumatic Brain Injury (TBI) is often characterized by cognitive problems, such as attention deficits that could significantly inhibit an individual’s productivity and independence in performing daily activities. We developed a self-report attention measure based on the International Classification of Functioning, Disability and Health (ICF) by connecting the ICF Attention Measure (ICF-AM) to meaningful descriptions of functional attention. The purpose of this study was to generate keyforms that link person ability to item response patterns. Methods: The ICF-AM consists of 52 self-report items that measure the impact of attention deficits on daily functioning. Ninety individuals with moderate and severe TBI were assessed with the ICF-AM. Forty-seven participants were recruited from outpatient rehabilitation centers and 43 people were recruited one or more years after TBI. The Rasch analysis program Winsteps 3.75 was used to generate item-person maps to define task difficulty and person ability, and keyforms were generated to show response patterns of each participant on the instrument and set up treatment goals. Results: The 52 items divided participants into 5 statistically distinct strata, which mean these 52 attention tasks could distinguish this sample into five hierarchical levels of attention ability. Keyforms showed distinct ability patterns for participants with different attention levels. Since the keyforms present patterns of items a participant can and cannot do, it can be used for a basis for developing
treatment plans for the rehabilitation interventions. Conclusions: This study demonstrates a practical application of generating a treatment framework of attention activities for individuals with TBI based on the ICF-AM. Keyforms based on ICF-AM can be used as a treatment framework for individualized treatment planning and goal setting. NIDRR H133G000227

207 Laterality of Mammary Stem and Progenitor Cell Populations During Normal Development, Jacquelyne P Robichaux; Brian W Booth; John W Fuseler; Ann F Ramsdell; Hollings Cancer Center, MUSC; Institute for Biological Interfaces of Engineering, Clemson University, Cell Biology and Anatomy, School of Medicine USC.

Mammary stem and progenitor cells play a critical role in breast cancer initiation and progression, and recently, the different mammary epithelial cell types have been proposed to correlate to different subtypes of breast cancer. Although mammary glands are believed to be identical due to their anatomical symmetry, our lab has found that in mice the left (L) and right (R) thoracic mammary glands (TMGs) are molecularly different; furthermore, preliminary data suggests the hypothesis that there are L-R differences in stem and progenitor cells during normal development of the TMGs. qRT-PCR of pubescent wild-type mouse TMGs showed L-R differences in genes that regulate stem and progenitor cell differentiation in both luminal and myoepithelial cell lineages. In addition, when pubescent mice were injected with a fluorescent deoxyuridine label, the LTMG had more cells that retained the label after 10 weeks. Characterization of these label retaining cells by others has shown that these cells have characteristics of adult stem and progenitor cells. Currently, L and R TMGs of pubescent mice are being sorted by FACS analysis to quantify L-R differences in stem and progenitor cell numbers. Sorted cells will be analyzed by qRT-PCR and in vitro assays to verify cell purity and functionality. The results of these experiments are predicted to show L-R differences in mammalian stem and/or progenitor cell populations that occur during normal development. L-R differences in stem and progenitor cell populations could suggest a developmental origin of L-R differences observed in breast tumor initiation and progression. NIH R21 HD068993

208 S1P Receptor Signaling in Mesenchymal Stem Cells, Sarah Tucke Marrison, Thomas Beckham, Joseph Cheng, Ping Lu, Xiang Liu, James S Norris; Microbiology and Immunology, MUSC.

Mesenchymal Stem Cells (MSCs) are a pluripotent cell population acquired most prominently from bone marrow with the capacity to differentiate into osteoblasts, chondrocytes, adipocytes, cardiomyocytes, fibroblasts and other cell types. The immunoprivileged nature of these cells combined with their ability to home to sites of injury enhances therapeutic interest in this stem cell population. Phase I/II clinical trials have been conducted to evaluate the therapeutic potential of these cells in graft vs. host disease, following acute myocardial infarction, multiple sclerosis, bone and cartilage disease, and many other applications. The signaling pathways that direct the maintenance, migration, and engraftment of these cells are therefore a subject of extensive ongoing research. One facet of MSC signaling that remains largely unexplored is that of sphingosine 1-phosphate and its associated receptors. Sphingosine 1-phosphate (S1P) is a biologically active sphingolipid with many known functions including proliferation, inhibition of apoptosis, inflammation, and angiogenesis. These activities are largely mediated by interactions with the 5 G-protein coupled S1P receptors (S1PR1-5). The goal of this project is to evaluate the role S1PR signaling on the maintenance of a proliferative, pluripotent stem cell population capable of migration to and engraftment at sites of injury. The project was motivated by preliminary data suggesting that inhibition of S1PR2 changes the proliferation and phosphorylation status of Erk. Complex regulatory factors govern the differential and complementary effects of S1PR signaling and as such we propose the evaluation of S1P1-3. These receptors were selected based on the ubiquity of their expression and previous literature conducted implicating signaling roles in other stem cell populations. Inhibition of S1P2 results in increased MSC proliferation and migration that may be the result of increased Erk phosphorylation whereas inhibition of S1P receptors 1 and 3 does not impact MSC migration, proliferation, or the Erk phosphorylation status. However, inhibition of S1PR1-3 results in decreased MSC differentiation into adipocytes and S1P2 inhibition result in decreased osteogenesis. These changes are paralleled by changes pluripotency factors known to impact MSC self-renewal. We therefore propose that manipulation of S1P receptors and S1P2 in particular have implication in the maintenance and self-renewal of MSCs. NIH POI CA97132, SCTR Voucher Program, MUSC MSTP, Hollings Cancer Center Abney Foundation

209 The 1,25(OH)2D3 Response in MKP-1-deficient Mice That Have Primary Hyperparathyroidism, Alfred C Griffin; Erica Nelson; Louis Luttrell; Keith L Kirkwood; DSTP, MUSC; Craniofacial Biology, MUSC; Endocrinology, MUSC.

Abstract not available.

210 Inhibition Of Histone Deacetylase (HDAC) Activity Promotes M2 Macrophage Polarization Post Myocardial Infarction Reducing Matrix Metalloproteinase-9 (MMP-9) Expression and Improving Left Ventricular F, Denise M Kimbrough, Santhosh K Mani, Harinath Kasiganesan, Donald R Menick; MUSC.

Background: Large increases in matrix metalloproteinase-9 (MMP-9) are associated with adverse extracellular matrix (ECM) remodeling following a myocardial infarction (MI). We found that treatment with an HDAC inhibitor repressed post-MI upregulation of MMP-9. Significant sources of MMP-9 in the post-MI left ventricle (LV) are M1 macrophages. Two phenotypes (M1 and M2) are expressed following MI, but this is dependent on the phase of ECM remodeling. We hypothesize that HDAC inhibition regulates the post-MI expression of MMP-9 by mediating M1 to M2 macrophage polarization. Methods: CD1 and MMP-9 β-gal reporter mice were induced with MI by LAD ligation then administered HDAC inhibitors: trichostatin A (TSA) and Vorinostat (SAHA) [class I and IIb], PD106 (class I), or Tubastatin A (HDAC 6) until termination at 5 or 7 days post-MI. Expression of MMP-9, M1, and M2 markers in cells or tissue were analyzed by immunohistochemistry, immunoblotting and qRT-PCR. Results: Immunohistochemistry revealed that infiltrating macrophages express MMP-9 at 5 and 7 days post-MI.
HDAC inhibition decreases this expression and does so without reducing presence of macropores within infarct. Immunoblotting shows TSA, SAHA and PD106, inhibit control levels and lipopolysaccharide (LPS) stimulated upregulation of MMP-9 in cultured RAW264.7 and in vivo. Immunofluorescence revealed that treatment with PD106, Tub A, and TSA leads to M1 to M2 morphology specific polarization and maintenance of anti-inflammatory, M2, phenotype even with LPS stimulation in culture. SAHA significantly reduced the upregulation of M1 macrophage markers (CD11c, IL-6, IL-1beta), while upregulating M2 (CD163, CH3L3, Mannose) markers (p<0.05) post-MI. TSA, SAHA and PD106, increased expression of M2 markers in LPS stimulated cultured macropores while decreasing M1 associated markers. Conclusions: Macrophage mediated secretion of MMP-9 is inhibited in vivo and in vitro by HDAC inhibition. Class I selective HDAC inhibition promotes M2 macropore polarization, which attenuates adverse remodeling by reducing MMP-9 expression. NHI R01 HL066223; AHA 09GRNT2020202; AHA 13PRE16840023

211 BMP Signaling and Epicardial Contribution to the Atrioventricular Junction. Marie M Lockhart1, Ajinee L Phelps2, Christina M Brown2, Rupak D Mukherjee3, Maurice J van den Hoff1, John B Burch1, Andy Wessels1; 1Regenerative Medicine and Cell Biology, MUSC, 2Biology, USC, 3Surgery, MUSC, 4Anatomy, Embryology, and Physiology, Academic Medical Center, Amsterdam, The Netherlands, 5Fox Chase Cancer Center, Philadelphia, PA.

Recent studies using mouse models that enable us to trace the fate of epicardial derived cells (EPDCs) have demonstrated that at the atrioventricular (AV) junction EPDCs contribute to the mesenchyme of the AV sulcus, the annulus fibrosis, and the parietal leaflets of the AV valves. Insight into the mechanisms that govern the contribution of EPDCs to these AV junctional tissues is slowly emerging. While it has been demonstrated that BMP signaling is required for AV cushion formation, its role in the context of EPDC contribution to the AV junction has remained unexplored. In order to gain insight into the role of BMP signaling in this process, we conditionally deleted the Bmp receptor BmpR1a/Alk3 in the epicardium and EPDCs using the mWt1/RES/GFP-Cre (Wt1Cre) mouse. Histological analysis of Wt1Cre;Alk3flx/flx specimens revealed compromised development of the AV sulcus and annulus fibrosis. Furthermore we observed that conditional deletion of Alk3 results in a sharp decrease in the number of EPDCs in the parietal leaflets of the AV valves. Interestingly, the loss of EPDCs within these leaflets results in increased leaflet size as well as a myxomatous valve phenotype in post-natal specimens. Preliminary results indicate that in addition to changes in valve morphology, Wt1Cre;Alk3flx/flx mice have conduction abnormalities. Combined, these data show that BMP signaling is important in the cascade of events that regulate the contribution of the EPDCs to the AV sulcus, annulus fibrosis, and the parietal leaflets of the AV valves. NCCR C06 RR018823; NCCR C06 RR015455; NCCR P20 RR016434; P30 GM103342; NIH-NHLBI R01HL084285; NIH 5T32 HL007260; AHA Pre-doctoral fellowship 00001134

212 β3 Integrin Promotes Protein Ubiquitination and Prosurvival Signaling in Cardiomyocytes. Dorea L Pleasant, Kamala Sundararaj, Rebecca Harston, Sundaravadival Balasubramanian, Dhandapani Kuppuswamy; Medicine, MUSC.

Cardiac hypertrophy occurs in response to stress, such as an increase in hemodynamic overload. Upon hypertrophic stimulus, β3-integrin, a cell surface receptor that mediates nonreceptor tyrosine kinases (NTKs), under-goes activation. Using β3-integrin germline knockout (β3/-/-) mice, our recent work shows that beta3-integrin is required for ubiquitin (Ub)-mediated prosurvival signaling during early pressure overload (PO) in cardiomyocytes. Further, attenuation of β3-integrin signaling during PO results in significant cardiomyocyte apoptosis and thus compromised ventricular function. Whereas β3-integrin is critical for cardiomyocyte survival, our additional work revealed that it contributes to cardiac fibrosis. Therefore, our goal is to further elucidate the prosurvival role of β3-integrin specifically in cardiomyocytes and its downstream key players, such as NTKs, E3 ligases, ubiquitin and pro-apoptotic proteins. We have generated mice with cardiomyocyte specific, conditional deletion of β3-integrin (CMAlgtb3) for use in PO studies. Towards achieving this goal, β3-integrin LoxP mice were obtained (Washington University, St. Louis) and bred with cardiac troponin-T (Tnnt2) -Cre mice (Albert Einstein College of Medicine, New York). Offspring have been genotyped, bred and appropriate colonies have been established. The resulting mice contain a double transgenic system for cardiac specific expression of Cre, under the control of Tnnt2 promoter, and temporal manner using a Tet-On system (reverse tetracycline transactivator, rtTA). CMAlgtb3 and wild-type (WT) mice were treated with or without doxycycline (DOX) and subjected to PO by transverse aortic constriction (TAC) for 72 h or 1 week to promote left ventricular hypertrophy (LVH). Towards our goal, protein and tissue from these mice were analyzed for changes in β3-integrin, NTKs, Ub, several apoptotic proteins including caspase-3 and cIAP1 (cellular inhibitor of apoptosis, an E3 ligase). These studies seek to identify potential targets and develop novel therapeutic methods to encourage cardiomyocyte survival and prevent/delay maladaptive changes in hyper-trophying myocardium. NIH RHL092124; NIH T32 HL07260

213 Interferon Alpha Reduces Nitric Oxide Production in Endothelial Cells By Altering Endothelial Nitric Oxide Synthase Transcription and Phosphorylation. Joy N J Buie1, Robin Muise-Helmericks3, Jim C Oates1; 1Microbiology and Immunology, MUSC, 3Regenerative Medicine and Cell Biology, MUSC, 4Rheumatology and Immunology, MUSC.

Introduction: Patients with systemic lupus erythematosus (SLE) develop atherosclerosis prematurely without conventional cardiovascular risk factors. Type I interferons are elevated in SLE patients and are strongly associated with vascular endothelial dysfunction (VED), a first step in the development of atherosclerosis. VED results from diminished expression of endothelial nitric oxide synthase (eNOS) and nitric oxide (NO) bioavailability. Herein, we examined the impact of interferon alpha (IFN-alpha) on eNOS gene and protein expression and on NO production in primary human umbilical vein endothelial cells (HUVECs). Methods: HUVECs were treated with of IFN-
alpha (1000IU) at 6hrs in the presence or absence of bradykinin (1 and 25nM). Cells were examined for eNOS gene expression using RT2PCR. mRNA stability was analyzed using an Actinomycin D (10ug/ml) based mRNA stability assay while changes in heteronuclear RNA (hnRNA) were examined using PCR. Protein abundance and post-translational modifications of eNOS (peNOS Ser1177 and Thr495) were evaluated using Western blot analyses. NO production was detected by flow cytometry using the NO sensitive dye DAF-FM (4-Amino-5-Methylamino-2',7'-Difluorofluorescein) Diacetate. Results: HUVECs treated with IFN-alpha at 1000IU exhibited a 50% reduction in eNOS gene expression after 6hrs (p<0.005). Changes in eNOS mRNA stability were insignificant, however, a 48% reduction in hnRNA expression was observed (p<0.05) suggesting that IFN alpha may impair eNOS transcription. IFN-alpha also reduced total eNOS expression and increased post-translational phosphorylation of eNOS at the threonine 495 site 1.7 fold. These changes were reversed by treatment with bradykinin (25nM). Lastly, pre-incubation with IFN-alpha lead to a 40% reduction in NO production (p<0.05). However, NO production was restored more than 50% with addition of bradykinin treatment. Conclusions: IFN-alpha quenches the expression and activation of eNOS along with subsequent NO synthesis. These data further support a role for IFN-alpha in the development of endothelial dysfunction that may lead to atherosclerosis in SLE populations.

214 Understanding the Role of Estrogen Receptor Alpha in Plasmacytoid Dendritic Cell Development and Function in Systemic Lupus Erythematosus

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Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease that affects women at a 9:1 ratio compared to men. Previous work in our laboratory showed that estrogen receptor alpha (ERa) deficient lupus prone mice have increased survival and less renal disease compared to wild type lupus prone mice. We hypothesize that ERa deficiency improves SLE by reducing the innate immune systems ability to respond to this immune activation. To study the innate immune response this research focuses on the role of unliganded ERa in Toll-like receptor (TLR) mediated type I interferon (IFN) production. ERa deficiency significantly reduced the expression of type I IFN signature genes in response to TLR7 and 9 agonists in bone marrow derived dendritic cells from lupus prone mice under estrogen free conditions. Since pDCs produce large amounts of type I IFNs, we investigated the impact of ERa on pDC development and production of IFN. When total bone marrow from lupus prone mice was cultured under estrogen free conditions, ERa deficiency significantly reduced the number of cells producing IFN in response to TLR7 and 9 ligands. ERa deficiency also reduced the percentage of pDCs obtained from estrogen free cultures of total bone marrow. To determine if ERa deficiency alters pDC numbers in vivo, bone marrow and spleen pDC numbers were measured. ERa deficiency significantly reduced the percent and number of pDCs in bone marrow while the percent and number of pDCs remained unchanged in the spleen. In conclusion, absence of ERa reduced the percentage of IFN producing cells and pDCs in estrogen free bone marrow cultures. Additionally, ERa deficiency reduced the number of pDCs in the bone marrow of lupus prone mice. The reductions in pDC number and function occurring in the absence of ERa may be responsible for ameliorating disease in lupus prone mice. UL1 TR000062; Ralph H. Johnson VAMC.

215 Collagen Homeostasis in the PDL is Dependent on the Regulation of Transglutaminase Activity By SPARC

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The periodontal ligament (PDL) is a connective tissue that joins the tooth to the alveolar bone socket. PDL is primarily composed of collagen type I, and has a high turnover rate of the extracellular matrix (ECM) as compared to other collagen rich tissues. The high turnover rate of PDL coupled with the ease of accessibility of this tissue, renders PDL as a prime model system for investigating the molecular mechanisms of collagen fibril assembly and deposition. Collagen binding proteins, such as SPARC, are critical in collagen secretion and incorporation into the ECM. SPARC is a matricellular protein with anti-proliferative and counter-adhesive activities in vitro. SPARC is also a substrate for transglutaminase (TG), an enzyme that forms irreversible covalent cross-links in the ECM. SPARC-null mice have significant deficiencies in collagen volume fraction, fiber thickness, and overall morphology in PDL, which was associated with decreased mechanical strength of SPARC-null PDL as compared to wild type PDL. In addition, SPARC-null mice have increased susceptibility to periodontal disease, as measured by alveolar bone and PDL collagen loss in response to lipopolysaccharide injections. We hypothesized that the decreased collagen fibril thickness in SPARC-null mice was dependent upon an increase in TG cross-linking of collagen I. Using a novel organ culture system we have demonstrated SPARC-null PDL has increased TG activity, including an increase in TG-modified collagen I. We have used cyanogen bromide fragmentation of collagen to further confirm TG-modification of collagen I. Furthermore, in vivo inhibition of TG activity in SPARC-null PDL increases collagen fibril thickness. These data suggest that SPARC is a regulator of TG cross-linking of collagen I, and that TG cross-linking is one component that determines collagen fibril thickness in PDL. 1F30DE023009; Veterans Administration Merit Award.

216 Are Specific Residency Program Characteristics Associated with the Pass Rate of Graduates on the ABFM Certification Examination?

Lisa D Mims, Peter J Carek; Family Medicine, MUSC.

Introduction: Board certification pass rate has become a measure of quality for Family Medicine residency programs. The effect of program characteristics on these pass rates has not been studied. The purpose of this study is to evaluate the effect of various program characteristics on first-time ABFM board pass rates. Methods: Using information from the Frieda Online, AAFP and NRMP, program characteristics were obtained. Three and five-year aggregate ABFM board pass rates were calculated.
Descriptive statistics were used to summarize the data. The relationship between program characteristics, such as accreditation status, initial match rates and participation in curriculum innovation and first-time board pass rates were analyzed using chi square. Significance was defined as p<0.05 level of confidence. Results: Fifty-two percent of residency programs have ABFM board pass rates ≥ 90%. Both three and five-year aggregate board pass rates were significantly associated with regional location (p=0.0020 & 0.0092, respectively), program size (p=0.0177 & 0.0017, respectively), and accreditation cycle length (p=0.0001 for both). Innovative curriculum, including opportunities for international experience (p=0.0001 for both) and alternative medicine (p=0.0075 & p=0.0003), were also significantly associated. Curriculum in integrative medicine was statistically significant for five-year aggregate board pass rate (p=0.0174) but not for the three-year aggregate group (p=0.1816). Location type (urban, suburban, rural, or inner-city), program structure, salary, moonlighting, availability of tracks, P4 participation, and additional training opportunities beyond the programs accredited length were not associated. Conclusion: The percent of first-time takers successfully completing the ABFM certification examination is associated with several residency program characteristics, including regional location, program size, accreditation cycle length, opportunities for international experiences, and curriculum in alternative medicine. The underlying issues, especially for location and program size, require additional study, as low pass rates have adverse effects on programs in terms of the RC-FM cycle length.

217 A Double-blind, Randomized, Placebo-controlled Clinical Trial Evaluating Fibrin Sealant in Thyroidectomy Closure, Colin W Fuller, Shaun A Nguyen, Marion B Gillespie, Joshua D Hornig; MUSC.

Fibrin sealants such as Tisseel and Evicel (derived from bovine and human plasma, respectively) use thrombin and fibrin in an aerosolized two-component system for achieving an intraoperative water-tight surface seal. Originally developed for use in cardiovascular anastomoses, these products may also prove beneficial for achieving hemostasis when bleeding occurs from a diffuse surface without obvious discreet vessels, such as split-thickness skin graft donor sites and the thyroidectomy surgical bed. Because of the thyroid gland's robust perfusion and proximity to vital neck structures, including the airway, hemotoma is the most devastating potential complication of thyroid surgery. To this end, many surgeons place a subcutaneous drain to prophylactically siphon peritracheal fluid collections, though debate exists as to which patients, if any, benefit from this. Within this context, fibrin sealants may provide sufficient or additional prophylaxis against these catastrophic complications. What’s more, the use of such a sealant may also shorten the time to safe drain removal, reducing postoperative discomfort, shortening hospital stay and saving valuable healthcare resources. We report the results of an ongoing double-blind, randomized, placebo-controlled clinical trial which seeks to evaluate Evicel's efficacy and safety in preventing hematoma and seroma - and in reducing drain output, drain time and hospital stay - for open total and hemithyroidectomies. At this time, the treatment group consists of 21 subjects, the placebo group 20 (N=41). After eliminating the highest and lowest two outliers in each group for each measure, drain time (p=0.002) and hospital stay (p=0.004) were significantly reduced in the Evicel group (34.6h, SD 11.13h; 39.8h, SD 13.1h respectively) vs. the placebo group (48.19h, SD 11.6h; 52.86h, SD 10.2h respectively). There was no significant difference in total drainage, nor in drainage in the first eight postoperative hours. No significant adverse events have occurred in either group. Ethicon, Inc.

218 Computational Model Predictions of Age and Hearing Loss Effects on Concurrent Vowel Identification, Ananthakrishna Chintanpalli, Jayne B Ahlstrom, Judy R Dubno; Otolaryngology - Head and Neck Surgery, MUSC.

Differences in formant and fundamental frequencies (F0) are important cues for segregating and identifying two simultaneously presented (concurrent) vowels. For older adults with normal and impaired hearing, concurrent vowel identification is substantially reduced, even when identification of single vowels is unaffected. To reveal mechanisms that may underlie these deficits, this behavioral and computational modeling study was designed to estimate age- and hearing-loss-related changes to the cochlea and auditory nerve (AN) that may alter phase locking to formants and F0s of concurrent vowels. Younger and older adults with normal hearing, and older adults with hearing loss listened to concurrent vowels with a range of F0 differences. Individual vowels were presented at 65 dB SPL for subjects with normal hearing and at 85 dB SPL for subjects with hearing loss, to minimize confounding effects of reduced audibility. Predictions from a computational AN model were used to estimate formant and F0 difference cues available for vowel identification by each of the three subject groups. Three versions of the model were developed based on known anatomical and physiological changes to the cochlea and AN due to increased age and hearing loss. For each group, average localized synchronized rate and template contrast were computed from AN responses to quantify phase locking to formants and F0s, respectively. Compared to scores for younger adults, identification of both vowels was reduced for older adults with normal hearing and further reduced for older adults with hearing loss. Preliminary model predictions revealed that phase locking to formants of both vowels declined with increased age and hearing loss, which differed based on vowel-pair formant characteristics. Assessment of vowel identification in the context of these model predictions may provide physiologically appropriate explanations of age- and hearing-loss-related peripheral-processing deficits for segregating and understanding target speech in complex listening environments. NIH/NIDCD

219 Multifunctional CD26hi Th17 Cells Eradiate Large Human Tumors, Michelle H Nelson, Stefanie Bailey, Logan Huff, Sreenath Kundimi, Chryystal Paulos; Microbiology & Immunology, MUSC.

Human CD4+ T cells differentiate into multiple effector subsets, but their distinct roles in anti-tumor immunity remain elusive. CD4+ T cell subsets enriched from bulk human CD4+ T cells [Th1 (CXCR3+), Th2 (CCR4+), and Th17 (CCR6+ or CD26hi)] were stimulated with anti-CD3 beads bearing agonists to either CD28 or ICOS and were then engineered with a chimeric antigen receptor that recognizes human mesothelioma. In vitro, ICOS costimulation proved superior to CD28 for augmenting the function of human Th1, Th2, CCR6+ Th17 and CD26hi Th17 cells, as indicated by elevated production of IFN-
gamma, IL-4 and IL-17A, respectively. Moreover, CD26hi Th17 cells possessed strikingly enhanced polyfunctionality compared to Th1, Th2 or CCR6+ Th17 cells, as demonstrated by their heightened capacity to co-secrete IL-17A, IFN-γ, IL-22, IL-2, and TNF-alpha simultaneously. Compared to other enriched T cell subsets, a greater percentage of CD26hi Th17 cells exhibit an effector memory phenotype. Additionally, CD26hi Th17 cells expressed higher levels of ICOS, but lower levels of the regulatory-associated molecule CD39 on their cell surface than the other subsets. In vivo, CD26hi Th17 cells more efficiently reconstituted immunodeficient hosts and persisted long-term. Furthermore, CD26hi Th17 cells possessed a superior ability to kill large human tumors (>150mm²) when infused into mice compared to Th1, Th2 or CCR6+ Th17 cells. These results suggest that the generation of multifunctional, long-lived human Th17 populations could be instrumental to the design of novel, effective T cell-based cancer therapies.

**220 Oligoamines Containing 3-5-3 Carbon Backbone Architecture Are Endowed with Both Anticancer and Antibacterial Activity.** Boobalan Pachaiyappan1, Shannon Nowotarski2, Wang Bo3, Melissa Sokolosky4, Steven Holshouser5, Robert Casero6, Yong-Mei Zhang7, Patrick Woster8; 1Drug Discovery and Biomedical Sciences, MUSC, 2Sidney Kimmel Comprehensive Cancer Center, John Hopkins University, 3Biochemistry and Molecular Biology, MUSC.

Small molecule oligoamines that mimic the naturally occurring polycationic alkylamines has garnered considerable attention from drug discovery perspective. In this presentation, I will share the promising effect of optimized oligoamines containing 3-5-3 linkers that are endowed with both anticancer and antibacterial activities. For the cancer project, we studied the efficacy of our novel compounds against the validated epigenetic target, lysine-specific demethylase 1 (LSD1). Among nine compounds tested, three of them displayed 95% inhibition or greater at 10 µM in a recombinant LSD1 assay. Compound BP-15, a substrate-competitive inhibitor (Ki = 2.4 µM), exhibited an IC50 of 4 µM against the Calu-6 human lung adenocarcinoma line in an MTS cell viability assay. Following treatment with BP-3, BP-5 and BP-15, Calu-6 cells exhibited a statistically significant increase in the mRNA expression for the aberrantly silenced tumor suppressor genes SFRP2, HCAD, GATA4, and p16. Structure-based modeling of 6b in LSD1 active site revealed key H-bonding and hydrophobic interactions that govern the enzyme-inhibitor binding. For the bacteria project, among the 18 oligoamines that were tested against Gram-negative Pseudomonas aeruginosa (Pa), 15 of them displayed an equal or lower MIC values compared to kanamycin. One of the best compounds, BP-7, displayed a MIC value of 8 µg/ml against Pa. In the time-kill kinetics experiment, compound BP-7 exhibited a concentration-dependent, rapid killing of Pa achieving a 6-log reduction (99% reduction) in viable cell numbers within 3 hours. Thus, the oligoamines disclosed in this presentation hold promise to be novel class of potential anticancer and broad-spectrum antibacterial agents with a scope for further optimization.

**221 Selective Class I and II Histone Deacetylation Inhibitors Alter Stability of HDAC-co-repressor Complexes.** Hsiao S Wang, Lillianne G Harris, Santhosh Mani, Donald R Menick; Cardiology, MUSC.

Introduction Alterations in expression and activity of different genes have been implicated in the pathogenesis of heart failure. Our lab has shown that HDAC-repressor complexes play a critical role in the upregulation Sodium Calcium Exchanger (Ncx1) and HDAC inhibition causes changes that attenuated cardiac remodeling during cardiac hypertrophy and heart failure. Thus, treatment with HDAC inhibitors has been proposed as a potential strategy for treatment of cardiac hypertrophy and heart failure. HDAC inhibitors repress deacetylase activity but we propose that they also affect HDAC confirmation and interaction with other protein factors. We hypothesize that HDAC inhibitors affect the stability of the co-repressor complex with specific transcription factors and that this effect is dependent on the transcription factor. Results: Inhibition of HDACs in adult cardiomyocytes results in the greater stabilization of HDACs with co-repressor molecules that were recruited to the Ncx1 promoter through Nxx2.5 transcription factor. Compared to pan-HDAC inhibitor (TSA), MS 275, a selective class I HDAC inhibitor demonstrated stronger association between HDACs and co-repressors, suggesting that class I HDACs may affect via a more complex interaction. These results compliment ChIP experiments which also demonstrate enhanced recruitment of Sin3a at the proximal promoter of Ncx1. However, HDAC-repressor complex recruitment to the BNP promoter through YY1 transcription factor decreased complex stability. In vivo analysis, HDAC5 knockout mice reveal that the Sin3a-HDAC1/2 repressor complex is not recruited to the Ncx1 promoter in the absence of HDAC5. Conclusions: This work gives insight into part of the molecular mechanism of how HDAC inhibitors can affect the stability of the HDAC co-repressor complex in cardiac hypertrophy and heart failure. In addition, we demonstrated the Class IIa HDACs are required for the recruitment of the Sin3a/HDAC1/2 co-repressor complex to specific transcription factors on the target promoter. AHA 09GRNT2020202; NIH T32 HL 007260; NIH RO1 HL066223

**222 Selective Inhibition of Class I But Not Class IIb Histone Deacetylases Exerts Cardioprotection From Ischemia-Reperfusion.** Sverre E Aune, Santhosh K Mani, Donald R Menick; Medicine, MUSC.

While inhibition of class I/II histone deacetylases (HDACs) protects the mammalian heart from ischemia reperfusion (IR) injury, class specific effects remain unexamined. We hypothesized that selective inhibition of class I HDACs would preserve left ventricular (LV) function following IR in isolated hearts. Male Sprague Dawley rats (n=6 per group) were i.p. injected with DMSO (vehicle), the class I HDAC inhibitor entinostat (MS-275), the HDAC6 (class IIb) inhibitor tubastatin A (TubA), or the class I/IIb inhibitor trichostatin A (TSA). After 24 h, hearts were isolated and perfused in Lagendorf mode at 75 mm Hg for 30 min, and then subjected to 30 min ischemia and 120 min reperfusion. Another group of hearts from vehicle treated animals were perfused in Langendorff mode for 30 min only (baseline). A saline filled balloon attached to a pressure transducer was placed in the LV to monitor contractile function. After perfusion, LV tissue was collected for measurements of antioxidant protein levels.
and infarct area. Following IR, infarct area, diastolic and systolic pressures, +dP/dtmax, +dP/dtmax and rate pressure product were significantly restored toward baseline levels with MS-275. TSA significantly preserved +dP/dtmax. Contractile function was not preserved in hearts treated with TubA vs vehicle. Mitochondrial superoxide dismutase (SOD2) and catalase protein in MS-275 hearts were increased following I-R. This was associated with a reduction in phosphorylation at the nuclear exclusion site of the SOD2/catalase transcription factor FoxO3a. TubA treatment was associated with significantly decreased catalase levels in comparison to baseline hearts. Class I HDAC inhibition elicits pharmacologic preconditioning by increasing endogenous antioxidant enzymes SOD2 and catalase, a result of nuclear retention of FoxO3a. The protective effects of HDAC inhibitors in I-R can be ascribed to selective inhibition of class I HDACs. Preliminary results suggest that inhibition of class I HDACs is also protective against IR in vivo. NIH T32 HL007260-37

223 Molecular Chaperone Gp96 is a Novel Therapeutic Target of Multiple Myeloma. Yunpeng Hua1, Shai White-Gilbertson1, Joshua Kellner1, Saleh Rachidi1, Ronald DePinho2, Gabriela Chiosis2, Zhai Li1, Bei Liu1; 1Microbiology & Immunology, MUSC, 2The University of Texas MD Anderson Cancer Center, *Molecular Pharmacology, Memorial Sloan Kettering Cancer Center.

Purpose: gp96 is a key downstream chaperone in the ER to mediate unfolded protein response (UPR) and the pathogenesis of multiple myeloma (MM) is closely linked to dysregulated UPR. In this study, we aimed to determine the roles of gp96 in the initiation and progression of MM in vivo and in vitro. Experimental design: We generated a mouse model with over-expression of XBP1s and conditional deletion of gp96 in B cell compartment simultaneously to identify the roles of gp96 in the development of MM in vivo. Using a shRNA system, we silenced gp96 in multiple human MM cells and examined the effect of gp96 knockdown on MM cells by cell proliferation, cell cycle analysis, apoptosis assay, immunohistochemistry and human myeloma xenograft model. The anti-cancer activity of gp96 selective inhibitor, WS13 was evaluated by apoptosis assay and MTT assay. Results: Genetic deletion of gp96 in XBP1s-Tg mice attenuates multiple myeloma. Silencing of gp96 causes severe compromise in human multiple myeloma (MM) cell growth through inhibiting Wnt-LRP-survivin pathway. We also confirmed that knockdown of gp96 decreased human MM growth in a murine xenograft model. The targeted gp96 inhibitor induced apoptosis and blocked MM cell growth, but did not induce apoptosis in pre-B leukemic cells. We have demonstrated that myeloma growth is dependent on gp96 both genetically and pharmacologically. Conclusions: gp96 is essential for MM cell proliferation and survival, suggesting that gp96 is a novel therapeutic target for multiple myeloma. South Carolina Clinical & Translational Research Institute KL2RR029880 and UL1RR029882; American Cancer Society IRG-97-219-14; NIH AI070603 and AI077283

224 Novel Membrane Targeting Antibacterials Containing Oligoamine Linkers. Bo Wang1, Boobalan Pachaiyappan1, Jordan D Gruber1, Patrick M Woster2, Yong-Mei Zhang1; 1Biochemistry and Molecular Biology, MUSC, 2Drug Discovery and Biomedical Sciences, MUSC.

Antibiotic resistance is one of the greatest threats to human health. The lack of new antibiotics being developed further exacerbates the problem of antibiotic resistance. In this study, a novel class of drug candidates containing oligoamine linkers were synthesized and evaluated for their antibacterial activities. Compared to the clinical antibiotic kanamycin, 9 of 18 oligoamines displayed lower MIC value against both Gram-positive and Gram-negative pathogenic bacteria including Staphylococcus aureus (Sa), Pseudomonas aeruginosa (Pa) and Escherichia coli (Ec). The most active compound, compound 15, was 4 times more potent than kanamycin against Sa, Pa and Ec, with MIC values of 2 µg/ml, 8 µg/ml and 2 µg/ml, respectively. Compound 15 was also found to have a synergistic effect with kanamycin against Sa, Pa and Ec. Moreover, compound 15 protected Caenorhabditis elegans against Pa infection and exhibited strong inhibition against drug-resistant biofilm growth, as well as promoted biofilm dispersal of Pa. Time-kill kinetics experiments showed compound 15 exhibited concentration-dependent, rapid killing of all the tested strains, achieving a 6-log reduction in viable cell numbers within 3 hours. Toxicity of compound 15 was determined both in 293T cell and C. elegans, and the selective indices ranged from 5.3 to 32. Interestingly, we found that compound 15 exhibited a strong membrane depolarizing effect on all the strains tested. Overall, the results demonstrated that the oligoamines hold promise as a new potential class of broad-spectrum bactericidal antibacterial agents with a unique mechanism of action. DOD/DM090161; SCTR 1402 UL1TR000062

225 Maximizing Intratumoral Drug Accumulation During Combination Therapy of Radiofrequency Ablation with Thermosensitive Liposomal Doxorubicin: A Computational Study and In-vivo Evaluation. Christian Rossmann, Dieter Haemmerich; Pediatrics, MUSC.

Radiofrequency ablation (RFA) is a clinical, image-guided cancer treatment utilizing localized heat delivered via minimally-invasive electrode. Recent studies suggest improved efficacy of combining RFA with localized drug delivery by liposomal drug carriers releasing doxorubicin (DOX) upon supraphysiological temperatures. The purpose of this study was to develop mathematical models for identification of optimal heating strategies to maximize local drug accumulation. We used three dimensional computer models to simulate RFA for 5 to 60 minutes with target tissue temperatures between 60 and 95°C and to predict the amount of DOX in plasma, interstitium and cells considering temperature-dependent liposomal release and tissue DOX uptake. Model results were evaluated via fluorescence image data of DOX concentrations in 9 excised swine livers of equivalent in-vivo experiments (30 min TDOX administration, 12 min ablation). Total amount of DOX deposited within the tumor tissue increased approx. linearly with total ablation time and was minimal for the 5min and maximal for 60 minute treatment (25 vs. 177µg). Increased delay between drug administration and RFA significantly decreased amount of
DOX delivered to the target site due to plasma clearance of liposomal drug carriers (59% DOX reduction for RFA 2h later administration). In both mathematical models and in vivo studies most DOX (80-95%) was delivered just outside the thermal lesion due to temperatures (40-45°C) triggering the release of DOX. Combination of RFA and liposomal DOX may reduce local tumor recurrence as it facilitates increased tissue destruction due to amount of DOX delivered within the margin. The computer simulation model allowed accurate prediction of intratumoral and peripheral drug accumulation and offers promising opportunities to optimize this combination therapy. Celsion Corporation

226 ER Chaperon Gp96: Essential Regulator for Melanoma Growth and Melanogenesis. Yongliang Zhang1, Kristi L Helke2, Saleh Moha Rachidi3, Sergio G Coelho4, Vincent J Hearing5, Shaoli Sun6, Bei Liu7, Zhihai Li1; 1Microbiology & Immunology, MUSC, 2Comparative Medicine, MUSC, 3Laboratory of Cell Biology, NCI, 4Pathology & Laboratory Medicine, MUSC.

Heat shock protein gp96 (HSP90b1, grp94) is an endoplasmic reticulum chaperone of the HSP90 family. Clinical relevance analysis show high gp96 expression is highly associated with melanoma transformation, progression and cancer patient survival. To address the underlying mechanism for clinical association between high level of gp96 and melanoma progression, we knockdown gp96 in malignant melanoma cell line B16 cells. We found gp96 inhibition does not suppress in vitro tumor proliferation, but robustly inhibit orthotopically transplanted melanoma growth. Mechanistic study demonstrates that gp96 deletion compromises VEGF-A expression and inhibited tumor-associated angiogenesis but independent of host adaptive immunity. These results suggest that altered tumor microenvironment upon gp96 knockdown was responsible for the delayed tumor growth in vivo. Unexpectedly, we also observed that melanin production was significantly inhibited in B16 knockdown cells (B16-KD), which correlated with the reduced tyrosinase activity and melanosome translocation but not its expression in B16-KD cells. Further, mice with melanocyte-specific deletion of gp96 displayed decreased pigmentation. Mechanistic study revealed that the defect in melanogenesis can be rescued by activation of the canonical Wnt pathway, consistent with the critical roles of gp96 in chaperoning Wnt-co-receptor LRP6. Thus, our study has uncovered two novel roles of gp96 in melanogenesis can be rescued by activation of the canonical Wnt pathway, consistent with the critical roles of gp96 in chaperoning Wnt-co-receptor LRP6. Thus, our study has uncovered two novel roles of gp96 in melanogenesis and in facilitating melanin synthesis. NIH AI070603, AI077283

227 The Role of MicroRNA in Cochlear Lateral Wall Degeneration of Age-related Hearing Loss. Michael W Moore5, Yazhi Xing6, Christopher T Hensley6, Victoria J Findlay7, Jeremy L Barth8, Hainan Lang9; 5Microbiology & Immunology, MUSC, 6Pathology, MUSC, 7Regenerative Medicine, MUSC.

Age-related hearing loss is the most common type of hearing loss in humans, affecting nearly two-thirds of adults greater than 70 years of age. Mounting evidence suggests that non-sensory inner ear cells, specifically spiral ligament fibrocytes in the cochlear lateral wall, are integrally involved in this aging process. Previous studies from our laboratory demonstrated that the replicative ability of cells in the cochlear aging wall decreases with age for unknown reasons. Cellular senescence contributes heavily to the tissue aging process as do microRNAs, small non-coding RNA involved in the regulation of gene expression. While microRNA expression has been studied in the inner ear over the last several years, none of these studies have specifically focused on lateral wall tissues of aged cochlea. We hypothesized that age-related expression changes of specific microRNAs have a negative effect on genes that regulate extracellular matrix stability and cell proliferation, resulting in non-sensory cell dysfunction and senescence. Our animal model utilized young (1-3 months) and older (18 months) CBA/CaJ mice from a colony with known slowly-progressive hearing loss. Auditory function for these animals was evaluated by measuring auditory brainstem response thresholds. Cochleae were then harvested and RNA isolated from the lateral walls for high-throughput microarray analysis of microRNA and mRNA. Comparisons of young versus aged samples identified 149 microRNAs and 1074 mRNAs expressed in an age-dependent manner. Bioinformatic analysis of differentially expressed microRNAs identified several candidates having potential mRNA targets linked to aging processes such as extracellular matrix replenishment and cell proliferation. Review of mRNA expression data confirmed that many of these putative targets had altered expression levels in aged samples. Expression profiles for several candidate microRNAs and their putative downstream mRNA targets were validated with real-time PCR. Further studies will assess changes in auditory thresholds following manipulation of candidate microRNA expression. NIH R01 DC7506; P50 DC0422

228 Heptanol Application to the Mouse Round Window: A Model for Studying Cochlear Lateral Wall Regeneration. Shawn M Stevens1, Yazhi Xing2, Christopher Hensley2, Juhong Zhu1, Judith R Dubno1, Hainan Lang3; 1Otolaryngology-Head and Neck Surgery, MUSC, 2Pathology and Laboratory Medicine, MUSC.

Objective: Identify cells capable of supporting cochlear lateral wall regeneration. Study Design: Prospective Controlled Trial; Basic Science Research. Background: Human presbyacusis occurs, in part, secondary to age-related degeneration of cochlear lateral wall structures such as the stria vascularis and spiral ligament fibrocytes. This degeneration is likely linked to diminished regenerative capacity of lateral wall cells with age. While lateral wall regeneration is known to occur after an acute insult, this process remains poorly understood and the cells capable of self-replication un-identified. We hypothesized that spiral ligament fibrocytes constitute these proliferative cells. Subjects and Methods: To test the hypothesis, an acute ototoxic insult was created in normal hearing, young adult mice via cochlear exposure to 1-heptanol. Sacrifice occurred at 1-60 days post-treatment. Auditory brainstem responses, EdU Assay and immunostaining were used to assess regeneration. Results: Post treatment hearing thresholds were elevated in nearly all treated mice. Selective fibrocyte apoptosis and strial injury were observed at the time of peak hearing loss around 1-7 days post-treatment. Cellular proliferation was detected in the region of type II fibrocytes during this time. Hearing thresholds plateaued at 7 days post-treatment followed by a significant recovery of both hearing and morphologic appearance. Permanent outer hair cell degeneration was observed. Conclusions: Heptanol application to the round window of young adult mice is a rapid, selective, and reliable technique for investigating proliferation in the cochlear lateral wall. The
data indirectly showed spiral ligament fibrocytes may be the proliferative cells of the cochlear lateral wall. Further studies of this process are needed. NIH R01 DC007506; NIH P50 DC000422

229 A Quantitative Increase in Regulatory T Cells (Treg) Controls Development of Vitiligo, Shilpak Chatterjee1, Jonathan Eby2, Hye-Kap Kang3, Amir A Al-Khami4, Navtej Kaur4, Osama Naga4, Caroline Le Poole2, Shikhar Mehrotra4; 1Surgery, MUSC, 2Pathology, Loyola University.

Vitiligo is a T cell mediated autoimmune disease of the skin, with CD8+ cytotoxic T cells held responsible for the progressive loss of melanocytes from the epidermis. Previous reports suggest that IFN-gamma is a critical cytokine involved in the development of vitiligo, and may be responsible for shifting the balance between CD8+ T cells to immunosuppressive Treg in favor of melanocyte reactive cytotoxic T cell responses. We thus propose that promoting regulatory responses at the expense of effector responses can overcome immune activation and halt the progression of vitiligo. To test this, we made use of a recently developed mouse model of vitiligo with spontaneous depigmentation, the h3TA2 mouse. First, we established the relative importance of IFN-gamma in disease development by comparing depigmentation in h3TA2 mice lacking expression of IFN-gamma and mice knockout for TNF-alpha or perforin. As depigmentation was significantly impaired only in IFN-gamma knockout mice, these models confirm a central role for IFN-gamma in vitiligo development while suggesting that neither TNF-alpha or perforin/granzyme are solely responsible for cytotoxicity of skin-infiltrating T cells towards melanocytes. We further observed that regulatory T cells were relatively abundant in IFN-gamma deficient h3TA2 mice, confirming an inhibitory role for IFN-gamma in Treg polarization and more importantly, suggesting that enhancing Treg function can be therapeutic in vitiligo and prevent progressive depigmentation. Indeed, depletion of Treg employing anti-CD25 antibodies fully restored the depigmentation phenotype in h3TA2, IFN-gamma knockout mice. We were thus poised to induce regulatory T cell responses in the h3TA2 mice using rapamycin, an FDA approved immunosuppressive drug commonly used to support organ transplantation. Rapamycin was well tolerated and induced lasting remission of vitiligo in mice treated at the onset of disease as well as in mice with established disease. We thus conclude that reduced regulatory responses are pivotal to the development of vitiligo in disease-prone mice, and that rapamycin may well be therapeutic for vitiligo patients with active disease. Surgery, MUSC; NIH R21 AR056524; NIH R01 AR057643; Cell Evaluation and Therapy Shared Resource, Hollings Cancer Center

230 Fli-1 is a Novel Regulator of the Proinflammatory Chemokines MCP-1 and RANTES, Mara L Lennard Richard, Tamara K Nowling, Xian K Zhang; Rheumatology, MUSC.

Regulation of proinflammatory cytokines and chemokines is a primary role of the innate immune response. Monocyte chemoattractant protein (MCP-1) and Regulated upon Activation, Normal T Expressed and Secreted (RANTES) are chemokines that recruit immune cells to sites of inflammation and have been shown to play a role in the pathogenesis of a variety of inflammatory mediated diseases including systemic lupus erythematosus. Expression of MCP-1 and RANTES is reduced in kidneys from mice with a heterozygous knockout of the Fli-1 transcription factor. Fli-1 is a member of the Ets family of transcription factors, which are evolutionarily conserved across several organisms including Drosophila, Xenopus, mouse and human. Ets family members bind DNA through a consensus sequence GGAAT, or Ets binding site (EBS). Transient transfection assays of the murine MCP-1 promoter indicate that the Fli-1 gene actively drives transcription in a dose-dependent manner while the Ets-1 transcription factor failed to drive transcription. Results indicate that while Ets-1 does not drive transcription from the MCP-1 promoter alone, it works synergistically with Fli-1 to enhance transcriptional activation. Synergistic enhancement of the MCP-1 promoter has also been observed between Fli-1 and the p65 subunit of NF-kappaB. Deletion analysis of the MCP-1 promoter indicates that proximal and distal regions of the promoter are important for activation of MCP-1. Transient transfection assays of the murine RANTES promoter indicate that the Fli-1 gene actively drives transcription in a dose-dependent manner. Surprisingly, Ets-1 acts differently on the RANTES promoter, driving transcription, albeit at a significantly lower level than Fli-1. Ets-1 and Fli-1 likely have at least one binding site in common on the RANTES promoter as Ets-1 acts as a dominant negative regulator of transcription from this gene locus. Taken together, these results demonstrate a previously undiscovered, novel transcriptional regulator of the proinflammatory chemokines MCP-1 and RANTES. NIAIMS AR056670; SCTR; NIH/NCR 0UL1 RR029882 and UL1 TR00062; Ralph H Johnson VA Medical Center

231 Higher Antioxidant Level with Decreased Mitochondrial Respiration and Glycolysis Correlates to Persistence of Human CD62Lhi T Cell, Pravin Kesarwani1, Amir A Al-Khami1, Gina Scurti2, Christina Voelkel-Johnson2, Elizabeth Garrett-Mayer3, Craig C Beeson4, Michael Nishiumi1, Shikhar Mehrotra4; 1Surgery, MUSC, 2Pathology, Loyola University, 3Microbiology & Immunology, MUSC, 4Biostatistics & Epidemiology, MUSC, 5Pharmacy, Drug Discovery and Biomedical Sciences, MUSC.

The mechanism and metabolic factors that attribute to the differential outcome of ex vivo expanded CD8+ T cells used for adoptive immunotherapy are not well understood. Here we show that CD62Lhi central memory (TCM) like phenotype bearing T cells exhibit increased expression of cell surface sulphhydril groups (-SH; thiols), a key target of redox regulation, and other anti-oxidant proteins as catalase, nuclear related factor 2 (NRF-2), superoxide dismutase 1 (SOD1) compared to T cells with CD62Llo effector memory (TEM) like phenotype. This increase of redox regulators in CD62Lhi T cells inversely correlates to the generation of reactive oxygen species (ROS), reactive nitrogen species (RNS), extent of T cell proliferation and glycolytic enzymes. Furthermore, tumor epitope specific TCR transduced T cells pretreated with a thiol donor N-acetylcysteine or rapamycin, a drug that favors the generation of a CD62Lhi TEM-like phenotype, also up-regulates cell surface thiols, anti-oxidative genes and down-regulates basal oxygen consumption rate, expression of mitochondrial biogenesis regulator PGC1-alpha, glycolytic enzymes leading to increased retrieval of CD62Lhi T cells in vivo. These data suggest that concomitantly increasing anti-oxidant capacity and
Introduction: Sphingosine kinase 1 (Sphk1) is a key enzyme in sphingolipid metabolism that produces sphingosine-1-phosphate (S1P), thus controlling cellular proliferation, migration, and cytokine production. We sought to study the effect of genetic deletion of Sphk1 on regulation of T-cell responses in a mouse model of melanoma by generating transgenic mice pMel on Sphk1 deficient background. Results: Our data suggests that Sphk1 deficient pMel mice showed reduced tumor progression after B16 murine melanoma were subcutaneously administered. In addition, the growth of B16 melanoma was slower when T-cells from the pMel or Sphk1-/− pMel transgenic mice were adoptively transferred to Rag−/− mice with established tumors. An increased infiltration of Sphk1−/−pMel T-cells was noticed at the tumor site as compared to WT controls. This suggests that loss of Sphk1 from T-cells was enhancing their ability to target the tumor site. We also found TGF-beta mediated suppression of IFN-gamma secretion was poorer in these T-cells suggesting that Sphk1−/− T-cells could have retained effectors function at the tumor site. While a comparative evaluation of T cells from pMel and Sphk1−/−pMel showed similarity in cell surface markers, activation status, proliferation and Th1 cytokine response upon TCR restimulation, we observed that Sphk1−/− T-cells showed greater IL-17 secretion. Under Th17/Tc17 polarizing conditions we also noticed a qualitative and quantitative increase in Th17 cells. Conclusion: It is possible that the enhanced anti-tumor T cell immunity noticed in Sphk1−/−pMel is dependent on the ability to make IL-17 and lesser susceptibility to suppression. **Dept. of Surgery; SCTR; Lipidomics Core, Cell Evaluation and Therapy Shared Resource, Hollings Cancer Center**

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**233 MKP-1 Regulates Early NFATc1-Dependent Osteoclastogenesis in RANKL-Induced Defined Progenitor Populations.** Michael S Valerio1, Bethany A Herbert1, Alfred C Griffin1, Keith L Kirkwood2, Craniocranial Biology, MUSC, 2Microbiology and Immunology, MUSC, 3Biochemistry and Molecular Biology, MUSC.

Osteoclasts (OC) are derived from the hematopoietic progenitors and respond to cytokines; macrophage colony stimulating factor (M-CSF) and receptor activator of NF-κB ligand (RANKL). The key event in this response is RANKL-driven activation of MAPK and NF-κB signaling pathways, resulting in nuclear translocation of transcription factor NFATc1, the master regulator of osteoclastogenesis. Regulation of this process is in part controlled by MAPK activity. MAPK phosphatase 1 (MKP-1), a protein tyrosine and threonine phosphatase (encoded by the gene Dusp1), functions to dephosphorylate and subsequently inactivate MAPK signaling. Objective: To evaluate the role of MKP-1 in RANKL-induced osteoclastogenesis. Materials and Methods: OCP, defined as B220/CD45negGR1negCD11bflow/negCD115pos, were obtained from WT and Dusp1−/− bone marrow through magnetic enrichment using CD11b-conjugated beads. OCP were stimulated with M-CSF (25ng/ml) and RANKL (50ng/ml) for 3 days. Cells were fixed or extracted for RNA and protein following stimulation. TRAP assay was used for OC enumeration. qPCR using Nfatc1, Tm7sf4 (DC-STAMP), Ocstomp and Acp5 primers determined mRNA content. Nuclear protein extracts were obtained to determine NFATc1 nuclear content using the TransAM ELISA kit. Results: Results indicate that Dusp1−/− derived OCP form less numerous, significantly smaller and less functional OC compared to WT controls. mRNA expression of the key OC genes, Nfatc1, Tm7sf4 (DC-STAMP), Ocstomp and Acp5 primers was reduced in Dusp1−/− OC. Finally, NFATc1 nuclear content was also significantly reduced in Dusp1−/− post-stimulation and use of p38 and JNK inhibitors rescued NFATc1 nuclear translocation. Conclusion: Collectively, our data supports that MKP-1, a negative regulator of MAPKs, is necessary in early osteoclastogenesis in response to RANKL-induced signaling. Interestingly, this data reveals that MKP-1 positively controls OC formation in response to RANKL by regulating NFATc1 nuclear translocation. Clinical Significance: These data help support the biological underpinnings of physiologically-induced OC formation, which may be useful in the development of novel therapeutic targets for bone-resorptive disease. **NIH R01DE018290 and T32DE017551-05**
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