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 4th, 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 SRD2011 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). 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, 203, 204, 205, 206, and 207. 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 SRD2011 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 4th. 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 11th 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, and for Health Disparities - 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 from 12:00 pm.

Awards Ceremony:
The Awards Ceremony will follow the Keynote Lecture (4:00 pm) in the Drug Discovery Auditorium, starting just after 5:00 pm. In each session there will be a 1st place prize of $500 and a 2nd place prize of $200. The Sigma Xi, Interprofessional Research, VAMC Research, and Health Disparities Awards 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 at approximately 11:00 am.
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 Student Research Day event

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The Student Research Day Committee

Christopher Davies, College of Graduate Studies; Thomas Dix, College of Pharmacy; Teri-Lynn Herbert, Library; Paul Jacques, College of Health Professions; Teresa Kelechi, College of Nursing; Maralyne Mitcham, College of Health Professions; Susan Reed, College of Dental Medicine; Mike Schmidt, College of Medicine; Debbie Shoemaker, College of Graduate Studies; Zachary Cope, Elizabeth Little and Vondina Brown, Student Representatives; Steven Kubalak, College of Graduate Studies (Chair).
SRD2011 – SCHEDULE

FRIDAY, NOVEMBER 4th – Research Presentations

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

ORALS – CHP building A, 151-A Rutledge Ave, 2nd Floor: Rooms 201 – 207: 11:45 am – 3:15 pm
Bioengineering Building (BE), 1st Floor, Room 112: 11:45 am – 3:15 pm

Schedule of Oral Sessions:

<table>
<thead>
<tr>
<th>Room</th>
<th>11:00 am</th>
<th>12:00 pm</th>
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<td>CHP206</td>
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</table>

Keynote Address: Drug Discovery Auditorium, 4:00 – 5:00pm

"From Sarcomeres to Signaling to Stem Cells"
By: Dr. Mark Sussman
Distinguished Professor of Biology
Chief Research Scientist, SDSU Heart Institute
Chair, Basic Cardiovascular Sciences Council, AHA
San Diego State University
San Diego, CA
LOCATION OF ORAL PRESENTATIONS – SESSIONS 13-20

College of Health Professions, Building-A, 151-A Rutledge Avenue, 2nd floor
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
Follow signs to Room BE 112, first floor of the new Bioengineering Building
Student Research Day 2011 - Program

POSTER PRESENTATIONS

Harper Wellness Center Gym

<table>
<thead>
<tr>
<th>Session</th>
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<tr>
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<td>Undergraduate – I</td>
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<td>8:30 am - 12:00 noon</td>
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<td>Session 2</td>
<td>Undergraduate – II</td>
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ORAL PRESENTATIONS

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

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<td>12:00-3:15</td>
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SESSION 1: Undergraduate I

001 The Effects of Beta-arrestin 1 and 2 Overexpression on TLR-induced Inflammatory Cytokine Expression in RAW 264.7, Rocky C Wong¹, Hongkuan Fan², Perry Halushka², James Cook², Sarah Ashton², Peifeng Li²; ¹CofC, ²Neuroscience, MUSC.

002 Retinyl Ester Accumulation in the Absence of Light, Colleen K Sheridan¹, Yiannis Koutalos²; ¹Biology, CofC, ²Ophthalmology, MUSC.

003 Analgesic Effects of Two Sessions of Postoperative Left Prefrontal Cortex Repetitive Transcranial Magnetic Stimulation, Luke Dong¹, Scott T Reeves¹, Jeffery J Borckardt², Mark S George², Peggy Edgerton¹, Alok Madan², Larry C Field¹; ¹Anesthesiology and Perioperative Medicine, MUSC, ²Psychiatry and Behavior Sciences, MUSC.

004 Determining the Variability in Developing Post-Stroke Pneumonia, Gabriela R Keeton, Daniel T Lackland; Neurosciences, MUSC.

005 The Role of NPY in the Anxiety Associated with Cocaine Abstinence, Sonam Bhimbra¹, Parrish Waters², Ronald E See²; ¹CofC, ²Neuroscience, MUSC.

006 Generation of Nicotinamide Adenine Dinucleotide Phosphate (NADPH) in Vertebrate Photoreceptors, Leopold Adler IV¹, Yiannis Koutalos², Chunhe Chen²; ¹Physics and Astronomy, CofC, ²Ophthalmology, MUSC.

007 Changes in Vasopressin Receptor Levels in Extended Amygdala Affect Anxiety During Cocaine Withdrawal, Sarah K Grothouse¹, R P Waters², Ronald E See²; ¹CofC, ²Neuroscience, MUSC.

008 Cocaine Self-Administration Modulates Vasopressin Receptors in the Extended Amygdala, Alana D Guziewicz¹, Parrish Waters², Ronald See²; ¹Biology, CofC, ²Neuroscience, MUSC.

009 Impact of Modafinil on Stress and Cue Reactivity in Cocaine Dependent Individuals, Charles D Leiner¹, Margaret M Moran-Santa Maria², Lisa Nunn², Ronald E See³, Aimee L McRae-Clark⁴; ¹Medicine, MUSC, ²Psychiatry & Behavioral Sciences, MUSC, ³Neurosciences, MUSC, ⁴Psychiatry & Behavioral Services, MUSC.

010 Effect of Intranasal Oxytocin on Marijuana Craving, Aaron M Schott, Amanda M Wagner, Erin N Lindley, Nathan Baker, Aimee McRae-Clark; Psychiatry and Behavioral Sciences, MUSC.

011 Modafinil Reverses Methamphetamine-Induced Memory Deficits On An Object-In-Place Task In Rats: Role Of Glutamate Receptor Expression, Meghin J Gilstrap¹, Carmela M Reiche³, Lauren A Ramsey³, Jackie F McGinty², Ron E See²; ¹Psychology/Neuroscience, CofC, ²Neurosciences, MUSC, ³Biology, CofC.

012 Oxytocin As A Neuromodulator Of The Stress Response System For Self-Administered Cocaine Animals, Stephanie R Johnson¹, Parrish R Waters², Ronald E See²; ¹Biology, CofC, ²Neuroscience, MUSC.
013 Novel Targets of Nkx2.5 Regulation in the Second Heart Field, Anthony J Horton, Kyu-Ho Lee; Regenerative Medicine and Cell Biology, MUSC.

014 In the ADAMTS5 Mouse Model of Myxomatous Valve Disease Increased Proteoglycans Contribute to Disease Progression, Kelsha M. Washington¹, Loren E. Dupuis², Marion A. Cooley², W. Scott Argraves², Christine B. Kern³; ¹Claflin University, ²Regenerative Medicine and Cell Biology.

015 Effects of a Connexin43 Mimetic Peptide on Myocyte-Fibroblast Adhesion in a 3D Model of Cardiac Injury, Hina Siddiqui¹, Emily L Ongstad², Robert G Gourdie²; ¹Biology, College of Charleston, ²Regenerative Medicine and Cell Biology.

016 Retrospective Noise Correction in Diffusional Kurtosis Imaging, Glenn R George, Tabesh Ali; Radiology and Radiological Science, MUSC.

017 Space Flight Causes Transcriptomic Changes in the Small Intestine Affecting Nutrition and Digestion, Max N Hughes¹, Scott W Argraves², Jeremy L Barth²; ¹Clemson University, ²Regenerative Medicine and Cell Biology.

018 The Effect of Fingolimod (FTY720) on Small Cell Lung Cancer and Non-Small Cell Lung Cancer, Jessica S Creel¹, Sahar Saddoughi², Besim Ogretmen²; ¹Chemistry, Winthrop University, ²Biochemistry & Molecular Biology, MUSC.

019 FOXO3a Transcription Factor Regulation By Thromboxane Receptor-β Signaling: Novel Mechanism for Malignant Transformation, Philip M Sobolesky¹, Julie Woolworth¹, Yuan Shao¹, Elizabeth Fowler¹, Dennis K Watson¹, Perry V Halushka², Omar Moussa³; ¹Pathology and Laboratory Medicine, MUSC, ²Pharmacology, MUSC.

020 Velcade and Organ Transplant Desensitization, Emma M Bradley, Omar Moussa, Yuan Shao; Pathology and Laboratory Medicine, MUSC.

021 Attitudes and Knowledge of Atrial Fibrillation Treatment and Stroke Prevention, Andrew B Gundran¹, Daniel T Lackland¹; ¹Psychology, Clemson, ²Neuroscience, MUSC.

022 Growth Failure In Early Neglect: A Comparison Of Neglected U.S. Children And International Adoptees, Doreen Condon¹, Brad Miller², John Himes², Andrea Summer³, Angela Larosa³, Eve Spratt³; ¹Pediatrics, MUSC, ²Univ of Minnesota, ³Medicine, MUSC.

023 Association of Willingness to Participate in Research Studies with Payment, Risk, and Time Among Individuals with Type 2 Diabetes, Kimberly T Arnold¹, Leonard Egede², Clara L Dismuke³, Joni Strom²; ¹CofC, ²Health Disparities, MUSC, ³VAMC.

024 A Comparison of the Impact of Community Support on Post-Disaster Mental Health Outcomes in Urban and Non-Urban Settings, Jenny S West¹, Matthew Price¹, Kirstin Grös¹, Jenna McCauley¹, Dan F Grös², Kenneth J Ruggiero¹; ¹Psychiatry, MUSC, ²Mental Health, VAMC.

025 Exploring Health Behaviors and Life Satisfaction Amongst Health Professional Students At the Medical University of South Carolina, Brian C Giinty, Elizabeth B Brown, Shirabrandy Garza, Emily A Jeffcoat, Laura C Patterson, Hazel L Breland; Occupational Therapy, MUSC.
026 Management of Hypertension At a Free Clinic and Emergency Department, Thomas E Miller III, Daniel Lackland; Neurosciences, MUSC.

027 Movement Patterns of Infants with Known Brain Abnormalities in the First 3 Months of Life, Allison E McFall¹, Laura Beth Meyer², Caitlin Judd³, Maggie Balleh³, Jessica Perkel⁴, Noelle Moreau⁵, Patty Coker-Bolt⁶, Dorothea Jenkins⁷; ¹Occupation Therapy, MUSC, ²Occupational Therapy, MUSC, ³Physical Therapy, MUSC, ⁴Pediatrics-Neonatology, MUSC.

028 An Exploration of Early Motor Delays and Early Intervention for an Extremely Premature Infant, Lisa M Johnson¹, Abbie K Martin¹, Jessica Perkel², Noelle Moreau³, Patty Coker-Bolt¹, Dorothea Jenkins²; ¹Occupational Therapy, MUSC, ²Pediatrics-Neonatology, MUSC, ³Physical Therapy, MUSC.

029 Infant Head Movements: Intrarater and Interrater Reliability Using Dartfish 2D Motion Kinematics, Caroline G Tuttle¹, Casey E Hudson¹, Jessica Perkel², Noelle Moreau³, Patty Coker-Bolt¹, Dorothea Jenkins²; ¹Occupational Therapy, MUSC, ²Pediatrics, MUSC, ³Physical Therapy, MUSC.

030 Early Motor Skill Differences in Low and High Risk Preterm Infants, Stacy G McGinnis¹, Rebecca K Wiesner¹, Jessica Perkel², Noelle Moreau², Patty Coker-Bolt¹, Dorothea Jenkins², Michelle Woodbury¹; ¹Occupational Therapy, MUSC, ²Pediatrics-Neonatology, MUSC, ³Physical Therapy, MUSC, ⁴Pediatrics – Neonatology, MUSC.

031 Differences in Muscle Architecture, Passive and Dynamic Range of Motion in High and Low Risk Preterm Infants, Margaret P Smart¹, Caitlin Judd³, Katy Holthaus¹, Jessica Perkel², Patricia Coker-Bolt³, Dorothea Jenkins¹, Noelle G Moreau¹; ¹Physical Therapy, MUSC, ²Pediatrics, MUSC, ³Occupational Therapy, MUSC.

032 Reliability of Lower Extremity Kinematics Obtained Using Two-Dimensional Video Analysis in Young Infants, Caitlin A Judd¹, Margaret P Smart¹, Katy Holthaus¹, Jessica Perkel², Patricia Coker-Bolt², Dorothea Jenkins¹, Noelle G Moreau¹; ¹Physical Therapy, MUSC, ²Occupational Therapy, MUSC, ³Pediatrics, MUSC.

033 Effect of Locus of Control on Clinical Outcomes for Diabetes, Bryan E Ashley, Melba A Hernandez-Tejada, Joni L Strom, Leonard E Egede; Medicine, MUSC.

034 Glycemic Control In VA Clinical Sites Compared To Non VA Sites Among Adults With Type 2 Diabetes, Jeanne B Lumpkin, Clara E Dismuke, Joni L Strom, Leonard E Egede; Medicine, MUSC.

035 Ethnic Differences in Control of Multiple Diabetes Risk Outcomes, Jamaeka N Reid, Cheryl P Lynch, Joni L Strom, Leonard E Egede; Medicine, MUSC.

036 Gender Differences in Composite Control of Cardiovascular Risk Factors, Rhonda Winchester, Cheryl P Lynch, Joni L Strom, Leonard E Egede; Medicine, MUSC.

037 Effect of Spirituality on Multiple Diabetes Outcomes, Chisom Ezenekwe, Melba A Hernandez-Tejada, Joni L Strom, Leonard E Egede; Medicine, MUSC.
The Impact of Group Motivational Interviewing on Treatment Utilization in Dually Diagnosed Veterans, Lauren S Jamison, Steven D LaRowe, Liz J Santa Ana; 1Medicine, MUSC, 2Substance Abuse Treatment Center, VA.

Free Clinic Vs Emergency Department Population Management of Diabetes Mellitus Types II: A Retrospective Study, Robert Bryant, Daniel Lackland, Michael Saeif; 1Medicine, MUSC, 2Epidemiology, MUSC, 3Emergency, MUSC.

Significantly Elevated Smoking Rates Across Drug Dependent Study Populations, David M Friedrich, Annie N Simpson, R Lewis, Aimee L McRae-Clark, Suzanne E Thomas, Sudie E Back, Karen J Hartwell; 1Medicine, MUSC, 2Biostatistics, Bioinformatics & Epidemiology, MUSC, 3SC Dept Health & Environmental Control, 4Psychiatry & Behavioral Sciences, MUSC.

Changes in Sleep Patterns in Medical School: Implications for Medical Errors, Aniruddh Anil Patel, Connor Freeman, Bernadette M Cortese, Thomas W Uhde; 1Medicine, MUSC, 2Psychiatry & Behavioral Sciences, MUSC.

Learning to Fish in an Ocean of Alcohol Research: Empirical Approaches to Study Design and Methodology in the Investigation of Stress, Alcohol, and Trauma, Joshua E Dowd, Carla K Danielson, Jenna L McCauley; Psychiatry and Behavioral Sciences, MUSC.

SESSION 4: Clinical-Professional-Masters II Basic/Clinical Sciences

Perifocal Diffusion Values in Assessing Prognosis of Brain Gliomas, Pritesh Topiwala, Vittoria M Spampinato, Zoran Rumboldt; 1Radiology, MUSC, 2Neuroradiology, MUSC.

Treatment of Cerebral Aneurysms: Does Size Matter?, Chelsey K Baldwin, Aquilla Turk; 1College of Medicine, MUSC, 2Neuro-interventional/Radiology, MUSC.

Attentional Control of Temporal Processing in Rats, Alexander R Matthews, Catalin V Buhusi; Neurosciences, MUSC.

EEG Alpha Band Asymmetry and MSCEIT Scoring in Depression, Christopher P Menzel, Ziad Nahas; Psychiatry, MUSC.

Prevalence and Predictors of Sleep Disorders in an Adult Sample with Type 2 Diabetes, Golsa Yazdy, Sujeev S Bains, Joni L Strom, L E Egede; Medicine, MUSC.

Effect Of Trust In Health Care Providers On Multiple Diabetes Outcomes, S Bouges, C P Lynch, J L Strom, L E Egede; Health Disparities Research, MUSC.

Is The Arm Activity Monitor A Reliable And Valid Tool To Measure Arm Use During Functional Activities In Stroke Rehabilitation?, Karla L Knuth, Kendra L Sprogis, Latisha D Washington, Michelle L Woodbury; 1Occupational Therapy, MUSC, 2Health Science and Research, MUSC.

The Role of the Tongue in Secondary Palate Elevation of Prrx1 Deficient Mice, Caitlin M Biggs, Michael J Kern; 1Dental Medicine, MUSC, 2Regenerative Medicine and Cell Biology, MUSC.

Effects of TGF-Beta on NIH-3T3 Cell Proliferation, Migration, and Apoptosis, Benton L Johnson, Steven W Kubalak, Jayne Bernanke; 1Medicine, MUSC, 2Regenerative Medicine and Cell Biology, MUSC.
053 The Varied Effect of NAC and Cocoa on LPS Stimulated IL-6 Release By Both Mononuclear Cells and Human Gingiva Fibroblasts, William A Stokes¹, Yan Huang²; ¹Medicine, MUSC, ²Endocrinology, MUSC.

054 Fli-1 Transcription Factor Affects Glomerulonephritis Development By Regulating Expression of Inflammatory Chemokine in Endothelial Cells in Kidney, eva Karam¹, Eiji Suzuki¹, Sarah Williams², Xian Zhang³; ¹Rheumatology & Immunology, MUSC, ²Rheumatology & Immunology, MUSC, ³Rheumatology & Immunology, MUSC & Ralph H. Johnson VA Medical Center.

055 Glucosylceramide and Lactosylceramide Accumulation in Lupus Nephritis: Biomarker or Mediator of Disease?, Andrew R Mather¹, Maria Jose Hernandez-Corbacho², Jennifer Schepp-Berglind², Jonathan Donahue², Ashley J Snider², James Oates², Leah J Siskind¹; ¹Biochemistry, MUSC, ²Medicine, MUSC.

056 Slug Expression Inhibits Vitamin D-mediated Sensitivity to Radiation in Colorectal Cancer, Eric Moretz¹, Victoria J Findlay², Silvia G Vaena¹, Savannah G Bandurraga², Michael S Ashenafi³, David T Marshall², Dennis K Watson³, Ramsay Camp¹; ¹Surgery, MUSC, ²Pathology and Laboratory Medicine, MUSC, ³Radiation Oncology, MUSC.

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

057 The Role of Tissue Transglutaminase-2 in the Modulation of Polymorphonuclear Leukocyte Function, David P LeBel, Meghan K Anderson, Titus A Reaves; Regenerative Medicine and Cell Biology, MUSC.

058 Fifteen-Year Experience with Peritoneovenous Shunts for Refractory Ascites Management, Sara C Smith¹, Charles Bratton², Helen Skaggs¹, David Taber³, Kenneth Chavin², Baliga Prabhakar²; ¹Medicine, MUSC, ²Surgery, MUSC, ³Pharmacy, MUSC.

059 Inhibiting Effect of Albumin on Biofilm Formation in Titanium Implants in Vivo, Shivam J Desai¹, Qian K Kang²; ¹Medicine, MUSC, ²Orthopaedic Surgery, MUSC.

060 The Effect of TDCS in Post-operative Pain Management of Total Knee Arthroplasty, Rahul S Loungani¹, Jeffrey J Borckardt², Scott Reeves³, Josh May¹; ¹Medicine, MUSC, ²Psychiatry & Behavioral Sciences, MUSC, ³Anesthesiology & Perioperative Medicine, MUSC.

061 Does Laptop Ergonomic Education Translate Into Ergonomic Action?, Alexis Cameron, Meg Judy, Sarah Johnson, Mira Kraft, Bailey Munson, Mariah Valentine, Peter Bowman; Occupational Therapy, MUSC.

062 Four Kinematic Variables to Measure Quality of a Reaching Movement in Stroke Rehabilitation, Christa M Barrett¹, Katie E Kirstein¹, Tania O McElveen¹, Michelle L Woodbury²; ¹Occupational Therapy, MUSC, ²Health Science and Research, MUSC.

063 Epidermal Growth Factor-induced Activation of Na+/H+ Exchanger in Orpk Cilia (+) and Orpk Cilia (-) Renal Cells From a Mouse Model of Polycystic Kidney Disease Involves Different Signaling Mechanisms, Alisha Joyner¹, Tanjina Akter², Mary G Blanton³, Maria N Garnovskaya³, Sonya D Coaxum³; ¹Medicine, MUSC, ²Rheumatology and Immunology, MUSC, ³Nephrology, MUSC.

064 Association of Mother-Infant Oral Mutans Streptococci and Infant Feeding Practices, Thao Trang N Latham¹, Susannah C Shirer², Carol L Wagner³, Bruce W Hollis³, Myla Ebeling³, Thomas C Hulsey³, Susan G Reed¹; ¹Craniofacial Biology, MUSC, ²Oral Rehabilitation, MUSC, ³Pediatrics-Neonatology, MUSC, ³Pediatrics-Epidemiology, MUSC.
065 Stroke Rehabilitation: Does Arm Movement Quality Relate to Amount of Functional Use During Reaching Tasks?, Meredith M Smith,1 Aaron J Hardee,1 Sheronda C Lucas,1 Claire C Marsh,1 Michelle L Woodbury,2 1Occupational Therapy, MUSC, 2Health Science and Research, MUSC.

066 Contributors To Ankle Proprioception For Static And Dynamic Tasks, Lisa M Floyd, Taylor C Holmes, Jesse Dean; Physical Therapy, MUSC.

067 Differences in Impulsivity Among Drug-Dependent Populations, Ja' Pel Sumpter, A Simpson, M Owens, A McRae-Clark, K Hartwell; Psychiatry, MUSC.

068 Radiation-Induced Xerostomia in Oral, Head and Neck Cancer Patients, Tiffany L Lovelace, Terry Day; 1Dental Medicine, MUSC, 2Otolaryngology - Head & Neck Surgery, MUSC.

069 Caffeine and Alcohol Intake and Nicotine Dependence Severity in Female Smokers, Christine N Riyad, Kevin M Gray; Psychiatry and Behavioral Sciences, MUSC.

070 Examination of the Role of HuR in the Post-Transcriptional Regulation of Nucleolin Expression in Breast Cancer Cells, Tracy TholaniKunnel, Sudeep Bose, Eleanor Spicer; 1Medicine, MUSC, 2Regenerative Medicine and Cell Biology, MUSC, 3Biochemistry and Molecular Biology, MUSC.

071 Noncanonical, Rapid Downstream Crosstalk Between TGFβ and Retinoic Acid Signaling Pathways As Revealed By the Proximity Ligation Assay, Craig Kutz, James Atkinson, Jayne Bernanke, Steven Kubalak; 1Medicine, MUSC, 2Graduate Studies, MUSC, 3Regenerative Medicine and Cell Biology, MUSC.

SESSION 6: Clinical-Professional-Masters IV Basic/Clinical Sciences

072 Tumor Location is an Independent Prognostic Factor in Head and Neck Merkel Cell Carcinoma, Olivia P MaDan, Valerie A Smith, Eric J Lentsch, 1Otolaryngology, MUSC, 2Otolaryngology-Head and Neck Surgery, MUSC.

073 Bilateral Amygdalal Lesions, Depression, and Suicide in an Adolescent with Neurocutaneous Melanosis, Dennis E Onwati, Nicholas I Batalis, 1Medicine, MUSC, 2Pathology & Laboratory Medicine, MUSC.

074 Who Needs an MRI? Laterality and Specificity of Prefrontal Craving Centers for Treatment with TMS, Morgan Jones, Colleen A Hanlon, Xingbao Li, Karen J Hartwell, Mark S George; 1Medicine, MUSC, 2Psychiatry & Behavioral Sciences, MUSC.

075 Effect of a Designated Reader and Cognitive Aid on Resident Performance During Simulation of Peri-operative Emergencies, Julius E Hamilton, Jarod Suber, Rieke Horst, Carlee Clark, Matthew McEvoy; Anesthesia and Perioperative Medicine, MUSC.

076 The Prevalence and Clinical Significance of Mycoplasma Genitalium in Our Gynecologic Patients: A Preliminary Review, Karla E Williams, Oluwatosin Jaiyeoba, David E Soper; Obstetrics and Gynecology, MUSC.

077 Demographic, Clinical, and Laboratory Characteristics of 155 Pediatric Nephrolithiasis Patients, Jeffrey J Tutman, Laura P Adams, Lauren J Becton, David J Sas; Pediatrics, MUSC.

078 Chemotherapy Tolerance in Colorectal Cancer Patients Post Liver Resection: A 5-year Retrospective Study At a Regional Teaching Hospital, Leah D Fryml, E Bleed, J Mills, W J Edenfield; 1Medicine, MUSC, 2Furman University, 3Wofford College, 4Cancer Center of the Carolinas.
079 Determining The Presence Of An Ear Advantage Yielding Increased Success Following Cochlear Implantation In The Elderly, Wasef K Muzaffar, Ted A Meyer; Otolaryngology-Head and Neck Surgery, MUSC.

080 Connexin 40 Remodeling in Purkinje Cardiomyocytes Post-Myocardial Infarction, Satara A Brown¹, Mary S Rackley², Brett S Harris³, Terrence X O'Brien⁴; ¹Medicine, MUSC, ²Cardiology, MUSC; Medicine, VAMC, ³Regenerative Medicine and Cell Biology, MUSC.

081 Unanticipated Effects of Adenosine on Microtubule Density, Flora M Simmons, Grace Wallenborn, George Cooper; Medicine, MUSC.

082 The Pitfalls of Automated Functional Analysis in Cardiac CT, Nelson E Seabrook, Pal Suranyi; Radiology, MUSC.

083 Generation of a Novel Bacteriostatic and Anti-collagenolytic Dental Adhesive Through the Incorporation of Polyacrylic Acid Modified Copper Nanoparticles Into Adhesive Resins, Andrew W Ambrose¹, Walter Renne¹, Michael Schmidt²; ¹Restorative Dentistry, MUSC, ²Microbiology, MUSC.

084 Salivary Morbidity Following Radioactive Iodine Treatment for Thyroid Carcinoma, Ashley E Mishoe¹, Isaac F Dingle², M Boyd Gillespie³, Eric J Lentsch⁴, Shaun A Nguyen⁵; ¹Pharmacy, MUSC, ²Medicine, MUSC, ³Otolaryngology-Head & Neck Surgery, MUSC.

085 Effects of Cortisol and Norepinephrine on the Expression of the Tumor Antigen MUC1 in DU-145 Prostate Cancer Cells, Kristina Andrijauskaite¹, Daniel J Fernandes¹, Nigel S Courtenay-Luck¹, Katherine Regan Sterba²; ¹Biochemistry, MUSC, ²Biostatistics and Epidemiology, MUSC.

086 Hypertonic Saline Immune Functions, Kevin M Phelan¹, Diane E Neaf², Samir Fakhry³; ¹Medicine, MUSC, ²Health Sciences, Walden, ³Surgery, MUSC.

SESSION 7: PhD I

087 Efficacy of Transcranial Direct Current Stimulation (tDCS) and Repetitive Transcranial Magnetic Stimulation (rTMS) for the Treatment of Fibromyalgia Syndrome: A Systematic Review, Nicole M. Marlow¹, Health S Bonilha², E Baron Short³; ¹Biostatistics and Epidemiology, MUSC, ²Health Sciences and Research, MUSC, ³Psychiatry and Behavioral Sciences, MUSC.

088 Associations Between Coping Styles, Diabetes Knowledge, Medication Adherence, and Self-Care Behaviors in Adults with Type 2 Diabetes, Brittany L Smalls¹, Rebekah J Walker¹, Melba A Hernandez-Tejada², Jennifer A Campbell², Kimberly S Davis², Leonard E Egede²; ¹Health Sciences and Research, MUSC, ²Medicine, MUSC, ³College of Charleston.

089 Association Between Fatalism, Medication Adherence and Self-care Behaviors in Adults with Type 2 Diabetes, Rebekah J Walker¹, Brittany L Smalls¹, M Hernandez-Tejada², Jennifer A Campbell², Kimberly S Davis², Leonard E Egede²; ¹Health Professions, MUSC, ²Medicine, MUSC.

090 Filamin-A Regulates Cardiac Valve Development Via a Novel Serotonin Pathway, Kimberly Sauls, Amanda Richards, Katherine Williams, Aimee Phelps, Andy Wessels, Roger Markwald, Russel Norris; Regenerative Medicine and Cell Biology, MUSC.
Amino Acids Starvation Response in Saccharomyces Cerevisiae, Role of Sphingolipids Gene ISC1, Alessandra Metelli¹, Alessandro Achilli², Hovirag Lancioni², Nora Babudri², Nabil Matmati¹; ¹Biochemistry & Molecular Biology, MUSC, ²University of Perugia.

Rational Development of Novel Biogenic Beta-Adrenergic Selective Agonists, Robert B Cameron, Christopher Lindsey, Lauren P Wills, Richard T Trager, Craig C Beeson, Rick G Schnellmann, Yuri K Peterson; Pharmaceutical & Biomedical Sciences, MUSC.

The Role of Th17 and Treg Cells During HNSCC Carcinogenesis, Danielle N Justis¹, Anna-Maria De Costa², Corinne Schuyler², Rita Young²; ¹Microbiology and Immunology, MUSC, ²Otolaryngology, MUSC.

An Analysis of Race and Age As Factors Associated with the Development of Lymphedema Following Breast Cancer Treatment, Sybil L Prince Nelson, Joan Cunningham; Biostatistics, MUSC.

The Analysis of Acute Stroke Clinical Trials with Responder Analysis Outcomes, Kyra M Robinson, Sharon D Yeatts, Viswanathan Ramakrishnan, Valerie L Durkalski; Biostatistics and Epidemiology, MUSC.

Spatial Exposure Modeling of Environmental Risk And Intellectual Delay Outcomes, Georgiana Onicescu¹, Andrew B Lawson¹, Suzanne McDermott², Marje Aelion³, Bo Cai²; ¹Biostatistics, MUSC, ²Univ. of South Carolina, ³Univ. of Massachusetts.

High Content Analysis of Dynamic Agonist Stimulated Receptor, G Protein, and Beta-arrestin Trafficking, Kathryn M Appleton¹, Mi-Hye Lee², Louis M Luttrell², Yuri K Peterson³; ¹Pharmaceutical and Biomedical Sciences, MUSC, ²Medicine, MUSC, ³Pharmacy, MUSC.

Complement Deficiency Ameliorates Acute Cigarette Smoke Induced Lung Injury, Sarah E Casey¹, Fei Qiao¹, Stephen Tomlinson², Carl Atkinson²; ¹Microbiology & Immunology, MUSC, ²Microbiology & Immunology. MUSC.

Activation Induced Cell Death in Adoptively Transferred T-Cells, Matt Scheffel¹, Chris Voelkel-Johnson¹, Shikhar Mehrotra²; ¹Microbiology & Immunology, MUSC, ²Surgery, MUSC.

Extracellular Heat Shock Protein 90 (eHsp90) Mediates EMT in Prostate Cancer Through the Polycomb Epigenetic Pathway, Krystal L Dole, Michael Hance, Jennifer Isaacs; Pharmacology, MUSC.

Dephosphorylation of C-terminal Tyrosine Residues Does Not Contribute to Ethanol Inhibition of Recombinant NMDA Receptors, Ben A Hughes, John J Woodward; Neurosciences, MUSC.

Matrix Metalloproteinases in Reinstated Cocaine Seeking, Alex W Smith, Armina T Wiggins, Peter W Kalivas; Neurosciences, MUSC.

Assessing Cognitive Flexibility Following Methamphetamine Self-administration, Brittney M Cox¹, Zackary A Cope², Aram Parsegian¹, David E Moorman¹, Stan B Floresco², Gary Aston-Jones¹, Ronald E See¹; ¹Neurosciences, MUSC, ²Psychology, Univ. of British Columbia.

Homer2 Deletion Prevents Chronic Ethanol-Induced Spine Enlargement in the Nucleus Accumbens, Natalie M Straight, Natasha N New, Justin T Gass, Patrick J Mulholland, Judson L Chandler; Neurosciences, MUSC.
106 Clinical Reasoning in Graduate Prelicensure Nurses, Suzanne M Sutton¹, Lynne Nemeth¹, Darlene Amendolair², Julie Moss²; ¹Nursing, MUSC, ²Mary Black School of Nursing, University of South Carolina Upstate.

107 Business Case for Pre-treatment Swallowing Exercises, Kendrea L Focht¹, Kit N Simpson¹, Terry A Day², Bonnie Martin-Harris²; ¹Health Sciences and Research, MUSC, ²Otolaryngology-Head and Neck Surgery, MUSC.

108 DNA Damage Activates MK2-mediated Cell Cycle Control By Transcriptional Regulation of Cyclin, Bethany A Herbert, Sudha Talwar, Yogendra Padwad, Viswanathan Palanisamy; Craniofacial Biology, MUSC.

109 Activation of Apoptotic Pathways Without Cell Death in an Inner-ear Immortomouse Cell Line, Kayla R Hill¹, Fu-Quan Chen¹, Ya-Jun Guan², Jochen Schacht², Su-Hua Sha¹; ¹Pathology and Laboratory Medicine, MUSC, ²Otolaryngology, University of Michigan.

110 The Vitamin D Receptor and Retinoid X Receptor Expression Related to DNMT Levels in a Murine Model of Colitis, Rebecca W Knackstedt, Vondina Moseley, Jay Morris, Michael Wargovich; MCBP, MUSC.

111 The Ratio of Alpha-1B-Glycoprotein to Zinc Alpha-2 Glycoprotein in Urine Is an Early and Accurate Predictor of Acute Kidney Injury, Joseph L Alge¹, Michael G Janch¹, Andrew D Shaw², Lakhmir S Chawla³, James A Tumlin⁴, John M Arthur¹; ¹Medicine, MUSC, ²Anesthesiology, Duke University, ³Anesthesiology and Critical Care Medicine, George Washington University, ⁴Medicine, University of Tennessee at Memphis.

112 Acid Ceramidase Over Expression in Response to Cigarette Smoke Exposure, Sarah T Marrison¹, Joseph C Cheng¹, Thomas H Beckham¹, Ping Lu¹, Angen Liu², Sarah Casey¹, Xiang Liu¹, James S Norris¹; ¹Microbiology and Immunology, MUSC, ²Rheumatology, MUSC.

113 Effects of Fli-1 on T Cell Function in Lupus, Fahmin Basher¹, Zainab Amani², Marlene Bunni², Tamara Nowling²; ¹Microbiology & Immunology, MUSC, ²Rheumatology, MUSC.

114 Absence of Estrogen Receptor Alpha Reduces Plasmacytoid Dendritic Cells and Type I Interferon Production in Lupus Prone Mice, Jennifer L Scott¹, Melissa Cunningham², Osama S Naga³, Gary Gilkeson⁴; ¹Microbiology and Immunology, MUSC, ²Jewish Hospital, University of Cincinnati, ³Medicine, University of Cincinnati, ⁴Medical Research Service, VA.

115 NAC and Vit D Treatment Improving Hypoxic Ischemic Injury in the Neonatal Rat Model, Danielle Clark¹, Jessica Perkel², Xingju Nie³, Inderjit Singh³, Dorothea Jenkins²; ¹MCBP, MUSC, ²Pediatrics, MUSC, ³CBI, MUSC.

116 Improving Treatment of Bacterial Infections in Deep Wounds, Angela A Alexander, Xuejun Wen; Clemson-MUSC Bioengineering.

SESSION 9: PhD III

117 Racial Disparities in Repeat Admissions for Ischemic Stroke Patients Less Than 65 Years of Age, Andrea D Boan¹, David L Bachman², Robert J Adams², Wuwei Feng², Brent M Egan³, Joyce S Nicholas¹, Andrew B Lawson¹, Daniel T Lackland²; ¹Biostatistics & Epidemiology, MUSC, ²Neuroscience, MUSC, ³General Internal Medicine, MUSC.

118 Optogenetic and Pharmacologic Modulation of Locus Coeruleus Noradrenergic Neurons: Effects on Behavioral Flexibility, Zackary A. Cope¹, Elena Vazey¹, David E. Moorman¹, Stan B. Floresco², Gary S. Aston-Jones¹; ¹Neurosciences, MUSC, ²Psychology, University of British Columbia.
119 Contribution of BDNF/TrkB Signaling in Rat Striatum in Response to Acute Amphetamine, Bok Soon Go, Jacqueline F McGinty; Neuroscience, MUSC.

120 Middle School Student's Perception of Nursing As a Career, Robin E Matutina, Teresa J Kelechi, Martina Mueller; Nursing, MUSC.

121 S1P Carrier-Dependent Effects on Endothelial Barrier: HDL-S1P Prolongs Endothelial Barrier Enhancement Compared to Albumin-S1P Via Effects on S1P1 Trafficking and Signaling, Brent A Wilkerson, G Daniel Grass, Shane B Wing, W Scott Argraves, Kelley M Argraves; Regenerative Medicine and Cell Biology.

122 Regulation of Invadopodia Formation and Activity By Emmprin (CD147), Daniel Grass, Momka Bratoeva, Bryan P Toole; Regenerative Medicine and Cell Biology, MUSC.

123 ERK2 Phosphorylation of Splicing Factor 45 (SPF45) Regulates SPF45 Alternative Splicing Site Utilization and Downstream Gene Expression, Adnan M Al-Ayoubi¹, Hui Zheng², Yuying Liu¹, Tao Bai³, Scott T Eblen¹; ¹Pharmacology, MUSC, ²Molecular Biology, The Scripps Research Institute, ³Neurology, U of Chicago.

124 Development of Selective Small Molecule Inhibitors of Heterotrimeric G-Protein Signaling for the Treatment of Ovarian Cancer, Kevin J Bigham¹, Starr E Hazard², Jonel Lirjoni³, Ellen Maher⁴, Joe B Blumer², Yuri K Peterson¹; ¹Pharmaceutical and Biomedical Studies, MUSC, ²Pharmacology, MUSC, ³Pharmacy, MUSC, ⁴Pharmacology, MUSC.

125 Mitochondrial Fusion is Linked to Bioenergetic Capacity and Cell Survival in a Cell-based Model of PDE6B-dependent Retinitis Pigmentosa, Anthony Leonard¹, Nathan Perron¹, Cecile Nasarre², Craig Beeson¹, Baerbel Rohrer²; ¹Pharmaceutical Sciences, MUSC, ²Ophthalmology, MUSC.

126 High Throughput Identification of Mitochondrial Toxicophores, Richard E Trager, Lauren Wills, Christopher Lindsey, Gyda Beeson, Craig Beeson, Rick Schnellmann, Peterson Yuri; Pharmaceutical and Biomedical Sciences, MUSC.

127 Microbial Electrosynthesis From CO2 By Mixed Communities, Chris Marshall, Harold May; Microbiology & Immunology, MUSC.

128 Pathogenic Natural Igm Antibodies Initiate The Inflammatory Response Important For Both Hepatic Ischemia/Reperfusion Injury And Liver Regeneration After Partial Hepatectomy, Keely L Morris¹, Fei Qiao¹, Songqing He¹, Carl Atkinson¹, Liudmila Kulik⁵, Michael V Holers⁵, Tomlinson Stephen¹; ¹Microbiology and Immunology, MUSC, ²Rheumatology, UCSM, ³Division of Rheumatology, UCSM.

129 Characterization of the Evolution of Immune Phenotype During the Development and Progression of Squamous Cell Carcinoma of the Head and Neck, Anna-Maria A De Costa¹, Danielle Justis¹, Corinne Schuyler¹, Rita Young¹; ¹Otolaryngology, MUSC, ²Research Services, VA.
130 The One-Year Attributable Cost of Post-Stroke Aphasia, Annie N Simpson¹, Heather Bonilha¹, Patrick D Mauldin², Kit N Simpson¹, Charles Ellis¹; ¹Health Science and Research, MUSC, ²Clinical Pharmacy & Outcome Sciences, MUSC.

131 Lights On, Relapse Off: Examining Optogenetic Inhibition of Relapse Neurocircuitry, Michael T Stefanik¹, Karl Deisseroth², Peter W Kalivas¹; ¹Neuroscience, MUSC, ²Psychiatry and Bioengineering, Stanford University.

132 Intra-prefrontal Cortical Infusion of Brain-derived Neurotrophic Factor Effects on Cocaine Seeking-induced Arc MRNA Induction, Nortorious T Coleman, Wei-Lun Sun, Jacqueline F McGinty; Neuroscience, MUSC.

133 Hematopoietic Stem Cell-Derived Carcinoma–Associated Fibroblasts Promote Tumor Progression, Lindsay T McDonald, Dayvia A. Laws, Amanda C. LaRue; Pathology, MUSC.

134 Anti-apoptotic Genes Family As a Novel Diagnostic Markers of Bladder Cancer, Elizabeth B Fowler¹, Philip M Sobolesky¹, Yuan Shao¹, Julie A Woolworth¹, Yuan Shao¹, Omar Moussa²; ¹Pathology, MUSC, ²Pathology, MUSC.

136 Life After Lung Cancer Resection: Exploring Rehabilitative Options to Improve Quality of Life, Melanie S. Jefferson¹, David O. Sword¹, Erica Rouvalis², Marvella E. Ford³; ¹CHP, MUSC, ²MUSC, ³HCC, MUSC.

137 AKT3 Promotes Nuclear Retention Of PGC-1 And ER Alpha By Regulation Of The Major Nuclear Export Protein, CRM-1, Daniel G Corum, Robin C Muise-Helmericks; Regenerative Medicine and Cell Biology, MUSC.

138 Effects of Perfluorooctane Sulfonate (PFOS) and Perfluorooctanoic Acid (PFOA) on IL-2 Production in the Human Jurkat T-cell Line, Kristin S Midgett¹, Margie Peden-Adams², Gary S Gilkeson¹, Diane L Kamen¹; ¹Microbiology and Immunology, MUSC, ²Harry Reid Center for Environmental Studies, University of Nevada-Las Vegas.

139 Fibulin-1 Deficiency Leads to Dysregulation of the Forkhead-Tbx1-Fgf8-FgfR-Map Kinase Pathway and DiGeorge Syndrome-like Phenotype, Victor M Fresco, Marion A Cooley, Waleed O Twal, Kyu-Ho Lee, Jeremy L Barth, W Scott Argraves; Regenerative Medicine and Cell Biology, MUSC.

140 Seamless Phase II/III Adaptive Dose Finding Design for Longitudinal Data in Safety/Efficacy Clinical Trials, Caitlyn N Ellerbe, Jordan Elm, Viswanathan Ramakrishnan, Valerie Durkalski; Biostatistics and Epidemiology, MUSC.

141 The Role of Estrogen-Related Receptors in Cardiomyocyte Metabolic Adaptation to Oxidative Stress, Kathryn Cribben¹, Paul McDermott²; ¹MCBP, MUSC, ²Medicine, MUSC.

SESSION 11: Postdocs-Residents-Fellows I

144 Positive Propylene Glycol in a Patient with Ethylene Glycol Toxicity, Roger W Stone, Yusheng Zhu; Pathology, MUSC.

145 XRCC1 399 Arg>Gln (28152G>A) Variation Correlates with Deterioration in Quality of Life Induced By Radiotherapy in Prostate Cancer Patients, Alina G Sofronescu, David T Marshall, Yusheng Zhu; Pathology and laboratory Medicine, MUSC.

146 Diabetes Empowerment, Medication Adherence and Self-care Behaviors in Adults with Type 2 Diabetes, Melba A Hernandez-Tejada, Jennifer A Campbell, Kimbery S Davis, Brittany L Smalls, Rebekah J Walker, Leonard E Egede; Medicine, MUSC.

147 Enhancing Behavioral Interventions for PTSD in Operation Enduring Freedom/Operation Iraqi Freedom Veterans: Influence of Personal and Environmental Factors, Matthew Price¹, Daniel F Gros², Martha Strachan³, Jenny S West¹, Kenneth J Ruggiero¹, Ron Acier³; Psychiatry, MUSC, ²Mental Health, VAMC.

148 Association Of Serum Concentrations Of 25-Hydroxyvitamin D And Gingival Inflammation During Pregnancy, Vivek Singh¹, Carol L Wagner², Bruce W Hollis², Myla Ebeling², Thomas C Hulsey², Susan G Reed³; ¹MSCR, MUSC, ²Pediatrics-Neonatology, MUSC, ³CDM, MUSC.

149 Phase I Trial of the HDAC Inhibitor LBH589 in Combination with Sorafenib in Patients with Renal Cell Carcinoma, Non Small Cell Lung Cancer and Soft Tissue Sarcomas, Charles M Butler, Lydia T Laboccetta, Alan Brisendine, Thomas E Keane, Harry A Drabkin; Hematology and Oncology, MUSC.

SESSION 12: Postdocs-Residents-Fellows II

150 Prognostic Factors for Nodal Spread in Thin (≤ 1 Mm) Melanoma: A Meta Analysis, Allison N Lundy¹, Kent E Armeson², Betsy Hill², Ashley C Parks³, Nestor F Esnaola¹, David J Cole¹, Ramsay Camp¹; Surgery, MUSC, ²Biostatistics and Epidemiology, MUSC, ³Medicine, MUSC.

151 Association Between Spirituality and Depression in Adults with Type 2 Diabetes, Joni L Strom, Cheryl P Lynch, Melba A Hernandez-Tejada, Leonard E Egede; Medicine, MUSC.

152 Role of OPA1 in Early Zebrafish Development, Jennifer J Rahn, Krista D Stackley, Sherine S.L. Chan; Pharmacy, MUSC.

153 EGCG, a Green Tea Polyphenol, Can Reverse Methylation Related Silencing of Genes in Human Colon Carcinomas, Jay Morris¹, Vondina R Moseley², Katie Coleman³, Michael Wargovich¹; ¹Pharmacology, MUSC, ²MSTP, MUSC, ³Western States Chiropractic College, Portland, OR.

154 Defining the Role of ICOS and CD28 Costimulation in TH17 Cell Activation, Differentiation and Tumor Immunity, Michelle Nelson¹, Logan W Huff¹, Carolyn E Rogers¹, Sreenath Kundimi¹, Chrystal M Paulos²; ¹Microbiology and Immunology, MUSC, ²Surgery, MUSC.
155 Role of Transcription Factor Fli-1 in Regulation of Dendritic Cell and Monocyte Development, Eiji Suzuki¹, Sarah Williams², Eva Karam¹, Xian Zhang¹; ¹Rheumatology and Immunology, MUSC, ²Ralph H. Johnson VAMC.

156 Defective Migration in Activator of G Protein Signaling 3-null Leukocytes in Response to CXCL12 and CCL19 Stimulation, Melissa B Branham-O’Connor¹, Ellen M Maher¹, Xian Zhang², Stephen M Lanier¹, Joe B Blumer¹; ¹Cell and Molecular Pharmacology and Experimental Therapeutics, MUSC, ²Medicine, MUSC.

157 RAT Pathway Synchronizes FGFR1 Signaling By Intracellular Sequestration and Controlled PM Delivery of the Receptor, Jagadish Kummetha Venkata¹, Claire Leist Hinsch¹, Demetri D Spyropoulos¹, Erika T Brown¹, Simon C Watkins², Vincent Dammai¹; ¹Pathology, MUSC, ²Cell Biology and Center for Biologic Imaging, University of Pittsburgh.

158 Effect of MKP-1 Knockout on Osteoclast Progenitor Populations and RANKL Induced Osteoclastogenesis, Valerio S Michael, Keith L Kirkwood; Craniofacial Biology, MUSC.

159 Effects of Inositol Phosphosphingolipid Phospholipase C1 Deletion on Trafficking of the Plasma Membrane ATPase (Pma1) in Cryptococcus Neoformans, Kaur Navtej¹, Mor Visesato¹, Maurizio Del Poeta²; ¹Biochemistry and Molecular Biology, MUSC, ²Craniofacial Biology, MUSC.

160 Insulin Like Growth Factor-1 Attenuates Intracellular Changes In Ventral Spinal Cord 4.1 Motoneuron Cells Damaged By Interferon-Gamma, Sookyoun Park¹, Kenkichi Nozaki¹, Arabinda Das¹, James S Krause², Naren L Banik¹; ¹Neurosciences, MUSC, ²Health Sciences and Research, MUSC.

161 Regulation Of Ogt And Oga And Their Impact On Insulin Signal Transduction, Kamala P Sundararaj, Katherine A Robinson, Maria Buse, Lauren Ball; Endocrinology, MUSC.

162 Factors Regulating the Subcellular Localization of Activators of G-protein Signaling 3: The Role of Serine/threonine Residues in the G-protein Regulatory Domain, Fatih M Kelesoglu, Sadik S Oner, Stephen M Lanier; Cell and Molecular Pharmacology, MUSC.

163 Reinstatement of Cocaine-seeking in Rats with an Addiction-prone Phenotype, R Parrish Waters, Amy B Young, Matt W Feltenstein, Ronald E See; Neurosciences, MUSC.

164 Neuronal and Behavioral Effects of Optogenetic Modulation of the Lateral Habenula, Margaret J Gill, Robert P Waters, Art C Riegel, Ron E See; Neuroscience, MUSC.

165 Proteomic Analysis Of Cerebral Spinal Fluid Reveals Candidate Biomarkers Of Domoic Acid Toxicosis In California Sea Lions, Benjamin A Neely¹, Jennifer Soper², Frances M D Gulland², John M Arthur³, Michael G Janich³; ¹Nephrology, MUSC, ²The Marine Mammal Center, ³Nephrology, MUSC, Research Service, Ralph H. Johnson VA Medical Center, Charleston, SC.

166 β-blockade Prevents P21-activated Kinase 1 (Pak1) Activation in an in Vitro Model of Cardiac Hypertrophy, Grace Wallenborn, Guangmao Cheng, Dhandapani Kuppuswamy, George Cooper; Medicine, Cardiology, MUSC.
ORAL PRESENTATIONS:
College of Health Professions (CHP) Building A: 11:45 – 3:15 pm
Bioengineering Building (BE) Room 112: 11:45 – 3:15 pm

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<td>12:30 - 12:45</td>
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<td><strong>167 Anxiogenic Effects of Cocaine Withdrawal in Rats</strong>, Kyle T Brown, Parrish R Waters, Ronald E See; Psychology, CofC.</td>
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<td>12:45 - 1:00</td>
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<td><strong>168 Structure-function Relationships in the Brain Using Imaging Across Multiple Spatial Scales</strong>, Grace Margaret A Dion, Zhongyang Lu, Manuel Levy, Prakash Kara; Neuroscience, MUSC.</td>
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<td><strong>169 Evaluating an Intervention to Increase Cancer Knowledge in Racially Diverse Communities in South Carolina</strong>, CoDanielle Green¹, Marvella E. Ford²; ¹SC State University, ²MUSC.</td>
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<td><strong>170 Pilot Study: Maternal Infant Neurobiology</strong>, Courtney H Marsh¹, Amy Wahlquist², Paul Nitert², Carol Wagner², Eve G Spratt²; ¹Medicine, MUSC, ²Pediatrics and Psychiatry, MUSC.</td>
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<td>1:30 – 1:45</td>
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<td>1:45 - 2:00</td>
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<td><strong>171 Importance of Lymph Node Metastasis in Head and Neck Sarcomas</strong>, Lewis J Overton, Valerie A Smith, Eric J Lentsch; Otolaryngology, MUSC.</td>
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<td>2:00 - 2:15</td>
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<td><strong>172 Using a Community-Based Participatory Research Approach to Create and Test a Culturally Sensitive Oral Health Educational Handbook-Hollywood Smiles Handbook</strong>, Christine M Hudson¹, Lynn J West¹, Elizabeth Carpenter², Renata Leite¹; ¹Center for Oral Health Research, MUSC, ²Hollywood, SC, Mayor's Office.</td>
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<td>2:15 - 2:30</td>
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<td><strong>173 A Unique Case of Anton's Syndrome</strong>, Elizabeth M Quattlebaum¹, Robert J Adams¹, Nolan Williams², Mark T Wagner³; ¹Neurosciences, MUSC, ²Psychiatry and Neurosciences, MUSC, ³Neuropsychology, MUSC.</td>
</tr>
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SESSION 14: Undergraduate IV: 12:30 – 2:30 pm: CHP 207

12:30 - 12:45
174 Selective MicroRNA Suppression in Thoracic Aortic Aneurysm: Relationship of MiR-29a to Aortic Size and Proteolysis, Charlotte R Ivey¹, Jeffrey A Jones², Elizabeth C O’Quinn¹, John A Elefteriades¹, Robert E Stroud², Francis G Spinale², John S Ikonomidis²; ¹Medicine, MUSC, ²Surgery, MUSC.

12:45 - 1:00
175 Nkx2.5 Regulates Hoxb4, MiR-10a, and Jarid2 Expression in the Developing Heart, Aaron M Blackshaw¹, Kyu-Ho Lee²; ¹CofC, ²MUSC Pediatric Cardiology.

1:00 - 1:15
176 Comparative Transcriptome Analysis to Identify Genes Regulating Elastogenesis, Sharon L Guffy¹, Erin L Pardue¹, Jeremy L Barth¹, Kathleen R Braun², Thomas N Wight², W Scott Argraves¹; ¹Regenerative Medicine and Cell Biology, MUSC, ²Benaroya Research Institute.

1:15 - 1:30
177 The Effect of Cytokines on T Cell Antioxidant Capacity, Jazzmine Clemons¹, Shikhar Mehrotra²; ¹Claiflin University (SURP), ²MUSC.

1:30 – 1:45 BREAK

1:45 - 2:00
178 Neurotransmitters Effected By Cocaine Addiction, Catherine M Claro, Parrish R Waters, Ronald E See; Neurosciences, MUSC.

2:00 - 2:15
179 MBD4 DNA Repair in Prostate Cancer, Sierra S. Brooks¹, David Turner²; ¹Voorhees College, ²MUSC.

2:15 - 2:30
180 Thioredoxin 1 As a Therapeutic Target in Advanced Prostate Cancer, DeAngelo Dinkins¹, Christina Voelkel-Johnson²; ¹SC State University, ²MUSC.

SESSION 15: Clinical-Professional-Masters V: 12:15 – 3:00: CHP 201

12:15 - 12:30
181 Pilot Study: Tolerability and Functionality of Two High-Fiber, Weight Loss Diets, William D Strickland¹, O’Neil M Patrick², Tonya Turner²; ¹Medicine, MUSC, ²Psychiatry, MUSC.

12:30 - 12:45
182 Prevalence of Vitamin D Deficiency in Obese Children and Adolescents, Jennifer N Paige, Janet Carter, Melissa Henshaw; Medicine, MUSC.

12:45 - 1:00
183 Predictors of Adequate Health Literacy In a Diverse Primary Care Sample with Type 2 Diabetes, Julie Teuber, Sujeev S Bains, Joni L Strom, L E Egede; Medicine, MUSC.

1:00 - 1:15

184 Multiple Cardiovascular Risk Factor Control (MCRFC) Across Sites of Care in Type 2 Diabetes, Jacob C DeWeerth, Clara E Dismuke, Joni L Strom, Leonard E Egede; Medicine, MUSC.

1:15 - 1:30

185 Effect Of Delayed Discounting On Multiple Diabetes Outcomes In Adults With Diabetes, Adam H Fox, Clara E Dismuke, Joni L Strom, Leonard E Egede; Medicine, MUSC.

1:30 – 1:45 BREAK

1:45 - 2:00

186 Differential Inflammatory Response Could Contribute To The Disparity Of Barrett's Esophagus and Esophageal Adenocarcinoma In European Versus African Americans, Jason B Wheeler¹, Dennis K Watson², Elizabeth Garrett-Mayer³, Carolyn E Reed⁴, ¹MSCR, MUSC, ²Pathology, MUSC, ³Biostatistics, MUSC, ⁴Surgery, MUSC.

2:00 - 2:15

187 Does Completion Lymphadenectomy Improve Survival for Patients with Sentinel Node-Positive Cutaneous Melanoma of the Head and Neck? Experience From the SEER Database, Valerie A Smith¹, Joan E Cunningham, PhD², Eric J Lentsch, MD¹; ¹Otolaryngology-Head and Neck Surgery, MUSC, ²Biostatistics and Epidemiology, MUSC.

2:15 - 2:30

188 Is Cirrhosis a Contraindication to Laparoscopic Cholecystectomy?, Juan José E Villar-Benavides, John McGillicuddy, Sapna Bazaz, David J Taber, Nicole A Weimert, Prabhakar Baliga, Kenneth D Chavin; Transplant Surgery, MUSC.

2:30 - 2:45

189 Taking On The Social Network: Biochemical Characterization Of Pqsd Activity In Alkylquinolone Synthesis In Pseudomonas Aeruginosa, Mo Wei Yang¹, Zdzislaw Szulc², Christopher Davies², Alvin Zhou³, Yong-Mei Zhang⁴; ¹Biochemistry, MUSC, ²Biochemistry and Molecular Biology, MUSC, ³Engineering, Clemson University.

2:45 - 3:00

190 Severe Hunter Syndrome (Mucopolysaccharidosis II) Phenotype Secondary to Large Deletion in the X Chromosome Encompassing IDS, FMR1, and AFF2 (FMR2), Day M Burruss¹, Tim C Wood², Lesby Espinoza³, Alka Dwivedi⁴, Kenton R Holden⁵; ¹Medicine, MUSC, ²Biochemical Genetics, GGC, ³Pediatrics, University of Honduras, ⁴Cytogenetics, GGC, ⁵Neurosciences, MUSC.
11:45 - 12:00  
**191 The Role of Complement Peptides, C3a, in Host Defense Against Candida, a Human Fungal Pathogen,** Geoff Bloomquist\(^1\), Caroline Westwater\(^2\); \(^1\)College of Dental Medicine, MUSC, \(^2\)Craniofacial Biology, MUSC.

12:00 - 12:15  
**192 RPE65 Protein is Present Within Human Cones to Enhance Photopigment Regeneration for Vision,** Peter H Tang\(^1\), Mona Buhusi\(^1\), Rosalie K Crouch\(^2\); \(^1\)Neuroscience, MUSC, \(^2\)Ophthalmology, MUSC.

12:15 - 12:30  
**193 Melatonin Attenuates Oligodendrocyte Cell Death and Myelin Loss,** Okwuchukwu G Obi\(^1\), Arabinda Das\(^2\), Narendra L Banik\(^2\); \(^1\)Medicine, MUSC, \(^2\)Neuroscience, MUSC.

12:30 - 12:45  
**194 The Role of the Prrx-1 Gene in Cell Proliferation During Secondary Palate Development,** Charles Moore\(^1\), Michael Kern\(^2\), Christine Kern\(^2\); \(^1\)Dental Medicine, MUSC, \(^2\)Regenerative Medicine and Cell Biology, MUSC.

12:45 - 1:00  
**195 Expression of Nucleobindin-2/Nesfatin-1 in Bone Tissue,** Tejas Doshi\(^1\), Lauren Ball\(^1\), Alexis Nagel\(^2\); \(^1\)Pharmacology, MUSC, \(^2\)Pharmacology, MUSC.

1:00 - 1:15  
**196 Mitochondrial Dysfunction in Degenerative Pathologies,** Danielle M Desjardins\(^1\), Craig Cano Beeson\(^2\); \(^1\)College of Graduate Studies, MUSC, \(^2\)College of Pharmacy / Pharmaceutical & Biomedical Sciences, MUSC.

1:15 - 1:30  
**197 The Effect of IRS-1 Modification By N-acetyl Glucosamine (O-GlcNAc) on the Insulin Response,** Tabatha B Davis\(^1\), Katherine Robinson\(^1\), Maria G Buse\(^1\), Lauren Ball\(^3\); \(^1\)Endocrinology, MUSC, \(^2\)Pharmacology, MUSC.

1:30 – 1:45  **BREAK**

1:45 - 2:00  
**198 Imbalance in Histone Acetyl Transferase and Histone Deacetylase Activity During Hypertrophy,** Christopher R Smith\(^1\), Mona S Li\(^1\), Olga Chernysh\(^2\), Elizabeth S Inks\(^3\), James C Chou\(^3\), Santhosh K Mani\(^1\), Donald R Menick\(^1\); \(^1\)Cardiology, MUSC, \(^2\)Cardiology, MUSC; \(^3\)Pharmaceutical and Biomedical Sciences, MUSC.

2:00 - 2:15  
**199 Interstitial Trafficking of MicroRNAs Within the Human Myocardium Following Ischemia-Reperfusion,** Ashley B Arana, Robert E Stroud, Risha Patel, Jeffery Jones, Francis G Spinale; Cardiothoracic Surgery, MUSC.

2:15 - 2:30
Progression of Arterial Stiffness and Coronary Atherosclerosis: Longitudinal Evaluation By Cardiac Computed Tomography, Shane Oberoi, U Joseph Schoepf, John Nance; Radiology, MUSC.

Radiation Dose and Image Quality At High-Speed CT Angiography of the Aorta: Intra-Individual and Inter-Individual Comparison with Conventional CT Angiography, E Lexworth Hanna¹, Paul Apfaltrer¹, J. Reid Spears¹, Garrett W Rowe³, Daniel Harris¹, Stefan O Schoenberg², Rozemarijn Vliegenthart¹, U Joseph Schoepf¹; ¹Radiology, MUSC, ²Clinical Radiology and Nuclear Medicine, University Medical Center Mannheim.

Stimulation of Human Aortic Endothelial Cells (HAEC) with OxLDL-IC Stimulates Fc Gamma Receptor Expression and Endothelial Dysfunction, Katalina Romero¹, Yanchun F Li², Gabriel Virella³, Maria Lopes-Virella³; ¹Medicine, MUSC, ²Endocrinology, Diabetes & Medical Genetics, MUSC, ³Microbiology & Immunology, MUSC.

Kaposi's Sarcoma-Associated Herpesvirus Induced Expression Of Emmprin On The Cell Surface Following De Novo Infection Of Endothelial Cells, Paul A Bomar, Christopher Parsons; Infectious Disease, MUSC.

SESSION 17: PhD V: 11:45 – 3:15 pm: CHP 202

Mammary Gland Laterality in Normal and Neoplastic Development, Jacqulyne P Robichaux¹, Joan E Cunningham², Demetri D Spyropoulos³, Ann F Ramsdell¹; ¹Regenerative Medicine and Cell Biology, MUSC, ²Biostatistics, Bioinformatics and Epidemiology, MUSC, ³Pathology and Laboratory Medicine, MUSC.

Identifying Cancer-Associated Inflammatory Genes: A Data-Mining Approach, Saleh M Rachidi¹, Tingting Qin³, Jim Zheng², Zihai Li¹; ¹Microbiology and Immunology, MUSC, ²Biochemistry and Molecular Biology, MUSC.

NAVIGATE: A Trial to Increase Patient Enrollment in Thoracic and Esophageal Cancer Clinical Trials, Kathleen B Cartmell¹, Marvella E Ford², Nestor F Esnaola³, Tricia A Adrales-Bentz⁴, Terri L Matson⁴, Carolyn E Reed⁴, Debbie C Bryant⁴, Anthony J Alberg¹,³, Lauren A Smith¹, James D Bearden⁴, Howard A Zaren⁷, Anita L Harrison⁴; ¹Health Professions, MUSC, ²Biostatistics & Epidemiology, MUSC, ³Medicine, MUSC, ⁴Hollings Cancer Center, MUSC.

MKP-1 Deficiency Enhances Epithelial Neoplasia in a Murine Oral Cancer Model, Xiaoyi Zhang, Hong Yu, Keith L Kirkwood; Craniofacial Biology, MUSC.

The Role of Bone Morphogenetic Protein 4 in the Developing Inflow and Outflow Regions of the Heart, Laura Briggs¹, Jayant Kakarla², Aimee Phelps³, Andy Wessels³; ¹Regenerative Medicine and Cell Biology, MUSC, ²Regenerative Medicine and Cell Biology, MUSC.
Does Acetylation Regulate MiRNA Expression in Myocardial Infarction?, Ludivine Renaud¹, Harinath Kasiganesan¹, Santhosh K Mani¹, Erhe Gao², Jeffrey A Jones³, Robert E Stroud³, Donald R Menick¹; ¹Cardiology, MUSC, ²Center for Translational Medicine, Thomas Jefferson University, ³Surgery, MUSC.

1:15 - 1:30

Risk Stratification of Sickle Cell Patients in a Primary Care Clinic, Justin E Marsden¹, Charles Ellis¹, William P Moran², Jingwen Zhang³, Patrick D Mauldin⁴; ¹Health and Rehabilitation Science, MUSC, ²General Internal Medicine and Geriatrics, MUSC, ³General Internal Medicine, MUSC, ⁴Pharmacy, MUSC.

1:30 – 1:45  BREAK

1:45 - 2:00

Natriuretic Peptides Protect the RPE From Advanced Glycation End Products-Induced Barrier Breakdown, Mohammad Dahrouj, Zsolt Ablonczy, Craig E Crosson; Ophthalmology, MUSC.

2:00 - 2:15

Valproic Acid (VPA) Reduces Retinal Ganglion Cell (RGC) Degeneration in a Rat Model of Ocular-Hypertensive Injury, Oday Alsarraf, Phillip W Yates, Craig E Crosson; Ophthalmology, MUSC.

2:15 - 2:30

Globin Regulatory Proteins As Components Of The Molecular Response To Hypoxia In Alveolar Epithelial Type II Cells, Robyn G Lottes¹, Danforth A Newton², Demetri D Spyropoulos³, John E Baatz²; ¹Molecular and Cellular Biology and Pathobiology, MUSC, ²Pediatrics and Neonatology, MUSC, ³Pathology and Laboratory Medicine, MUSC.

2:30 - 2:45

A Comparison of the Differentiative Capacities of Induced Pluripotent Stem Cell (iPSC)-Derived Fibroblasts and Other Primary Fibroblasts in Hypoxia, Emily M Allen¹, Demetri D Spyropoulos², John E Baatz⁴; ¹Marine Biomedicine and Environmental Science, MUSC, ²Pathology, MUSC, ³Pediatrics, MUSC.

2:45 - 3:00

Pseudomonas Aeruginosa: Utilizing Two Guns of Virulence - Swarming Motility and Biofilm Formation, Jordon D Gruber, Souzan Abdel-Samie, Yong-Mei Zhang; Biochemistry, MUSC.

3:00 - 3:15

Regulation of Sphingosine Kinase 1 By P53-Dependent Proteolysis, Brittany L Carroll, Linda A Heffernan-Stroud, Lina M Obeid; Biochemistry, MUSC.

SESSION 18: PhD VI: 11:45 – 3:15 pm: CHP 204

11:45 - 12:00

The E3 Ubiquitin Ligase EDD Regulates Platinum Resistance and is a Novel Therapeutic Target for Epithelial Ovarian Cancer, Amber T Bradley¹, Hui Zheng¹, Angela Ziebarth⁶, Wayne Sakati¹, Gabriel Lopez-Berestein⁴, Anil K Sood⁵, Charles N Landen², Scott T Eblen¹; ¹Cell and Molecular Pharmacology and Experimental Therapeutics, MUSC, ²Obstetrics and Gynecology, University of Alabama Birmingham, ³Gynecologic Oncology, University of Texas MD Anderson Center.
12:00 - 12:15
**218 Development Of A Clinically Relevant Murine Model Of Pancreatic Cancer**, Clayton S Lewis, Jody T Mack, Charles D Smith; Pharmaceutical and Biomedical Sciences, MUSC.

12:15 - 12:30
**219 Defining the Role of FLI1 in Breast Cancer**, Melissa N Scheiber¹, Patricia M Watson², Victoria J Findlay¹, Tihana Rumboldt¹, Dennis K Watson¹; ¹Pathology, MUSC, ²Medicine, MUSC.

12:30 - 12:45
**220 Regulation of Telomerase By Sphingosine Kinase 2/Sphingosine-1-Phosphate Signaling in Lung Cancer**, Shanmugam Panneer Selvam¹, Yuri K Peterson², Christopher R Gault³, Lina M Obeid ³, Jennifer S Isaacs⁴, Sarah Spiegel⁵, Charles D Smith ², Besim Ogretmen¹; ¹Biochemistry and Molecular Biology, MUSC, ²Pharmaceutical Sciences, MUSC, ³Medicine, MUSC, ⁴Pharmacology and Experimental therapeutics, MUSC, ⁵Biochemistry and Molecular Biology, VCU.

12:45 - 1:00
**221 Sphingosine 1-phosphate and Acid Ceramidase Modulate the Subcellular Localization of the PTEN Tumor Suppressor**, Thomas H Beckham, Xiang Liu, Joseph C Cheng, Ping Lu, Tucker Marrison, Jim S Norris; Microbiology and Immunology, MUSC.

1:00 - 1:15
**222 Bioactive Sphingolipids Regulate Cardiac Hypertrophy and Autophagy in Lipid Overload: A Role for Myristate and Its Derivatives**, Sarah E Brice¹, An Van Laer², Catalin F Baicu², Tuoyu Geng¹, Harinath Kasiganesan², Michael Zile², L. Ashley Cowart¹; ¹Biochemistry & Molecular Biology, MUSC, ²Cardiology, MUSC.

1:15 - 1:30
**223 Fibulin-1 Regulation of HB-EGF/ErbB1 Signaling in Cardiac Valvulogenesis**, Keerthi Harikrishnan, Marion A Cooley, Waleed O Twal, Victor M Fresco, Christine B Kern, William S Argraves; Regenerative Medicine & Cell Biology, MUSC.

1:30 – 1:45  BREAK

1:45 - 2:00
**224 An Integrated Bioinformatic and Biochemical Approach to Identifying Caspase Activity During the Aging Process of Karenia Brevis**, Jillian G Johnson, Frances M Van Dolah; Marine Biomedicine and Environmental Sciences, MUSC.

2:00 - 2:15
**225 SPARC and the Collagenous Extracellular Matrix of the Periodontal Ligament**, Jessica M Trombetta-eSilva¹, Amy D Bradshaw²; ¹Dental Medicine, MUSC, ²Medicine, MUSC.

2:15 - 2:30
**226 MKP-1 is Required for Canonical 1,25(OH)2D3-signaling and Osteoclastogenesis**, Alfred C Griffin, Keith K Kirkwood; Craniofacial Biology, MUSC.

2:30 - 2:45
**227 The Contribution of Fatty Acid Amides to Prymnesium Parvum Toxicity**, Matthew J Bertin¹, Paul V Zimba², Kevin R Beauchesne³, Kevin M Huncik³, Peter Moeller³; ¹Marine Biomedicine and Environmental Sciences, MUSC, ²Pharmaceutical Sciences, MUSC, ³Medicine, MUSC.
2:45 - 3:00

**228** Estrogen Receptor Agonists Protect Against Glutamate Excitotoxicity In Spinal Cord Slice Cultures, Joshua A Smith¹, Arabinda Das¹, Gerald C Wallace¹, Swapan K Ray², Naren L Banik¹; ¹Neurosciences, MUSC, ²Pathology, Microbiology, & Immunology, USC School of Medicine.

3:00 - 3:15

**229** Changes in Prefrontal Cortex Catecholamine and Glutamate Levels During Cued Vs. Drug Primed Reinstatement of Methamphetamine-seeking in Rats, Aram Parsegian, Ronald E See; Neurosciences, MUSC.

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**SESSION 19: PhD VII: 11:45 – 3:15 pm: Bioengineering Building  BE112**

11:45 - 12:00

**230** A Novel Function of Bves Revealed By Bimolecular Interaction Studies, Claire L Hinsch, Jagadish Kummetha-Venkata, Vincent Dammai; Pathology and Laboratory Medicine, MUSC.

12:00 - 12:15

**231** Endogenous Opioids Mediate Left Dorsolateral Prefrontal Cortex RTMS-induced Analgesia, Joseph J Taylor¹, Jeffrey J Borckardt², Mark S George³; ¹Neuroscience, MUSC, ²Psychiatry, MUSC, ³Psychiatry, Radiology and Neuroscience, MUSC.

12:15 - 12:30

**232** Interleukin-10 And Kupffer Cells Protect The Fatty Liver From Ischemia And Reperfusion Injury, Alton Sutter¹, Justin Ellett², Kenneth Chavin²; ¹Microbiology and Immunology, MUSC, ²Surgery, MUSC.

12:30 - 12:45

**233** The Role Of Acid Ceramidase In The Failure Of Radiation Therapy For Prostate Cancer, Joseph C Cheng¹, S Tucker Morrison¹, Thomas H Beckham¹, Thomas E Keane², David T Marshall³, Xiang Liu¹, James S Norris¹; ¹Microbiology & Immunology, MUSC, ²Urology, MUSC, ³Radiation Oncology, MUSC.

12:45 - 1:00

**234** Elevation of CerS6 Expression Triggers Compensation Via the Ceramidase Pathway in Colon Cancer Cells, Tejas S Tirolkar, Christina Voelkel-Johnson; MCBP, MUSC.

1:00 - 1:15

**235** Identification and Characterization of PP2C Activation By Ceramide, David M Perry¹, Kazuyuki Kitatani², Patrick Roddy¹, Mohamad El-Osta¹, Yusuf Hannun¹; ¹Biochemistry, MUSC, ²Tottori University.

1:15 - 1:30

**236** The Role of the Cancer-associated Sm-like Oncogene on Apoptotic Messages and Chemotherapeutic Sensitivity in Pancreatic Cancer, Elizabeth C Little¹, Ernest R Camp², Cindy Wang², Dennis K Watson³, Patricia M Watson³, David J Cole²; ¹Microbiology and Immunology, MUSC, ²Surgery, MUSC, ³Pathology, MUSC.

1:30 – 1:45  BREAK
1:45 - 2:00

237 Transcriptional Regulation of Cartilage Link Protein in the Developing Heart, Marie M Lockhart¹, Elaine Wirrig², Aimee Phelps¹, Andy Wessels³; ¹Regenerative Medicine and Cell Biology, MUSC, ²University of Cincinnati.

2:00 - 2:15

238 Cubilin is Essential for Maintaining Blood HDL Levels, Obaidullah Aseem¹, Brian T Smith², Marion A Cooley¹, W Scott Argraves³; ¹Regenerative Medicine and Cell Biology, MUSC, ²Regenerative Medicine and Cell Biology, MUSC.

2:15 - 2:30

239 Phosphoregulation of the Cx43 Carboxy-terminus in Cardiac Injury, Joseph A Palatinus, Robert G Gourdie; Regenerative Medicine and Cell Biology, MUSC.

2:30 - 2:45

240 PGlcNAc Nanofibers From a Marine Diatom Stimulate a Scarless Wound Healing Program, Haley B Lindner¹, Aiguo Zhang², Juanita Eldridge¹, Arun Seth², Rick Visconti¹, Amy Bradshaw³, John Vournakis⁴, Robin C Muise-Helmericks¹; ¹Regenerative Medicine and Cell Biology, MUSC, ²Sunnybrook Research Institute, University of Toronto, ³Medicine, MUSC, ⁴Marine Polymer Technologies.

2:45 - 3:00

241 Histone Deacetylase Inhibitor Suberoylanilide Hydroxamic Acid Normalizes the Levels of Very Long Chain Fatty Acids in Human Skin Fibroblasts From X-Adrenoleukodystrophy Patients and Downregulates the Expression of Proinflammatory Cytokines in Abcd1/2 Silenced Mouse Astrocytes, Jaspreet Singh, Mushfiquddin Khan, Inderjit Singh; Pediatrics, MUSC.

3:00 - 3:15

242 Regulation of Mitochondrial Protein Biosynthesis By Formylation and Deformylation of Methionyl-tRNA, Kyle C Strickland, Sergey A Krupenko; Biochemistry, MUSC.

SESSION 20: Postdocs-Residents-Fellows III: 12:00 – 3:15 pm: CHP 205

12:00 - 12:15

243 Biased Agonism of the Angiotensin AT1 Receptor Induces the Akt-mediated Activation of the Mammalian Target of Rapamycin, Ryan T Kendall, Louis M Luttrell; Medicine, MUSC.

12:15 - 12:30

244 Lack of Nitric Oxide Synthases Increases Lipoprotein Immune Complex Deposition in the Aorta and Elevates Plasma Sphingolipid Levels in Lupus, Mohammed M Al Gadban¹, Jashalynn German², Jean-Philip Truman¹, Ellen C Riemer¹, Waleed O Twal¹, Kent J Smith¹, Jim C Oates³, Samar M Hammad¹; ¹Regenerative Medicine and Cell Biology, MUSC, ²Graduate Studies, MUSC, ³Rheumatology & Immunology, MUSC.

12:30 - 12:45

245 Connexin43 Interacts with Voltage-Gated Sodium Channel 1.5 in the Perinexus of Cardiomyocytes, J Matthew Rhett, Jane Jourdan, Robert G Gourdie; Regenerative Medicine and Cell Biology, MUSC.

12:45 - 1:00
246 Prognostic Importance of Age, Gender, and Subtype in Differentiated Thyroid Cancer, Samuel L Oyer¹, Valerie A Smith², Eric J Lentsch¹; ¹Otolaryngology, MUSC, ²Medicine, MUSC.

1:00 - 1:15

247 Use of Hybrid Torque+Position Controller Towards More Realistic Movement Profiles of Neurally Controlled Devices, Pratik Y Chhatbar, Joseph T Francis; SUNY Downstate Medical Center.

1:15 - 1:30

248 The SR Protein Kinase Clk1 Phosphorylates SPF45 and Regulates Its Degradation and Splice-Site Selectivity, Yuying Liu, Adnan Al-Ayoubi, Hui Zheng, Jennifer Bethard, Scott T Eblen; Cell and Molecular Pharmacology and Experimental Therapeutics, MUSC.

1:30 – 1:45 BREAK

1:45 - 2:00

249 High Throughput Antifungal Drug Screening, Visesato Mor, Erika Bullesbach, Maurizio Del Poeta; Biochemistry, MUSC.

2:00 - 2:15

250 Chromosomal Instability and Virulence: A Study with Cryptococcus Neoformans, Narendra K Bairwa, Visesato Mor, Maurizio Del Poeta; Biochemistry, MUSC.

2:15 - 2:30

251 The Sphingolipid Delta 8 Desaturase SLD8 is Involved in the Pathogenesis of Cryptococcus Neoformans, Shriya Raj, Maurizio Del Poeta; Biochemistry & Molecular Biology, MUSC.

2:30 - 2:45

252 Apoptosis-Associated Proteomic Changes in C6 Glioma Cells on Alpha-Hydroxy C16-Ceramide Treatment, Venkatesh Kota¹, Vishnu M Dhople², Nancy Smythe¹, George Fullbright¹, Zdzislaw Szulc¹, Alicja Bielawska¹, Hiroko Hama¹; ¹Biochemistry and Molecular Biology, MUSC, ²Functional Genomics, University of Greifswald.

2:45 - 3:00

253 Cellular Morphogenesis Under Stress is Influenced By the Sphingolipid Pathway Gene ISC1 and DNA Integrity Checkpoint Genes in Saccharomyces Cerevisiae, Tripathi Kaushlendra, Nabil Matmati, W Jim Zheng, Yusuf A Hannun, Bidyut K Mohanty; Biochemistry & Molecular Biology MUSC.

3:00 - 3:15

254 RANK Ligand Regulation of Autophagy in Oral Squamous Cell Carcinoma Tumor Cells, Yuvaraj Sambandam, Kumaran Sundaram, William L Ries, Sakamuri V Reddy; Pediatrics, MUSC.
001  The Effects of Beta-arrestin 1 and 2 Overexpression on TLR-induced Inflammatory Cytokine Expression in RAW 264.7, Rocky C Wong1, Hongkuan Fan2, Perry Halushka2, James Cook3, Sarah Ashton2, Peifeng Li2; 1CoF, 2CofC, 3Neuroscience, MUSC.

Previous findings from our laboratory and others indicated that beta-arrestin 1 and 2 regulate the immune system’s inflammatory response. Beta-arrestin 1 and 2 negatively regulate NF-KappaB activation and beta-arrestin 1 and 2 differentially regulate ERK 1 and 2 activation. Both beta-arrestin 1 and 2 positively regulate lipopolysaccharide (LPS)-induced inflammatory response and endotoxemia. We hypothesize that overexpression of beta-arrestin 1 or 2 differentially regulates TLR-induced inflammatory cytokine expression in RAW 264.7 macrophage cell lines. To address this hypothesis, we determined the effect of overexpression of beta-arrestin 1 or 2 on TLR4 ligand LPS and TLR2 ligand Pam3CSK4-induced TNF-alpha and IL-6 production in RAW cell lines by using ELISA. Our results demonstrate that LPS and Pam3CSK4 significantly induced TNF-alpha and IL-6 production in RAW cells expressing the control vector or beta-arrestin 1 or 2. RAW cells that overexpressed beta-arrestin 2 produced more TNF-alpha than RAW cells expressing control vector in response to LPS (p<0.05, n =3). There is no difference between RAW cells expressing control vector and RAW cells expressing beta-arrestin 1 or 2 in response to Pam3CSK4. This data suggest that beta-arrestin 2 positively regulate TLR4 induced TNF-alpha production, but has no effect on TLR2 induced inflammatory cytokine production. Beta-arrestin 1 has no effect on LPS and Pam3CSK4 induced TNF-alpha or IL-6 production. These observations support our hypothesis that beta-arrestin 1 and 2 differentially regulate cytokine expression in RAW 264.7 cell lines. Understanding the role of beta-arrestins in TLR induced inflammatory cytokine production may lead to novel therapeutic strategies to treat sepsis. MUSC College of Graduate Studies; NIH AI079248; and NIH GM27673

002 Retinyl Ester Accumulation in the Absence of Light, Colleen K Sheridan1, Yiannis Koutalos3; 1Biology, CofC, 2Ophthalmology, MUSC.

Retinyl esters are the substrates for generation of the visual chromophore, 11-cis-retinal. These esters are stored in the retinal pigment epithelium. In the light, 11-cis-retinal is isomerized and these esters are mobilized to replenish it. In mice lacking RPE65, the enzyme that catalyzes the formation of the 11-cis isomer, a build up of esters occurs. We hypothesized that in the absence of light, significantly larger amounts of retinyl esters accumulate in the retinal pigment epithelium. Wild-type mice (129/sv) were age matched and dark-adapted for various lengths of time over the course of one-month. Whole eyecups were collected and retinyl esters were extracted. Esters were then quantified using normal phase HPLC. This data was compared to the quantity of retinyl esters found in wildtype mice raised in cyclic light and in RPE65 deficient mice. Accumulation of esters in mice dark-adapted up to 29 days surprisingly showed very little difference from light adapted mice. Quantities of retinyl esters in both groups of wildtype mice were much lower than in RPE65 deficient mice. A model to explain the results is presented. NIH grant EY014850, Foundation Fighting Blindness and Research to Prevent Blindness

003 Analgesic Effects of Two Sessions of Postoperative Left Prefrontal Cortex Repetitive Transcranial Magnetic Stimulation, Luke Dong1, Scott T Reeves1, Jeffery J Borckardt2, Mark S George2, Peggy Edgerton1, Alok Madan3, Larry C Field1; 1Anesthesiology and Perioperative Medicine, MUSC, 2Psychiatry and Behavior Sciences, MUSC.

BACKGROUND: Recent preliminary trials found that a single postoperative 20 minute repetitive transcranial magnetic stimulation (rTMS) treatment over the left prefrontal cortex was associated with a significant reduction in postoperative patient-controlled morphine use. This study sought to reproduce these results and to determine the value of adding a second rTMS treatment 4 hours after surgery on postoperative opioid use and postoperative pain. METHODS: One hundred twelve participants who underwent gastric bypass surgery completed this study. Participants received two 20-minute treatments of Real or Sham postoperative rTMS. Each participant was randomized double-blind to one of four study groups for the two treatments (Real-Real, Sham-Real, Real-Sham, or Sham-Sham). Patient-controlled hydromorphone pump usage was tracked throughout each participant's postoperative hospital stay. RESULTS: There were no differences among groups with respect to the mean total PCA (mg) hydromorphone use (F(3,111)=2.32, ns) nor to the cumulative PCA usage curve slopes during the 36-hour post-operative period (F(1,111)=0.12, ns) before or after controlling for chronic opioid use status. While a trend was evident for a real TMS advantage after the first treatment (p=.11), no differences emerged during the period after the first TMS treatment but before the second in either the mean PCA dilaudid usage or the slopes of the PCA use curve during that period. CONCLUSIONS: The results of this study failed to reproduce the analgesic effect of rTMS in a postoperative setting seen in previous studies. Total PCA opioid use and cumulative PCA usage curve slopes were comparable among randomized groups. The addition of a second treatment also failed to have a positive analgesic effect. Future studies should be geared toward better understanding variables that might influence TMS effects on pain perception in the
perioperative setting and a dose-finding study seems warranted given the previous successful trials of TMS for post-operative pain management. Foundation for Anesthesia Education and Research (FAER) and Medical Student Anesthesia Research Fellowship (MSARF)

004 Determining the Variability in Developing Post-Stroke Pneumonia, Gabriela R Keeton, Daniel T Lackland; Neurosciences, MUSC.

Stroke-associated pneumonia (SAP) is the leading cause of death in the post-acute phase of stroke. The patterns and factors associated with SAP are unclear, limiting the ability to identify a consistent profile of a high-risk patient. The purpose of this study is to identify factors associated with SAP by assessing type of stroke, age, race, and gender. A cohort of 643 stroke patients with SAP was assembled from the South Carolina Hospital Discharge Database (2008-2009). Only patients with an ischemic (ISC) or hemorrhagic (HEM) stroke were considered, and pneumonia was a secondary diagnosis. Statistical analysis was conducted to determine SAP variability. More HEM patients (4.61%) developed SAP than ISC patients (2.96%), and almost double the number of HEM patients with SAP died than ISC patients with SAP. A statistically significant difference was detected between age and race in SAP development. Age is the best predictor for SAP, but there is a clear racial disparity in the multivariate analysis between type of stroke, age, and race. This data suggests that there is an association between stroke severity, SAP, and the strength that demographic variables carry in predicting SAP development. However the association between SAP and stroke severity merits further investigation. Cardiovascular Biology Grant

005 The Role of NPY in the Anxiety Associated with Cocaine Abstinence, Sonam Bhimba1, Parrish Waters2, Ronald E See3; 1CoC, 2Neuroscience, MUSC.

Cocaine withdrawal is associated with multiple negative states, including anxiety, and the resumption of cocaine use often alleviates these symptoms. Neuropeptide Y (NPY) is an endogenous 36 amino acid neuropeptide abundantly found in the central nervous with Y(1) and Y(2) receptors densely expressed in the cortex, hippocampus, and amygdala. These areas of the brain are particularly associated with mood disorders and stress response, including the anxiety associated with cocaine withdrawal. The goal of this study is to investigate the role of NPY in changes that occur in the brain during withdrawal from cocaine abuse. We used an animal model of cocaine addiction, in which animals self-administer cocaine in daily sessions and then experience forced abstinence. Following cocaine self-administration and abstinence, we measured anxiety using the elevated plus-maze, and central levels of NPY and NPY receptors using the protein quantification techniques, western blotting and ELISA. Animals exhibited increased levels of anxiety during abstinence, and preliminary data suggest that there is a correlation between anxiety and the levels of NPY found in the brain, such that decreased levels of NPY produce anxiogenic effects. Our results indicate that NPY is a significant factor in the anxiety involved with drug addiction. NIH P20 RR-016461

006 Generation of Nicotinamide Adenine Dinucleotide Phosphate (NADPH) in Vertebrate Photoreceptors, Leopold Adler IV1, Yiannis Koutalos2, Chunhe Chen2; 1Physics and Astronomy, CoFC, 2Ophthalmology, MUSC.

The reduced form of nicotinamide adenine dinucleotide phosphate (NADPH) is the main source of reducing equivalents for reactions in the cytosol. Living vertebrate photoreceptor cells were used as model system to examine the generation of NADPH in real time. Photoreceptors contain a high concentration of a visual pigment than contains an 11-cis retinyl chromophore, which is used to detect light. The process of detecting light is initiated by the photosomerization of the visual pigment chromophore to all-trans. Subsequently, the chromophore is released from the pigment in the form of all-trans retinal. Utilizing NADPH as the reducing agent, all-trans retinal is then reduced to all-trans retinol. The formation of all-trans retinol can be measured in single cells from its fluorescence, using fluorescence imaging. Since the formation of all-trans retinol requires NADPH, the system can be used to study the generation of NADPH. Previous analyses of the kinetics of the reduction of all-trans retinal to all-trans retinol have taken NADPH to be in great excess. However, in bright light conditions, photoreceptors have a high demand for NADPH, due to constant release of all-trans retinal from photo-activated rhodopsin. The kinetics of the release of all-trans retinal has previously been independently determined and is known to be significantly faster than the formation of all-trans retinol. This time delay between the release of all-trans retinal and the formation of all-trans retinol, reflects limited availability of NADPH and can be used to estimate the rate of NADPH production. A numerical model of the formation of all-trans retinol that incorporates the production of NADPH as a first order process has been developed.

007 Changes in Vasopressin Receptor Levels in Extended Amygdala Affect Anxiety During Cocaine Withdrawal, Sarah K Grothouse1, R P Waters2, Ronald E See3; 1CoFC, 2Neuroscience, MUSC.

Relapse is a major obstacle in the treatment of cocaine addiction, and a primary trigger of relapse is the anxiety associated with abstinence. Vasopressin is modified by cocaine taking, and may contribute to this anxiety. We modeled cocaine addiction using an animal model of cocaine addiction, in which rats self-
administered cocaine during daily 6 hour sessions. After 14 days of access to cocaine and 42 hours of abstinence, anxious behavior was measured using the elevated plus maze. Using western blotting, we measured levels of vasopressin receptors in the extended amygdala of animals that self-administered cocaine and saline controls. Our results demonstrate heightened levels of anxiety in our cocaine-exposed animals, and suggest that changes in vasopressin receptor levels may underlie these behavioral changes. NIH P20 RR-016461

008 Cocaine Self-Administration Modulates Vasopressin Receptors in the Extended Amygdala. Alana D Guziewicz1, Parrish Waters2, Ronald See3; 1Biology, CoF, 2Neuroscience, MUSC.

Relapse is a major obstacle in the treatment of cocaine addiction, and a major contributor to relapse is the anxiety associated with abstinence from cocaine. Vasopressin is a neurotransmitter that is highly involved in anxiety, and evidence suggests that it could play a central role in the anxiety associated with cocaine withdrawal through activation of stress related brain centers. To investigate this possibility we used rats trained to self-administer cocaine to study behavioral and physiological changes during cocaine addiction and withdrawal. We analyzed levels of vasopressin and vasopressin receptors in the brains of the animals using the immunohistochemical method of protein detection. These levels were compared to those of control animals that self administered saline. Data collection is ongoing, and we have detected increased anxiety levels in animals that self administered cocaine. Preliminary evidence suggests a modulation of vasopressin receptors in the brain regions that mediate anxiety, such as the amygdala, BNST, and nucleus accumbens. NIH P20 RR016461

009 Impact of Modafinil on Stress and Cue Reactivity in Cocaine Dependent Individuals. Charles D Leiner1, Margaret M Moran-Santa Maria2, Lisa Nunn2, Ronald E See3, Aimee L McRae-Clark4; 1Medicine, MUSC, 2Psychiatry & Behavioral Sciences, MUSC, 3Neurosciences, MUSC, 4Psychiatry & Behavioral Services, MUSC.

Background: Cocaine dependence is a major health disorder in the US. Attempts to find effective medications for attenuating drug craving and relapse have been unsuccessful. Factors leading to relapse include stress and drug-cues, but knowledge of the compounding effects of these factors is still lacking. Modafinil combined with psychotherapy, has shown promise in facilitating abstinence. The focus of the present study was to evaluate the impact of modafinil on stress-reactivity and combined stress- and cue-reactivity in cocaine dependent individuals (CDI). Methods: Modafinil (400mg) was given to CDI for three days. Subjects were then randomized to a Trier Social Stress Test (CDI+M+S; n = 13) or no-stress activity (CDI+M+NS; n = 11). Subjects were then exposed to cocaine-related cues. Outcome variables included HR, MAP, serum cortisol, subjective stress and drug craving levels. These preliminary data were obtained from an on-going study, preventing access to placebo data. Thus, to examine the impact of modafinil on stress reactivity, data from the modafinil pretreated groups were compared with data from a previous clinical study of cocaine dependent subjects (CDI+S; n=33) and healthy controls (HC+S; n=36) who were also exposed to the Trier. Results: Peak change in MAP measured five minutes after the Trier was significantly greater in the CDI+M+S, CDI+S, HC+S groups than CDI+M+NS group (p<0.001). All other measures were not significant between groups (p<0.05). Analysis of area under the curve for subjective data revealed no significant difference between groups in either subjective craving or stress (p>0.05). There were no significant differences between stress and no-stress modafinil-pretreated groups in any outcome measure in response to the cocaine cues (p>0.05). Conclusions: These preliminary data suggest modafinil alone may not attenuate stress reactivity and cocaine craving. This supports findings in recent studies that modafinil treatment alone has little impact on drug craving and abstinence. NIH/NCCR UL1 RR029882; 5R01DA021690-05; and NIDA R25DA020537

010 Effect of Intranasal Oxytocin on Marijuana Craving. Aaron M Schott, Amanda M Wagner, Erin N Lindley, Nathan Baker, Aimee McRae-Clark; Psychiatry and Behavioral Sciences, MUSC.

Marijuana is the most commonly used illicit drug in the United States. Previous models show that stress plays a large role in the motivation to abuse substance, such as marijuana. The neuropeptide oxytocin has been shown to impart anxiolytic effects, ranging from trust and social bonding to calmness and mood enhancement. In this study, we investigated whether intranasal administration of oxytocin would attenuate the drug craving response to a psychosocial stress task in marijuana-dependent individuals. Individuals age 18-65 years meeting DSM-IV criteria for marijuana dependence were randomized to receive either oxytocin (40IU) or placebo nasal spray prior to completing the Trier Social Stress Task (TSST). Craving was assessed using the Marijuana Craving Questionnaire (MCQ) immediately prior to and immediately following completion of the TSST. Differences in MCQ pre- and post-TSST were compared across groups using the Wilcoxon Rank Sum Test. There was an attenuation of the craving response in the oxytocin group (n=5) as compared to the placebo group (n=6) in the Emotion and Expectancy domains of the MCQ (p=0.010 and p=0.021, respectively). A trend for attenuation in the overall MCQ score (p=.090) in the oxytocin group compared to the placebo group was also observed.
Although this is an ongoing pilot study with a small sample size to date, this preliminary analysis suggests that oxytocin may reduce stress-induced craving in marijuana-dependent individuals.

**011 Modafinil Reverses Methamphetamine-Induced Memory Deficits On An Object-In-Place Task In Rats: Role Of Glutamate Receptor Expression.** Meghin J Gilstrap¹, Carmela M Reichel², Lauren A Ramsey³, Jackie F McGinty⁴, Ron E See⁵; ¹Psychology/Neuroscience, CofC, ²Neurosciences, MUSC, ³Biology, CofC.

Chronic methamphetamine (meth) frequently results in persisting cognitive deficits in animals and humans. We demonstrate here that contingent meth impairs memory on an object-in-place task, which measures the ability to identify an object relative to its location and surrounding objects. We also evaluated whether modafinil reversed this cognitive impairment. Rats self-administered i.v. meth (0.02 mg/infusion) on and FR1 schedule of reinforcement (7 days for 1 hr/day, followed by 14 days for 6 hr/day), or received yoked saline infusions. After one week of withdrawal, rats were tested for object-in-place recognition memory. In brief, rats explored four objects for five minutes in a closed test chamber. Ninety minutes later, the location of two objects was changed in order to assess memory for object location and the total time spent at each object was recorded. Half the rats received either vehicle or modafinil (100 mg/kg) immediately after familiarization. Our results revealed that saline-treated rats spent more time interacting with the objects in changed locations, while meth-treated rats distributed their time relatively equally among all objects, regardless of location. Meth-treated rats that received modafinil showed a reversal in the deficit; that is, they spent more time exploring the objects in the new locations. Our results demonstrate both meth-induced cognitive deficits on an object-in-place task and the subsequent reversal of these deficits by modafinil. Comparisons of glutamate NMDA receptor levels in brain areas involved in memory tasks (e.g. prefrontal cortex, perirhinal cortex, and hippocampus) will be presented. Characterization of meth-induced impairments of glutamate NMDA receptors (e.g. NR1, NR2A, and NR2B) in frontal and temporal cortical areas and their subsequent alteration by modafinil may identify neurobiological substrates that are the basis for the behavioral effectiveness of modafinil and its potential use as a treatment in meth addiction. *P20DA022658, and F32DA029344.

**012 Oxytocin As A Neuromodulator Of The Stress Response System For Self-Administered Cocaine Animals.** Stephanie R Johnson¹, Parrish R Waters², Ronald E See²; ¹Biology, CofC, ²Neuroscience, MUSC.

Anxiety during withdrawal from drugs of abuse is a major contributor to relapse. Although multiple systems influence this phenomenon, oxytocin has emerged as a potential contributor to withdrawal mediated anxiety. To better understand the role of oxytocin in cocaine withdrawal associated anxiety, we used an animal model of cocaine addiction, in which rats self-administer cocaine during daily 6 hour sessions for 14 days; a group of yoked saline animals served as controls. Following self-administration and 2 days of abstinence, we assessed anxiety levels using the elevated plus maze (EPM). We used the protein quantification technique, Western Blotting, to identify potential changes in oxytocin receptor levels in the extended amygdala of animals that self-administered cocaine. Animals that self-administered cocaine exhibited higher levels of anxiety-like behavior on the EPM, and preliminary evidence suggests that changes in central oxytocin receptor levels may influence this change in behavior. *NIH P20 RR-016461*

**013 Novel Targets of Nxx2.5 Regulation in the Second Heart Field.** Anthony J Horton, Kyu-Ho Lee; Regenerative Medicine and Cell Biology, MUSC.

Abstract not available.

**014 In the ADAMTS5 Mouse Model of Myxomatous Valve Disease Increased Proteoglycans Contribute to Disease Progression.** Kelsha M Washington¹, Loren E Dupuis², Marion A Cooley², W Scott Argraves³, Christine B Kern²; ¹Clalfin University, ²Regenerative Medicine and Cell Biology, MUSC.

Abstract not available.

**015 Effects of a Connexin43 Mimetic Peptide on Myocyte-Fibroblast Adhesion in a 3D Model of Cardiac Injury.** Hina Siddiqui¹, Emily L Ongstad², Robert G Gourdie²; ¹Biology, College of Charleston, ²Regenerative Medicine and Cell Biology, MUSC.

Abstract not available.

**016 Retrospective Noise Correction in Diffusional Kurtosis Imaging.** Glenn R George, Tabesh Ali; Radiology and Radiological Science, MUSC.

Diffusional kurtosis imaging (DKI) is a novel, non-invasive, magnetic resonance imaging (MRI) technique that can be used to measure the properties of water diffusion in vivo to assess tissue microstructure and pathophysiology. DKI is an extension of conventional diffusion tensor imaging (DTI), which, unlike DTI, does not assume that water diffusion is Gaussian. Since movement of water in biological tissues is often non-Gaussian, DKI provides a more accurate representation of water diffusion patterns than DTI. The additional information contained in DKI has been shown to be useful in assessing disease-related tissue changes. To access this complementary information, MRI data should be obtained at higher diffusion weightings than required.
Spaceflight causes physiological changes affecting bones, muscle and cardiovascular systems. Another consequence of spaceflight is an alteration in the levels and locations of nutrients in the body. For example, calcium, iron, zinc, and vitamins K, D and folate all undergo changes as a consequence of spaceflight. Attempts to address this deficiency through vitamin and mineral dietary supplements have not been entirely effective, suggesting the possibility that spaceflight affects normal mechanisms of nutrient absorption. Given the importance of the small intestine for nutrient absorption, we hypothesize that spaceflight causes alters function of the small intestine, thereby influencing nutritional status. To test this, gene expression profiling was conducted on small intestine samples (n=4) from mice flown for 11 days on space shuttle mission STS-108. Analysis of spaceflight samples detected differential expression of 155 genes as compared to samples from mice maintained on earth (fold change >2, p <0.05, estimated false discovery <5%). A majority of these genes were also found to be differentially expressed in response to fasting, which was evident based on analysis of published microarray studies. An unbiased analysis of the genes affected by spaceflight revealed that several biological processes were significantly represented, including cell cycle, oxidoreductase activity, and response to temperature. Gene expression data was further analyzed to examine functional categories predicted to be affected by spaceflight (i.e., biased analysis). Among the categories examined, several showed an apparent response to spaceflight, including digestion, response to stress, and oxidative stress. Differential expression was validated for six genes representative of functional categories implicated as affected by spaceflight through either the unbiased and/or biased analyses. These results provide new insight into spaceflight-induced changes in intestinal functional. Furthermore, they suggest that agents promoting appetite and protecting against oxidative stress may improve small intestine function in space, thereby improving astronaut nutritional status.

**018 The Effect of Fingolimod (FTY720) on Small Cell Lung Cancer and Non-Small Cell Lung Cancer**, Jessica Creel, Sahar Saddoughi, Besim Ogretmen, Jessica Creel, Sahar Saddoughi, W Scott Argraves, Max N Hughes, Jeremy L Barth, S Balagopal, W Scott Argraves, Clemson University, Regenerative Medicine and Cell Biology, MUSC, Winthrop University, Biochemistry & Molecular Biology, MUSC.

Ceramide, a bioactive sphingolipid, has been shown to exert anti-proliferative functions against lung cancers via PP2A-dependent degradation by directly binding to the inhibitor 2 of PP2A (I2PP2A), which results in PP2A activation. The clinical relevance of the ceramide-I2PP2A interaction in lung cancer progression was explored using 10 patient lung adenocarcinoma tissues, with their paired pathologically non-cancerous adjacent lung tissues. In these samples, I2PP2A is overexpressed in about 70% of the tumors and the C18-ceramide levels are decreased within the majority. These data suggested to us a novel hypothesis, that the lack of ceramide in combination with increased levels of I2PP2A, modulate PP2A-dependent degradation in lung tumors. Thus, reactivating PP2A tumor suppressor signaling may be an attractive therapeutic strategy for lung cancer. Our current studies have been focused on a new sphingosine analog, FTY720, which was recently FDA approved for multiple sclerosis. In this study, FTY720 was used to treat both H1341 SCLC and A549 NSCLC at various doses, and the IC50 was determined to be 10μM for each cell line. To investigate cell death pathways required for FTY720 anti-cancer effects, Necrostatin, a necrotic cell death inhibitor, was used in combination with FTY720. Inhibition of the necrotic pathway resulted in a 33% protection from cell death by FTY720. To investigate the role of PP2A in the FTY720 mediated cell death of lung cancer cells, Okadaic Acid, a PP2A inhibitor, was used and resulted in a 30% protection from FTY720. To further understand FTY720’s anti-cancer mechanism in-vivo, A549 xenographs were implanted on the flanks of SCID mice and treated daily with 10mg/kg of FTY720 (oral) leading to a significant reduction in tumor volume compared to control. In conclusion, these data indicate that FTY720 may be an exciting new therapeutic option to clinically target
019 FOXO3a Transcription Factor Regulation By Thromboxane Receptor-β Signaling: Novel Mechanism for Malignant Transformation, Philip M Sobolesky1, Julie Woolworth1, Yuan Shao2, Elizabeth Fowler1, Dennis K Watson1, Perry V Halushka2, Omar Moussa3, 1Pathology and Laboratory Medicine, MUSC, 2Pharmacology, MUSC.

The mechanisms of malignant transformation of urothelial cells is currently unknown. Previous data from our group have shown the thromboxane receptor isoform β (TP-β) is overexpressed in 80% of bladder cancer patients and TP-β can induce oncogenic transformation of the immortalized urothelial cell line SV-HUC. Thromboxane signaling occurs through Ga12 and β-arrestin 2, which in turn activates AKT and ERK. The aim of the current studies is to elucidate the mechanism of cellular transformation induced by activated TP-β signaling. We utilized a protein-protein interaction array approach to screen for TP-β binding partners. Forkhead box transcription factor 3a (FOXO3a) was identified as one of the proteins that directly interact with TP-β. Immunoprecipitation studies followed by western blot analysis confirmed the interaction. FOXO3a is a transcription factor with tumor suppressor activities and regulates genes involved in cellular processes such as cell cycle arrest, apoptosis, metabolism, DNA repair, and cellular stress resistance. shRNA knockdown of FOXO3a was sufficient to transform SV-HUC cells in vitro evidenced by loss of contact inhibition. TP-β agonist stimulation with U46619 activated AKT and ERK which resulted in increased phosphorylation of FOXO3a at both Ser253 and Ser294 AKT and ERK phosphorylation sites, respectively. Phosphorylation of FOXO3a causes transcriptional inactivation and transportation out of the nucleus where it becomes targeted for degradation. In our bladder cancer model we have shown that FOXO3a upregulates the transcription of manganese superoxide dismutase (MnSOD). MnSOD has been shown to remove reactive oxygen species (ROS) from the cell. Previous studies have shown that ROS can stabilize TP-β by changing the subcellular localization. Our proposed model is that malignant transformation could be a result of feedback loop mechanism where TP-β stimulation causes decreased FOXO3a transcriptional activity thereby decreasing MnSOD levels, and enhancing ROS levels which in turn stabilize TP-β. NIH R01CA127905

020 Velcade and Organ Transplant Desensitization, Emma M Bradley, Omar Moussa, Yuan Shao; Pathology and Laboratory Medicine, MUSC.

Abstract not available.

021 Attitudes and Knowledge of Atrial Fibrillation Treatment and Stroke Prevention, Andrew B Gundран1, Daniel T Lackland2, 1Psychology, Clemson, 2Neuroscience, MUSC.

Atrial fibrillation is the most common heart arrhythmia in the United States affecting around 2.3 million people, of which the majority of patients affected are the elderly. One of the major risks associated with atrial fibrillation is the five to seven fold increase of ischemic stroke risk. A survey named Afib STROKE was conducted by Harris Interactive on behalf of Boehringer Ingelheim Pharmaceuticals, Inc, in collaboration with National Stroke Association between April 8, 2010 – June 28, 2010 involving 507 patients with non-valvular atrial fibrillation (55.1% female, 44.9% male; mean age 67.59). The data was analyzed to assess attitudes and knowledge of patients and physicians about atrial fibrillation to identify factors in more informed and compliant patients and determine the facts and information that should be communicated to patients to fully understand their condition, treatment, and stroke prevention. Patients that recall discussing their atrial fibrillation with their physicians when first diagnosed had a higher likelihood of being informed about atrial fibrillation and stroke prevention. The amount of time discussed had different impacts on how informed patients were about certain aspects of atrial fibrillation as some as knowledge of some aspects of atrial fibrillation would increase with time while others would decrease demonstrating no significance in how informed a patient would be. The study has suggested the impact of communication and education between patients and physicians, especially when first diagnosed with atrial fibrillation. In addition, it has highlighted the importance of the patient-physician relationship and helped recognize what needs to be communicated to patients about atrial fibrillation and stroke prevention. MUSC SURP

022 Growth Failure In Early Neglect: A Comparison Of Neglected U.S. Children And International Adoptees, Doreen Condon1, Brad Miller2, John Himes2, Andrea Summer3, Angela Larosa4, Eve Spratt3; 1Pediatrics, MUSC, 2Univ of Minnesota, 3Medicine, MUSC.

Early adversity, including neglect and deprivation, can have a profound and long-lasting impact on growth in children. This has been well-studied in international adoptees, but less is known about the impact of neglect in U.S. children. In this prospective cohort study, children ages 3 to 10 were recruited from primary care clinics, an international adoption clinic, and from the general population via advertisement. Children were stratified into three groups a) U.S. neglect (USN); b) previously institutionalized international adoptee (IA); and, c) Control (CTL). After screening interview of parent/guardian, children underwent physical examination, anthropometry,
behavioral and psychometric screening, cognitive testing and collection of saliva, urine and serum. Of the children enrolled (n=60; 17 USN, 15 IA, 28 CTL), Height SDS showed significant differences between groups (USN -0.03, IA -0.50, CTL +0.29, p<0.05, but age adjusted means were not statistically different (p=0.07). Age-adjusted Head circumference (HC) was significantly smaller (p<0.05) in IAs (50.1 cm) than USN (51.1) and CTL (51.7). There was a trend toward heavier weight SDS in USN (+0.10) than IA (+0.59, p=0.06). When mean IGF-1 was adjusted for age and weight SDS, there was a significant difference (p<0.05) between CTL and abused groups (USN 157.8 ng/dL, IA 129.4, control 124.3). The degree of growth failure in height and HC in IAs is similar to that seen in other studies. Compared to IAs and the reference population, USN have higher growth factors that may be related to increased weight in this group. The difference between these two dysinhibited populations may be a relative access to nutrition in USN compared to IA children that could result in excessive weight gain. Further studies are necessary to understand the relationship of early neglect in U.S. children to later growth problems and obesity. K23MH-63111; MUSC DART and SCTR

023 Association of Willingness to Participate in Research Studies with Payment, Risk, and Time Among Individuals with Type 2 Diabetes. Kimberly T Arnold1, Leonard Egede2, Clara L Dismuke3, Joni Strom1; 1CoF, 2Health Disparities, MUSC, 3VAMC.

There are several factors that influence a patient's willingness to participate in research studies including personal values, trust in the healthcare system, and an assessment of personal benefit (payment and risk). Bentley and Thacker (2004)9 found that monetary payment had positive effects on respondents' willingness to participate in research, regardless of risk, but it did not blind them to the risks involved in the studies. This study was conducted to discover the effects of payment, risk, and time on the willingness of patients with type 2 diabetes to participate in research studies. The hypothesis is patients will be more willing to participate in research studies with higher payment levels and lower levels of risk and time. A sample of 534 patients with type 2 diabetes was recruited from the MUSC University Internal Medicine Clinic, the Franklin C. Fetter Health System, and the Ralph H. Johnson VA Medical Center primary care clinic. To assess patient willingness to participate in research modules, subjects rated various research designs that involved different levels of risk, payment, and time. We used the Dickert and Grady model of payment for research from the study by Bentley and Thacker for this analysis. There was a negative correlation between risk and willingness with a Pearson correlation coefficient of -0.42862 and p value of 0.1262, but was not statistically significant at p<0.05. There was also a negative correlation between time and willingness with a Pearson correlation coefficient of -0.52286 and statistically significant p value of 0.0551. There was a positive correlation between payment and willingness with a Pearson correlation coefficient of 0.48885 and a p value of 0.0761, but was not statistically significant. The patients involved in this study were concerned with time more than payment or risk. NIDDK T35 grant

024 A Comparison of the Impact of Community Support on Post-Disaster Mental Health Outcomes in Urban and Non-Urban Settings. Jenny S West1, Matthew Price1, Kirstin Grös1, Jenna McCauley1, Dan F Grös2, Kenneth J Ruggiero1; 1Psychiatry, MUSC, 2Mental Health, VAMC.

Exposure to disasters is associated with increased risk for immediate and long-term psychological distress (Carr et al, 1997; Kessler et al, 2008; Weisler, Barbee, & Townsend, 2006). Previous research has shown a strong association between self-rated health, social support, and community support following a natural disaster (Ruggiero et al, 2009; Acierno et al, 2007; Bourque et al, 2006). However, relatively little research has examined the extent that community support impacts post-disaster psychological distress across urban and non-urban areas. Community support is a critical variable when examining health disparities across urban and non-urban areas. Support within the community may play a greater role in buffering the mental health impact of disaster among non-urban areas by offsetting potentially limited access to professional services (e.g. mental health professionals). The present study compared the moderating effect of community support on the association between disaster exposure and mental health outcomes in urban and non-urban residents of Galveston and Chambers counties after Hurricane Ike. Eight hundred and seventy-one adults completed telephone based surveys 12-17 months after the hurricane. A multi-group structural equation modeling was used to evaluate differences in the conditional effect of community support on the association between disaster exposure and mental health symptoms across urban and non-urban areas. Findings suggested that for participants living in non-urban areas, increased community support reduced the association between mental health problems and disaster exposure, b = 0.81, p < 0.001. However, there were no significant associations between community support and mental health problems for those living in Urban areas, b = -0.54, p = 0.18. These findings suggest that the effect of community support is stronger in non-urban environments. Efforts to address the psychological fallout of a natural disaster in non-urban areas should capitalize on the potentially strong impact of community support. Further research is needed to better understand the reduced role of such support in urban settings.
025 Exploring Health Behaviors and Life Satisfaction Amongst Health Professional Students At the Medical University of South Carolina, Brian C Ginty, Elizabeth B Brown, Shirabrandy Garza, Emily A Jeffcoat, Laura C Patterson, Hazel L Breland; Occupational Therapy, MUSC.

Transitioning to post-secondary education often leads to the development of health-risk behaviors in areas such as alcohol, tobacco, nutrition, physical activity, and sleep patterns, placing students at an increased likelihood of developing long-term unhealthy behavior patterns. First-year health professional graduate students already have and will continue to acquire knowledge and exposure to health risks. Nonetheless, currently there is little known about the relationship between their knowledge and the health behaviors they actually practice. Given the prevalence of health-risk behaviors in the general college-age population, there is a need to gather preliminary information on the health and wellness of first-year health professional graduate students. The current project is an extension of a project conducted in 2010 (HR# 20302). This study examined health behaviors practiced by first-year health professional graduate students at the Medical University of South Carolina (MUSC) enrolled in the medical doctor (MD), occupational therapy (OT), physical therapy (PT), and physician assistant (PA) graduate clinical education programs. A survey of behavioral risk factors was adapted based on the Behavioral Risk Factor Surveillance System Survey Questionnaire (BRFSS) to examine the health behaviors practiced among first-year health professional students. The survey will be administered to approximately 150 first-year students enrolled in graduate clinical education programs in the College of Health Professions and the College of Medicine. Our anticipated results are that by the first-year health professional graduate students will identify their current practiced health behaviors, it will enhance their ability to facilitate health education as a means of promoting positive health behaviors of their future clients as well as improve health behaviors and eventual life satisfaction as health professional live the lifestyle they advocate to their patients.

026 Management of Hypertension At a Free Clinic and Emergency Department, Thomas E Miller III, Daniel Lackland; Neurosciences, MUSC.

Abstract not available.

027 Movement Patterns of Infants with Known Brain Abnormalities in the First 3 Months of Life, Allison E McFall, Laura Beth Meyer, Caitlin Judd, Maggie Balleh, Jessica Perkel, Noelle Moreau, Patty Coker-Bolt, Dorothea Jenkins, Occupation Therapy, MUSC, Occupational Therapy, MUSC, Physical Therapy, MUSC, Pediatrics-Neonatology, MUSC.

Cerebral Palsy (CP), the most prevalent childhood movement disorder, is characterized by abnormalities in the developing brain. Children with CP demonstrate impairments of the motor system, abnormal muscle tone, presence of primitive reflexes, atypical postural reactions, and delays in motor skill development. The period of time shortly after infant brain injury is critical to the developing brain and provides a window of time in which early intervention could enhance an infant's later functional outcome. A detailed knowledge of how to define the atypical motor development in infants with CP is a critical step in providing therapeutic interventions to improve outcomes for these infants. The specific aims of this study are to identify, within the first 3 months of life, atypical patterns of movement and muscle development in two infants with known brain abnormalities. Infant motor tests, motion kinematics, and muscle ultrasound were performed on each infant at 6-weeks, and 12-weeks to establish preliminary normative data on differences in motor skill acquisition and muscle development. Preliminary results reveal that each child fell within the average range on infant motor assessments at 6 and 12 weeks. However, further video analysis of these motor assessments found that both infants exhibited atypical quality of movement in terms of use, frequency of movement, asymmetry, and compensatory movement patterns. Additionally, muscle ultrasound detected abnormalities of the gastrocnemius muscle architecture at 6 and 12 weeks in length of the muscletendon unit and ankle range of motion. Although both infants had known brain abnormalities, neither infant qualified for early intervention services using current screening and assessment tools. Findings of this study demonstrate the need for more sensitive assessments of early abnormal motor and muscle patterns in high risk infants which could facilitate targeted intervention during early development, prior to the onset of significant clinical deficits associated with CP.

028 An Exploration of Early Motor Delays and Early Intervention for an Extremely Premature Infant, Lisa M Johnson, Abbie K Martin, Jessica Perkel, Noelle Moreau, Patty Coker-Bolt, Dorothea Jenkins, Occupation Therapy, MUSC, Pediatrics-Neonatology, MUSC, Physical Therapy, MUSC.

There are approximately 9,000 preterm births in South Carolina each year, representing 14.3% of live births. Extremely premature infants are at greatest risk for developing cerebral palsy (CP), developmental delay
(DD), vision and hearing loss although many preterm infants are not diagnosed with CP until 18-24 months of age. States address this at risk population by providing early intervention (EI) services, however many at risk infants do not receive EI until late in the first year of life. The stress of extreme prematurity and early delays can greatly affect the developmental outcomes of infants as well as the family. The purpose of this study is to identify early markers of CP and DD in an extremely premature infant while examining the perspective of the mother on raising an infant with early motor delays. This mixed methods case study consisted of a review of the infant’s medical records, an analysis of infant motor assessments at term, 6 and 12 weeks corrected age, MRS/DTI data, and parent interview. Results indicated that the infant was below average on motor assessments at term and 6 weeks, and low average at 12 weeks corrected age. MRS revealed the presence of lactate peaks nearly 13 weeks after birth, indicating continued abnormal glucose consumption in the basal ganglia and watershed areas. The infant, however, did not qualify for EI services and was not referred to therapy until 6 months of life. This case study demonstrates the difficulties surrounding early diagnosis of CP and DD in extremely premature infants. Future studies should focus on improving detection and early diagnosis of infants with CP and DD. In addition, a closer inspection of the EI process for extremely premature infants could lead to implementation of services prior to the onset of significant deficits associated with CP and DD. Specialized Center of Research (SCOR)

029 Infant Head Movements: Intrarater and Interrater Reliability Using Dartfish 2D Motion Kinematics, Caroline G Tuttle1, Casey E Hudson1, Jessica Perkel2, Noelle Moreau3, Patty Coker-Bolt1, Dorothea Jenkins4; 1Occupational Therapy, MUSC, 2Pediatrics, MUSC, 3Physical Therapy, MUSC.

Typical and atypical motor development in infants is assessed according to age-based developmental motor milestones. Many early infant motor tests involve observations of head movements since an infant’s ability to successfully participate in daily activity requires head control for vision, play, feeding, and bonding with family. In a typically developing three month old, the head should be kept in line with the body due to improved strength of the infant’s neck muscles. The ‘Pull-to-Sit’ test is one early developmental motor test to examine early head control. This test looks at the amount of an infant’s head movement during the ‘Pull-to-Sit’ test. Fifteen infants were tested during 6 and 12 week assessments and head movements were examined at 30, 45, 60, 75, and 90 degrees in the sagittal plane during the ‘Pull-to-Sit’ test. Each of the examiners followed a specific protocol for using the Dartfish software to analyze the infants’ sagittal plane head movements during this test. Interclass Correlation Coefficients were excellent, intrarater reliability values were .99 and interrater reliability values were .96. Results of this study suggest that the Dartfish kinematic motion software is a reliable measure for analyzing early sagittal plane head movements in infants. The use of 2D motion analysis may improve the accuracy of assessing head movement in early infancy which could lead to the early identification of infants with abnormal head movements at greatest risk for future developmental delay. MUSC Specialized Center of Research (SCOR)

030 Early Motor Skill Differences in Low and High Risk Preterm Infants, Stacy G McGinnis1, Rebecca K Wiesner1, Jessica Perkel2, Noelle Moreau3, Patty Coker-Bolt1, Dorothea Jenkins4, Michelle Woodbury5; 1Occupational Therapy, MUSC, 2Pediatrics – Neonatology, MUSC, 3Physical Therapy, MUSC, 4Pediatrics – Neonatology, MUSC.

Cerebral palsy is the most common cause of physical disability in children. Extremely premature infants are at greatest risk for developing CP. The current time frame for the diagnosis of CP is between 18-24 months. Unfortunately, due to late diagnosis, occupational and physical therapists are unable to provide supportive programs that could decrease the onset of significant clinical deficits associated with CP. The most well studied method used to diagnose CP is Magnetic Resonance Imaging (MRI), but there are important safety concerns for using imaging with vulnerable premature infants and testing should target infants at greatest risk for later delays. In order to improve the timely detection and diagnosis of children with CP, a description of motor skill development in the first three month of life is crucial. The purpose of this study is to identify early motor skill patterns in low and high risk infants. This pilot trial will determine quantifiable motor skill patterns in preterm infant at term and 12-weeks corrected age. A detailed knowledge of differences between high and low risk preterm infants will improve the referral of at risk infants for diagnostic imaging studies and early intervention services. Seventeen preterm infants, 8 females and 9 males, were tested at term, 6 weeks, and 12 weeks corrected using the Test of Infant Motor Performance (TIMP). Descriptive exploratory analysis and Rasch statistical analyses were used to differentiate motor skill patterns between high and low risk preterm infant groups. Low and high risk infants demonstrate specific motor skill patterns of the head, upper, and lower extremity at term and 12-weeks corrected age. These motor skills can be ordered on a
Dorothea Jenkins

in Young Infants

Obtained Using Two

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warrant further investigation. High risk for developing CP. These novel results occur much

weeks of CGA, suggesting that MA adaptations may

summary, gastrocnemius MA differences can be

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Only GSMT increased in HPT, suggesting that the

gastrocnemius muscle size increased in LPT on

were detected in DROM. Conclusion: MTU length

and 12 weeks in HPT (p < 0.05). No group differences

were detected between preterm infants at low risk (LPT) and

high risk (HPT) for future developmental disabilities

before 12 weeks of age. Methods: Three LPT and

three HPT infants were assessed at 6 and 12 weeks of

corrected gestational age (CGA). Medial gastrocnemius MA was measured using 2-D Bmode ultrasound imaging and included musculotendinous unit (MTU) length, cross sectional area (CSA), muscle thickness (MT), and combined gastrosoleus thickness (GSMT). Dynamic ankle ROM (DROM) during standing was measured with 2-D video analysis software. Passive ankle ROM (PRM) was measured with a standard goniometer. Non-parametric data analysis was performed. Results: At 6 weeks, PROM measures were greater in LPT compared to HPT (p < 0.05). LPT MTU and CSA increased from 6 to 12 weeks and were greater than HPT at both time points (p < 0.01). Only MTU and GSMT increased between 6 and 12 weeks in HPT (p < 0.05). No group differences were detected in DROM. Conclusion: MTU length increased in both groups from 6 to 12 weeks, while gastrocnemius muscle size increased in LPT only. Only GSMT increased in HPT, suggesting that the soleus may be less affected in high risk infants. In summary, gastrocnemius MA differences can be detected between LPT and HPT infants before 12 weeks of CGA, suggesting that MA adaptations may occur much earlier than previously thought in infants at high risk for developing CP. These novel results warrant further investigation. MUSC Specialized Center of Research (SCOR)

031 Differences in Muscle Architecture, Passive and Dynamic Range of Motion in High and Low Risk Preterm Infants. Margaret P. Smart1, Caitlin Judd1, Katy Holthaus1, Jessica Perkel2, Patricia Coker-Bolt3, Dorothea Jenkins2, Noelle G Moreau1; 1Physical Therapy, MUSC, 2Pediatrics, MUSC, 3Occupational Therapy, MUSC.

Introduction: Prematurity is a known risk factor for developing cerebral palsy (CP). Older children with CP have altered muscle architecture and often develop contractures of the gastrocnemius muscle. However, it is unknown when these muscle changes first manifest in development. The purpose of this study was to determine whether gastrocnemius muscle architecture (MA) and range of motion (ROM) differences can be detected between preterm infants at low risk (LPT) and high risk (HPT) for future developmental disabilities before 12 weeks of age. Methods: Three LPT and three HPT infants were assessed at 6 and 12 weeks of corrected gestational age (CGA). The infants were recorded with a single video camera aligned perpendicular to the sagittal plane during supported standing and supine kicking. Markers were placed on bony landmarks to calculate hip, knee, and ankle maximum joint angles in flexion and extension using Dartfish software. The number of kicks per leg was also calculated. Two novice raters and an expert rater with experience using Dartfish software were compared for interrater reliability. Interrater reliability was determined for the expert rater only. Results: Interrater reliability for the standing and supine kinematic measures were good to excellent with ICC values between.73 and.98, except for hip flexion which had moderate reliability. Interrater reliability for standing measurements was good to excellent (.77 to.97). Supine measurements were moderate to excellent (.68 to.97) except for knee extension with fair reliability. Dorsiflexion and plantarflexion in standing and supine hip extension had the highest interrater reliability (ICC >.89). The interrater and intrarater reliability for kick counts were moderate to excellent (.69 to.99). Discussion: The results of this study suggest that standing 2-D measurements of lower extremity joint angles are more reliable than supine measurements. In addition, standing plantarflexion and dorsiflexion had the highest intra and interrater reliability. Overall, Dartfish software proved to be a reliable tool to analyze the 2-D kinematics of infants at six weeks CGA. MUSC SCOR

033 Effect of Locus of Control on Clinical Outcomes for Diabetes. Bryan E Ashley, Melba A Hernandez-Tejada, Joni L Strom, Leonard E Egede; Medicine, MUSC.

Diabetes, like many chronic diseases, requires important behavioral changes to be successfully treated. Thus, the impact of cognitive and behavioral traits on glycemic control is large. Locus of control (LOC), referring generally to how much control one perceives over one’s health, appears related to positive health outcomes. Specifically, the internal dimension of LOC (i.e., believing one can actually exert influence on one’s health outcomes) is most related to outcomes in prior research. The goal of this study was to establish the association between an individual’s locus of control and glycemic management. Surveys were collected in three different clinics in the Charleston, SC and included an 18 question Multi-

032 Reliability of Lower Extremity Kinematics Obtained Using Two-Dimensional Video Analysis in Young Infants. Caitlin A Judd1, Margaret P Smart1, Katy Holthaus1, Jessica Perkel1, Patricia Coker-Bolt2, Dorothea Jenkins3, Noelle G Moreau1; 1Physical Therapy, MUSC, 2Occupational Therapy, MUSC, 3Pediatrics, MUSC.

Background: There is need for quantitative physiological markers to identify early signs of cerebral palsy (CP) in at-risk infants. However, it is crucial that the quantitative tools utilized are sensitive and reliable. The purpose of this study was to investigate the interrater and intrarater reliability of 2-D measurements of lower extremity joint angles during standing and supine kicking. Methods: Five infants born between 24 and 39 weeks were assessed at 6 weeks corrected gestational age (CGA). The infants were recorded with a single video camera aligned perpendicular to the sagittal plane during supported standing and supine kicking. Markers were placed on bony landmarks to calculate hip, knee, and ankle maximum joint angles in flexion and extension using Dartfish software. The number of kicks per leg was also calculated. Two novice raters and an expert rater with experience using Dartfish software were compared for interrater reliability. Interrater reliability was determined for the expert rater only. Results: Interrater reliability for the standing and supine kinematic measures were good to excellent with ICC values between.73 and.98, except for hip flexion which had moderate reliability. Interrater reliability for standing measurements was good to excellent (.77 to.97). Supine measurements were moderate to excellent (.68 to.97) except for knee extension with fair reliability. Dorsiflexion and plantarflexion in standing and supine hip extension had the highest interrater reliability (ICC >.89). The interrater and intrarater reliability for kick counts were moderate to excellent (.69 to.99). Discussion: The results of this study suggest that standing 2-D measurements of lower extremity joint angles are more reliable than supine measurements. In addition, standing plantarflexion and dorsiflexion had the highest intra and interrater reliability. Overall, Dartfish software proved to be a reliable tool to analyze the 2-D kinematics of infants at six weeks CGA. MUSC SCOR
Background: Diabetes affects 8.3% of the US population. Glycemia (HbA1c) is the main outcome target for clinicians in managing diabetes. There is little evidence regarding the association of facility type with HbA1c levels. We examined the association of facility type with HbA1c level in a population of adults with type 2 diabetes.

Methods: 534 individuals with type 2 diabetes were recruited from a private hospital affiliated clinic (MUSC), a Federally Qualified Health Center (FQHC), and a VA facility. We performed chi² tests to examine socio-economic characteristics by facility. We examined the unadjusted association of HbA1c level with facility type, using one-way ANOVA and Bonferroni tests. We estimated the independent association of facility type with HbA1c levels using linear regression and adjusting for covariates. Results: At FHQC, individuals were predominantly Black (84.83%), female (65.56%), 50-64 (52.81%), unmarried (70.66%), high-school graduates (43.75%), unemployed (72.30%), uninsured (45.76%) with less than $10,000 income (54.34%). At VA, individuals were predominantly Black (51.88%), male (97.51%), 50-64 (46.47%), married (52.08%), some college (47.48%), unemployed (79.17%), government insured (75.00%), had $35,000 plus income. At MUSC, individuals were predominantly Black (65.13%), female (66.41%), 65 plus (42.15%), unmarried (59.5%), equally less than high school (30.23%) and high school (30.23%) educated, unemployed (75.38%), government insured (74.71%), had $35,000 plus income. In unadjusted analysis, VA was associated with 0.799 lower HbA1c and MUSC with 0.767 lower HbA1c relative to the FQHC. After adjusting for all covariates, VA was associated with 0.519 lower HbA1c (95% CI -1.023:-0.016), MUSC was associated with 0.505 lower HbA1c (95% CI -0.935:-0.075) relative to the FQHC. Age 65 and older was associated with 0.657 lower HbA1c (95% CI -1.139:-0.174), government insured with 0.491 lower HbA1c (95% CI -0.955:-0.028). Conclusion: After adjusting for socio-economic factors, VA and private facility was associated with lower HbA1c levels relative to FQHC.
036 Gender Differences in Composite Control of Cardiovascular Risk Factors. Rhonda Winchester, Cheryl P Lynch, Joni L Strom, Leonard E Egede; Medicine, MUSC.

Women with diabetes are at greater risk than men of developing cardiovascular disease (CVD) and worse outcomes. CVD risk factors are also less well-controlled in women than men. However, gender differences in composite control of these risk factors in diabetes are less clear; therefore, this study sought to understand this relationship. Data were collected from participants with type 2 diabetes at 3 primary care settings (MUSC Internal Medicine, federally qualified health centers, and the Veterans Affairs primary care). Participants completed surveys to gather demographic data (personal characteristics, socioeconomic status, self-rated health). For the outcome, composite risk factor control (glycosylated hemoglobin, HbA1c; blood pressure, BP; and low-density lipoprotein-cholesterol, LDL-C), were obtained from medical records. STATA v11 was used to analyze demographic differences by gender with chi-square tests and the independent effect of gender on composite control (odds ratio, OR, with 95% confidence interval, CI) with multiple regression. Of 534 participants, 56.3% were male (41.4% white, 55.8% black, 2.9% other) and 43.7% female (20.3% white, 78.4% black, 1.3% other). Significant gender differences showed that, compared to males, more females were <50 years old (12.3% versus 22.2%), not married (47.9% versus 74.4%), had less than high school education (18.2% versus 31.4%), and lower income (23.5% versus 50.3%). A higher proportion of males than females had good BP (≥130/80mmHg), LDL-C (<100mg/dL), and composite control (all p<0.001). In multivariate analyses adjusted for demographic variables, males had an OR of 1.70 (95%CI 1.17, 2.48) for good LDL control, OR 1.66 (95%CI 1.16-2.38) for good BP control, and OR 3.14 (95%CI 1.70-5.79) for good composite control than females. Findings demonstrate poorer composite risk factor control among women than men. This suggests that management of CVD risk in women with diabetes is inadequate. Therefore, more aggressive efforts should target women in attaining early risk factor control.

037 Effect of Spirituality on Multiple Diabetes Outcomes. Chisom Ezenekwe, Melba A Hernandez-Tejada, Joni L Strom, Leonard E Egede; Medicine, MUSC.

Health care and disease management researchers have again turned attention to the connection between religiosity/spirituality (R/S) and health. One way R/S may moderate health outcomes is through increasing the likelihood of positive health behaviors in chronic diseases that are affected by behavior such as Type 2 diabetes (T2DM). However, the topic of increased pro-

038 The Impact of Group Motivational Interviewing on Treatment Utilization in Dually Diagnosed Veterans. Lauren S Jamison\(^1\), Steven D LaRowe\(^2\), Liz J Santa Ana\(^2\); \(^1\)Medicine, MUSC, \(^2\)Substance Abuse Treatment Center, VA.

Motivational Interviewing is widely researched, but this research has been almost exclusively conducted in the context of individual interventions and not group interventions. The present study is, to our knowledge, the first to examine Group Motivational Interviewing (GMI) within a substance abusing population of veterans. This report summarizes the effect of GMI on treatment utilization. Veterans (n=46) at the Ralph H. Johnson VA Medical Center with current alcohol dependence or abuse and a non-substance-related major Axis I psychiatric disorder were assigned to "Treatment as Usual" (TAU) or GMI. Participants engaged in four sessions. GMI sessions were directed at developing a sense of discrepancy between personal goals and current behavior and enhancing change talk among participants, while TAU sessions consisted of educational workshops. The dependent variable was the number of individual and group mental health, substance abuse, VA housing, and work therapy visits in the 6 months prior to and following treatment. Patients in the GMI group showed more treatment utilization over time than those in the TAU group, with significance at post-treatment months.
Diabetes is a growing epidemic in the industrialized world with a total of 25.8 million Americans being diagnosed with the disease and an annual increase of 1.9 million new cases each year. Many of the minorities that are affected cannot afford health insurance and do not receive proper management of this chronic disease. The free clinic (FC) is an ambulatory care center which individuals with little or no health care may use as their primary home for proper management and monitoring of chronic illnesses such as diabetes. The emergency department (ED) is a health center that specializes in emergency medicine, and acute complications of chronic illness but is not equipped to maintain and monitor chronic illnesses. Still there is an increase in individuals with chronic illnesses that frequent the emergency room more than the free clinic. The Barrier Island free clinic and Medical University of South Carolina Emergency Department (ED) patient records for diabetes mellitus Type II of calendar year 2009 were used to determine if there was a significant difference in management of diabetes among subgroups of the populations. The Pearson Chi-Square test statistic and p-value were used to determine whether there was any statistically significant difference between the subgroups within their population and between the subgroups and the two different populations. There was no statistical difference found in any of the subgroups when they were compared to one another within their respective population. However, when the subgroups of the FC and ED were compared to one another there was an increased incidence of the black and <65 subgroups visiting the ED. Future research should look into the quality of care given by each medical center and whether there is an increase in referrals from the ED to a free clinic for the proper management of care. NIH HD055885-02; NIH P50AA010761; DA022424; K23 DA021228; CTSA UL1 RR029882

Changes in Sleep Patterns in Medical School: Implications for Medical Errors. Aniruddh Anil Patel1, Connor Freeman2, Bernadette M Cortese3, Thomas W Uhde2; 1Medicine, MUSC, 2Psychiatry & Behavioral Sciences, MUSC.

Abstract not available.

Learning to Fish in an Ocean of Alcohol Research: Empirical Approaches to Study Design and Methodology in the Investigation of Stress, Alcohol, and Trauma. Joshua E Dowd, Carla K Danielson, Jenna L McAuley; Psychiatry and Behavioral Sciences, MUSC.

Introduction: Many studies have investigated the relationship between trauma exposure, stress reactivity, and drinking behavior (Gerra et al, 2000; Buckner et al, 2007). However, because of the broad range of traumatic experiences, the myriad of psychological problems associated with traumatic...
experiences, and the complex etiology of alterations in stress reactivity, it is challenging to design an experiment that examines the desired question while minimizing or measuring these potential confounds. Therefore, it is important to consider all of the methodological decisions that are part of designing a well-focused scientific study. The purpose of this study is to highlight and discuss the methodological considerations involved in examining the interaction of PTSD, distress tolerance, and genetic vulnerabilities among trauma-exposed young adults with regard to their response to stress and subsequent drinking behavior. Methods: One participant was used as a case study to establish the feasibility of the proposed methods. This participant was assigned to the control condition and, as such, read a travel magazine, received a priming dose of alcohol, and then participated in a Beer Taste Test. Stress levels and blood alcohol levels were multiply assessed. Amount of alcohol consumed was the primary dependent variable. Results: Stress levels remained relatively constant throughout the experiment and the amount of alcohol consumed was similar to the participant’s self-reported typical drinks per day. Conclusion: The stability of stress levels under the control condition provides support for the control promoting low stress. Also, the correspondence between self-reported typical drinks per day and alcohol consumed during the experimental control condition supports the validity of the Beer Taste Test in measuring typical drinking behavior. Finally, adherence to experimental protocol will reduce potential measurement confounds and maximize the ability to detect a relationship between trauma exposure and drinking behavior under acute stress, including possible mediators. MUSC DART; and NIAAA P50 AA010761

043 Perifocal Diffusion Values in Assessing Prognosis of Brain Gliomas, Pritesh Topiwala, Vittoria M Spampinato, Zoran Rumboldt, Radiology, MUSC, Neurointerventional/Radiology, MUSC.

Abstract not available.

044 Treatment of Cerebral Aneurysms: Does Size Matter? Chelsea K Baldwin, Aquilla Turk, College of Medicine, MUSC, Neuro-interventional/Radiology, MUSC.

Indication for treatment of very small cerebral aneurysms (VSCA) is controversial. In the past, treatment of unruptured aneurysms (UA) was recommended due to the serious prognosis associated with aneurysmal subarachnoid hemorrhage (aSAH), morbidity 20-25%(rosenorn) and mortality 50-60%(rosenorn), in contrast to the low morbidity 2.6-7% (van Rooij, rosenorn, Laterna) and mortality 0-1.3% (rosenorn, van Rooij) of invasive treatment of UA. However in recent studies aneurysmal size has become a point of contention in the decision to treat UA invasively. Studies suggest that invasive treatment of VSCA should rarely be recommended due to an increased rate of intraprocedural complications when compared to larger aneurysms (Schuette, Pierot, Sluzewski, Nguyen), and with a presumably insignificant rate of natural rupture, ranging from 0.05% to 0.5% per year dependent on history of Subarachnoid hemorrhage from another aneurysm (ISUIA, Pierot, Burns). Weibers and colleagues concluded that patients without a history of aSAH, the rate of rupture of aneurysms less than 10mm was 0%. Conversely it has also been reported that VSCA that present as ruptured in the clinical setting as such a rate that suggests that their natural history is not as benign as proposed, 1/3 of ruptured aneurysms were <5mm and 75% less than 10mm (Taylor et al). The current study shows that 25.6% of ruptured aneurysms presenting to our institution, Medical University of South Carolina, are very small cerebral aneurysm (VSCA: <4mm). VSCA were not found to have significantly higher rates of complications and procedural difficulties when treated invasively. Electively coiled VSCA had better outcomes than VSCA treated after rupture. The current study concludes that VSCA make up a significant number of presenting ruptured aneurysm. Their treatment is feasible regardless of rupture status, however outcomes are best if treated electively; therefore elective treatment of incidental very small cerebral aneurysms is recommended.

045 Attentional Control of Temporal Processing in Rats, Alexander R Matthews, Catalin V Buhusi; Neurosciences, MUSC.

Humans and other animals process temporal information as if they use an internal "stopwatch" that can be "stopped" and "reset." The stop/reset mechanism of interval timing can be examined by observing the effect of short interruptions (gaps) or distractor (unfamiliar) events during the timed interval. For example, pigeons delay responding and restart (reset) timing all over again when the timed visual signal is interrupted by a dissimilar gap (of low intensity). Similarly, rats stop timing during a dark visual gap, but reset after a brief illuminated gap. In summary, previous results in humans and lower animals like rats and pigeons suggest that the stop/reset of interval timing is controlled by an attentional mechanism. We recently proposed a time-sharing model assuming two concurrent processes_time accumulation and memory decay controlled by the discriminability of the interrupting event_whose interplay results in a continuum of responses, from run to stop and reset. Here we test this model in rats by manipulating the intensity of auditory distracters (experiment 1), by dissociating the role of distracter intensity, distracter similarity with the inter-trial interval, and dissimilarity from the timed auditory signal (experiment 2), and by local infusions of selective drugs into critical brain sites (experiment
3). Computational modeling (experiment 4) demonstrates that an attentional time-sharing mechanism accounts for the experimental results. MH065561; and MH073057

**046 EEG Alpha Band Asymmetry and MSCEIT Scoring in Depression**, Christopher P Menzel, Ziad Nahas; Psychiatry, MUSC.

Electroencephalography Alpha Asymmetry has been studied over the past few decades with regards to depression. However a consensus as to the exact locations and mechanisms by which cortical hyper- and-hypoactivation occur in depressed subjects has not yet been reached. This study attempts to identify the locations of highest alpha asymmetry and any correlation between alpha asymmetry and emotional intelligence using the MSCEIT, a test used to evaluate emotional intelligence in depressed patients relative to the control. This study used EEG to determine alpha power at 5 distinct electrode pairs in the Prefrontal Cortex and one electrode pair in each of the Central, Parietal, and Occipital brain regions, totaling 8 locations. The logarithm of each pair was computed in a right minus left configuration to determine relative alpha frequency, or alpha asymmetry. This study found that there was asymmetry present between all leads but that only the Occipital electrode pair reflected statistically significant data. However with regards to MSCEIT scores, both Total and the Managing Emotions branch of the MSCEIT reflected positive correlations with the depressed patient alpha asymmetries. This is an important step in understanding asymmetrical EEG activity in depression and in the determination of what brain regions are involved in the link between depression and emotional intelligence. MUSC DART

**047 Prevalence and Predictors of Sleep Disorders in an Adult Sample with Type 2 Diabetes**, Golsa Yazdy, Sujeev S Bains, Joni L Strom, L E Egede; Medicine, MUSC.

Objective: To determine the overall prevalence and sociodemographic predictors of sleep disorders in a diabetic population. Methods: Validated surveys were distributed at three clinics in Charleston, SC. Data was obtained regarding sociodemographic factors and sleep disorders. 683 patients were recruited over a 10-week period. Sleep disorder questions assessed quality of sleep/rest. Logistic regression models were used to assess sociodemographic predictors of sleep disorders. Results: In our sample, 66% were white race, 85% were 50 years old or older, 56% were male, 60% were unmarried, 58% had < high school education, 76% were unemployed, 18% were uninsured, 35% had <$10,000 income, and 72% reported their health status as either better or the same as last year. Among the sleep disorders, 41% reported sleeping < 7 hours daily, 64% reported snoring, 65% reported unintentionally nodding off for at least 1 day a month, and 10% reported unintentionally nodding off while driving at least 1 day a month. In our logistic regression models, less than 7 hours sleep was less likely among those with poor health status (p<0.001) and participants at the VA site (p=0.006). Unintentionally nodding off was associated with black race (p=0.004) and unintentionally nodding off while driving was less likely among black (p=0.001) and hispanic/other race (p=0.03). No sociodemographic variables were significantly associated with snoring. Conclusions: OSA risk factors are prevalent in this population of patients with diabetes. The relationship between sociodemographic characteristics and varying sleep disorders need to be investigated to establish a possible mechanism by which they are linked. MUSC Center for Health Disparities

**048 Effect Of Trust In Health Care Providers On Multiple Diabetes Outcomes**, S Bouges, C P Lynch, J L Strom, L E Egede; Health Disparities Research, MUSC.

Diabetes is the seventh leading cause of death claiming the lives of 25.8 million Americans. This chronic disease increases the risk of macrovascular and microvascular complications and heart disease. In order to reduce the number of patients suffering from this high burden condition, a greater understanding of the obstacles hindering care to patients with diabetes is needed. Studies have shown a positive relationship between trust in primary care provider, patient adherence to medication and health related quality of life in patients with diabetes. In addition, a strong correlation has been shown between increased patient satisfaction in healthcare services and lowered glycated hemoglobin levels, better continuity of care and greater trust in the medical system. A sample of 534 patients with type 2 diabetes was recruited from three primary care clinics (an academic Internal Medicine clinic, a federally qualified health center, and a Veterans Affairs (VA) primary care clinic). Self-identified type 2 diabetic patients completed a survey about their personal characteristics, belief systems and preferences, health related knowledge, behaviors and attitudes. The predictor variable, trust, was measured by a 17-item multidimensional trust in health care systems scale (MTHCSS) scored on a 5-point scale with a minimum score of seventeen and a maximum score of eighty-five. Higher scores indicate greater trust in the healthcare system. The primary outcome was glycemic control measured by glycosylated hemoglobin A1C (HbA1c). Mean scores of the trust index will be compared between older (≥65 years of age) and younger (<65 years of age) individuals. When examining the mean differences in trust scores, individuals ≥65 years of age had significantly higher trust scores compared to those younger than 65 year old (p=0.0030). In addition, age had a significant impact on glycemic control (p=0.0019) and diastolic blood pressure (p<0.0000).
Based on our preliminary results, trust was not a predictor of glycemic control. Age on the other hand did affect glycemic levels and diastolic blood pressure. Further studies are needed to determine why trust was not a predictor of glycemic control in this particular study when current literature shows different. NIH 5T35DK007431-27

049 Is The Arm Activity Monitor A Reliable And Valid Tool To Measure Arm Use During Functional Activities In Stroke Rehabilitation? Karla L Knuth1, Kendra L Sprogis1, Latisha D Washington1, Michelle L Woodbury2; 1Occupational Therapy, MUSC, 2Health Science and Research, MUSC.

Background: Stroke affects nearly 800,000 people in the US annually. The vast majority of stroke-survivors (>75%) have persistent upper extremity (UE) motor impairment restricting self-care and role-related activity performance. The overall goal of neurorehabilitation is to restore patients' functional abilities; however the impact of rehabilitation on functional arm use is not well defined because of inadequate measurement tools. The Arm Activity Monitor (AAM) is a new device for measuring functional arm use, but, its measurement properties are not established. Objective: Determine the test-retest reliability and face validity of the AAM. Methods: This research work-in-progress is a prospective cohort study enrolling 20 subjects; 10 individuals 3+ months post-stroke and 10 neurologically healthy age-matched controls. At two testing sessions subjects will perform 8 standardized functional tasks while wearing AAMs on each wrist. Session 1 and session 2 AAM data will be compared with a two-way mixed-model intraclass correlation coefficient (ICC). Additionally, from videotapes, 3 trained raters will count subjects’ purposeful UE movements. Rater-counts will be compared to AAM-counts with spearman’s rho correlation coefficients. Correlations >0.90 indicate strong agreement, >0.75 adequate agreement. Results: 4 subjects have been enrolled. Preliminary analysis indicates AAM test-retest ICC=0.89, and spearman’s rho correlation=0.40. Conclusions: Preliminary data suggest the AAM reliably measures arm use from session to session. However, there was poor agreement between rater-counts and AAM-counts which calls into question its face validity. Raters counted obvious reach-to-grasp motions as did the AAM. However, the AAM also counted other, less-obvious, arm motions such as movement corrections, balance reactions, fidgeting and movement speed alterations. Possibly, the construct “arm use” as measured by the AAM is broader than “arm use” defined by our raters. Although promising, the preliminary data do not support using the AAM to measure stroke-rehabilitation outcomes because of unresolved questions regarding the interpretability of its data. Ralph H. Johnson VAMC Career Development-2 Award B6332W

050 The Role of the Tongue in Secondary Palate Elevation of Prrx1 Deficient Mice. Caitlin M Biggs1, Michael J Kern2, 1Dental Medicine, MUSC, 2Regenerative Medicine and Cell Biology, MUSC.

Palate morphogenesis is very complex with many changes in the palatal shelves that will give rise to the palate, as well as concurrent changes in other oral structures. For example, in wild type mice the tongue is between the two vertical palatal shelves at embryonic day E13.5, but by E14.5 it descends allowing the vertical palatal shelves to elevate to their final horizontal position; then they extend and fuse. Previous work revealed that the palatal shelves of the homozygous null Prrx 1 (-/-) mice grew normally through day E13.5, but were still vertical and malpositioned by day E14.5. One possible explanation is that the tongue physically inhibits the shelves from elevating. To determine the role of the tongue in the elevation of the Prrx1 mutant palatal shelves, we used a serum-free tissue explant technique after removing the mandible and tongue. Our results demonstrated that the Prrx1 mutant shelves failed to elevate and thus failed to fuse in the in vitro culture system. This supports the role of Prrx1 in palate morphogenesis, specifically in the aspect of palatal shelf elevation. Wateree Dreams Foundation

052 Effects of TGF-Beta on NIH-3T3 Cell Proliferation, Migration, and Apoptosis, Benton L Johnson1, Steven W Kubalak2, Jayne Bernanke2; 1Medicine, MUSC, 2Regenerative Medicine and Cell Biology, MUSC.

Transforming growth factor beta (TGF-β) is a cytokine involved in many cellular processes such as cell growth, apoptosis, migration, epithelial-mesenchymal transition (EMT), heart cell-cell signaling, and tumor response1. TGF-β is secreted by many cell types, and depending on the target cell, various responses can be expected. From a pharmacological perspective, TGF-β mechanistic pathways could be targets for future cancer treatments. TGF-β’s effects on fibroblasts at various concentrations are not as well understood. To assay migration, NIH 3T3 cells were scratched and treated with varying concentrations of TGF-β. Treatment with TGF-β at any concentration increased cell migration compared to the untreated cells. Data suggests there may be multiple intracellular mechanisms influenced by TGF-β. Future studies are required to understand how these mechanisms react to different concentrations of TGF-β.

053 The Varied Effect of NAC and Cocoa on LPS Stimulated IL-6 Release By Both Mononuclear Cells and Human Gingiva Fibroblasts, William A Stokes1, Yan Huang2; 1Medicine, MUSC, 2Endocrinology, MUSC.

IL-6 is a cytokine that is secreted by many cells and results in an increase in the acute immune response.
Elevated IL-6 levels have been implicated in many diseases such as atherosclerosis. LPS is derived from bacterial cell walls, and can stimulate IL-6 secretion in both U937 and HGF through a TLR-4 mediated signal cascade. NAC and Cocoa inhibit LPS-stimulated secretion of IL-6 differently in U937 and HGF. NAC inhibits >50% IL-6 secretion after 24 h incubation in both U937 and HGF. Cocoa inhibits >50% IL-6 secretion after 24 h in U937, but the inhibition in HGF is only 20%. The change in the effects of Cocoa on the two cell lines is likely caused by a difference in the TLR-4 signal transduction pathway in the two cells.

**054** Fli-1 Transcription Factor Affects Glomerulonephritis Development By Regulating Expression of Inflammatory Chemokine in Endothelial Cells in Kidney.

Eva Karam¹, Eiji Suzuki¹, Sarah Williams¹, Xian Zhang³;
¹Rheumatology & Immunology, MUSC, ²Rheumatology & Immunology, Ralph H. Johnson VA Medical Center.

Expression of Fli-1, a member of the Ets family of transcription factors, is implicated in the development of glomerulonephritis in murine models of systemic lupus erythematosus (SLE). Lupus nephritis is a major cause of death in both animal models and human patients, and is characterized by immune complex formation and inflammatory cell infiltration. Expressions of monocyte chemotactic protein-1 (MCP-1) and Chemokine (C-C motif) ligand 5 (CCL5) has been demonstrated to initiate inflammatory cell infiltration in the kidneys of lupus mice. In this study, we examined the role of Fli-1 on chemokine production and inflammatory cell infiltration in conjunction with nephritis development in NZM2410 mice, an animal model of SLE. We generated Fli-1 heterozygous knockout NZM2410 mice (Fli1+/−) and wild-type (WT) littermate (Fli1+/+) mice. The expression levels of MCP-1 and CCL5 in the kidneys from 18-week-old mice were analyzed by real-time PCR. The endothelial cells were isolated from kidneys and production of MCP-1 and CCL5 in these cells were investigated. We first examined the expression of MCP-1 and CCL5 in the kidneys from both Fli-1+/− and WT controls. Expression of MCP-1 and CCL5 in the kidneys from 18-week old Fli-1+/− NZM2410 mice was significantly decreased compared to that from WT littermates. Next we isolated endothelial cells from kidneys of both Fli-1+/− and WT NZM2410 mice. There was a significant reduction in MCP-1 production in endothelial cells from Fli-1+/− NZM2410 mice compared to WT NZM2410 mice. The productions of MCP-1 and CCL5 in endothelial cells transfected with specific Fli-1 siRNA were significantly reduced compared to cells transfected with negative control siRNA. Our data indicate that Fli-1 affects glomerulonephritis development by regulating expression of inflammatory chemokine MCP-1 and inflammatory cell infiltration in the kidneys. The lower expression of Fli-1 results in decreased expression of MCP-1 in endothelial cells from the kidneys with significantly reduced infiltration of inflammatory cells, which leads to reduced glomerulonephritis in NZM2410 mice. NIH AR056670; and Medical Research Service, VA

**055** Glucosylceramide and Lactosylceramide Accumulation in Lupus Nephritis: Biomarker or Mediator of Disease?

Andrew R Mather¹, Maria Jose Hernandez-Corbacho², Jennifer Schepp-Berglind², Jonathan Donahue³, Ashley J Snider³, James Oates³, Leah J Siskind¹; ¹Biochemistry, MUSC, ²Medicine, MUSC.

Abstract not available.

**056** Slug Expression Inhibits Vitamin D-mediated Sensitivity to Radiation in Colorectal Cancer.

Eric Moretz¹, Victoria J Findlay², Silvia G Vaena¹, Savannah G Bandurraga¹, Michael S Ashenafi³, David T Marshall³, Dennis K Watson³, Ramsay Camp³; ¹Surgery, MUSC, ²Pathology and Laboratory Medicine, MUSC, ³Radiation Oncology, MUSC.

Vitamin D (VD) has demonstrated an inconsistent therapeutic effect in various cancers and molecular pathways regulating VD response are poorly described. Recently, the reciprocal relationship between VD and epithelial-to-mesenchymal transition (EMT) has been described. Therefore, we hypothesize that VD will enhance radiation sensitivity in colorectal cancer (CRC) by regulating EMT. VD receptor (VDR) and E-cadherin levels (Western blot analysis), as well as Snail and Slug mRNA (transcriptional EMT regulators) levels (qRT-PCR) were assessed in eight human CRC cell lines at baseline and in response to VD treatment. HCT116 and DLD1 cells were stably transfected under antibiotic selection using pCMV-3Tag-1 vector expressing Slug (Slug HCT116/DLD1) or Snail cDNA (Snail HCT116/DLD1) and compared to empty-vector transfected cells (empty HCT116/DLD1). Boyden chamber assay was used for migration evaluation. Radiation sensitivity was assessed by in vitro clonogenic analysis after 10 days following 24 hr pre-treatment with 1 μM 1α,25(OH)2D3 (VD) or EIOH (vehicle) and subsequent 0-6 Gy radiation treatment. Human CRC cells demonstrated variable VDR and E-cadherin levels. SW620 cells demonstrated decreased E-cadherin protein expression and the highest relative Slug expression (p<0.05). LoVo cells demonstrated no VDR. VD treatment decreased Slug expression in the DLD1 and HCT116 cells (p<0.05) and stimulated SW620 cell Slug levels at 48 hours (3-fold increase, (p<0.0005), VD pre-treatment of DLD1 and HCT116 cells inhibited migration (p<0.02) and enhanced radiation sensitivity at 4 Gy by 57 (P<0.01) and 62% (P<0.05) respectively compared to vehicle. Conversely, VD pre-treatment had no effect on SW620 cells. Similarly, Slug HCT116 cells demonstrated...
resistance to VD radiation sensitizing effect compared with empty HCT116 cells. VD enhanced radiation sensitivity in CRC cells, although high Slug expression conferred resistance to this effect. Novel VD therapeutic strategies appear promising as radiation sensitizers, but should be individualized based on expression of EMT molecular markers.

057 The Role of Tissue Transglutaminase-2 in the Modulation of Polymorphonuclear Leukocyte Function, David P LeBel, Meghan K Anderson, Titus A Reaves; Regenerative Medicine and Cell Biology, MUSC.

Polymorphonuclear leukocyte (PMN) migration across epithelial surfaces is a major concern in inflammation involving mucosal surfaces. Inflammatory bowel disease includes Crohn’s Disease and Ulcerative Colitis, and presents as a series of inflammatory conditions involving dysregulated and excessive PMN migration across the intestinal epithelium; patient symptoms are more pronounced during such migration. Tissue Transglutaminase (TGM)-2 is an enzyme that catalyzes calcium-dependent crosslinks of an amino group and has been implicated in a variety of cellular functions that include GTPase activity (shown to affect PMN adhesion), cell growth, and wound healing. Antibodies to TGM-2 are present in patients with Celiac Disease (inflammation localized to the small intestine) and a majority of Crohn’s Disease patients also have Celiac Disease. Despite this information, the role of TGM-2 in PMN functions has not been widely explored. Using immunofluorescence, we determined that TGM-2 has both an extracellular and intracellular deposition in PMN. Treatment of PMN with an inhibitor of TGM-2 appears to promote translocation of the leukocyte specific integrin CD11b to the surface of PMN. Cellular adhesion studies revealed that TGM-2 can inhibit PMN attachment to fibrinogen (precursor to fibrin and a ligand for CD11b) by nearly 50%. This result suggests that TGM-2 may have a role in blood coagulation and/or a role in CD11b mediated activities. Transwell migration experiments reveal that TGM-2 can inhibit fMLP-directed migration more than 50%. Consisting of formylated bacterial peptides, fMLP promotes PMN migration toward such peptides. The fMLP receptor is a G-protein coupled (7TM spanning) receptor that regulates the PMN response by facilitating migration through an up-regulation of adhesion and migration receptors. Using Flow Cytometry experiments, we determined that TGM-2 affects PMN adhesion and migration by modulating the PMN-fMLP receptor. These data highlight TGM-2 as a potential target molecule in the treatment of mucosal inflammation that involves aberrant PMN transmigration. NIH 5T35DK7431-27

058 Fifteen-Year Experience with Peritoneovenous Shunts for Refractory Ascites Management, Sara C Smith1, Charles Bratton2, Helen Skaggs3, David Taber4, Kenneth Chavin2, Baliga Prabhakar2; 1Medicine, MUSC, 2Surgery, MUSC, 3Pharmacy, MUSC.

Peritoneovenous shunts (PVS) have been used to control the morbidity of ascites associated with liver disease. The goal of this study was to review our experience with PVS, as a primary treatment for ascites and as a bridge to transplant. We performed a retrospective cross-sectional analysis of all patients who received a PVS from November 1995 to February 2010 at our institution. Variables included demographics, etiology of liver disease, lab data, and operations performed. Outcomes included shunt patency, and complications for each patient. Fifty-five primary shunt insertions, 29 shunt revisions, 27 shunt removals, and five shunt replacements were performed in 53 patients. The mean MELD score for the subjects was 16 ± 7.5 prior to shunt insertion. Mean assisted shunt patency duration was 152 days (median 65 days), with a range from 3 to 967 days. At one, three, six, and twelve months 82%, 55%, 40%, and 35% were patent, respectively. At the end of follow-up, shunt patency was 16%. Ten patients went on to receive a liver transplant after implantation of PVS. Orthotopic liver transplant (OLT) is the definitive treatment for end stage liver disease (ESLD) patients suffering from ascites. However, our results indicate that PVS, with proper maintenance, can serve as an effective technique for palliative care in these patients who are not candidates for transplant. Transplant candidates may also benefit from placement of a PVS to mitigate the morbidity of ascites until transplantation. Though PVS placement was intended to bridge to liver transplantation, few patients underwent transplant after PVS in this cohort of patients; only 19% of subjects received a liver transplant post-shunt insertion. Whether as a bridge to transplant or as palliation, peritoneovenous shunts can be a beneficial procedure to alleviate ascites in ESLD patients.

059 Inhibiting Effect of Albumin on Biofilm Formation in Titanium Implants in Vivo, Shivam J Desai1, Qian K Kang2; 1Medicine, MUSC, 2Orthopaedic Surgery, MUSC.

Bacterial infection is an extremely serious complication after orthopaedic surgeries namely because of the biofilm mode of growth of the infecting bacteria. Postoperative infections often require removing the implant altogether so more preventative measures are needed to inhibit bacterial adhesion. This study aimed to evaluate whether titanium surfaces coated with cross-linked albumin could reduce bacterial biofilm in vivo. Titanium discs were coated with bovine serum albumin cross-linked with carbodiimide. The discs
were placed subcutaneously into 8 rats and challenged with S. aureus. 7 days after the infection, the discs were retrieved and evaluated using confocal fluorescent microscopy and dilution plate enumeration. The results show that the albumin coating disrupted and prevented strong bacterial biofilm formation. The discs covered with albumin displayed 80% fewer colony forming units. These results imply that implants coated with cross-linked albumin coating may offer viable prophylaxis to reduce infection in any implantation surgery. Summer Health Professions Grant

060 The Effect of TDCS in Post-operative Pain Management of Total Knee Arthroplasty, Rahul S Loungani1, Jeffrey J Borckardt2, Scott Reeves3, Josh May1; 1Medicine, MUSC, 2Psychiatry & Behavioral Sciences, MUSC, 3Anesthesiology & Perioperative Medicine, MUSC.

Abstract not available.

061 Does Laptop Ergonomic Education Translate Into Ergonomic Action? Alexis Cameron, Meg Judy, Sarah Johnson, Mira Kraft, Bailey Munson, Mariah Valentine, Peter Bowman; Occupational Therapy, MUSC.

There is limited research regarding ergonomic laptop/notebook computer use. This study examined the effects of an educational session on proper laptop/notebook computer ergonomics knowledge and behaviors of graduate students. The hypothesis is that graduate students participating in a 30 minute educational session will increase their ergonomic knowledge and improve their positioning during laptop/notebook computer use. A convenience sample of 42 graduate students from the College of Health Professions at the Medical University of South Carolina participated in this study of which 20 were assigned to the experimental group and the remainder to the control group. All of the participants were administered a pre-test regarding their knowledge of proper laptop/notebook computer ergonomics. The experimental group then received a 30 minute didactic and interactive educational session designed to increase students' knowledge and influence their behavior regarding proper laptop/notebook computer ergonomics. Approximately a month later, two versions of a post-test were administered to all participants to measure changes in knowledge and behavior as a result of either the intervention and the quiz or the quiz alone. In addition, in-class behaviors were observed to determine if post-test results are consistent with actual behavior. This study will provide data on whether an ergonomic educational session will make a difference regarding graduate student knowledge and behaviors during laptop/notebook computer use.

062 Four Kinematic Variables to Measure Quality of a Reaching Movement in Stroke Rehabilitation, Christa M Barrett1, Katie E Kirstein1, Tania O McElvene1, Michelle L Woodbury2; 1Occupational Therapy, MUSC, 2Health Science and Research, MUSC.

Introduction: In the USA, 800,000 strokes occur annually; 75% of survivors experience contralosensal arm paralysis because of ischemic-related neural damage. Impaired arm motor function limits patients' abilities to accomplish meaningful self-care, vocational, and social activities. Neuro-rehabilitation aims to improve activity/participation by reducing impairment. Kinematic analyses precisely quantify impairments of each arm segment and joint, but the relationship of separate variables to an overarching construct, arm movement quality, is not known. Objective: To verify whether 4 arm kinematic variables (reaching path curvature, trunk movement, elbow range of motion and time of peak velocity) represent movement quality in neurologically healthy individuals and people with stroke. Methods: This was a secondary analysis of existing data obtained during a larger, funded Veteran's Administration stroke rehabilitation study. The sample included 52 individuals, ages 45-88 years, ±6.4 years post single first-time stroke; and 15 neurologically healthy individuals ages 21-78 years. Kinematic analyses were conducted during fast-paced reaching-to-target. Using a 1-factor Confirmatory Factor Analysis (MPlus v. 6), we tested the hypothesis that 4 variables worked together to measure arm movement quality. The goodness of model fit (maximum log-likelihood) was defined as a significant Chi-square Model Fit Test (p<0.05) and Root Mean Square Error of Approximation (RMSEA) <0.05. Results: The 1-factor model fit the data (Chi-square= 64.173, 4df, p<0.001; RMSEA = 0.03). Factor loadings ranged from 0.30-0.89. Residual variances ranged from 0.20-0.91 with time of peak velocity having the lowest loading and highest residual variance. Conclusions: Results suggest that arm movement quality can be measured by 4 kinematic variables. The optimal variables are those that quantify reaching-path curvature, trunk movement, and elbow range of motion. These kinematic variables could be used by neurorehabilitation therapists/scientists to measure the quality of reaching movements which will enable better documentation of treatment efficacy and patient progress in stroke rehabilitation. VA, Ralph H. Johnson VAMC Career Development-2 Award B6332W

063 Epidermal Growth Factor-induced Activation of Na+/H+ Exchanger in Orpk Cilia (+) and Orpk Cilia (-) Renal Cells From a Mouse Model of Polycystic Kidney Disease Involves Different Signaling Mechanisms, Alisha Joyner1, Tanjina Akter2, Mary G Blanton3, Maria N Garnovskaya3.
Association of Mother-Infant Oral Mutans Streptococci and Infant Feeding Practices, Thao Trang Latham1, Susannah C Shirer2, Carol L Wagner3, Bruce W Hollis4, Myla Ebeling3, Thomas C Hulse5, Susan G Reed1; 1Craniofacial Biology, MUSC, 2Oral Rehabilitation, MUSC, 3Pediatrics-Neonatology, MUSC, 4Pediatrics-Epidemiology, MUSC.

Mutans streptococci (MS) bacteria are an initiator in early childhood caries. MS can be found in the infants’ oral cavity as early as 24 hours after birth. One large study of predentate, Caucasian, six-month-old infants, found that breast-fed (n=113) compared with bottle-fed infants (n=17) were at higher risk for predentate oral MS. Mothers with infected infants were also more likely to have higher MS levels compared to mothers of uninfected infants. Increased maternal contact was speculated to account for these differences. In South Carolina we study a large population of Caucasian, African-American and Hispanic mother-infant pairs. The primary objective of our research is to compare presence and quantity of oral MS in our population of infants and mothers by race/ethnicity, and by feeding method (lactating and non-lactating mothers).

Information is collected by interviewer questionnaire from the mothers of infants within 2 weeks of birth, at 6 months, and at 18 months during an ongoing NIH study of vitamin D and lactation. Data include age of child, method of feeding, nighttime feeding habits, oral hygiene habits, type of formula, and additional sugars consumed. Oral MS levels are made using the Dentocult®SM Strip mutans test kit. Double data entry and Stata IC version 11.0 is used for analyses. Preliminary data for 101 mother-infant pairs over 15 months are summarized. There were 67 infants of lactating mothers and 34 infants of non-lactating mothers. Overall, 31/92 (34%) of mothers were positive for oral MS (7 not evaluable) and 8/94 (8.5%) of infants were positive for oral MS (7 not evaluable). There were 3 mother-infant pairs positive for oral MS in the lactating group (10 pairs not evaluable) and no pairs positive in the non-lactating group (1 pair not evaluable). Additional data for another 100 mother-infant pairs is currently under analysis in this ongoing study. SCTR; NIH/NCRR UL1 RR029882; NIH/NCRR P20 RR-017696; 5R01HD043921; RR01070; and DE017551

Stroke Rehabilitation: Does Arm Movement Quality Relate to Amount of Functional Use During Reaching Tasks? Meredith M Smith1, Aaron J Hardee1, Sheronda C Lucas1, Claire C Marsh1, Michelle L Woodbury2; 1Occupational Therapy, MUSC, 2Health Science and Research, MUSC.

Background: Stroke is the leading cause of disability in the US. Approximately 75% of stroke survivors experience residual arm dysfunction, limiting independence in daily activities. Neurorhabilitation aims to improve functional arm use, with the assumption that quality of movement is related to amount of use. However, there is a paucity of research examining whether such a relationship exists. Functional arm use can be measured in two ways: 1) therapist-observation and 2) new technology such as the Arm Activity Monitor (AAM). Objective: To determine the relationship between quality of arm movement and amount of arm use in post-stroke individuals during functional reaching tasks. Methods: This research work-in-progress is a prospective cohort study enrolling 20 subjects; 10 individuals 3+ months post-stroke and 10 neurologically healthy age-matched controls. At two videotaped testing sessions subjects will perform 8 standardized functional tasks while wearing AAMs on each wrist. Three trained raters will observe and count subjects’ purposeful UE movements. Subjects will attend an additional session for UE motion analysis. Kinematic variables measuring UE movement capacity and coordination will be compared to AAM-counts and rater-counts with spearman’s rho correlation coefficients. Results: 4 subjects have been enrolled. Preliminary analysis indicates rater-observed counts are positively correlated with kinematic measures (coefficients range from 0.40 to 0.80), while, in contrast, AAM-counts are inversely correlated with kinematic measures (coefficients range from -0.40 to -1.0). Conclusion: Results suggest that arm movement quality is associated with functional arm use when measured by raters but not when measured by the AAM. In our study, raters only count purposeful movements, while AAMs sensibly measure both purposeful and non-purposeful movements. Higher AAM-counts might result from multiple movement attempts due to poor movement quality. Because AAMs do not exclusively measure purposeful movements they may not be useful for therapists who want to measure functional arm use. VA; and Ralph H. Johnson VAMC Career Development-2 Award B6332W

Contributors To Ankle Proprioception For Static And Dynamic Tasks, Lisa M Floyd, Taylor C Holmes, Jesse Dean; Physical Therapy, MUSC.

Traditional thought suggests that during active muscle contractions, fusimotor drive enhances proprioceptive information. Alternatively, the “sense of effort” required to overcome gravitational torque may also improve proprioceptive sense. We tested these competing explanations with subjects in a gravity-eliminated position using both static and dynamic conditions. Eight young (23±1 yrs) healthy subjects laid on their right side with a splint maintaining knee extension. Ankle motion was limited to plantarflexion and dorsiflexion by sneakers bolted to a frame with a
potentiometer aligned with the axis of motion. Surface EMG electrodes monitored tibialis anterior (TA) and soleus (SO) muscle activity. During static trials, subjects matched a constant target ankle position (neutral; 10° plantarflexion; 20° plantarflexion), while dynamic trials used a target sine wave trajectory (5° amplitude, 8s period; 5° amplitude, 4s period; 10° amplitude, 4s period). Both static and dynamic trials included three conditions: Passive (experimenter positioned ankle while subject relaxed); Active (subject used visual feedback to position the ankle); Weighted (identical to the Active with an additional dorsiflexion torque of ~3Nm applied by a weight attached over a pulley posterior to axis). Once the subject reported awareness of their ankle position/motion, they actively recreated the target without visual feedback. Performance was quantified as the absolute value of error between the target and subject-generated positions in static trials and amplitudes in dynamic trials. Neither TA nor SO exhibited measurable activity during Passive trials; TA activity dominated Active trials; SO activity dominated Weighted trials. However, errors did not differ (p>0.05), suggesting that fusimotor drive alone does not improve proprioception. Learned sense of effort may thus provide proprioception information. Therefore, the relationship between sense of effort and joint position may need to be relearned in clinical populations to improve function.

067 Differences in Impulsivity Among Drug-Dependent Populations, Ja’Pel Sumpter, A Simpson, M Owens, A McRae-Clark, K Hartwell; Psychiatry, MUSC.

Background: The role of impulsivity in substance abuse has been receiving an increased attention from both researchers and clinicians. Previous studies have focused on the relationship between impulsivity and the compulsive aspects of drug use. Current research suggests that impulsivity is an important factor in both the initiation and maintenance of substance use disorders. Objective: To measure and examine differences in impulsivity between cocaine, marijuana, and nicotine dependent subjects and explore impulsivity as a risk factor of drug abuse. Method: In this study, impulsivity was compared among cocaine, marijuana, and nicotine dependent subjects in several studies conducted at MUSC. Participants completed the Barratt Impulsiveness Scale (BIS-11) and were interviewed regarding lifetime drug use. Drug dependence was confirmed SCID. Results: Results revealed that participants who were marijuana accompanied with smoking are more impulsive than cocaine smokers, cocaine nonsmokers, and smokers, respectively. Categorically, cocaine nonsmokers had a greater impulsivity in the non-planning subscore (26.32, p<0.0001) while marijuana nonsmokers measured at a much higher impulsivity cognitive subscore (20.58, p=0.0001). There was no significant difference among groups in the motor subcategory. Conclusions: This study shows a statistically significant difference between impulsivity among varying drug-dependent groups, which may further the understanding of impulsive factors contributing to ongoing drug use and addiction. Additionally, the results reported here may aid researchers aim at identifying pharmacologic and tailored cognitive behavioral methods of addressing impulsivity based on drug of abuse. NIDA R21DA22424; NIDA P50DA016511; NIDA R33 DA036085-03; and NICHD K12 HD05885-02

068 Radiation-Induced Xerostomia in Oral, Head and Neck Cancer Patients, Tiffany L Lovelace, Terry Day; Dental Medicine, MUSC, Otolaryngology - Head & Neck Surgery, MUSC.

Xerostomia, the subjective perception of dry mouth, is a common side effect associated with radiation therapy for head and neck cancer. Injury of the major and minor salivary glands included in the radiation field results in atrophy of the secretory components and varying degrees of xerostomia. The type and severity of the condition are related to radiation dose, fraction size, and duration of treatment. Because xerostomia is often a life-long condition that can have a major impact on oral health and quality of life, much research has been devoted to treatment and prevention strategies. The purpose of this research was to perform a systematic review of the literature to assess treatment and prevention strategies for xerostomia induced by radiation therapy and to evaluate the best form of management. It was found that the main strategies include agents and procedures such as amifostine, pilocarpine, salivary substitutes, cevimeline, acupuncture, and salivary gland transfer. In a preliminary analysis of 22 prospective studies, the use of these treatment and prevention strategies have resulted in varying degrees of success in the reduction of xerostomia. Further analysis of the data is underway in the form of a systematic review of the literature and meta-analysis to determine which treatment strategy and which prevention option results in the greatest improvement of chronic xerostomia. This study also aims to determine if preventive techniques administered before radiation therapy are superior to treatment of xerostomia following radiation therapy.

069 Caffeine and Alcohol Intake and Nicotine Dependence Severity in Female Smokers, Christine N Riyad, Kevin M Gray; Psychiatry and Behavioral Sciences, MUSC.

Background: Tobacco use is the single most preventable cause of disease, disability, and death in the United States today. The co-administration of other psychoactive compounds with cigarettes may have implications for tobacco-related health outcomes. Smokers are more likely than non-smokers to consume caffeine and alcohol, and nicotine dependent smokers tend to consume more caffeine and alcohol.
than non-dependent smokers, but few studies have explored the relationships between severity of nicotine dependence and frequency of caffeine and alcohol use among established daily smokers. Methods: During baseline assessment, 122 nicotine dependent women enrolled in a smoking cessation study recorded alcohol and caffeine use using the Smoking History Survey, and completed the Fagerström Test for Nicotine Dependence (FTND) to assess severity of nicotine dependence. Spearman correlations were used to assess the relationships between FTND score and alcohol and caffeine consumption. Results: Analysis revealed a significant positive correlation between caffeine intake and FTND score (r=0.366, p<0.0001) but a significant negative correlation between weekly alcohol use and FTND score (r=0.272, p=0.002). Conclusion: These findings suggest that the positive relationship between cigarette smoking and caffeine consumption, previously reported in smokers versus non-smokers and dependent versus non-dependent smokers, extends to established nicotine dependent smokers. In contrast, alcohol consumption may have a more complex relationship with cigarette smoking. While smokers versus non-smokers and dependent versus non-dependent smokers are more likely to consume alcohol, severity of nicotine dependence among established smokers is negatively correlated with alcohol use in the present sample. It may be that highly dependent smokers have crossed a threshold, beyond which alcohol plays a diminished role in maintenance of smoking. NIDA R25DA020537, and P50DA016511

070 Examination of the Role of HuR in the Post-Transcriptional Regulation of Nucleolin Expression in Breast Cancer Cells, Tracy Tholanikunnel1, Sudeep Bose2, Eleanor Spicer1; 1Medicine, MUSC, 2Regenerative Medicine and Cell Biology, MUSC. Nucleolin has been found to be highly overexpressed in the cytoplasm of chronic lymphocytic leukemia (CLL) cells, which leads to stabilization of the proto-oncogene bcl-2 mRNA (Otake et al, 2007). The biochemical mechanisms leading to up-regulation of nucleolin in CLL and other cancers is unknown. The focus of this project will be to obtain information about trans-acting factors that regulate nucleolin mRNA stability and translation, using MCF-7 breast cancer cells as a model. Specifically, the focus will be to determine if the RNA regulatory protein HuR plays an important role in nucleolin mRNA metabolism. The results of this work are designed to contribute to an understanding of the mechanisms of up-regulation of nucleolin expression in proliferating cells.

071 Noncanonical, Rapid Downstream Crosstalk Between TGFβ and Retinoic Acid Signaling Pathways As Revealed By the Proximity Ligation Assay, Craig Kutz1, James Atkinson2, Jayne Bernanke3, Steven Kubalak3; 1Medicine, MUSC, 2Graduate Studies, MUSC, 3Regenerative Medicine and Cell Biology, MUSC. The importance of transforming growth factor beta (TGFβ) and retinoic acid (RA) signaling in a variety of physiological and pathological processes has been well documented. Yet, despite the traditional canonical roles of these signaling pathways independently, there are few reports exploring unconventional crosstalk between them. Our lab has previously found novel interactions of downstream Smad cofactors in TGFβ signaling directly binding to intracellular receptors for retinoid acid, retinoid X receptor alpha (RXRα). Importantly, this interaction takes place faster and at traditionally suboptimal concentrations of RA (low nM range), suggesting a role for unliganded retinoid receptors independent of transcriptional regulation. Using a novel form of in situ immunohistochemistry, the proximity ligation assay, direct intracellular protein-protein interactions between RXRα and TGFβ signaling cofactors were explored. We found that in addition to canonical interactions between Smad2 and Smad4, RXRα demonstrates direct interactions for both these TGFβ cofactors. In particular, we are the first to show that RXRα binds with Smad4. The RXRα/Smad4 interaction increased with TGFβ treatment, but was blunted with administration of RA. These results are critical because they suggest that unliganded retinoid receptor modulation may be more extensive than originally perceived and may regulate heterologous signal pathways independent of retinoid receptor-driven transcription. Whether these effects are a result of direct heterodimerization or a novel multimeric complex is the focus of future studies. R01 HL83116

072 Tumor Location is an Independent Prognostic Factor in Head and Neck Merkel Cell Carcinoma, Olivia P MaDan1, Valerie A Smith1, Eric J Lentsch2; 1Otolaryngology, MUSC, 2Otolaryngology-Head and Neck Surgery, MUSC. Merkel cell carcinoma (MCC) is a rare and aggressive tumor of the skin, which most frequently arises in the head and neck. The purpose of this study was to explore the relationship between tumor location and prognosis among patients with MCC of the head and neck. Using the Surveillance Epidemiology and End Results (SEER) database, we identified patients with MCC of the head and neck. We compared clinicopathologic characteristics and disease specific survival (DSS) between patients with head and neck MCC at different anatomic subsites. DSS was estimated by the Kaplan-Meier method; and a multivariable regression model was constructed to
determine independent predictors of DSS. Of the 2104 patients identified in SEER database, 61.0% were male. The mean age at diagnosis was 77.5 years. The most common anatomic subsite was the face (61.1%). Scalp tumors were significantly larger (10.4% >5cm, p=0.0001) and more likely to present with distant metastasis (8.7%, p=0.08) than other head and neck tumors. Lip tumors had the highest rate of invasion into bone, cartilage, and skeletal muscle (13.7%, p=0.012); and ear tumors had the highest rate of nodal metastasis (63.2%, p=0.011). Scalp/neck and lip primary sites were significantly associated with worse survival on univariable analysis (p=0.0054 and p=0.0007, respectively); however, the lip was the only site that was independently associated with worse survival on multivariable analysis (HR 1.8, p=0.005). We are the first to report lip primary site as an independent predictor of worse survival in head and neck MCC. More aggressive treatment of patients with MCC of the lip may be warranted in order to improve outcomes.

073 Bilateral Amygdalal Lesions, Depression, and Suicide in an Adolescent with Neurocutaneous Melanosis, Dennis E Orwat1, Nicholas I Batalis2; 1Medicine, MUSC, 2Pathology & Laboratory Medicine, MUSC.

This report concerns a case in which suicide by self-immolation occurred in an adolescent with neurocutaneous melanosis (NCM). A rare neurocutaneous syndrome, NCM has often been reported to occur concomitantly with psychiatric and neurologic disorders. While symptomatic disease is most often encountered in children, symptomatic disease at any age typically results in rapid morbidity and mortality. NCM may have a large influence on pre-mortem behavior and determination of cause of death, and it is important to be aware of its morphology and potential significance when encountered at autopsy.

074 Who Needs an MRI? Laterality and Specificity of Prefrontal Craving Centers for Treatment with TMS, Morgan Jones1, Colleen A Hanlon2, Xingbao Li2, Karen J Hartwell2, Mark S George2; 1Medicine, MUSC, 2Psychiatry & Behavioral Sciences, MUSC.

Background: Transcranial magnetic stimulation (TMS) is a non-invasive brain stimulation technique that is being used as a treatment in multiple clinical populations. While emerging evidence suggests that it may be beneficial for treating substance dependence, the target location for stimulation is unclear. The aim of the present study was to determine if there was a consistent location of brain activity associated with drug-related cue reactivity among individuals for use as a treatment target. Method: 26 nicotine-dependent subjects viewed smoking and neutral visual cues while allowing themselves to crave cigarettes. Functional MRI BOLD scans from each participant were analyzed to locate the peak activation point during craving. Selection of the clusters of peak activity was restricted to areas in the frontal cortex. Points from all individuals were averaged to find a mean location that could potentially be used for treatment. Results: The location of peak activity when viewing drug related cues was in the left prefrontal cortex for 22 of the 26 participants. Sixteen of those were primary activation points; the remaining 6 were secondary activation peaks—those subjects’ primary prefrontal activation was on the right side. The location of the group mean was in the ventral medial frontal cortex (X, Y, Z: -19.64, 44.41, 4.55). Across the group, there was an approximately 6 cm of variability in the location of peak activity in each coordinate plane (X, Y, Z: -3 to -54,11 to 65, -20 to 46). Conclusion: According to these data, the variability between individual activation points during craving is too great to be encompassed by TMS stimulation at a single location and, thus, every patient should receive an fMRI to determine his or her exact craving center so that TMS can be effectively administered as an addiction treatment. However, the data also showed that there is a cohort of subjects whose left prefrontal activation points are very tightly clustered. Perhaps further investigation will reveal a similarity within these subjects that will allow effective treatment for this subgroup. DART, NIDA R25DA020537, NIDA DA19231

075 Effect of a Designated Reader and Cognitive Aid on Resident Performance During Simulation of Peri-operative Emergencies, Julius E Hamilton, Jarod Suber, Rieke Horst, Carlee Clark, Matthew McEvoy; Anesthesia and Perioperative Medicine, MUSC.

Abstract not available.

076 The Prevalence and Clinical Significance of Mycoplasma Genitalium in Our Gynecologic Patients: A Preliminary Review, Karla E Williams, Oluwatosin Jaiyeoba, David E Soper; Obstetrics and Gynecology, MUSC.

Recent studies suggest that Mycoplasma genitalium is a sexually transmitted disease (STD) that causes non-chlamydial, non-gonococcal lower and upper genital tract infections including urethritis, cervicitis, endometritis, and pelvic inflammatory disease (PID). However, the demographic profile of infected women, associated risk factors, disease presentation, and association with other microorganisms is not well understood. We conducted a cross sectional study with an objective to determine whether M. genitalium is implicated in non-chlamydial, non-gonococcal sexually transmitted infection, cervicitis, and PID. Our specific aims were to determine the microorganisms’s prevalence, clinic significance, associated risk factors for infection, and co-infections. A sample size of 400 was estimated using a power calculation. Demographic information, sexual history, endocervical
and vaginal swabs were collected for 32 nonpregnant women aged 18 years and older. Quantitative PCR analysis was conducted on the original samples, concentrated samples, and purified, concentrated samples respectively. Our preliminary results show a sample majority being African Americans (78%) between the ages of 18 and 25 years (72%) which correlates well with the CDC recommendation for women aged 25 years and younger to receive annual STD screenings. Majority of our patients revealed a history of one or more STDs (56%), and 53% of patients presented to their visit with gynecologic symptoms. Three patients were positive for Trichomonas vaginalis, and four tested positive for bacterial vaginosis. All patients tested negative for gonorrhea, chlamydia, or M. genitalium. The fact that all of the patients thus far have tested negative for M. genitalium correlates well with previous studies that reveal a 3-7% prevalence rate. The CDC reports that South Carolina ranks third in the United States for chlamydial and gonorrheal infections, twenty-seventh in primary and secondary syphilis infections, and fifteenth in HIV/AIDS cases. Early identification and treatment will help to reduce the risk of complications, economic burden, and the transmission of STDs.

077 Demographic, Clinical, and Laboratory Characteristics of 155 Pediatric Nephrolithiasis Patients, Jeffrey J Tutman, Laura P Adams, Lauren J Becton, David J Sas; Pediatrics, MUSC.

Background: Evidence suggests that the incidence of nephrolithiasis is increasing in children, yet there are few data documenting characteristics of pediatric stone formers. We sought to describe various characteristics of our stone-forming pediatric population. A description of pediatric nephrolithiasis patients of this size and scope has not been performed in almost two decades. Methods: We searched the MUSC EMR database for the ICD-9 codes for nephrolithiasis and urolithiasis. From patients with stones confirmed by imaging, we collected data on over 120 demographic, clinical, laboratory, evaluation, management, and follow-up variables on each patient. Results: Data from 155 subjects was collected and analyzed. Forty-nine percent of our patients were female. Seventy-three percent of our patients lived in urban environments. The ratio of urban-to-rural pediatric stone formers was lower than the general pediatric population (2.7 vs 3.5). The mean age of presentation tended to be earlier in males than females (8.2 vs. 9.4 years). Males with stones were more likely to be obese than females with stones (20.5% vs. 12.4%). Males with stones were also more likely to be obese than the general pediatric population, while females with stones were less likely to be obese. Patients presenting from ages 2-11 were less likely to be obese than the general pediatric population, while patients presenting from 12-18 were more likely to be obese. Ninety-eight percent of the 54 stones that were analyzed contained calcium. The most common abnormalities seen on LithoLink 24 hour urine analysis were low citrate (79%), supersaturation of calcium oxalate (70%), and supersaturation of calcium phosphate (63%). Conclusions: Our data summarize many characteristics of pediatric stone formers and reveal intriguing results regarding urine chemistry, obesity, and differences related to gender. Further investigation into potential contributors to the increasing incidence of pediatric nephrolithiasis is warranted.

078 Chemotherapy Tolerance in Colorectal Cancer Patients Post Liver Resection: A 5-year Retrospective Study At a Regional Teaching Hospital, Leah D Fryml1, E Bleed2, J Mills3, W J Edenfield4; 1Medicine, MUSC, 2Furman University, 3Wofford College, 4Cancer Center of the Carolinas.

Colorectal cancer (CRC) patients who receive liver resections for hepatic metastases commonly receive perioperative chemotherapy--neoadjuvant, adjuvant, or both. There is currently little data regarding the possible reduced tolerance to chemotherapy in patients status-post liver resection, as measured by the number and proportion of treatment delays and dose reductions experienced. This retrospective review of 40 patients at a single cancer center revealed no conclusive evidence linking decreased tolerance to liver resection; however, data does suggest that, for each commonly used chemotherapy drug, doses are more frequently delayed adjuvantly than neoadjuvantly. In addition, it was found that patients who experience low tolerance of chemotherapy preoperatively are more likely to experience low tolerance postoperatively.

079 Determining The Presence Of An Ear Advantage Yielding Increased Success Following Cochlear Implantation In The Elderly, Wasef K Muzaffar, Ted A Meyer; Otolaryngolgy-Head and Neck Surgery, MUSC.

Several studies have revealed, despite similar audiometric scores between ears, there is an asymmetric activation of auditory cortex preferentially for speech centers. In right-handed individuals these centers will be present on the left cerebral cortex while for the left-handed, they may be in one or both hemispheres. This finding coupled with a known decline in auditory pathways with aging has led to the credence implanting the right ear with a cochlear implant will cause a greater improvement in hearing performance. New literature has supported the notion of a right ear advantage present clinically in the elderly following cochlear implantation. This study aims to demonstrate if this right ear advantage is reproducible over different populations. A retrospective analysis of audiometric data for 50 patients divided by into groups based on the ear implanted was performed. Results compared right-ear versus left-ear implantation.
performance on speech perception tests (Hearing in Noise test, Consonant-Vowel Nucleus-Consonant words, and phonemes) pre-operatively and 1 year post-operatively. At 1 year, no statistically significant improvement was found for HINT (p = 0.47), CNC (p = 0.48), and phoneme (p = 0.55) test scores for either ear. While an asymmetry may exist in the activation and number of pathways to the contralateral auditory cortex, a clear advantage in outcome depending on the ear implanted is not apparent. As clinicians continue to establish cochlear implantation criteria for the elderly, right ear advantage is not a dependable marker for evaluation of a patient’s future performance.

080 Connexin 40 Remodeling in Purkinje Cardiomyocytes Post-Myocardial Infarction, Satara A Brown1, Mary S Rackley2, Brett S Harris3, Terrence X O’Brien2; 1Medicine, MUSC, 2Cardiology, MUSC; Medicine, VAMC, 3Regenerative Medicine and Cell Biology, MUSC.

Purkinje cardiomyocytes are specialized cardiomyocytes that connect to working cardiomyocytes to facilitate contraction of the heart muscle. Cx40 is the predominant connexin found in gap junctions of Purkinje cardiomyocytes; however, Cx43 and Cx45 are predominant in working cardiomyocytes. In working cardiomyocytes following myocardial infarction (MI), Cx43 remodeling occurs, which is indicated by lateralization of Cx43 and ensuing arrhythmias. We hypothesized that in murine Purkinje cardiomyocytes, MI will cause disorganization of Cx40 expression at gap junctions. A Cx40EGFP/+ transgenic mouse model post-surgical ligation of the left anterior descending artery was utilized to conduct this study. EGFP, enhanced green fluorescence protein, allowed identification of Purkinje cardiomyocytes. Antibodies to detect pan-cadherin and Cx40 were used in immunofluorescence staining of tissues. Immunofluorescence and confocal microscopy were employed to image gap junctions and intercalated disks in EGFP areas. Differences in Cx40 expression, cadherin expression, and colocalization of Cx40 and cadherin in control mice and mice that have experienced MI were quantified. Findings were similar to reported alterations in Cx43, which is believed to contribute to arrhythmias in working cardiomyocytes. Cx40 remodeling was indicated by decreased Cx40 expression, decreased cadherin expression, and decreased colocalization of Cx40 and cadherin in the Purkinje cell areas. Cx40 expression decreased by 56%, cadherin expression decreased by 69%, and colocalization decreased by 24%. This indicated that gap junctions were deficient and relocated from their normal locations at intercalated disks following MI. Alterations in Cx40 in Purkinje cells may be responsible for life-threatening arrhythmias that can occur post-MI. Changes in the murine population may parallel changes that occur in humans; therefore, these findings in the mouse model may potentially translate into treatment for post-MI arrhythmias in the future. NIH 1R25 HL096316

081 Unanticipated Effects of Adenosine on Microtubule Density, Flora M Simmons, Grace Wallenborn, George Cooper; Medicine, MUSC.

Increased microtubule density is one factor in the impairment of contractility and growth in pathological hypertrophy. This increase in microtubule density is caused by MAP4, a microtubule associated protein, decoration along microtubules. This, in turn, hyperstabilizes microtubules, impairing the heart’s ability to compensate with contraction or growth. There is a pathway developed that leads to MAP4 decoration of microtubules, beginning with catecholamine induced activation of Pak1. Adenosine is an endogenous nucleoside that has anti-adrenergic effects in the heart. Adenosine has recently been showed to decrease the catecholamine induced increase in microtubule density. This research looked at the three receptor agonists of adenosine, A1, A2A, and A3 to find which one is responsible for the cardioprotective effects, ie, decreasing ∆-tubulin and pPak1. Isolated feline cardiomyocytes were treated with isoproterenol, A1, A2A, and A3 for courses of 1, 4, 24, and 48 hours. It was found that A1 agonist in the presence of β-adrenergic stimulation provided cardioprotection by decreasing ∆-tubulin and pPak1 after 4 hours. A1 agonist treatment on control cells actually behaved in a cardiotoxic manner, increasing ∆-tubulin and pPak1. A2A and A3 did not decrease ∆-tubulin or pPak1 by very much, leading us to believe that the three receptors act synergistically to provide cardioprotection. NIH Minority Summer Fellowship

082 The Pitfalls of Automated Functional Analysis in Cardiac CT, Nelson E Seabrook, Pal Suranyi; Radiology, MUSC.

The primary purpose of this study was to identify the pitfalls of fully automated functional analysis of cardiac CT. Secondly, we examined the accuracy of the reported values, using the manually corrected analysis as the standard of reference. In this IRB approved study, eighty-nine (89) cardiac triple rule-out studies were retrospectively re-analyzed to calculate volumetric global function. First, the software automatically calculated the ejection fraction (EF), end systolic (ESV) and end diastolic (EDV) left ventricular volumes. Next, the manual analysis of cardiac function was performed, correcting the mitral valve plane where necessary by two reviewers in consensus. Additionally, medical records were reviewed and reported values were collected. Using the manually corrected analysis as the standard, the errors of functional analysis were calculated for the automated and the reported values using paired t-tests. Eighty-nine (89) studies were examined with an average age of 54.5 years. Residents reported quantitative
functional data for 81 patients. There were significant (p<0.01) differences among EFs calculated automatically (61.1±12.2%), the reported values (64.8±10.0%), and manually (71.6±7.6%). The mean difference in EF between automated and manual calculations was -10.5% (range -55.4 to 4.9). The mean difference in EF between reported and manual calculations was -7.9% (range -27.8 to 13.2%). The average automated, reported and manually corrected values for the EDV were 126.1±36.1, 121.8±32.5 and 126.9±30.3mL, respectively. The average ESV was 51.0±27.7, 44.0±20.4 and 37.0±15.7mL for automated, reported and manual calculations, respectively. The automated calculations significantly underestimated EF. Although reported values partially corrected for the underestimation, they were significantly lower than the standard. The ESV was systematically overestimated by the automated software due to placing the mitral valve plane at a higher level, obtaining smaller stroke volumes and decreasing EF. This can be deleterious to patients when clinical decisions are based on EF.

083 Generation of a Novel Bacteriostatic and Anti-collagenolytic Dental Adhesive Through the Incorporation of Polyacrylic Acid Modified Copper Nanoparticles Into Adhesive Resins, Andrew W Ambrose¹, Walter Renne¹, Michael Schmidt²; ¹Restorative Dentistry, MUSC, ²Microbiology, MUSC.

Recurrent caries as a result of bacterial microleakage is the primary cause of failure associated with resin based composites placed in the posterior dentition. The aim of this study was to assess the ability of antimicrobial copper to mitigate microleakage through its continuous microbiocidal activity leading toward long term stability. Clinical isolates of Streptococcus mutans were obtained. The isolates were then grown in brain heart infusion broth overnight and a growth curve with corresponding viability counts was determined over a period of two days. An increase in the viable count numbers matched the corresponding optical density from the growth curve for both the exponential growth phase and the stationary phase. With the ability to predict the number of colony forming units based on the corresponding optical density value one has the ability to consistently perform experiments with the S. mutans when there is a specific quantity desired. Further experiments will include comparing the effects of the presence or absence of copper nanoparticles in dental adhesives on S. mutans and determining the bond strength of the adhesives containing the copper nanoparticles.

084 Salivary Morbidity Following Radioactive Iodine Treatment for Thyroid Carcinoma, Ashley E Mishoe¹, Isaac F Dingle², M Boyd Gillespie³, Eric J Lentsch⁴, Shaun A Nguyen⁵; ¹Pharmacy, MUSC, ²Medicine, MUSC, ³Otolaryngology-Head & Neck Surgery, MUSC.

Background: Thyroid cancer is the most common endocrine malignancy and its prevalence has been rising steadily over the past fifty years. It is estimated that nearly 45,000 new cases were diagnosed in 2010. Radioactive iodine (RAI) is standard treatment in cases of papillary and follicular thyroid carcinomas where there is residual thyroid tissue following thyroidectomy or in cases of suspected or known metastases. The long-term salivary side effects and the prevalence of sialoadenitis requiring treatment following RAI for thyroid carcinoma have not been well described with validated questionnaires or with similarly designed studies. Purpose: The primary aim of this study is to evaluate swallowing-related quality of life using the M.D. Anderson Dysphagia Inventory (MDADI) and the University of Michigan Xerostomia scale (XeQOLS) while controlling for RAI dosage and time since RAI. Secondary endpoints include impairment in global head and neck quality of life using the University of Washington- Quality of Life Scale (UW-QOL) and prevalence of sialoadenitis using a sialoadenitis screening survey. Methods: The present study is a cross-sectional survey of surviving patients seen at the MUSC Hollings Cancer Center for cancer of the thyroid gland and were treated with RAI between 2000 and 2011. Patients were identified by review of the Hollings Cancer Registry and quality assurance databases of the Departments of Otolaryngology- Head & Neck Surgery, Pathology and Radiation Oncology. Each patient was mailed a study packet that included an introductory letter, a Baseline Questionnaire, three validated surveys, including the MDADI, the UW-QOL, and the XeQOLS, and a stamped return envelope. A phone call was made to patients who had not returned surveys within 1 month of mailing. Results: Pending. Conclusions: Data collection is still proceeding and is expected to be complete by the end of the year.

085 Effects of Cortisol and Norepinephrine on the Expression of the Tumor Antigen MUC1 in DU-145 Prostate Cancer Cells, Kristina Andrijauskaite¹, Daniel J Fernandes¹, Nigel S Courtenay-Luck¹, Katherine Regan Sterba²; ¹Biochemistry, MUSC, ²Biostatistics and Epidemiology, MUSC.

There is growing experimental and clinical evidence that psychological stress can affect cancer progression and the survival of cancer patients. The glucocorticoid cortisol and the catecholamine norepinephrine are known to be the mediators of psychological stress. Experimental studies indicate that elevated levels of these stress hormones may promote tumor growth, angiogenesis, and metastasis. In this study, we used DU-145 prostate cancer cell line to investigate the effects of cortisol and norepinephrine on MUC1, a tumor marker which is associated with tumor cell metastasis and is aberrantly glycosylated and up-regulated in most human epithelial carcinomas. Experiments investigating the effect of cortisol and
norepinephrine on the DU-145 cells growth revealed that both stress hormones increased the proliferative rate of these cells. The protein expression of MUC1 levels were assessed by ELISA and flow cytometry. The ELISA assays showed that physiologically relevant concentrations of cortisol found in the tumor microenvironment (10-7 M) enhanced the expression of MUC1 by 2-fold after 6 or 10 days when compared to untreated control cells. In addition, flow cytometric analyses revealed that DU-145 cells treated for 3 and 6 days with cortisol up-regulated the cell-surface expression of MUC1 by 2-fold. A 10 day exposure to cortisol up-regulated the MUC1 expression by approximately 7-fold. Norepinephrine did not enhance the expression of MUC1 at any time period. Also, the mRNA levels of MUC1 were increased by approximately 4-fold when cells were treated for 6 and 10 days with cortisol, while norepinephrine had no effect on MUC1 mRNA levels. In addition, preliminary data on assessing stress hormones effect on cells invasiveness indicates that cortisol may alter the invasive potential of DU-145 cells. Taken together, our findings suggest that cortisol may affect cancer progression by up-regulating the tumor antigen MUC1. This study provides for the first time a biochemical link between psychosocial stress and tumor invasiveness in prostate cancer cells.

086 Hypertonic Saline Immune Functions, Kevin M Phelan¹, Diane E Neal², Samir Fakhry³, 1Medicine, MUSC, 2Health Sciences, Walden, 3Surgery, MUSC.

Abstract not available.

087 Efficacy of Transcranial Direct Current Stimulation (tDCS) and Repetitive Transcranial Magnetic Stimulation (rTMS) for the Treatment of Fibromyalgia Syndrome: A Systematic Review, Nicole M. Marlow¹, Health S Bonilha², E Baron Short³; ¹Biostatistics and Epidemiology, MUSC, ²Health Sciences and Research, MUSC, ³Psychiatry and Behavioral Sciences, MUSC.

OBJECTIVE: To systematically review the literature to date applying repetitive transcranial magnetic stimulation (rTMS) or transcranial direct current stimulation (tDCS) for patients with fibromyalgia syndrome (FMS), summarizing procedures (including brain site, frequency, intensity, duration, total sessions, scheduling), FMS symptom outcomes, and levels of evidence. METHOD: Electronic bibliographic databases screened included PubMed, Ovid MEDLINE, PsychINFO, CINAHL, and Cochrane Library. The keyword “fibromyalgia” was combined with (“transcranial” and “stimulation”) or “TMS” or “tDCS” or “transcranial magnetic stimulation” or “transcranial direct current stimulation”. Reference sections of studies meeting inclusion criteria were screened for relevant publications. RESULTS: Nine of 23 studies were included, 5 each for rTMS (high-frequency M1 = 2, low-frequency DLPFC = 2, high-frequency DLPFC = 1) and tDCS (anodal-M1 = 1, anodal-M1/DLPFC = 3). Eight were double-blinded randomized clinical trials. Outcomes reviewed included pain, quality of life, tender points, depression, adverse events, and drop-outs. Most (80%) rTMS studies with pain outcome results reported significant decreases, while all tDCS studies with pain outcome results reported significant decreases. Greater longevity of pain reductions was observed for excitatory M1 rTMS/tDCS. Completion rates ranged from 80% to 100% for active-stimulation groups, much higher than such results reported in the literature for FDA approved FMS pharmaceuticals. CONCLUSION: Excitatory rTMS/tDCS at M1 may play a vital role among multidisciplinary treatment components for FMS, particularly for patients who are unable to find adequate symptom relief with other therapies. Further work into optimal stimulation parameters and standardized testing methodologies are needed to clarify the efficacy and effectiveness of these neuromodulation techniques for treating fibromyalgia.

NIH NIAIM S60 AR049459 and KL2 RR029880

088 Associations Between Coping Styles, Diabetes Knowledge, Medication Adherence, and Self-Care Behaviors in Adults with Type 2 Diabetes, Brittany L Smalls¹, Rebekah J Walker¹, Melba A Hernandez-Tejada², Jennifer A Campbell³, Kimberly S Davis⁴, Leonard E Egede⁵; ¹Health Sciences and Research, MUSC, ²Medicine, MUSC, ³College of Charleston.

Literature on diabetes and psychological factors show that some actions and thoughts that compose coping styles relate to compliance with treatment and self-care prescriptions. The goal of this study is to examine different coping styles and how these are related to diabetes management in adults with type-2 diabetes. The study had 378 subjects, recruited from the MUSC Internal Medicine Clinic and Franklin C. Fetter Health Center, who completed the following measures: 24-item diabetes knowledge questionnaire, Summary of Diabetes Self-Care Scale, COPE-S, and the 8-item emotional-approach coping questionnaire. Our study population was comprised of 83% Non-Hispanic Blacks, 69% women, 22% 65 years or older, 68% were not married, 26% had less than a high school education, 60% unemployed, 39% uninsured, 47% had a yearly income of less than $10,000, and 24% had worsening health status. Significant correlations were observed between both types of coping: emotional expression (EE) and emotional processing (EP) (r=0.070, p<0.0001). EE was related to diabetes knowledge (r=0.18, p<0.001) and EP to foot care (r=0.14, p<0.015). However, both were related to diet (EE r=0.18, p<0.001; r=0.16, p<0.005); exercise (EE r=0.20, p<0.004; EP r=0.23, p<0.001); and blood sugar testing (EE r=0.13, p<0.023; EP r=0.15, p<0.008). In the linear regression model, EP was significantly associated with medication adherence (β-
0.17, 95% -0.32, -0.015), diabetes knowledge (β 0.76, 95% 0.29, 1.24), diet (β 0.52, 95% 0.24, 0.81), exercise (β 0.51, 95% 0.19, 0.82), blood sugar testing (β 0.54, 95% 0.16, 0.91), and foot care (β 0.32, 95% -0.23, 0.67). Contrarily, EE was associated with diet (β 0.38, 95% 0.13, 0.64), exercise (β 0.54, 95% 0.27, 0.82), blood sugar testing (β 0.42, 95% 0.00, 0.76) and foot care (β 0.36, 95% 0.60, 0.66), but was not associated with diabetes knowledge. In conclusion, coping styles related to emotional processing and emotional expression was significantly associated with improved diabetes management. NIH T35DK007431

089 Association Between Fatalism, Medication Adherence and Self-care Behaviors in Adults with Type 2 Diabetes, Rebekah J Walker1, Brittany L Smalls1, M Hernandez-Tejada2, Jennifer A Campbell2, Kimberly S Davis3, Leonard E Egede2; 1Health Professions, MUSC, 2Medicine, MUSC.

Fatalism refers to a complex psychological cycle characterized by perceptions of hopelessness, meaninglessness, powerlessness, and despair (Powe and Weinrich, 1999; Egede and Ellis 2009). Few studies have examined the effect of fatalism on health outcomes. The objective of this study was to examine the association between fatalism and medication adherence and self-care behaviors in adults with diabetes. Data on 378 subjects with Type 2 diabetes were examined. Fatalism was measured with a 12-item scale; medication adherence was assessed with the 4-item Morisky scale; diabetes knowledge was measured with a 24-item diabetes knowledge questionnaire; and self-care behaviors were assessed with the Summary of Diabetes Self-care Scale. Multiple linear regression was used to assess the independent effect of fatalism on medication adherence and self-care controlling for covariates. Subject description is as follows: 83% were Non-Hispanic Blacks, 69% were women, 22% were 65 years or older, 68% were not married, 26% had less than high school education, 60% were unemployed, 39% were uninsured, 47% had a yearly income <$10,000, and 24% had worsening health status. Fatalism correlated significantly with medication adherence (r = 0.24, p<0.001), diet (r=-0.26, p<0.001), exercise (r=-0.20, p<0.003), blood sugar test (r=-0.19, p<0.007); however there was not significant association with diabetes knowledge or foot care. In the linear regression model, fatalism was significantly associated with medication adherence (β 0.24, 95% CI -0.010, 0.338); diet (β -0.05, 95% CI -0.077, -0.027), exercise (β -0.04, 95% CI -0.067, -0.011), and blood sugar test (β -0.04, 95% CI -0.08, -0.013); however, there was not significant association with knowledge or foot care. In this group, fatalism largely predicted poorer health behaviors. Thus, fatalism may be an important aspect of patient psychology to consider when deigning interventions, and patients with this personality characteristic or life outlook may benefit from specific intervention. NIH NIDDK T35DK007431

090 Filamin-A Regulates Cardiac Valve Development Via a Novel Serotonin Pathway, Kimberly Sauls, Amanda Richards, Katherine Williams, Aimee Phelps, Andy Wessels, Roger Markwald, Russel Norris; Regenerative Medicine and Cell Biology, MUSC.

Linkage and sequencing studies identified mutations in the filamin-A gene in humans with valvular heart disease. This defines filamin-A as an indispensable regulator of valve structure and function. By performing 3D-modeling and motif scanning, we observed these filamin-A mutations occur around putative transamidating sites for the enzyme, Transglutaminase-2 (TG2). Herein we demonstrate that TG2 is required for post-translational modification of filamin-A via the covalent incorporation of serotonin molecules (aka “serotonylation”). As a consequence, valve fibroblasts exhibit enhanced contractile function resulting in extracellular matrix compaction. In the case of either filamin-A point mutations or genetic removal of filamin-A from the cardiac valves during development, matrix compaction is disrupted resulting in enlarged tissues. These findings illustrate a novel contribution of serotonin, TG2 and filamin-A to cardiac development and suggest a mechanistic basis for the pathogenesis of filamin-A mediated valvulopathies. Additionally these data provide evidence of a developmental origin for valvular heart disease.

091 Amino Acids Starvation Response in Saccharomyces Cerevisiae, Role of Sphingolipids Gene ISC1, Alessandra Metelli1, Alessandro Achilli2, Hovirag Lancioni2, Nora Babudri3, Nabil Matnati3; 1Biochemistry & Molecular Biology, MUSC, 2University of Perugia.

The Saccharomyces cerevisiae ISC1 gene has a 30% homology to mammalian neutral sphingomyelinase 2 (nSMase2). This enzyme catalyses the hydrolysis of three complex sphingolipids, inositol phosphorylceramide (IPC), mannosylinositol phosphorylceramide (MIPC), and mannosylidinositol phosphorylceramide (M(IP)2C back to ceramide. Ceramide is a known bioactive lipid that functions in signal transduction, inflammation, cancer, apoptosis and stress response. In yeast, cells depleted in ISC1 gene (isc1Δ) exhibit a higher sensitivity to several compounds such as hydrogen peroxide (H2O2), hydroxyurea (HU) and methyl methanesulfonate (MMS). Here we investigated the role of Isc1 in yeast cells response to amino acids starvation. isc1Δ cells lose 80 % viability after 24 hours of amino acids starvation, 96% after 48 hours, and 98% after 72 hours, compared to wild type strain (WT). Starvation for a single or all auxotrophic amino acids has the same effect. Deletion of ISC1 gene shows the most severe sensitivity to amino acids starvation, compared
with the deletion of other genes in the sphingolipid pathway such as CSG2, SUR4, SCS7, IPT1 and SUR1. In starvation, autophagy plays a very important role in providing recycled amino acids to the cells. We have found that isc1Δ cells during amino acids starvation had no accumulation of autophagic bodies in the vacuoles. Intravacuolar autophagic bodies accumulation occurs when autophagy is active. In fact WT cells accumulated autophagic bodies in the vacuoles during starvation. Our results indicate that first, survival after 24, 48 and 72 hours starvation to amino acids is compromised in cells lacking ISC1 gene, and second, autophagic bodies accumulation in the vacuol is an Isc1 dependent event. Isc1 emerges as a new component involved in the autophagic response to amino acids starvation in Saccharomyces cerevisiae.

092 Rational Development of Novel Biogenic Beta-Adrenergic Selective Agonists, Robert B Cameron, Christopher Lindsey, Lauren P Wills, Richard T Trager, Craig C Beeson, Rick G Schnellmann, Yuri K Peterson; Pharmaceutical & Biomedical Sciences, MUSC.

Abstract not available.

093 The Role of Th17 and Treg Cells During HNSCC Carcinogenesis, Danielle N Justis¹, Anna-Maria De Costa², Corinne Schuyler², Rita Young²; ¹Microbiology & Immunology, MUSC, ²Otolaryngology, MUSC.

Head and neck squamous cell carcinoma (HNSCC) is an important public health problem worldwide with more than 500,000 new cases diagnosed each year. Despite advances in treatment, the 5-year survival rate remains at 20-65%. Patients with HNSCC tend to be systemically immuno-compromised, including a substantial increase in the immunosuppressive regulatory T cell (Treg) population. Tregs have recently been shown to have a reciprocal relationship with the Th17 cell population, an emerging effector T cell subset with an ambiguous role in carcinogenesis. The current project aims to investigate the changes in expression of Th17 cells and IL-17a during HNSCC development. Evaluation of cytokine levels in lysates of normal/adjacent, premalignant and HNSCC tissue from human subjects revealed an increase in IL-17A levels in premalignant tissue compared to control with a subsequent decrease in IL-17A levels in HNSCC tissue compared to premalignant. Based on the human data, a mouse model of carcinogen-induced HNSCC development was used to analyze Th17 and IL-17A expression in lymph node cells of control, premalignant and HNSCC-bearing mice. Similar to the human data, there was an increase in percentage of Th17 cells and IL-17A production in lymph nodes of mice with HNSCC compared to premalignant lesion-bearing mice. These data indicate that Th17 cells have a role in the immune reaction to premalignant lesion development. This role may be suppressed during the ultimate progression to HNSCC, a phenomenon that may be related to the increase in Treg cells. In order to elucidate the relationship between Th17 cells and Treg cells during HNSCC carcinogenesis, we plan to explore the mechanisms behind the responses of the Th17 cell population to products of premalignant and HNSCC tissue.

095 An Analysis of Race and Age As Factors Associated with the Development of Lymphedema Following Breast Cancer Treatment, Sybil L Prince Nelson, Joan Cunningham; Biostatistics, MUSC.

Lymphedema is the arm- and hand- swelling condition that plagues many women following surgery for breast cancer. In the After Breast Cancer Study (ABC study), potential participants were recruited through Palmetto Health in Columbia SC in 2002 and 2003. Five hundred eighty breast cancer survivors responded to an extensive survey which asked for physical characteristics such as race, age, and weight as well as general medical history. The goal of this analysis was to determine if race was a major factor of lymphedema or whether it increased the odds of acquiring the disease in any way. In these data, it was found that overall, black women are twice as likely to develop lymphedema than their white counterparts. When stratified by age, this ratio changes. Black women under 50 years of age are 1.79 times as likely to develop lymphedema than white women under fifty. Black women between 50 and 70 are 3.74 times as likely and black women over 70 are 4.37 times as likely than white women over 70. One limitation of this study is that it is based on survey data which may not be a representative subsection of society. It was found that a combination of race and age was an indicator for developing lymphedema. The literature shows that obesity has long been a risk factor for lymphedema, but age and race are also an important factor as, independent of BMI, black women have increasingly higher odds of developing lymphedema as age increase. This finding will be studied further in the context of other risk factors. More investigation is planned as to the socioeconomic and marital status of participants as well as time since diagnosis and choice of treatment.

096 The Analysis of Acute Stroke Clinical Trials with Responder Analysis Outcomes, Kyra M Robinson, Sharon D Yeatts, Viswanathan Ramakrishnan, Valerie L Durkalski; Biostatistics and Epidemiology, MUSC.

Abstract not available.
097 Spatial Exposure Modeling of Environmental Risk And Intellectual Delay Outcomes, Georgiana Onicescu¹, Andrew B Lawson¹, Suzanne McDermott², Marje Aelion³, Bo Cat²,¹, Biostatistics, MUSC, ², Unv. of South Carolina, ³, Univ. of Massachusetts.

The main objective of this retrospective cohort research project is to model the relationship between mothers’ residence during pregnancy, residential soil chemicals and the development of mental retardation or developmental delay (MR/DD) in their children. The data consists of pregnant women in South Carolina insured by Medicaid during January 1, 1996 and December 31, 2001 and the study location is the southern part of South Carolina. The current analysis is a subset of the original data including only mother-baby pairs who either did not move or moved to a known location, therefore having non-missing soil chemical data during pregnancy. Data analysis includes Bayesian hierarchical logistic regression models having as outcome child MR/DD status and as independent variables penalized splines of soil chemical values. NIH R01 ES012895-04A2

098 High Content Analysis of Dynamic Agonist Stimulated Receptor, G Protein, and Beta-arrestin Trafficking, Kathryn M Appleton¹, Mi-Hye Lee², Louis M Luttrell³, Yuri K Peterson³; ¹Pharmaceutical and Biomedical Sciences, MUSC, ²Medicine, MUSC, ³Pharmacy, MUSC.

Mechanisms driving functional selectivity downstream of differentially stimulated G protein couple receptors (GPCRs) are not well understood. It is hypothesized that pathway selective ligands of GPCRs regulate specific receptor endosome trafficking of beta-arrestin and G-proteins. Utilizing the parathyroid hormone 1 receptor (PTH1R) and the beta2-adrenocceptor (beta2AR) as models, temporal protein trafficking was characterized as induced by multiple ligands which elicit multiple phenotypic responses through the same receptor. We present a time resolved cell based method for assaying dynamic events proximal to receptors during agonist selective signaling using the InCell Analyzer 2000. By coupling live cell fluorescence microscopy using with high-content multi-parametric object classification, this method is optimized to quantitatively differentiate efficacy profiles for receptor ligands with regards to G-protein and beta-arrestin2 coupling. Real-time protein trafficking profiles were compared to real-time second messenger fluxes. The FLIPR Tetra platform was utilized for the measurement of calcium transients using a calcium sensitive dye, and intracellular cAMP dynamics in living cells as monitored in real-time using the GloSensor cAMP assay. Multiple full and biased agonists of the PTH1R and beta2AR were used for a comparative analysis. Pathway selective agonist trafficking displayed differences in the timing, localization, and colocalization of receptor and beta-arrestin at the plasma membrane and in cytosolic signalingsomes. Analysis of multiple ligands indicates a spectrum of pathway selectivity following agonist stimulation including differential regulation of effector colocalization and second messenger flux. This data furthers our understanding of altered responses and interactions induced by selective receptor ligands which regulate both convergent and divergent signaling to produce diverse cellular phenotypes.

099 Complement Deficiency Ameliorates Acute Cigarette Smoke Induced Lung Injury, Sarah E Casey, Fei Qiao, Stephen Tomlinson, Carl Atkinson; Microbiology & Immunology, MUSC.

Cigarette smoke is the single largest risk factor in emphysema development. The pathogenesis is complex, but inflammation plays a key role in lung damage and destruction. The complement system is a powerful mediator of inflammation and excessive activation can result in tissue damage. Studies performed more than a decade ago demonstrated that components within cigarette smoke have the capacity to activate the alternative pathway of complement in vitro by modification of C3. The aims of this study are to determine whether cigarette smoke exposure in-vivo results in complement activation and if complement deficiency protects against acute cigarette smoke induced lung damage. C57Bl6 complement sufficient, C3 (deficient all pathways of complement) and fB (deficient alternative pathway) deficient animals were exposed to 4 3R4F reference cigarettes twice a day for three days. Twelve hours following the final exposure mice were sacrificed for analysis. Results show acute cigarette smoke resulted in complement deposition in lungs, increased lavage concentrations of C3 and C5, and increased gene transcription for C3, C4, C5 and fB. To assess whether complement activation plays a role in acute smoke induced lung damage lavage and lung samples from wild type, C3 and fB deficient mice were compared. Deficiency in either C3 or fB resulted in a significant reduction in histological lung damage, inflammatory cell infiltration, lung myeloperoxidase levels and pro-inflammatory cytokines as compared to wild type. Smoke exposure results in increased complement production, gene transcription and deposition in vivo. Exposure of complement deficient mice to acute cigarette smoke results in a significant reduction in inflammatory cell infiltration and cytokine production, which results in a concomitant reduction in lung injury as compared to wild type controls. Taken together these data support a role for complement in the initiation of lung inflammation and damage as a result of cigarette smoke inhalation.
100 Activation Induced Cell Death in Adoptively Transferred T-Cells. Matt Scheffel, Chris Voelkel-Johnson, Shikhar Mehrotra; Microbiology & Immunology, MUSC; Jennifer Isaacs; Pharmacology, MUSC.

Patient outcomes for melanoma skin cancer are highly dichotomous based on stage of initial detection. Stage I melanoma is generally curable via surgery; however, once the cancer has metastasized, a favorable prognosis quickly diminishes (five year survival ~15%). The advent of melanoma tumor specific antigens (i.e. MART-1, tyrosinase, etc) has allowed for immunotherapies to be an effective treatment for late stage disease. Current immunotherapies either use patient autologous tumor-infiltrating lymphocytes or transduce a melanoma antigen specific T-cell receptor onto patient nonspecific T-cells. These therapies have greatly improved patient outcomes for late stage melanoma. However persistence of adoptively transferred T-cells continues to represent a major hurdle for therapeutic efficacy. Our overall hypothesis is that activation induced cell death (AICD) contributes to poor persistence of adoptively transferred T-cells and that increasing resistance to cell death will improve persistence and subsequent therapeutic efficacy. AICD is an immune-homeostatic mechanism by which activated T-cells undergo cell-death upon repeated exposure to cognate antigen. An immediate goal of this project is to understand how these T-cells die upon antigenic stimulation. Previous research on this project indicates that AICD is a caspase-independent necrotic form of cell death facilitated by JNK, AIF, and reactive oxygen species (ROS). Currently we seek to determine if AICD is modulated by p53. The p53 inhibitor, pifithrin-alpha, rescues T-cells from AICD, and p53 protein expression is upregulated in response to antigenic stimulation. Ongoing experiments will confirm AICD protection via a p53 knock-out mouse model and will also further characterize the localization and post-translational kinetics of p53 involved in AICD. Future directions will seek to relate p53, as well as JNK and AIF, as upstream or downstream factors of ROS accumulation as we believe ROS to be a likely therapeutic target to attenuate AICD via redox regulation. 

101 Extracellular Heat Shock Protein 90 (eHsp90) Mediates EMT in Prostate Cancer Through the Polycomb Epigenetic Pathway. Krystal L Dole, Michael Hance, Jennifer Isaacs; Pharmacology, MUSC.

Prostate cancer is the second leading cause of cancer deaths in men, mainly due to metastases to the bone. While the key drivers of metastasis are still unclear, activation of the metastatic program is widely believed to involve the molecular processes of epithelial to mesenchymal transition (EMT). During the EMT process, epithelial tumor cells lose the cell-cell adhesion protein E-cadherin. Loss of this protein promotes increased cell motility and tumor dissemination. Extracellular heat shock protein 90 (eHsp90) is a secreted protein that has recently been found to promote both tumor cell motility and metastasis. However, the mechanism of action and potential role of eHsp90 in prostate cancer remains unknown. We have found that eHsp90 is a critical mediator of EMT. Treatment of epithelial prostate cancer cells with eHsp90 decreases E-Cadherin, increases mesenchymal proteins, and subsequently increases motility. In addition, EMT is complex program that is often regulated by epigenetic factors. Chromatin modifiers histone deacetylases 1 and 2 (HDAC1/2) and enhancer of zeste homolog 2 (EZH2) are frequently upregulated in metastatic prostate cancer and are also events associated with activation of EMT. Notably, we find these three epigenetic proteins to be upregulated in accordance with eHsp90-mediated induction of EMT events. Inhibition of these proteins with small molecule inhibitors reverses the eHsp90 suppression of E-Cadherin, supporting their involvement in eHsp90’s EMT inducing activity. These results demonstrate a novel pathway in which prostate cancer cells secrete eHsp90 to mediate EMT events and increase metastatic potential. A further understanding of this pathway may lead to efforts designed to target eHsp90 as a therapeutic approach to reduce the incidence and lethality of prostate cancer.

102 Dephosphorylation of C-terminal Tyrosine Residues Does Not Contribute to Ethanol Inhibition of Recombinant NMDA Receptors. Ben A Hughes, John J Woodward; Neurosciences, MUSC.

N-methyl-D-aspartate (NMDA) receptors are ion channels activated by the neurotransmitter glutamate and are highly expressed by neurons. These receptors are critical for excitatory synaptic signaling and inhibition of NMDA receptors leads to impaired cognition and learning. Ethanol inhibits NMDA currents at concentrations associated with intoxication, and this action may underlie some of the behavioral effects of ethanol. Although numerous putative mechanisms have been suggested, how ethanol inhibits these receptors remains unclear. Recent findings in the literature suggest that ethanol, via facilitation of tyrosine phosphatase activity, may dephosphorylate key tyrosine residues in the C-terminus of NR2B subunits resulting in diminished channel function. To directly test this hypothesis, we engineered NMDA receptor mutants that contained phenylalanine in place of tyrosine at three different sites and transiently expressed them in human embryonic kidney (HEK) cells. Whole-cell patch clamp electrophysiology was used to record glutamate-activated currents in the absence and presence of ethanol (10 – 600mM). Analysis of the dose-response curves showed no significant difference in ethanol IC50 values between
wild-type receptors and Y1252F, Y1336F, Y1472F or triple Y-F mutants. These findings suggest that the ethanol inhibition of recombinant NMDA receptors is unlikely to involve dephosphorylation of C-terminal tyrosine residues. *NIH R37 AA009986*

### 103 Matrix Metalloproteinases in Reinstated Cocaine Seeking

Alex W Smith, Armina T Wiggins, Peter W Kalivas; Neurosciences, MUSC.

Chronic cocaine use is associated with behavioral, neurochemical and morphological changes within glutamatergic projections connecting the PFC to the nucleus accumbens (NAc). Cocaine induced glutamatergic plasticity in PFC-NAc circuitry contributes to dysregulation of glutamate homeostasis and the vulnerability to reinstate cocaine-seeking. Matrix metalloproteinases (MMPs) are a family of proteolytic enzymes that degrade the extracellular matrix to promote synaptic growth and reorganization. The endogenous inhibitors of MMPs are a family of 4 proteins termed tissue inhibitors of metalloproteinases (TIMPs), each of which inhibit all MMPs but with differing binding affinity profiles. The balance between MMPs and TIMPs determines MMP activity. MMPs are required for the maintenance of LTP, a finding that has inspired substantial experimentation into the involvement of MMPs in learning and memory, as well as in drug addiction. We hypothesize that increased MMP activity in the NAc produced by chronic cocaine self-administration is required for reinstated cocaine-seeking. In order to test this hypothesis, we used an operant cocaine self-administration paradigm to test the effects of acute MMP inhibition (by nonspecific MMP inhibitor FN-439) on reinstatement of cocaine seeking, as well as MMP-specific inhibitors against MMPs-2, -3, and -9. Rats were trained in cocaine self-administration and then extinction training, and reinstatement was induced by a 15mg/kg IP cocaine injection and cues indicating the availability of cocaine. The acute treatment condition utilized a within-subjects crossover design, where animals received either an MMP inhibitor or vehicle prior to two consecutive reinstatement sessions. In addition, in vivo zymography was used as a direct measure of gelatinase (MMP-2/9) activity prior to reinstatement. Results indicate that MMP activity is increased following chronic cocaine self-administration and that this increase is attenuated 30 minutes following reinstatement, and inhibition of MMP activity attenuates reinstatement to cocaine-seeking. *NIH R01 DA 03906-26*

### 104 Assessing Cognitive Flexibility Following Methamphetamine Self-administration

Brittney M Cox¹, Zackary A Cope², Aram Parsegian³, David E Moorman¹, Stan B Floresco², Gary Aston-Jones¹, Ronald E See ¹; ¹Neurosciences, MUSC, ²Psychology, Univ. of British Columbia.

Methamphetamine (meth) addiction has been implicated in cognitive deficits in working memory, attention and executive function, all of which are regulated by the prefrontal cortex. Neuroimaging studies have shown decreased prefrontal activation in meth addicts. Furthermore, prefrontal cortex impairments in rodent models have shown analogous cognitive deficits. The rodent attention set shift task has been used to demonstrate selective cognitive flexibility deficits in rats following escalated meth self-administration. Here, we used an automated attention set-shifting task (AASST) conducted in an operant chamber (analogous to the Wisconsin card sorting task) to determine whether performance impairments are seen after limited access meth self-administration, a regimen most commonly used for drug self-administration studies. Compared to other rodent set-shifting procedures, this task allows greater temporal resolution for tracking behavior, more detailed analysis of the types of errors, and greater face validity to human studies. The use of the AASST in conjunction with meth self-administration also allows direct comparison of drug history and cognitive performance within the same animal. The self-administration and set-shifting tasks were conducted in distinct chambers; the AASST chamber was equipped with levers and the self-administration chamber with nose poke ports. Discriminative light cues that differed by color and location served as conditioned stimuli. Meth experienced rats showed robust nose poke responding for meth, with an average intake of 1.8 ± 0.25 mg/kg/day and 36 ± 9.9 active nose pokes in the active port by the last day of self administration (2 hr session). We have successfully incorporated self-administration with the AASST and will discuss these preliminary findings. In the cognitive analysis, we will report trials to criterion and errors to criterion by type: perseverative, regressive, and never reinforced, during a visual-cue discrimination, shift to response discrimination (extra-dimensional shift), and a response reversal. *NIH DA022658; DA06214; and 5T32DA007288-20*

### 105 Homer2 Deletion Prevents Chronic Ethanol-Induced Spine Enlargement in the Nucleus Accumbens

Natalie M Straight, Natasha N New, Justin T Gass, Patrick J Mulholland, Judson L Chandler; Neurosciences, MUSC.

Homer2 is a post-synaptic density protein that acts to tether glutamate receptors to the cell’s internal calcium store. Current research shows that Homer2 knockout (KO) mice have an increased latency to right after acute IP ethanol and these mice do not show locomotor sensitization after chronic alcohol exposure. This implicates Homer2 in alcohol-associated behavioral plasticity. We investigated alcohol-associated plasticity of dendritic spines in the Homer2 KO mouse. Wildtype (WT) and KO mice received an acute injection of 4 g/kg ethanol (i.p, 20% v/v in saline) and
their latency to right was measured. In a separate study, WT and KO mice were administered 3g/kg ethanol every other day over 16 days for a total of 8 injections. Immediately after the first and eighth injections, the locomotor activity of each mouse was monitored for 15 minutes. 24 hours after the last injection, diolistic labeling coupled with confocal imaging were used to determine chronic ethanol-associated changes in density and morphology of dendritic spines in the nucleus accumbens (NAc) core. There was no significant effect of genotype on the righting response after acute ethanol injection. Also, deletion of Homer2 didn’t alter the locomotor response to acute ethanol injection, and chronic ethanol did not produce locomotor sensitization in either genotype. Spine density values were similar between WT and KO mice in saline-treated mice, and chronic ethanol exposure didn’t alter spine density in either genotype. Preliminary data also indicate that chronic IP injection of ethanol alters the morphology of dendritic spines of NAc neurons in WT, but not Homer2 KO mice. Specifically, only WT mice showed increased spine volume after chronic ethanol exposure. Deletion of Homer2 also prevented chronic ethanol-induced enlargement of the head size of mature, mushroom spines. Together these data implement Homer2 in the regulation of alcohol-associated plasticity of dendritic spines in NAc neurons. NIH AA010983; and AA017922

106 Clinical Reasoning in Graduate Prelicensure Nurses, Suzanne M Sutton1, Lynne Nemeth1, Darlene Amendolair2, Julie Moss3; 1Nursing, MUSC, 2Mary Black School of Nursing, University of South Carolina Upstate.

Background/rationale: Clinical reasoning by nurses is considered essential for today’s complex health care system. Literature reveals that content saturation, disconnect between theory and clinical education and failure to integrate clinical reasoning into the nursing curriculum hinder the ability to practice clinical reasoning by nursing students. Clinical reasoning uses multiple levels of knowledge, experience and cognition to organize data, consider situational context and the patient’s perspective and desires in providing patient care. Inability to perform clinical reasoning results in failure to rescue, errors and patient injury and death. Aims: 1) explore how baccalaureately prepared prelicensure nurses describe clinical reasoning in providing patient care and 2) discover teaching-learning methods used to teach clinical reasoning, as described by baccalaureately prepared prelicensure nurse graduates. Methods: This qualitative study was designed using grounded theory to investigate how nurse graduates define clinical reasoning and how it was taught during their nursing education. Using purposeful sampling, participants were recruited during the final semester of a BSN program at a small southeastern university via school of nursing website and email. Using techniques described by Charmaz, interview transcripts were analyzed and coded using NVivo software to uncover contributory themes and concepts. Results: Ten participants volunteered and seven completed this study. Participants: 1) were unable to theoretically define clinical reasoning, but described it as a multi-step, cognitive process in clinical decision-making and patient care; 2) could use clinical reasoning because they have experience or will develop it with further experience; 3) believed clinical reasoning was taught, but that practicums need to be changed to better relate to theoretical content and provide more diverse experiences; 4) described an inconsistency between instructors who stressed tasks rather than “thinking like a nurse” (as the application of clinical reasoning). Conclusions: Curricula should link clinical reasoning and learning outcomes with clinical education and theoretical content.

107 Business Case for Pre-treatment Swallowing Exercises, Kendrea L Focht1, Kit N Simpson2, Terry A Day2, Bonnie Martin-Harris3; 1Health Sciences and Research, MUSC, 2Otolaryngology-Head and Neck Surgery, MUSC.

Objectives/Hypothesis: Dysphagia is a common post-treatment morbidity for patients with head and neck cancer treated with chemoradiation. Previous studies have demonstrated that pre-treatment swallowing exercises may improve post-cancer treatment swallowing function and quality of life. We constructed a decision analysis model to estimate the incremental cost-effectiveness ratio (ICER) of this strategy compared with current standard care-post-treatment swallowing exercises. Study Design: Cost-effectiveness analysis. Methods: A transition state model was constructed to estimate the ICER of pre-treatment swallowing exercises on a cohort of 100 hypothetical patients. Quality of life estimates were obtained through convenient sampling. Costs were estimated from Medicare reimbursement data. Sensitivity analyses evaluated changes in efficacy, quality of life weights, and costs. Results: Pre-treatment swallowing exercises were less costly and resulted in a greater gain in quality-adjusted life-years (QALYs) when compared to post-treatment swallowing exercise intervention following chemoradiation treatment for head and neck cancer. Compared with current standard care using post-cancer treatment swallowing exercises, the pre-treatment exercise intervention provides a dominant ICER of $142,972 per QALY gained. Sensitivity analysis adjusting both costs and utility had minimal impact on these results as the ICER continued to be dominant. Conclusions: Implementing pre-treatment swallowing exercises offers a clinical benefit in patients treated with chemoradiation for head and neck cancer with significant cost savings relative to the current standard of care. The results from this analysis are a useful
108 DNA Damage Activates MK2-mediated Cell Cycle Control By Transcriptional Regulation of Cyclin, Bethany A Herbert, Sudha Talwar, Yogendra Padwad, Viswanathan Palanisamy; Craniofacial Biology, MUSC.

DNA damage induces activation of the p38 mitogen activated protein kinase pathway (p38 MAPK) leading to activation of MAPK-activated protein kinase 2 (MK2), a phosphorylation substrate of p38. RNA binding proteins such as TTP, HuR, hnRNP A0, and TIAR are known substrates of MK2. Consequently, both cyclin A1 and B1, protein regulators of mitosis, are targeted by proteins HuR and TTP. Interestingly, MK2 activity is necessary in the G2/M cell cycle checkpoint after DNA damage. Depletion of MK2 has also been shown to sensitize p-53 deficient cells to chemotherapeutic drugs. The role of doxorubicin, a chemotherapeutic drug, in the induction of the p38 pathway in cell cycle control via MK2 and cyclin has yet to be elucidated. We hypothesize the chemotherapeutic doxorubicin may alter cell cycle control through induction of the p38-MK2 pathway. Previously, we have observed cyclin B1 as a downstream mRNA target of MK2. Screening of six oral cancer cell lines yielded increased cyclin B1 mRNA in comparison to normal human oral keratinocytes. The fold change of cyclin B1 mRNA was highest in oral squamous cell carcinoma 74B cells, which were further used for experimentation. By western blot analysis, 74B cells treated with doxorubicin express phosphorylated MK2 protein, confirming that MK2 is activated. To assess the function of MK2 in the stabilization of cyclin B1 mRNA following doxorubicin treatment, MK2 was transiently knocked down using siRNA. Quantitative real-time PCR results from this mRNA decay experiment using actinomycin-pulse chase analysis suggest that the half-life of the cyclin B1 transcript is shorter in 74B cells transfected with siMK2. These results indicate that MK2 is activated upon DNA damage and silencing MK2 destabilizes cyclin B1 mRNA. Currently, we are exploring if MK2 regulates phosphorylation of RNA-binding proteins to control the cell cycle through transcriptional regulation of cyclin in oral cancer. NIH R00DE018165; NRSA, T32

109 Activation of Apoptotic Pathways Without Cell Death in an Inner-ear Immortomouse Cell Line, Kayla R Hill³, Fu-Quan Chen¹, Ya-Jun Guan², Jochen Schacht², Su-Hua Sha¹; ¹Pathology and Laboratory Medicine, MUSC, ²Otolaryngology, University of Michigan.

Aminoglycoside antibiotics and cisplatin are the major ototoxic drugs resulting in permanent hearing loss due to the inability of mammalian sensory cells to regenerate. Understanding the mechanism of pathogenesis is the first step in designing effective treatment and prevention of drug-induced hearing loss. In-vitro systems greatly enhance the efficiency of biochemical and molecular investigations through easy access and manipulation. HEI-OC1, an inner ear cell line from the immortomouse, expresses markers for auditory sensory cells and, therefore, is a potential tool to study the ototoxic mechanisms of drugs like aminoglycoside antibiotics or cisplatin. We are currently investigating aminoglycoside-induced signaling pathways and cell death using HEI-OC1 cells. HEI-OC1 cells efficiently took up fluorescently tagged gentamicin and responded with changes in a variety of cell death and survival signaling pathways. Within hours, the C-jun N-terminal kinase pathway and transcription factor AP-1 were activated. At later times, the “executioner caspase”, caspase 3, was activated. These responses were robust and elicited by both gentamicin and kanamycin. However, despite the initiation of apoptotic pathways and transient changes in nuclear morphology, cell death was not observed. Furthermore, beta-glactosidase measurements ruled out senescence in gentamicin-treated cells. The ability to withstand treatment with aminoglycosides but not with cisplatin suggests that this cell line may be helpful in providing some insight into the differential actions of the two ototoxic drugs and possibly into mechanisms of intrinsic repair capabilities after aminoglycoside insult. NIH R01 DC-03685

110 The Vitamin D Receptor and Retinoid X Receptor Expression Related to DNMT Levels in a Murine Model of Colitis, Rebecca W Knackstedt, Vondina Moseley, Jay Morris, Michael Wargovich; MCBP, MUSC.

Abstract not available.

111 The Ratio of Alpha-1B-Glycoprotein to Zinc Alpha-2 Glycoprotein in Urine Is an Early and Accurate Predictor of Acute Kidney Injury, Joseph L Alge², Michael G Janech¹, Andrew D Shaw³, Lakhmir S Chawla³, James A Tumlin², John M Arthur³; ¹Medicine, MUSC, ²Anesthesiology, Duke University, ³Anesthesiology and Critical Care Medicine, George Washington University.

Abstract not available.
112 Acid Ceramidase Over Expression in Response to Cigarette Smoke Exposure. Sarah T Marrison1, Joseph C Cheng1, Thomas H Beckham1, Ping Lu1, Angen Liu2, Sarah Casey1, Xiang Liu1, James S Norris1, 1Microbiology and Immunology, MUSC, 2Tissue Biorepository, Hollings Cancer Center, MUSC.

Abstract not available.

113 Effects of Fli-1 on T Cell Function in Lupus. Fahmin Basher1, Zainab Amani2, Marlene Bunni2, Tamara Nowling2, 1Microbiology & Immunology, MUSC, 2Rheumatology, MUSC.

Systemic lupus erythematosus is an autoimmune disease characterized by abnormal activation of T and B cells and consequent production of autoantibodies, inflammation, and deposition of immune complexes in peripheral organs. Overexpression of the transcription factor Fli-1 in non-autoimmune mice leads to a lupus-like disease state, while reduction of Fli-1 expression results in decreased T cell infiltration in the kidney as well as decreased inflammation and increased survival. In this study we investigated effects of Fli-1 on T cell function in both non-autoimmune and autoimmune mouse models with respect to proliferation and apoptosis. While a decrease in proliferation was seen in wildtype C57BL/6 mice compared to Fli-1+/-, no differences were observed in pre-disease MRL/lpr mice. Fli-1’s known anti-apoptotic effects were observed in the B6 mice, with a decrease in early apoptosis in wildtype mice compared to Fli-1+/-, and a similar trend was seen in the MRL model, with CD4+ cells exhibiting increased and CD8+ cells decreased early apoptosis. We adaptively transferred T cells isolated from young wildtype MRL/lpr mice into Fli-1+/- and vice versa, and monitored serum levels of IgG, IgM, IgA, anti-dsDNA antibodies, anti-GBM antibodies, and proteinuria over 12 weeks. IgG levels in Fli-1+/- mice receiving wildtype cells, and wildtype mice receiving Fli-1+/- cells exhibited a modest increase but still significantly lower than wildtype controls. Conversely, IgM levels did not differ significantly between wildtype and Fli-1+/- recipients. These results indicate that presence of lower levels of Fli-1 in endogenous or transferred T cells can protect from disease with respect to circulating antibodies such as IgG but that reduced expression of Fli-1 may affect the ability of the T cells to regulate B cell production of autoantibodies.VA Merit Review 101 BX000115

114 Absence of Estrogen Receptor Alpha Reduces Plasmacytoid Dendritic Cells and Type I Interferon Production in Lupus Prone Mice. Jennifer L Scott3, Melissa Cunningham2, Osama S Naga2, Gary Gilkeson2, 1Microbiology and Immunology, MUSC, 2Medical Research Service, VA.

Systemic Lupus Erythematosus (SLE) is an autoimmune disease that affects women at a 9 to 1 ratio compared to men. Based on this observation, estrogen and its receptors, estrogen receptor α and β (ERα/β), have been speculated to play a role in SLE. To study the role of ERα, a lupus prone (NZM 2410) murine model deficient in the receptor was developed. These ERα -/- lupus prone mice have longer survival times and less renal disease compared to their wild type counterparts. To account for this difference, our laboratory has investigated their immunological profiles. We found that many inflammatory cytokines are decreased in ERα -/- lupus prone mice. These cytokines include IL-1, IL-6, IL-23, and MCP-1. Another cytokine that we investigated was type I interferon (IFN) and the body’s major producer of type I IFN, the plasmacytoid dendritic cell (pDC). This area is relevant because SLE patients have increased expression of type I IFN regulated genes. Additionally, type I IFN therapy for malignancy can induce lupus symptoms in patients. Regarding this cytokine, our findings show a decrease in pDCs in ERα -/- lupus prone mice compared to wild type lupus prone mice. These pDCs account for 60% of total bone marrow derived dendritic cells in wild type lupus prone mice, but only 35% in the ERα -/- lupus prone mice. Additionally, the pDCs from ERα -/- lupus prone mice produce decreased levels of type I IFN. Given these findings, the next step will be determining the mechanism by which ERα deficiency reduces inflammatory cytokines and attenuates disease.

115 NAC and Vit D Treatment Improving Hypoxic Ischemic Injury in the Neonatal Rat Model. Danielle Clark1, Jessica Perkel2, Xingju Nie3, Inderjit Singh2, Dorothea Jenkins2, 1MCBP, MUSC, 2Pediatrics, MUSC, 3CBI, MUSC.

Neonatal hypoxic ischemic (HI) injury can be a devastating ending to an apparently normal pregnancy. Current standard of treatment is hypothermia, a neuroprotective therapy that decreases oxygen consumption and preserves energy levels in the brain. In this study, we compared hypothermia treatment alone, combination therapy with N-acetylcysteine (NAC), and triple therapy with NAC and Vitamin D in a neonatal HI rat model. NAC has antioxidant and anti-inflammatory properties and been shown to improve behavioral testing and infarct volume. Vitamin D (Vit D), an immunomodulator, is depleted during inflammatory processes. In one report, Vit D treatment was neuroprotective in neonatal hypoxic ischemic encephalopathy. We hypothesized triple therapy of hypothermia, NAC and Vit D will result in better outcomes than hypothermia treatment alone or with NAC in the rat HI model. Using a standard HI model on PND seven rats, we randomized ten rats to each treatment, giving IP injections of saline, NAC, or NAC and Vit D daily for seven days followed by PO for four days. Behavioral testing was done daily for
negative geotaxis and every three days for other measures until sacrifice at eleven days post HI insult. Infarct volume, as measured by gross brain pathology scoring, showed a trend of improvement in triple therapy rats compared with other treatments. A trend in behavioral improvement with triple therapy was also observed in first day of successful negative geotaxis, measure of neurological reflexes and locomotion. Poor brain pathology scores showed a significant association with post injury poor weight gain or weight loss. Spleen weight was significantly adversely affected by eleven days post injury and correlated with both worse brain pathology scores and post injury weight loss. In conclusion, our data may provide insight into future possible treatment combinations as well as predicting outcome severity using a non-invasive measure.

116 Improving Treatment of Bacterial Infections in Deep Wounds, Angela A Alexander, Xuejun Wen; Clemson-MUSC Bioengineering.

Surgical site wound infection and infection due to trauma results in billions of dollars in medical costs each year. Antibiotic prophylaxis and wound debridement are commonly used to treat these infections, however surgical debridement requires invasive techniques and increasing antibiotic-resistant bacteria, especially in biofilm development, warrants the need for alternative solutions to treat these infections. In this work, charged polymer fibers were used to immobilize and kill bacteria. Polymer fibers were charged to induce reactivity with bacteria and promote adhesion. The efficiency of bacteria immobilization on the charged fibers was evaluated in vitro using S. aureus in a bacteria adhesion study. Charged fibers showed enhanced adhesion and immobilization of bacteria and exhibited bactericidal activity. This finding has significant implications for advancements in treatment of deep wound infections because it eliminates the problem of antibiotic resistant bacteria. In addition, this potential new technology in infection treatment may lead to other applications for charged materials to prevent infection.

117 Racial Disparities in Repeat Admissions for Ischemic Stroke Patients Less Than 65 Years of Age, Andrea D Boan¹, David L Bachman², Robert J Adams², Wuwei Feng³, Brent M Egan⁴, Joyce S Nicholas⁵, Andrew B Lawson⁵, Daniel T Lackland⁶, ¹Biostatistics & Epidemiology, MUSC, ²Neuroscience, MUSC, ³General Internal Medicine, MUSC.

Abstract not available.

118 Optogenetic and Pharmacologic Modulation of Locus Coeruleus Noradrenergic Neurons: Effects on Behavioral Flexibility, Zackary A Cope¹, Elena Vazey¹, David E Moorman¹, Stan B Floresco², Gary S Aston-Jones¹; ¹Neurosciences, MUSC, ²Psychology, University of British Columbia.

Many modern theories of behavioral control posit a pivotal role for the locus coeruleus (LC) in appropriately directing attention according to utility and task demands. The Adaptive Gain Theory (AGT), based upon unit recordings in behaving monkeys and neural network modeling, proposes that focused attention is facilitated by low tonic (baseline) LC activity with high phasic (bursting) responses associated with decision completion preceding a behavioral response. Conversely, when utility of an ongoing behavior wanes, phasic firing of LC decreases and tonic activity increases to facilitate disengagement from the previous goal and exploration of other contingencies. Adaptive behavior depends on an ability to flexibly switch between these modes as dictated by homeostatic and environmental demands. Impairments in these processes are thought to underlie numerous disorders such as autism, drug addiction, attention deficit hyperactivity disorder and cognitive inflexibility seen in schizophrenia and Parkinson’s disease. However, it remains to directly test these hypotheses in a task that manipulates reward contingencies and task demands. According to AGT, tonic stimulation following a rule change should decrease perseveration and trials to reach criterion on the new task. We used recently developed optogenetic techniques to specifically stimulate noradrenergic LC neurons (see Vazey et al, SFN 2010). We show that tonic stimulation of LC on trials following a rule change enhances cognitive flexibility in rats in an automated set-shifting task in an operant chamber. Specifically, LC tonic activation during early trials following an extradimensional shift (EDS) decreased perseverative responding to the previously rewarded dimension, relative to non-stimulated EDSs. Delivery of optogenetic stimulation to LC neurons was also verified by differential Fos expression in the LC nucleus following 15 min of unilateral tonic activation. Additionally, we report preliminary results in this same paradigm using atomoxetine, a selective noradrenergicuptake inhibitor. R37-DA06214; and R01-MH092868

119 Contribution of BDNF/TrkB Signaling in Rat Striatum in Response to Acute Amphetamine, Bok Soon Go, Jacqueline F McGinty; Neuroscience, MUSC.

Abstract not available.

120 Middle School Student’s Perception of Nursing As a Career, Robin E Matutina, Teresa J Kelechi, Martina Mueller; Nursing, MUSC.

Purpose: The American Association of Colleges of Nursing (AACN) (2008) predicts that by the year 2025, there will be a nursing shortage of 500,000 RNs. This study seeks to demonstrate that recruitment interventions geared toward educating middle school students about nursing and nursing specialties would significantly improve the perception of nursing as a future career choice, thereby increasing the number of
students who choose nursing as a career. If educating middle school students about nursing significantly increases nursing school enrollment and graduation rates, the nursing shortage may be positively impacted, thus positively impacting health care for society. Subject Population: The sample population was taken from Hanahan Middle School in Berkeley County, South Carolina. The target population was middle school students of African American, Asian American, Hispanic American, Pacific Islander, and white races. Participants were middle school students 9 to 15 years of age in Grades 7 and 8. Research Design: A pre-test/post-test design tested the effects of the intervention on a group of middle school students compared to a control group. The intervention consisted of an interactive computer program describing nursing careers developed by Microburst Learning. Instrument: The instrument used to collect data was the Indiana survey which is divided into two parts: (1) a career section, and (2) a nursing section. The survey is a 5-point Likert scale, ranging from “strongly agree” to “strongly disagree.” The instrument was used to measure two outcomes, perception and ideal career choice. Procedure: The pre-survey assessed students’ perceptions of nursing as an ideal career choice. The intervention group was given the Microburst Learning computer program describing nursing. After the intervention, the students completed a post survey. The survey responses were compared to determine the effectiveness of the interventions. *Sigma Theta Tau Gamma Omicron*

121 S1P Carrier-Dependent Effects on Endothelial Barrier: HDL-S1P Prolongs Endothelial Barrier Enhancement Compared to Albumin-S1P Via Effects on S1P1 Trafficking and Signaling. Brent A Wilkerson, G Daniel Grass, Shane B Wing, W Scott Argraves, Kelley M Argraves; Regenerative Medicine and Cell Biology.

Abstract not available.

122 Regulation of Invadopodia Formation and Activity By Emmprin (CD147). Daniel Grass, Momka Bratoeva, Bryan P Toole; Regenerative Medicine and Cell Biology, MUSC.

A defining feature of malignant tumor progression is cellular penetration through the basement membrane and interstitial matrices that separate various cellular compartments. Accumulating evidence supports the notion that invasive cells employ specialized structures termed invadopodia, which are actin-based, lipid raft-enriched membrane protrusions abundant in membrane-type-1 matrix metalloproteinase (MT1-MMP) and several signaling proteins, to breach these structural barriers. CD147 (emmprin; basigin), an immunoglobulin superfamily protein that is associated with tumor invasion and metastasis, induces the synthesis of various matrix metalloproteinases in multiple systems. In this study we show that up-regulation of CD147 is sufficient to induce MT1-MMP expression, invasiveness, and formation of invadopodia-like structures in non-transformed, non-invasive, breast epithelial cells. We also demonstrate that CD147 and MT1-MMP are in close proximity within these invadopodia-like structures and in membrane sub-fractions with the properties of lipid rafts. Moreover, manipulation of CD147 levels in invasive breast carcinoma cells causes corresponding changes in MT1-MMP expression, invasiveness, and invadopodia formation and activity. These findings indicate that CD147 regulates invadopodia formation and activity, most likely via assembly of MT1-MMP-containing complexes within lipid raft domains of the invadopodia. *DOD W81XWH-10-1-0083; NIH R01CA073839; NIH R01CA082867; and MUSC SCTR*

123 ERK2 Phosphorylation of Splicing Factor 45 (SPF45) Regulates SPF45 Alternative Splicing Site Utilization and Downstream Gene Expression. Adnan M Al-Ayoubi1, Hui Zheng2, Yuying Liu1, Tao Bai1, Scott T Eblen1; 1Pharmacology, MUSC, 2Molecular Biology, The Scripps Research Institute, 3Neurology, U of Chicago.

Abstract not available.

124 Development of Selective Small Molecule Inhibitors of Heterotrimeric G-Protein Signaling for the Treatment of Ovarian Cancer, Kevin J Bigham1, Starr E Hazard2, Jonel Lirjoni3, Ellen Maher4, Joe B Blumer5, Yuri K Peterson1; 1Pharmaceutical and Biomedical Studies, MUSC, 2Pharmacology, MUSC, 3Pharmacy, MUSC, 4Pharmacology, MUSC.

G-protein coupled receptors (GPCRs) are a widely expressed class of cell surface receptors that are frequently over-expressed in tumor cells. Their ligands are also commonly found in high concentrations at metastatic sites. Overactive signaling at the level of hormone, receptor, or G-protein can initiate and potentiate cellular transformation and other diseases. Heterotrimeric G-proteins, the immediate downstream effectors of GPCRs, present an attractive approach to regulate GPCR signaling cascades. For many cancers, such as ovarian, a disproportionate number of the overexpressed GPCRs couple to Gαi subunits. In ovarian cancer, for example, the Gαi-coupled receptors CXCR4, α2-AR, and LPA receptors are particularly important in the development of the disease phenotype. Each year there are ~22,000 new cases and ~14,000 deaths resulting from ovarian cancer indicating a need for substantial improvement in treatment options. Due to the rapid onset of ovarian cancers, screening protocols for patients is not as effective as in other cancers and necessitates the development of more directed and efficacious treatments. We hypothesize that direct inhibition of overactive G-protein signaling is cytotoxic to ovarian cancers. Here, we describe for the first time the development of selective small molecule inhibitors
which bind to and stabilize the GDP-bound form of the Gαi. This type of inhibition has the advantage of circumventing the need to directly address the upstream component of GPCR-related signaling in cases of mutations, polymorphisms, and expression-related defects often seen in cancer. Pharmacologic regulation of both receptor-dependent and independent signaling through specific heterotrimeric subunits will provide a unique window into a major signaling axis while providing data and compounds for further therapeutic development.

125 Mitochondrial Fusion is Linked to Bioenergetic Capacity and Cell Survival in a Cell-based Model of PDE6β-dependent Retinitis Pigmentosa, Anthony Leonard¹, Nathan Perron¹, Cecile Nasarre², Craig Beeson¹, Baerbel Rohrer²; ¹Pharmaceutical Sciences, MUSC; ²Ophthalmology, MUSC.

Retinitis Pigmentosa (RP) is a progressive retinal degenerative disease with limited therapies. Intracellular metabolism is reduced with the onset of cell death in the rd1 mouse model of RP (i.e., lack of function of PDE6β resulting in calcium cytotoxicity; Acosta et al, 2005; Lohr et al, 2006). The present study was undertaken to establish a molecular mechanism for a novel class of neuroprotective compounds in a cell-culture based model of PDE6beta-dependent RP. The mouse retina-derived 661w cone photoreceptor cell line was grown under standard conditions. Calcium cytotoxicity was induced by either treating the cells directly with Ca2+ ionophore A23187 or by opening the cGMP-gated cation channels using phosphodiesterase inhibitor IBMX. Cell viability was measured using tetrazolium dye reduction; mitochondrial respiratory capacity was analyzed via Seahorse extracellular flux assays; levels of relevant proteins were analyzed via Western blots of cell lysates; and mitochondrial morphology was visualized in live cells by nonyl acridine orange dye staining with DAPI then imaging and quantitation using automated fluorescent microscopy. Similarity of compounds was determined using hierarchical clustering based on pairwise similarity of Tanimoto coefficients (Tc). Twenty two compounds diminished uncoupled mitochondrial respiration. Based on chemical similarity (Tc=55), five clusters of three or more compounds were identified. Toxicant clusters were analyzed using 3D pharmacophore models. A 2D-QSAR model of a toxic adenosine like cluster provided a binary prediction of mitochondrial toxicity. These models were used to identify preliminary groups of chemical scaffolds related to mitochondrial toxicity. An informatic search of the ChemBridge 50,000 compound small molecule diversity library using predictive models revealed 24 potential toxicants (0.48% of the library) which were experimentally validated using RPTC respirometry and revealed one compound to be mitochondrial toxic (enrichment factor of 2083). In conclusion, respirometric assays with primary cultures of RPTC enabled the high-throughput evaluation of mitochondrial toxicity for a diverse set of 1760 compounds. Five discrete toxicophores associated with mitochondrial toxicity were elucidated. These toxicity data were utilized to create and validate predictive cheminformatic models and identify novel mitochondrial toxicophores. NIH GM084147 and the BLRD of the VA

126 High Throughput Identification of Mitochondrial Toxicophores, Richard E Trager, Lauren Wills, Christopher Lindsey, Gyda Beeson, Craig Beeson, Rick Schnellmann, Peterson Yur; Pharmaceutical and Biomedical Sciences, MUSC.

Many environmental, pharmaceutical, and industrial compounds negatively affect human health by exerting toxic effects on mitochondria. Currently there is a major need for reliable methods to predict mitochondrial toxicity. A novel respirometric assay was used to identify compounds and develop a database of mitochondrial toxicants. We hypothesize that distinct classes of chemotypes can be identified and used to predict previously unrecognized mitochondrial toxicity for known compounds and new chemical entities. A diverse group of 1760 compounds were tested at 5 μM in primary cultures of rabbit renal proximal tubule cells (RPTCs) using the Seahorse Biosciences Extracellular Flux analyzer. Cell counting of RPTCs was performed by staining with DAPI then imaging and quantitation using automated fluorescent microscopy. Similarity of compounds was determined using hierarchical clustering based on pairwise similarity of Tanimoto coefficients (Tc). Twenty two compounds diminished uncoupled mitochondrial respiration. Based on chemical similarity (Tc=55), five clusters of three or more compounds were identified. Toxicant clusters were analyzed using 3D pharmacophore models. A 2D-QSAR model of a toxic adenosine like cluster provided a binary prediction of mitochondrial toxicity. These models were used to identify preliminary groups of chemical scaffolds related to mitochondrial toxicity. An informatic search of the ChemBridge 50,000 compound small molecule diversity library using predictive models revealed 24 potential toxicants (0.48% of the library) which were experimentally validated using RPTC respirometry and revealed one compound to be mitochondrial toxic (enrichment factor of 2083). In conclusion, respirometric assays with primary cultures of RPTC enabled the high-throughput evaluation of mitochondrial toxicity for a diverse set of 1760 compounds. Five discrete toxicophores associated with mitochondrial toxicity were elucidated. These toxicity data were utilized to create and validate predictive cheminformatic models and identify novel mitochondrial toxicophores. NIH GM084147 and the BLRD of the VA

127 Microbial Electrosynthesis From CO₂ By Mixed Communities, Chris Marshall, Harold May; Microbiology & Immunology, MUSC.

Abstract not available.
**128** Pathogenic Natural IgM Antibodies Initiate The Inflammatory Response Important For Both Hepatic Ischemia/Reperfusion Injury And Liver Regeneration After Partial Hepatectomy, Keely L Morris¹, Fei Qiao¹, Songqing He¹, Carl Atkinson¹, Liudmila Kulik², Michael V Holers², Tomlinson Stephen¹; ¹Microbiology and Immunology, MUSC, ²Rheumatology, UCSM.

Complement activation and inflammation are linked to both hepatic ischemia/reperfusion injury (IRI) and to liver regeneration. The complement activation products C3a and/or C5a are known to be involved in the priming phase of liver regeneration. Here, we report on the complement activation event and initiation of a post-ischemic and post-resection inflammatory response. Previous studies using models of intestine, heart, brain and hindlimb IRI have shown that natural IgM Abs trigger complement activation upon reperfusion. These natural Abs bind to neoepitopes exposed on post-ischemic endothelium and activate the lectin and/or classical pathway to induce injury that is dependent upon alternative pathway amplification. Utilizing separate models of hepatic IRI and 70% partial hepatectomy (Phx), we characterized injury and regeneration in Ab-deficient (Rag1-/-) mice, with and without reconstitution with different IgM mAbs. Rag1-/- mice were protected from hepatic IRI, but had significantly increased injury and an impaired regenerative response after Phx. Injury in the IRI model (ALT, necrotic index) and the regenerative response in the Phx model (mitotic index, BrdU staining) were restored to wild type levels in Rag1-/- mice injected of B4 or C2 IgM mAbs, specific for annexin IV and a subset of phospholipids, respectively. Analysis of liver sections after either IRI or Phx showed IgM deposition co-localized with C3 deposition. There was no detectable IgM or C3 in sections from untreated Rag1-/- mice. These studies show that different pathophysiologically important epitopes recognized by IgM natural Abs are similarly expressed after hepatic IR and Phx, and that these Abs play a critical role in initiating the inflammatory response that is important for injury after IR and for regeneration after Phx. NIH F30 DK089696-02

**129** Characterization of the Evolution of Immune Phenotype During the Development and Progression of Squamous Cell Carcinoma of the Head and Neck, Anna-Maria A De Costa¹, Danielle Justis¹, Corinne Schuyler², Rita Young¹; ¹Otolaryngology, MUSC, ²Research Services, VA.

Squamous cell carcinoma of the head and neck (HNSCC) is an aggressive malignancy associated with manipulation of immune mechanisms, representing a significant obstacle to effective immunotherapeutic intervention. One way to avoid this obstacle would be to initiate therapy prior to establishment of immune escape, yet little is known about the development of immune evasion during the transition to malignancy. The goal of the present study is to further investigate the phenotype of the immune system during progression to HNSCC by determining the expression and function of immune cells in draining lymph nodes of mice treated with the carcinogen 4NQO until they develop premalignant oral lesions and eventually HNSCC. Lymph nodes of HNSCC-bearing mice were found to contain a much greater number of cells, including a greater number of both conventional (Tconv) and regulatory (Treg) T cells, compared to lymph nodes of control and premalignant lesion-bearing mice. Analysis of T cell functional markers showed that premalignant lesion-bearing mouse lymph nodes consist of a much greater percentage of Tconv cells expressing markers for activation, memory, and exhaustion compared to both control and HNSCC-bearing mice. Analysis of intracellular cytokine staining and cytokine release revealed that lymph nodes cells from both premalignant lesion-bearing and HNSCC-bearing mice include increased levels of Th1/Th17 cells, with no concurrent differences in levels of Th2 cells, compared to control mice. The data show that while there is the expected increase in immunosuppressive Tregs in lymph nodes when HNSCC is present, there is also an unexpected increase in immune populations usually associated with a beneficial anti-tumor response, including Tconv cells and Th1/Th17 cells. In addition, the results demonstrate that the premalignant stage of HNSCC development is associated with a robust immune response involving an increase in inflammatory Th1/Th17 cells. RO1 CA128837; and RO1 DE018268

**130** The One-Year Attributable Cost of Post-Stroke Aphasia, Annie N Simpson¹, Heather Bonilha¹, Patrick D Mauldin², Kit N Simpson¹, Charles Ellis¹; ¹Health Science and Research, MUSC, ²Clinical Pharmacy & Outcome Sciences, MUSC.

Background and Purpose: Aphasia is a disorder that frequently occurs after stroke. Little is known about the contribution of aphasia to the cost of care for patients who experience stroke. Methods: We retrospectively examined a cohort of South Carolina Medicare beneficiaries who experienced an ischemic stroke in 2004 to determine the attributable cost of aphasia. We defined attributable costs as the cost of caring for patients with aphasia after stroke that was over and above the cost of general stroke-relate care. Univariate analyses were used to compare demographic, comorbidity, and severity differences between individuals with post-stroke aphasia and those without aphasia. Differences in charges to Medicare due to stroke were examined using a Gamma distributed generalized linear multivariable model with a log link function. Results: We found that in 2004, 3,200 Medicare beneficiaries experienced an ischemic stroke in South Carolina. Among those, 398
had an ICD-9 diagnostic code indicating post-stroke aphasia. Patients with aphasia experienced longer length of stays (p<.0001), greater morbidity (p<.001), and greater mortality (p<.01). The 1-year attributable cost of aphasia to Medicare was $2,051 greater than the average cost of stroke for patients without aphasia (p<.001). In adjusted models that controlled for relevant covariates, the attributable 1-year cost of aphasia was estimated at $1,703 (p<.01). Conclusions: Aphasia contributes to greater costs to the healthcare system, above the cost of stroke alone. Clearly understanding the impact of aphasia on stroke-related care costs is critical to resource allocation and utilization in the current cost-containment climate. VA CDA 07-012-3

131 Lights On, Relapse Off: Examining Optogenetic Inhibition of Relapse Neurocircuitry. Michael T Stefanik1, Karl Deisseroth2, Peter W Kalivas3; 1Neuroscience, MUSC, 2Psychiatry and Bioengineering, Stanford University.

The aberrant need to obtain drug-related rewards can have disastrous consequences. Pharmacological and electrophysiological studies have implicated the nucleus accumbens (NA) as a key neural substrate in the brain’s reward system. Its function has also been shown to be altered after exposure to cocaine. While previous methods have been sufficient to give us a general picture of circuit function, they lack the specificity to adequately determine the significance of the NA and its connections to other crucial structures mediating drug seeking. One major output of the NA, the ventral pallidum (VP), has also been shown to be changed after exposure to cocaine, yet little is known about precisely how this interaction contributes to relapse. The current work examines the effects of optogenetic inhibition of the NA and the connections between the NA and VP during the reinstatement of cocaine seeking. Male Sprague-Dawley rats underwent surgeries for viral microinjections, implantation of bilateral guide cannulae and intra-jugular venous catheters. During surgery, microinjections of adeno-associated virus (AAV) containing the coding sequence for the chloride pump halorhodopsin (eNpHR3.0) or the proton pump archaerhodopsin (ArchT) with either a synapsin or CAG promoter, respectively, were made into the NA or VP. Both opsins hyperpolarize neurons when activated by laser light. Animals then went through 12 days each of cocaine self-administration followed by extinction training (2 hr/day). Following extinction, animals underwent cue and cocaine prime-induced reinstatement along with the presence/absence of optically induced inhibition. Optical inhibition of the NA with either construct inhibited the reinstatement of drug seeking behavior, in line with previous studies. Ongoing experiments are designed to test effects of optical inhibition on the reciprocal connections between the NA and VP. These data will help to elaborate on the complex interconnections between neural structures that give rise to drug-seeking behaviors. NIDA DA015369; and NIDA 5T32DA7288-20

132 Intra-prefrontal Cortical Infusion of Brain-derived Neurotrophic Factor Effects on Cocaine Seeking-induced Arc mRNA Induction. Notorious T Coleman, Wei-Lun Sun, Jacqueline F McGinty; Neuroscience, MUSC.

Activity-regulated cytoskeleton-associated protein (Arc) is an immediate-early gene that is localized to activated synaptic sites in a NMDA receptor-dependent manner. Its activity also depends upon activation of BDNF (brain-derived neurotrophic factor). BDNF acts by helping to support the survival of existing neurons and it induces dendritic growth, enables glutamate transmission, and alters transcription and synaptic plasticity. Previous studies in this lab showed that a single intra-cranial infusion of BDNF suppresses cocaine-seeking after one week of abstinence. Further, after two weeks of abstinence, rats with a cocaine history had greater increases of Arc mRNA in the dorsomedial PFC (dmPFC) than rats with a saline history when re-exposed to the operant chamber. The purpose of this study was to investigate whether a single infusion of BDNF into the dmPFC immediately after the end of cocaine self-administration would prevent alterations in Arc expression in the brains of cocaine-seeking animals after one week of abstinence. Male Sprague-Dawley rats were trained to criteria to self-administer cocaine 2 hr/day for 10 days. Immediately following the last self-administration session, they received an intra-dmPFC infusion of either BDNF or phosphate-buffered saline. Rats went through one week of abstinence and then were placed back into the operant chamber for a one-hour context relapse test. Rats were immediately euthanized without anesthesia and brains were processed using in situ hybridization to determine Arc mRNA levels. We found that a single intra-dmPFC infusion of BDNF only slightly decreased cocaine-seeking after one week of abstinence. However, histology revealed that several of the infusion cannulae placements were actually restricted to the anterior cingulate instead of the prelimbic cortex. Therefore, BDNF infusion did not affect cocaine-induced relapse or Arc mRNA levels in the dmPFC. In future studies, the coordinates of the intra-cranial cannulae will be adjusted and the effects of intra-PFC BDNF on the expression of Arc and other immediate early genes, such as Zif-268, in the dmPFC will be investigated. T32 DA07288; P50 DA15369; and IMSD Grant R25GM072643
133 Hematopoietic Stem Cell-Derived Carcinoma–Associated Fibroblasts Promote Tumor Progression, Lindsay T McDonald, Dayvia A Laws, Amanda C LaRue; Pathology, MUSC.

Cells and paracrine factors of the tumor microenvironment play a central role in tumor angiogenesis, invasion, migration and proliferation, making the tumor microenvironment an exciting therapeutic target. Among the most prominent cell types in the tumor stroma are fibroblasts, termed carcinoma-associated fibroblasts (CAFs). We have identified a novel population of CAFs and CAF precursors (circulating fibroblast precursors, CFPs) that are of hematopoietic stem cell (HSC) origin. Our lab has previously shown that these cells preferentially migrate and differentiate in response to tumor and their inhibition results in decreased tumor size. While these studies have identified a unique HSC-derived CAF population, the mechanisms by which these cells promote tumorigenesis are unknown. Based on these findings, we hypothesize that HSC-derived CFPs/CAFs directly affect tumor progression. To address this hypothesis, we examined the ability of HSC-derived fibroblast populations to affect tumor cell proliferation, migration and invasion. Our preliminary data showed that CFPs increased proliferation, migration and invasion of Lewis Lung Carcinoma (LLC) cells in vitro. Our in vivo studies show that co-injection of CAFs with LLCs promoted tumor growth. To begin to elucidate the mechanism by which CFPs/CAFs effect tumor cells, we conducted ELISA, flow cytometric and immunohistochemical analysis. Our findings suggest a role for TGFβ in CFP/CAF promotion of tumor progression. Given that these HSC-derived CAFs comprise a significant (8-10%) component of the solid tumor this population represents a valuable therapeutic target. VA MERIT Award; and NIH/NCI

134 Anti-apoptotic Genes Family As a Novel Diagnostic Markers of Bladder Cancer, Elizabeth B Fowler, Philip M SoBolesky, Yuan Shao, Julie A Woolworth, Omar Moussa; Pathology, MUSC.

Abstract not available.

136 Life After Lung Cancer Resection: Exploring Rehabilitative Options to Improve Quality of Life, Melanie S Jefferson1, David O Sword1, Erica Rouvailles2, Marvela E Ford3; 1CHP, MUSC, 2MUSC, 3HCC, MUSC.

Background: Lung cancer (LC) is the leading cause of cancer death in the United States. Survival outcomes following resection are less than optimal. Post-operative rehabilitation programs are safe and feasible for LC patients. More research investigating the multidisciplinary management of LC patients is needed. The goal of this formative study was to examine the perceptions and experiences of physical therapists (PT) with rehabilitative care for resected LC patients. Methods: The Interclassification of Functioning, Disability, and Health (ICF) Model provided the theoretical framework. Using the ICF Model, two audiotaped focus groups (FG) were conducted. The sessions were transcribed and analyzed using content analysis and theme identification. Results: A total of 20 PTs (10 per FG) participated. The results were organized by each domain of the ICF model; health condition, activities, participation, and personal and environmental factors. Health Condition Common knowledge of risk factors and clinical implications for developing early stage LC were conveyed in both focus groups. Activities The inpatient PTs communicated the need for multidisciplinary management of newly resected LC patients such as early progressive mobilization and activities of daily living (ADL) deficits. Participation All of the PTs felt that a post-operative aerobic and strengthening rehabilitation program would be beneficial for newly resected LC patients. Personal and Environmental Factors Personal motivational factors such physician referrals, and being able to return to home, work and leisure time activities were among the most imperative for encouraging patients to enter into a rehabilitation program. Conclusions: It is imperative to gain the perspectives of rehabilitation scientists to effectively design and implement rehabilitation protocols. This could ultimately contribute to the establishment of clinical exercise rehabilitation guidelines that not only impact the field of rehabilitation, but are pivotal in furthering the evidence to support exercise-based rehabilitation into the LC continuum for improved survival outcomes.

137 AKT3 Promotes Nuclear Retention Of PGC-1 And ER Alpha By Regulation Of The Major Nuclear Export Protein, CRM-1, Daniel G Corum, Robin C Muise-Helmericks; Regenerative Medicine and Cell Biology, MUSC.

Previous work from our laboratory has shown a requirement for Akt3 in modulating mitochondrial biogenesis in primary endothelial cells. This is due to the ability of Akt3 to indirectly affect subcellular localization of PGC-1 alpha (PGC-1α), a master regulator of mitochondrial biogenesis. Blockade of Akt3 expression results in a cytoplasmic accumulation of PGC-1α, thus affecting its nuclear activity. Our studies show that knockdown of Akt3 expression by shRNA causes up-regulation of CRM-1 protein expression. CRM-1, the major nuclear export protein, appears to be an Akt3 substrate, as mutation of a putative Akt phosphorylation site results in stabilization of CRM-1 protein. Inhibition of CRM-1 using Leptomycin B blocks nuclear export causing nuclear accumulation of PGC-1α. Additionally, the PGC-1α associated protein, estrogen receptor alphas (ERα) subcellular localization is similarly affected by Akt3 inhibition. In silico analysis shows two putative nuclear
export sequences (NES1 and NES2) within PGC-1α and two within ERα. Site directed mutagenesis of PGC-1α NES1 or NES 2 results in near complete nuclear accumulation of PGC-1α under conditions of Akt3 blockade, indicating both NES sites are required for CRM-1 transport. The Akt3 dependent reduction in PGC-1/ERα nuclear accumulation results in decreased expression of both PGC-1α and ERα dependent genes. Since our data show that Akt3 blockade results in both reduced mitochondrial biogenesis and content, we tested the effect of Akt3 blockade on autophagy. Akt3 blockade results in increased autophagy and is independent of the effect of Akt1 knockdown on autophagy, as Leptomycin B treatment decreases autophagosome formation. Taken together these findings suggest that Akt3 controls the transcriptional activity of ERα and PGC-1α by modulation of their nuclear/cytoplasmic localization, thus regulating the balance of mitochondrial growth and autophagy. Future studies will confirm the role of the putative NES sequences in ERα subcellular localization and delineate the Akt3-dependent molecular pathways regulating autophagy. NIH/LB R01HL084565

138 Effects of Perfluorooctane Sulfonate (PFOS) and Perfluorooctanoic Acid (PFOA) on IL-2 Production in the Human Jurkat T-cell Line. Kristin S Midgett1, Margie Peden-Adams2, Gary S Gilkeson1, Diane L Kamen1; 1Microbiology & Immunology, MUSC; 2Harry Reid Center for Environmental Studies, University of Nevada-Las Vegas.

The potential human health effects of perfluorinated compounds such as perfluorooctane sulfonate (PFOS) and perfluorooctanoic acid (PFOA) are becoming an increasing concern in the United States and worldwide. Both PFOS and PFOA have been shown to alter various immune functions suggesting that they are immunotoxic. PFOS specifically has been shown in rodent studies to decrease T-cell IL-2 production, which is characteristic of autoimmune diseases such as systemic lupus erythematosus (SLE). Along with PFOS, PFOA has been detected in human blood, but had not previously been investigated for modulation of IL-2 production. The current study assessed the effects of PFOS and PFOA on IL-2 production in the human Jurkat T-cell line. Cells, stimulated with PHA/PMA or anti CD-3/anti CD-28, were dosed with 0, 0.05, 0.1, 0.5, 1, 5, 10, 50, 75, or 100 μg/ml of PFOS or 0, 0.005, 0.01, 0.05, 0.1, 0.5, 1, 5, or 10 μg/ml of PFOA. Jurkat cells stimulated with PHA/PMA exhibited decreased IL-2 production beginning at 50 μg PFOS/ml. However, cells stimulated with anti-CD3/anti-CD28 exhibited no alteration in IL-2 production. PFOA exposure in cells stimulated with PHA/PMA resulted in significant decreases in IL-2 production at 10 μg PFOA/ml, but cells stimulated with anti-CD3/anti-CD28 exhibited no alteration in IL-2 production. Addition of the PPAR-alpha antagonist GW6471 to PFOS dosed cells stimulated with PHA/PMA resulted in decreases in IL-2 production starting at 50 μg PFOS/ml. However, the addition of GW6471 to PFOA exposed cells stimulated with PHA/PMA ameliorated the PFOA-induced decrease in IL-2 production. These data suggest that PFOS affects T-cell IL-2 production via PPAR-alpha-independent mechanisms and that PFOA-induced suppression of IL-2 production may be PPAR-alpha-dependent. Further studies utilizing cells from SLE patients who have varying blood levels of PFOS and PFOA are underway to further investigate the role of PFOS and PFOA as environmental triggers of SLE. MUSC SCTR, NIH/NCRR UL1 RR029881, NIH/NIHES 1 R21 ES017934

139 Fibulin-1 Deficiency Leads to Dysregulation of the Forkhead-Tbx1-Fgf8-FgfR-Map Kinase Pathway and DiGeorge Syndrome-like Phenotype. Victor M Fresno, Marion A Cooley, Waleed O Twal, Kyu-Ho Lee, Jeremy L Barth, W Scott Argraves; Regenerative Medicine and Cell Biology, MUSC.

DiGeorge syndrome (DGS) is a complex and variable disorder that includes defects of the cardiovascular system, pharyngeal glands and head. Most of the tissues affected in DGS are derived from the pharyngeal arches, which are populated by migrating neural crest cells (NCCs). Motility, guidance and survival of NCCs contributing to the pharyngeal arches are under the control of the Forkhead-Tbx1-Fgf8-FgfR-Map kinase pathway. Fibulin-1 (Fbln1) is an extracellular matrix protein required for motility, guidance and survival of NCCs contributing to the pharyngeal arches. Deficiency of Fbln1 in mice leads to defects of the heart, pharyngeal glands and head that resemble abnormalities of human DGS. Using DNA microarray and qPCR analysis we have evaluated the impact of Fbln1 deficiency on the expression of genes in this pathway. In pharyngeal arch tissues from Fbln1-deficient embryos, levels of transcripts encoding proximal components of the Forkhead-Tbx1-Fgf8-FgfR-Map kinase pathway, Fgf8, Foxc1 and Foxc2 and Tbx1, were reduced. In addition, levels of transcripts encoding downstream components of the pathway, Fgfr and FgfR, were also decreased. Similarly, in embryonic fibroblasts from Fbln1-deficient mice, levels of Tbx1 and Fgfr transcripts were decreased (p=0.03 and p=0.002, respectively) when the cells were cultured on fibronectin substrata. In P19 cells differentiated along the cardiomyocyte lineage, we observed that siRNA knockdown of Fbln1 resulted in reduced expression of Fgfr. Conversely, expression of Fbln1 in cells that normally do not express Fbln1 led to an increase in the expression of Fgfr. Together, the findings indicate that Fbln1 is a new positive effector of the Forkhead-Tbx1-Fgf8-FgfR-Map kinase pathway. NIH HL095067; MUSC SCTR; and CTSA TL1RR029881
140 Seamless Phase II/III Adaptive Dose Finding Design for Longitudinal Data in Safety/Efficacy Clinical Trials, Caitlyn N Ellerbe, Jordan Elm, Viswanathan Ramakrishnan, Valerie Durkalski; Biostatistics and Epidemiology, MUSC.

Abstract not available.

141 The Role of Estrogen-Related Receptors in Cardiomyocyte Metabolic Adaptation to Oxidative Stress, Kathryn Cribben1, Paul McDermott2, 1MCBP, MUSC, 2Medicine, MUSC.

In the ischemic heart, metabolic adaptation of the cardiomyocyte to hypoxia is critical to sustain myocardial structure and function. These metabolic adaptations are dependent on Estrogen-Related Receptors (ERRs), which are members of the nuclear hormone receptor superfamily of transcription factors. ERRs regulate expression of genes involved in fatty acid metabolism, oxidative phosphorylation, and mitochondrial biogenesis. The purpose of these studies is to determine the regulatory mechanisms governing expression of the alpha, beta and gamma isoforms of ERR in cardiomyocytes undergoing oxidative stress. Adult feline cardiomyocytes in primary culture were electrically stimulated to contract at 1 Hz under normoxia (21% oxygen), hypoxia (0.5% oxygen), or hypoxia followed by reoxygenation. Expression of ERR isoforms and target genes was measured by QRT-PCR. Distribution of mRNA-ribosomal complexes was measured by fractionation of polysomes on a linear sucrose gradient. SABiosciences QRT-PCR arrays provided a high throughput tool for prospective target gene identification. Expression of ERR-alpha mRNA was significantly increased by 3.5-fold over 24 hours of hypoxia compared to normoxic controls. In contrast, ERR-beta mRNA expression increased 11-fold after 12 hours of hypoxia, and this increase was maintained over 24 hours. Subsequent reoxygenation for 24 hours caused a partial (25%) reduction in ERR-alpha expression, but ERR-beta expression returned to baseline levels. Hypoxia also increased mRNA expression of PGC-1alpha, an ERR co-activator, by 16-fold over 24 hours, while reoxygenation reduced expression back to baseline levels by 24 hours. 1) Hypoxia in cardiomyocytes induced rapid and substantial increases in ERR-beta and PGC-1alpha expression compared to ERR-alpha expression; 2) reoxygenation returned expression of ERR-beta and PGC-1alpha to baseline levels; 3) hypoxia caused a smaller, yet sustained increase in ERR-alpha expression. NIH and VA


Scaffold-based bone tissue engineering is an emerging concept for regeneration of long bone within skeletal defects. A common limitation of many scaffold-based strategies is the lack of sufficient guidance cues that encourage aligned osteon formation characteristic of cortical bone microstructure. In cortical bone, osteocytes are arranged within ostecns, forming a highly aligned structure oriented parallel to the load-bearing axis. To promote and organize initial cell attachment within a defect, scaffold properties such as geometry should be well-controlled. Thus, the objective of this work was to produce scaffolds that would support attachment and alignment of pre-osteoblast cells. Poly(lactic-co-glycolic acid) (PLGA 80:20) scaffolds having an overall cross-section of 500 um were fabricated using a custom extrusion apparatus. Pellets were melt spun at a feed rate of 5 mL/min, and drawn at a rate of 0.5 mm/s. Scaffolds with round, 4-, 6- and 8-branched with microchannel grooves geometry were cultured with human embryonic palatal mesenchymal stem cells (HEPM, ATCC CRL 1486) for 24 hours. Scaffolds were then fixed in 4% paraformaldehyde and stained with DAPI for fluorescence imaging. The longitudinal orientation of HEPM with respect to the long axis of the scaffolds was determined for each geometry. Cells preferentially aligned on the grooved microchannel scaffolds when compared to the rounded scaffolds (two-way ANOVA, P<.005). For cells cultured on microchannel scaffolds, the mean angle of deviation from the scaffold long axis was less than 10°. In comparison, cells cultured on rounded scaffolds demonstrated a near random orientation (mean deviation angle 50°) with reference to the longitudinal axis of the scaffolds. Grooved scaffolds when compared with rounded scaffolds promote both the initial attachment, and alignment of pre-osteoblast cells. This study suggests that aligned PLGA scaffolds, which act as osteon templates, may enhance the initial stages of bone healing through the induction of directional cell growth.

143 Nhanes Survey Analysis of Sexual Minority Women, April D Taylor, Kit N Simpson, Michael Saladin; Health Sciences and Research, MUSC.

Introduction: Traditionally, health disparities in minority populations have been described for groups defined based on their race, ethnicity, age, and gender. Much less is known about how sexual orientation influences access to and use of care, and risk factors for chronic conditions such as obesity. The assessment of sexual minority populations is often difficult, as inclusion in national population databases is limited. The purpose of this paper is to compare a small de-identified sample of self-identified sexual minority (lesbian) women from the publicly available 2007-2008 continuous National Health and Nutrition Examination Survey (NHANES) to a demographically matched sample of heterosexual women in an effort to elucidate
factors that are associated with increased body mass index. Methods: Sexual orientation was determined using the sexual behavior questionnaire. Propensity score matching was used to obtain a demographically matched sample of heterosexual women, matched by family income, education, and race. The final dataset (n=119) was constructed by performing an additional match by hand based on the 5 closest matches in age. Results: The mean body mass index (BMI) for the lesbian women 30.9 (SD 8.2) was slightly higher than the heterosexual women 29.1 (SD 6.9), but was not significantly different. It is known that the annual medical care costs of obesity are generally higher than those for someone of normal weight. However, healthcare utilization in the past 12 months among lesbians was significantly less (p <.01) than heterosexual women, despite there being no significant difference in health insurance coverage (p =.13). Lesbian women were also more likely to report having an excellent/good diet (approaching significance: p =.07), regardless of elevated BMI. Discussion: Implications for research include the continued need to address potential disparities in sexual minority health by inclusion of the population among core variables of national survey instruments. MUSC SCTR; and NIH/NCRR UL1 RR029881

144 Positive Propylene Glycol in a Patient with Ethylene Glycol Toxicity, Roger W Stone, Yusheng Zhu; Pathology, MUSC.

Background: Both ethylene glycol and propylene glycol can be used as antifreeze. Propylene glycol is also used as a solvent in many medications. Ingestion of both can cause increased serum osmolality and anion gap acidosis, but ethylene glycol is much more toxic. However, large doses of propylene glycol can be toxic. We report a case in which the patient initially presented with ethylene glycol poisoning, but later showed a high level of propylene glycol. Methods: The patient was a 61 year old female who was found unconscious. Upon arrival to our hospital, the patient was in respiratory failure with evidence of an increased anion gap metabolic acidosis, increased serum osmolal gap, and negative volatiles. Ethylene glycol and propylene glycol in the patient’s serum were analyzed with a laboratory developed capillary column gas chromatography assay. The patient was treated with hemodialysis, continuous veno-venous hemofiltration and fomepizole. The patient also received phenytoin and lorazepam for a witnessed seizure. Ethylene glycol and propylene glycol were subsequently measured 13 hours and 38 hours later. Results: On admission, ethylene glycol was elevated at 22 mg/dL and propylene glycol was undetectable. Thirteen hours later, the ethylene glycol level was undetectable but propylene glycol was detected at 27 mg/dL. The medication list revealed that the patient was given phenytoin and a high dose lorazepam drip which contain propylene glycol. The lorazepam was discontinued and the following day the propylene glycol level decreased to 13 mg/dL and ethylene glycol remained undetectable. Conclusion: The positive propylene glycol in this patient is caused by medications. This case study supports the notion that propylene glycol accumulation is a common phenomenon that is becoming increasingly recognized in the ICU. Furthermore, it highlights the importance of identifying and reporting this potentially harmful compound whenever glycols analysis is performed.

145 XRCC1 399 Arg>Gln (28152G>A) Variation Correlates with Deterioration in Quality of Life Induced By Radiotherapy in Prostate Cancer Patients, Alina G Sofronescu, David T Marshall, Yusheng Zhu; Pathology and Laboratory Medicine, MUSC.

Background: Radiotherapy is a common treatment for prostate cancer patients (PCaP). Some patients develop adverse radiotherapeutic effects (AREs): lower urinary tract irritation, erectile dysfunction, rectal bleeding. Factors associated with AREs were not well defined, although some genetic variables were implicated. X-ray repair cross complementing protein 1 (XRCC1) is involved in DNA repair. The objective of this study is to identify a potential association between XRCC1 399 Arg>Gln (28152G>A) and deterioration in Quality of Life (QoL) due to urinary symptoms caused by radiotherapy in patients with PCa. Methods: A cohort of 67 PCa patients treated with radiotherapy was observed for one year post-treatment. The QoL due to urinary symptoms was assessed by grading urinary conditions using the scores recommended by the American Urological Association. It was considered a deterioration in QoL if a patient’s baseline score before treatment was less than or equal to 3, but greater than or equal to 4 after treatment. Peripheral blood samples were used to isolate genomic DNA. XRCC1 genotypes were determined using TaqMan SNP assay. The association between deterioration in QoL and XRCC1 genotype was analyzed using two-sided Fisher’s exact test. The differences were considered statistically significant if p < 0.05. Results: In these 67 patients, 41 were wild-type (GG) and 26 were variant (GA + AA) of XRCC1. In the wild-type group, only one patient experienced deterioration in QoL due to urinary symptom induced by radiotherapy, while in the variant group, 8 patients had deterioration in QoL. The incidences of deterioration in QoL were 0.024 and 0.307 in the wild-type and variant groups, respectively, and the difference between these two groups were statistically significant (p = 0.0016). Conclusion: Our data suggest that the variant genotype of XRCC1 399 Arg>Gln (28152G>A) is associated with a higher incidence of deterioration in QoL due to urinary symptoms in PCaP post-radiotherapy treatment. NCRR M01 RR001070; and #21648 from the Departments of
146 Diabetes Empowerment, Medication Adherence and Self-care Behaviors in Adults with Type 2 Diabetes, Melba A Hernandez-Tejada, Jennifer A Campbell, Kimbery S Davis, Brittany L Smalls, Rebekah J Walker, Leonard E Egede; Medicine, MUSC.

Diabetes empowerment refers to the ability to make decisions about controlling one’s disease by possessing both the knowledge required to make informed decisions, as well as resources to necessary implement these decisions. Some data support the utility of patient empowerment in treatment of chronic diseases. The objective of this study was to examine the relationship between diabetes empowerment and medication adherence and self-care behaviors. Patients were 378 adults with type-2 diabetes presenting for care to Southeastern university internal medicine clinic and nearby low income public clinic. Measures included the 8-item Diabetes Empowerment Scale, the 24-item Diabetes Knowledge Scale, and the Summary of Diabetes Self-care Behaviors (e.g., foot care, blood sugar testing, diet, exercise). Statistical analyses included Pearson’s correlation and multiple linear regression to assess the association and independent effect of diabetes empowerment on the other variables. 83% of participants were Non Hispanic blacks, 69% were women, 22% were 65 year or older, 68% were not married, 26% had less than high school education, 60% were unemployed, 39% were uninsured, 47% had yearly income <$10,000, and 24% had worsening health status. Empowerment was significantly correlated with adherence to medication (r = -0.17, p<0.003); diabetes knowledge (r=0.16, p<0.006); diet (r=0.24, p<0.000); exercise (r=0.25, p<0.000); blood sugar testing behavior (r=0.11, p<0.04); foot care (r=0.18, p<0.015). In the regression model, Diabetes Empowerment was significantly associated with medication adherence (beta -0.03, 95% -0.05, -0.014), diabetes knowledge (beta 0.90, 95% 0.019, 0.15), diet (beta 0.92, 95% 0.53, 0.13), exercise (beta 0.10, 95% 0.59, 0.15), blood sugar test (beta 0.67, 95% 0.13, 0.12), foot care (beta 0.82, 95% 0.03, 0.13). Thus, Diabetes Empowerment was related to positive self-care behaviors, better diabetes knowledge and medication adherence. Emphasis on empowerment and self-efficacy is relevant to improve outcomes in the management of diabetes. NIH/NIDDK T35DK007431

147 Enhancing Behavioral Interventions for PTSD in Operation Enduring Freedom/Operation Iraqi Freedom Veterans: Influence of Personal and Environmental Factors, Matthew Price1, Daniel F Gros2, Martha Strachan3, Jenny S West1, Kenneth J Ruggiero1, Ron Acierro2; 1Psychiatry, MUSC, 2Mental Health, VAMC. The lack of social support has consistently been identified as a relevant factor in the development, maintenance, and treatment of PTSD populations (Brewin, Andrews, & Valentine, 2000; Kilpatrick et al, 2007; Whealin, Ruzek, & Southwick, 2008; Wilcox, 2010; Zoellner, Foa, & Brigid, 1999). Prospective studies with combat veterans have supported the erosion model of social support in the development of PTSD (King et al, 2006). This model posits increased PTSD symptoms leads to diminished social support over time. Additional epidemiological work that has investigated mental health and functional impairment in recently returning (OEF/OIF) has suggested that interpersonal problems coincide with the onset of PTSD. Despite research that suggests OIF/OEF Veterans experience high rates of PTSD and associated interpersonal problems, no studies have examined social support in relation to treatment response in this group. The current study examined the role of four functional aspects of social support - emotional/informational support, positive social interactions, affectionate support, and tangible support – on pretreatment PTSD symptom severity and treatment response in a sample (n = 120) of OEF/OIF Veterans receiving exposure-based psychotherapy. Participants were recruited from the Ralph H Johnson VAMC. Multilevel modeling suggested that emotional/informational support was significantly related to the rate of change in PTSD symptoms such that increased emotional support was associated with better treatment response, β14 = 0.11, p < 0.05. However, affectionate support, tangible support, and positive social interaction were not associated with the rate of change in PTSD symptoms. The social support subscales explained 11% of the variance in treatment response. Together, these findings suggest that specific types of social support may have an important influence on the course of exposure treatment. Increased emotional support is theorized to enhance outcomes by increasing adherence to the treatment protocol and perceptions of safety which improved overall engagement and learning from exposures.

148 Association Of Serum Concentrations Of 25-Hydroxyvitamin D And Gingival Inflammation During Pregnancy, Vivek Singh1, Carol L Wagner2, Bruce W Hollis3, Myla Ebeling4, Thomas C Hulsey5, Susan G Reed3; 1MSCR, MUSC, 2Pediatrics-Neonatology, MUSC, 3CDM, MUSC.

A previous study of NHANES III data of 13 to >90 year olds suggested that low serum concentrations of vitamin D are associated with gingival inflammation and that marginal gingivitis may be a useful model to study the anti-inflammatory effects of vitamin D in humans. The purpose of our study was to see if this inverse association of serum concentration of vitamin D and gingival inflammation was reflected in a population of women during pregnancy. The women
were aged 16-45 years and the data collected at 16 weeks of pregnancy and within 2 weeks post-partum. The major outcomes of circulating serum vitamin D was measured as circulating serum 25(OH) D concentration and marginal gingivitis was measured as bleeding on probing (bleeding of the soft tissue around the tooth in response to gentle periodontal probing). The mesio-buccal sites of two randomly selected quadrants and excluding third molars were used as in the study of the NHANES III data. Of the 263 women with vitamin D and periodontal data at 16 weeks of pregnancy, 12 smokers were excluded leaving 251 women in the analyses. To distinguish gingival inflammation from periodontal disease, mesio-buccal sites with attachment loss > 2mm were excluded. The mean age of the women was 27.1 SD 5.4 years. By quintile of 25(OH)D, the women in the highest quintile had 29% lower proportion of periodontal sites with bleeding on probing (BOP). There was an inverse linear relationship between 25(OH)D and bleeding on probing after adjusting for age, race/ethnicity, sex and BMI. When classified by vitamin D deficiency (<20ng/ml), insufficiency (>20≤29ng/ml) and sufficiency (>30ng/ml), there was an approximate 35% decrease in proportion of periodontal sites with BOP as we move from deficient to sufficient group. Further analyses are ongoing. Higher serum 25(OH)D concentration may reduce the gingival inflammation in pregnant women. SCTR, NIH/NCRR UL1 RR029882, NIH/NCCR P20 RR-017696, 5R01HD043921, RR01070, and TE DE017551

149 Phase I Trial of the HDAC Inhibitor LBH589 in Combination with Sorafenib in Patients with Renal Cell Carcinoma, Non Small Cell Lung Cancer and Soft Tissue Sarcomas, Charles M Butler, Lydia T Laboccetta, Alan Brisendine, Thomas E Keane, Harry A Drabkin; Hematology and Oncology, MUSC.

Abstract not available.

150 Prognostic Factors for Nodal Spread in Thin (≤1 Mm) Melanoma: A Meta Analysis, Allison N Lundy1, Kent E Armeson2, Betsy Hill2, Ashley C Parks3, Nestor F Esnola4, David J Cole5, Ramsay Camp1, 1Surgery, MUSC, 2Biostatistics and Epidemiology, MUSC, 3Medicine, MUSC.

BACKGROUND: Although national guidelines recommend sentinel lymph node biopsy (SLNB) for T1b and greater melanomas, the procedure is controversial for thin (≤1 mm) tumors given the low rate of nodal spread. Several retrospective studies have identified possible pathologic predictors of SLN metastasis. We conducted a meta-analysis to determine the likelihood of association of these histologic variables with nodal spread in thin melanoma, which may help identify optimal candidates for SLNB. METHODS: We systematically searched PubMed and MEDLINE for studies (1992-2011) in which SLN biopsy was performed in patients with thin melanoma. Pathologic features of the primary tumor (Breslow thickness, Clark level, ulceration, regression, and mitotic rate) in both node-negative and node-positive patients were examined. Studies were combined using either fixed or random effect Mantel-Haenszel meta-analytic methods. Publication bias was assessed using rank correlation tests and funnel plots. Odds ratios (OR) and summary estimates were calculated for each variable. RESULTS: Twenty studies (3202 patients) met the inclusion criteria; 171 patients (5.4%) had a positive sentinel node biopsy. The factors significantly associated with nodal spread were ulceration (OR 3.3; 95% CI 1.8-6.0), depth >0.75 mm (OR 2.4; 95% CI 1.5-3.8), and Clark level 4/5 (OR 1.8; 95% CI 1.3-2.6). The rate of SLN positivity in these groups was higher: 9.4% (ulceration), 7.7% (depth 0.75-1 mm), and 7.5% (Clark 4/5). High mitotic rate was borderline significant (OR 3.1; 95% CI 1.0-9.7), with substantial heterogeneity across studies. Regression did not significantly correlate with sentinel node status. CONCLUSIONS: Increased depth (>0.75 mm), Clark level 4 or 5, and ulceration in thin melanomas are associated with an increased likelihood of SLN positivity. Study heterogeneity precluded definitive analysis of the effect of mitotic rate. Thin melanoma patients with high risk pathologic features should be strongly considered for sentinel lymph node biopsy.

151 Association Between Spirituality and Depression in Adults with Type 2 Diabetes, Joni L Strom, Cheryl P Lynch, Melba A Hernandez-Tejada, Leonard E Egede; Medicine, MUSC.

Comorbid depression complicates glycemic control in patients with diabetes. Potentially protective factors have received little attention; therefore, we examine the association between spirituality and depression among patients with type 2 diabetes. This prospective study included 201 adult participants with diabetes from an indigent clinic of an academic medical center. Participants completed validated surveys on spirituality and depression. The Daily Spiritual Experience Scale (DSES) measured a person’s perception of the transcendent (God, the divine) in daily life. The Center for Epidemiologic Studies-Depression scale assessed depression. Linear regression analyses examined the association of spirituality as the predictor with depression as the outcome, adjusted for confounding variables. Greater spirituality was reported among females, non-Hispanic blacks (NHB), those with lower educational levels, and those with lower income. The unadjusted regression model showed greater spirituality was associated with less depression. This association was mildly diminished but still significant in the final model. Depression scores also increased (greater depression risk) with females and those who were unemployed, but decreased with older age and NHB race/ethnicity. Treatment of depression symptoms may be facilitated by incorporating the
152 Role of OPA1 in Early Zebrafish Development. Jennifer J Rahn, Krista D Stackley, Sherine SL Chan; Pharmacy, MUSC.

Autosomal dominant optic atrophy (ad-OA) is a complex disease characterized by progressive vision loss chiefly due to selective degeneration of the retinal ganglion cells (RGCs) followed by ascending optic atrophy. Mutations within the nuclear encoded gene Opa1 are responsible for ~70% of ad-OA cases. OPA1 is a dynamin-related GTPase located in the inner mitochondrial membrane that plays several critical roles in the cell including regulating mitochondrial fusion, cristae remodeling, and cytochrome c release. It is not yet fully understood how defects in OPA1, which is ubiquitously expressed, can impact a specific cell type, and how mitochondrial defects in the RGCs lead to the complex phenotype observed in ad-OA patients. We are interested in investigating the role of OPA1 using the zebrafish (Danio rerio) model system. Zebrafish have been used for several decades as powerful developmental models due largely to the ease with which development can be observed in the embryo. We have successfully used morpholino antisense technology to transiently knockdown the OPA1 homologue in zebrafish embryos. Depletion of OPA1 was verified by western blot and Q-RTPCR from 48hpf to 4dpf. We observed a specific phenotype in the OPA1-deficient embryos that included increased volume in the hindbrain ventricle, smaller head and eye size, defects in circulation, and a reduced touch response and swim speed. Ultimately these fish develop edema in the pericardia, yolk, and eyes that result in death by 7dpf. In this model, depleted OPA1 did not affect mitochondrial DNA copy number but did result in a slightly lower basal oxygen consumption rate. We are continuing work to fully characterize the physical and mitochondrial defects that result from depletion of OPA1. Our studies will aid in our understanding of OPA1 and mitochondrial function in development and may help elucidate the connections between OPA1 dysfunction and the development of optic atrophy. *NIH/NIEHS R00ES01555*

153 EGCG, a Green Tea Polyphenol, Can Reverse Methylation Related Silencing of Genes in Human Colon Carcinomas. Jay Morris1, Vondina R Moseley2, Katie Coleman3, Michael Wargovich1; 1Pharmacology, MUSC, 2MSTP, MUSC, 3Western States Chiropractic College, Portland, OR.

Silencing of regulatory genes through hypermethylation of CpG islands is an important mechanism in tumorigenesis. In colon cancer, RXRα, an important dimerization partner with other nuclear transcription factors, is silenced through this mechanism. We found that colon tumors in mice had lower levels of RXRα protein and expression levels were restored by treatment with green tea. The degree of promoter methylation of the RXRα gene was reduced in these animals. To translate these findings to human colon cancer we treated CpG Island Methylator Phenotype sensitive and insensitive (CIMP+ & CIMP-) human colon cancer cell lines with epigallocatechin gallate (EGCG - major polyphenolic compound in green tea). We hypothesized that CIMP + cell lines which epigenetically silence key regulatory genes would demonstrate silencing of RXRα and that EGCG would restore its expression. To test this we used the following human colon cancer cell lines: HCT116, SW48, HCT15 - CIMP+; HT29, SW480, SW620 - CIMP- and IEC-6 - normal control. We found EGCG to restore RXRα activity levels in the CIMP+ line, in a dose dependent manner (0, 50, 100 & 150 μM EGCG was tested for 48 and 72 hour durations ). EGCG also reduced RXRα promoter methylation in one CpG island from a CIMP+ line compared to a CIMP- line. EGCG produced methylation changes in several other colon cancer related genes but did not cause a decrease in global methylation. Numerous epidemiological reports have shown the benefits of green tea consumption in reducing colon cancer risk but to date no studies have shown that some of the risk reduction may be related to the epigenetic regulation of key genes by constituent tea polyphenols. Our results here show that EGCG, a common tea polyphenolic compound, modulates the reversal of gene-silencing involved colon carcinogenesis and a possible avenue for colon cancer treatment. *NCI CA96694*

154 Defining the Role of ICOS and CD28 Costimulation in TH17 Cell Activation, Differentiation and Tumor Immunity. Michelle Nelson1, Logan W Huff2, Carolyn E Rogers1, Sreenath Kundimi1, Chrystal M Paulos2; 1Microbiology and Immunology, MUSC, 2Surgery, MUSC.

TH17 cells play an essential role in regulating host defense and exacerbating various autoimmune diseases, but their role in tumor immunity remains incompletely elucidated. We found that CD28 abrogates TH17 expansion and function, while the inducible costimulator (ICOS) augments the generation of polyfunctional TH17 cells. Of clinical importance, ICOS-expanded TH17 cells were superior at killing tumors compared to CD28. The objective of our studies is to identify the role of ICOS and CD28 in differentiating and optimally expanding TH17 cells that mediate tumor regression. We have polarized human CD4+ T cells towards either Th0 or Th17 with anti-CD3/anti-CD28 or anti-CD3/anti-ICOS beads. ICOS costimulation appears to influence the generation of TH17 cells, as determined by CCR4 and CCR6 expression, more so than the cytokine milieu.
during activation. The TH17 chemokine phenotype persists following polarization. Stimulating ICOS, rather than CD28, reduces cell proliferation, likely due to a lack of autocrine IL-2 production. In optimizing our culture conditions we have begun altering the published TH17 culture conditions and discovered that additional IL-2, given on day zero, enhances cells’ expansion. Additionally, culturing cells with beads bound with anti-CD3/anti-ICOS and a small amount of anti-CD28 appears to increase cell proliferation. Both of these culture condition changes appear not to jeopardize our desired TH17 phenotype. Understanding how ICOS stimulation and optimal culture conditions promote TH17 polarization will be instrumental in advancing adoptive cell transfer therapy in cancer treatment.

155 Role of Transcription Factor Fli-1 in Regulation of Dendritic Cell and Monocyte Development, Eiji Suzuki, Sarah Williams, Eva Karam, Xian Zhang; 1Rheumatology and Immunology, MUSC, 2Ralph H. Johnson VAMC.

Background: The Fli-1 gene is a member of the ets family of transcription factors that is expressed in hematopoietic cells, and has important roles in the immune system. Dendritic cell and monocytes have a critical role in immunity and autoimmunity. In this study, we demonstrate Fli-1 plays an important role in regulating the development of monocytes and dendritic cells. Method: C57BL/6 (B6) mutant Fli-1 mice (Fli-1 ΔCTA) express a truncated Fli-1 protein that lacks the C-terminal transactivation domain. Fli-1 ΔCTA and wild-type B6 mice were sacrificed at the ages of 8-12 weeks. Bone marrow cells, spleen cells and peripheral blood mononuclear cells were prepared from each mouse and analyzed with Flow cytometry. To further reveal the molecular mechanisms, multipotent progenitors (MPP) were sorted from cultured bone marrow cells from both wild-type and Fli-1 ΔCTA mice. The expression of FMS-like tyrosine kinase 3 ligand (Flt3L) in MPP was measured by real-time PCR. Result: Common dendritic cell precursor population in bone marrow from Fli-1 ΔCTA B6 mice was significantly higher than that from wild-type controls. The cell number of CD8+ and double negative conventional dendritic cells and macrophages in spleen from Fli-1 ΔCTA B6 mice were significantly higher compared to wild type littersmates. Pre-conventional dendritic cells, plasmacytoid dendritic cells and monocytes in peripheral blood from Fli-1 ΔCTA B6 mice were significantly higher compared to wild-type littersmates. The expression of Flt3L in MPP obtained from Fli-1 ΔCTA B6 mice was significantly increased compared to wild-type controls. Conclusion: Our results demonstrate that Fli-1 plays an important role in myeloid cell development and the CTA domain in Fli-1 protein negatively regulates the myeloid cell development. We also demonstrated that Fli-1 affects myeloid cell development by directly or indirectly regulating the expression of Flt3L, a key molecule during dendritic cell development.

156 Defective Migration in Activator of G Protein Signaling 3-null Leukocytes in Response to CXCL12 and CCL19 Stimulation, Melissa B Branham-O'Connor, Ellen M Maher, Xian Zhang, Stephen M Lanier; 1Cell and Molecular Pharmacology and Experimental Therapeutics, MUSC, 2Medicine, MUSC.

Activator of G-protein Signaling 3 (AGS3/Gpsm1), via regulation of G-protein signaling, plays central functional roles in cell division, synaptic plasticity, addictive behavior and neuronal development. In addition to its expression in the CNS, AGS3 is also expressed in peripheral tissues and lymphoid organs such as spleen and thymus as well as in bone marrow-derived dendritic cells (BMDCs). AGS3 expression is upregulated in B cells stimulated with LPS or anti-IgM, in T cells stimulated with anti-CD3 and IL-2 and in BMDCs stimulated with LPS. As part of a broad effort to define the extent of functional diversity of AGS regulated-events in vivo, we generated AGS3 null mice. Defects in Galpha-i signaling effect lymphocyte differentiation as well as some humoral responses to antigens; therefore, we measured lymphocyte populations and serum Ig levels as well as chemokine-directed chemotaxis of lymphocytes and BMDCs from wild-type and AGS3 null mice. We discovered defects in migratory capabilities of AGS3 null BMDCs and B-cells based on transwell chemotaxis assays. We also used a BRET-based system to monitor AGS3-Galphai interactions and observed CXCL12-regulated interaction of AGS3-RLuc and Galpha-i-1-YFP. In addition, we also observed Galpha-i-1-dependent BRET between AGS3-RLuc and CXCR4-Venus which was regulated by CXCL12, suggesting a role for the AGS3-Galphai complex in the integration of signals from chemokine receptors. These studies expand the functional repertoire for AGS3 and other GPR proteins in the immune system providing unexpected venues for the potential development of therapeutic agents. MH90531; NS24821; F32MH65092; and GM086510

157 RAT Pathway Synchronizes FGFR1 Signaling By Intracellular Sequestration and Controlled PM Delivery of the Receptor, Jagadish Kummeth Venkata, Claire Leist Hinsch, Demetri D Spyropoulos, Erika T Brown, Simon C Watkins, Vincent Dammai; 1Pathology, MUSC, 2Cell Biology and Center for Biologic Imaging, University of Pittsburgh.

Newly synthesized Receptor Tyrosine Kinases (RTK) are presumed to be continuously transported to the plasma membrane (PM) via post-Golgi vesicles (PGVs). Here, we identify that PGVs carrying Fibroblast Growth Factor Receptor-1 (FGFR1), a RTK prominent in development and disease, are sequestered in a novel intracellular compartment and
These results reveal important differences between
where significantly larger than wild counterparts.

on day 7 of the trap staining, revealing that OC formed
type of cells formed in WT vs KO CD

formed over time when comparing CD11blo WT vs

staining showed reduced number of osteoclasts
population compared to controls. Data from the TRAP
reduction in CD11blo a

response to treatment with CON or MCSF+RANKL for

hypothesis, osteoclast progenitor cells were flushed

populations. OC progenitor cells respond to RANKL

population of the receptor and establishes the first example of a

PM delivery of FGFR1. Thus, RAT pathway

mechanistically, the cytosol exposed FGFR1 C-terminus orchestrates a

sequence of events that involves inactivation of the inhibitory Rab2a and stimulation of localized activation of

Rab8a. Finally RabA-exocyst participated in eKiss and run1 PM delivery of FGFR1. Thus, RAT pathway

signaling to the microenvironment through regulated PM translocation of the receptor and establishes the first example of a

RTK sequestered for delayed PM fusion.

WT and KO and the various sub-populations in a
number of early, mid and late osteoclastogenic markers, which may explain the abnormal size and
number of osteoclasts formed in the subpopulations.

Taken together, our data shows that studying sorted
progenitor populations in response to KO resulted in
highly variable findings, indicating that some subsets
within the hematopoetic lineage are more greatly
affected than others during ostoclastogenesis. R01-
DE018290-01

159 Effects of Inositol Phosphosphingolipid
Phospholipase C1 Deletion on Trafficking of the
Plasma Membrane ATPase (Pma1) in
Cryptococcus Neoforms, Kaur Navate1, Mor
Visesato1, Maurizio Del Poeta2; 1Biochemistry and
Molecular Biology, MUSC, 2Craniofacial Biology,
MUSC.

The proton pumping H+- ATPase, Pma1, is one of the
most abundant integral membrane proteins of the
yeast plasma membrane. Pma1 activity controls the
intracellular pH and maintains the electrochemical
gradient across the plasma membrane, two essential
cellular functions. Defective in targeting Pma1 to the
plasma membrane is accompanied by failure of the
Pma1 to associate with lipid rafts mainly containing
phytoceramide. In the pathogenic fungus
Cryptococcus neoforms, deletion of the inositol
phosphosphingolipid phospholipase C1 (delta-isc1),
the gene encoding an enzyme that produces
phytoceramide from inositol sphingolipids, produces a
C. neoforms mutant with impaired Pma1 activity
and, thus, sensitive to low pH. However, the
mechanism(s) by which Isc1 regulates Pma1 in C.
neoforms is not known. In this study, we
investigated the involvement of Isc1 on Pma1
oligomerization, transport and stability at the plasma
membrane using immunofluorescent and molecular
methods. These studies will provide new insights on
how Isc1 regulates Pma1, with important implications
for the understanding of permissive fungal growth at
low pH. NIH AI56168, and NCRR RR17677

160 Insulin Like Growth Factor-1 Attenuates
Intracellular Changes In Ventral Spinal Cord 4.1
Motoneuron Cells Damaged By Interferon-Gamma,
Sookyoung Park1, Kenkichi Nozaki1, Arabinda Das1,
James S Krause2, Naren L Banik1; 1Neurosciences,
MUSC, 2Health Sciences and Research, MUSC.

Insulin like growth factor-1 (IGF-1) is a neuroprotective
growth factor which promotes neuronal survival by
blocking apoptosis. It also attenuates calpain
expression and maintains calpastatin levels. In order
to examine whether IGF-1 exerts its neuroprotective
roles against extracellular inflammatory stimulation, we
treated ventral spinal cord 4.1 (VSC4.1) cells with
interferon-gamma (IFN-γ). We identified that IFN-γ
caused apoptotic changes and increased the Bax:Bcl-
2 and calpain:calpastatin ratios and expression of

158 Effect of MKP-1 Knockout on Osteoclast
Progenitor Populations and RANKL Induced
Osteoclastogenesis, Valerio S Michael, Keith L
Kirkwood; Craniofacial Biology, MUSC.

Osteoclasts (OCs) are large multinucleated bone-
resorbing cells of hematopoetic lineage which from
stimuli such as macrophage colony stimulating factor
(MCSF) and receptor activator of NF-kB ligand
(RANKL) produced by osteoblasts and lymphocyte
populations. OC progenitor cells respond to RANKL
through induction of inflammatory cascades such as
MAP kinases (MAPK). Deletion of the phosphatase
MKP-1, which functions to deactivate MAPK, has been
shown to up-regulate inflammatory p38 and JNK
MAPK signaling, as well as to increase
osteoclastogenesis in mice. Given the diversity of the
hematopoetic lineage, the objective of this study was
to determine if subpopulations of osteoclast precursor
cells are responsive to MKP-1 deletion. To test this
hypothesis, osteoclast progenitor cells were flushed
from WT and MKP-1 KO mice and cells were sorted
into CD11bhi (Macrophage (MΦ)), CD11blo (MΦ
lineage) and CD11b- (non-MΦ) populations. Cells
were plated for TRAP staining and RNA activity in
response to treatment with CON or MCSF+RANKL for
3, 5, 7 and 9 days post-sort. Sorting revealed a
reduction in CD11blo and CD11b- cells in the KO
population compared to controls. Data from the TRAP
staining showed reduced number of osteoclasts
formed over time when comparing CD11blo WT vs
KO. However, a distinct difference was seen in the
type of cells formed in WT vs KO CD11blo populations
on day 7 of the trap staining, revealing that OC formed
where significantly larger than wild counterparts.
These results reveal important differences between
apoptosis related proteases (Caspase-3 and -12) in a dose-dependent manner. Post-treatment with IGF-1 attenuated these changes. In addition, IGF-1 treatment also decreased expression of inflammation related transcription factor (Nuclear factor-kappa B:Inhibitor of kappa B ratio) and cyclooxygenase-2 in VSC41 motoneuron cells. Furthermore, both IGF-1 receptors (α and β) and estrogen receptors (α and β) were activated by treatment with IGF-1. These results indicate that IGF-1 prevents apoptotic cell death in neuronal cells via interaction between estrogen receptor and IGF-1 receptor signaling. Thus, the cross-talk between these receptors may be a target for therapy to attenuate motoneuronal cell death in inflammatory central nervous system disease, such as multiple sclerosis. NIH/NIDDS

161 Regulation Of Ogt And Oga And Their Impact On Insulin Signal Transduction, Kamala P Sundararaj, Katherine A Robinson, Maria Buse, Lauren Ball; Endocrinology, MUSC.

One mechanism hypothesized to contribute to insulin resistance and the complications associated with diabetes is the altered regulation of O-GlcNAc transferase (OGT) and O-GlcNAcase(OGA). These enzymes are responsible for the addition and removal of N-acetylglucosamine (O-GlcNAc) to protein Ser/Thr residues. To understand the molecular mechanisms in the pathophysiologic status of diet induced obese and diabetic animals, we examined C57BL/6 male mice that were fed with two kinds of diets for 12 to 16 weeks: a normal chow diet (NCD), a high fat diet (HFD). The liver specific knock out of IRS-1/2 mice were also fed with NCD and HFD. The mRNA and protein expression levels of OGT, OGA, GCK, PCK, G6P, IRS-1 and IRS-2 in liver tissues from the two groups were measured. In the present study, we have found that the hepatic expression of OGT in NCD and HFD mice are increased with feeding. We also observed decreased hepatic OGT expression in HFD mice compared with the NCD mice in both fasted and fed state. Moreover, we found that the level of hepatic OGT expression was further decreased in HFD mice with the liver specific knock out (KO) of IRS-1/2. Conversely, the hepatic OGA expression was opposite to that of OGT. Interestingly, in HFD mice the hepatic O-GlcNAc modification was increased in both fasted and fed condition compared with the NCD mice. This increase was further augmented in liver specific IRS-1/2 KO HFD mice compared with the NCD IRS-1/2 KO mice. In conclusion, these studies show for the first time that IRS-1/2 mediated insulin signaling is essential for hepatic OGT and OGA expression and OGT decrease in HFD IRS1/2 KO mice may play a protective role.

162 Factors Regulating the Subcellular Localization of Activators of G-protein Signaling 3: The Role of Serine/threonine Residues in the G-protein Regulatory Domain, Fatih M Kelesoglu, Sadik S Oner, Stephen M Lanier; Cell and Molecular Pharmacology, MUSC.

Group II Activators of G-protein Signaling (AGS) proteins contain one to four G-protein regulatory motifs (GPR) that serve as docking sites for Gαi/o/t. The GPR-Gα signaling module is regulated by guanine nucleotide exchange factors and provides unexpected signaling diversity for the “G-switch”. AGS3, which contains seven tetratricopeptide repeats (TPR) and four GPR motifs, is involved in a wide range of biological functions including asymmetric cell division, autophagy and addictive behavior. AGS3 oscillates between different subcellular domains (cell cortex, spindle pole, aggresomes, autophagic vesicles and the Golgi apparatus) in a regulated manner. Interaction of AGS3 with Gαi or FRMPD1 stabilizes AGS3 at the cell cortex, whereas disruption of the TPR motif stabilizes the protein in the aggresome pathway. We asked if AGS3 trafficking was regulated by phosphorylation. As a first approach to this issue, we determined the subcellular distribution of a mutant GFP-tagged AGS3 in which 24 S/T residues in the GPR domain of the protein were changed to alanine to eliminate S/T phosphorylation in this region. Wild type AGS3-GFP, AGS3-GFP-GPRphosphonull and AGS3-GFP-Q182H (TPR mutant) were expressed in HEK-293 cells and the subcellular distribution determined by immunofluorescence microscopy. In contrast to wild type AGS3, both the GPRphosphonull and TPR mutant distributed to preaggresomal structures in the cytosol. These data suggest that trafficking of AGS3 into or out of the aggresome pathway is regulated by phosphorylation. Experimental strategies currently focus on defining the key S/T residues and kinases or phosphatases involved with this regulation. Dysregulation of the subcellular location of AGS3 may contribute to pathologies involving altered protein processing through the aggresomal and autophagic pathways. NIH DA025896; Bezmialem Foundation University

163 Reinstatement of Cocaine-seeking in Rats with an Addiction-prone Phenotype, R Parrish Waters, Amy B Young, Matt W Feltenstein, Ronald E See; Neurosciences, MUSC.

Studies that use a variant of the rat self-administration model of cocaine abuse have identified rats that possess a highly addiction-prone phenotype. During a chronic regimen of cocaine self-administration, these addiction-prone animals develop traits that indicate compulsive and unrestrained drug seeking and taking. Furthermore, and central to the clinical relevance of these animals, addiction-prone rats exhibit enhanced levels of reinstatement to drug seeking when
presented with a priming dose of cocaine, or cocaine associated cues. We utilized the methods described in these studies to further investigate the reinstatement behavior of animals that express this addiction-prone phenotype. Animals self-administered cocaine daily during three 40-minute sessions, separated by 15-minute periods during which contextual cues for cocaine were removed and cocaine was unavailable. After 65 days of cocaine self-administration, we assessed addiction phenotypes of all rats using a progressive ratio test, withholding cocaine upon operant responding, and associating cocaine infusions with an aversive stimulus (shock). Following tests, operant behavior was extinguished, and animals underwent reinstatement testing in the presence of yohimbine (2.5mg/kg IP), cocaine associated cues, or non-contingent injections of cocaine (10mg/kg IP).

Data indicate a correlation between progressive ratio scores, extinction behavior, and operant responses during cued reinstatement tests, suggesting an addiction-prone phenotype in some animals (those with exhibiting high scores in these tests). However, throughout the study all animals exhibited low levels of operant responding in the context unassociated with cocaine, indicating good discrimination by all individuals, even those with high scores on tests of addiction. Furthermore, when we associated cocaine infusions with a shock, lever pressing was inhibited (to nearly zero) in all animals. Thus, although some aspects of the proposed addiction-prone phenotype are present in our animals, our data suggest that all of the parameters of this phenotype are not universally expressed in rats that are prone to addiction. RO1 DA010462

164 Neuronal and Behavioral Effects of Optogenetic Modulation of the Lateral Habenula. Margaret J Gill, Robert P Waters, Art C Riegel, Ron E See; Neuroscience, MUSC.

A novel neural circuit has been identified that projects from the lateral habenula (LHb) to the rostromedial tegmental nucleus (RMTg) and the ventral tegmental area (VTA). This circuitry has been suggested to act as an “on/off” circuit in aversive and appetitive processes, as presentation of aversive stimuli activates the LHb, while reward predicting stimuli inhibit LHb neurons. Characterization of this circuitry has major implications for our understanding of motivated behaviors, as it strongly regulates ascending dopamine pathways. The current study examined whether optical stimulation of LHb neurons transfected with halorhodopsin (eNpHR) would attenuate neuronal firing using in vitro electrophysiology. Additionally, we examined whether optical stimulation of LHb efferents transfected with eNpHR altered locomotor activity in an open field or anxiogenic behavior on an elevated plus maze. Adeno-associated virus (AAV) containing the coding sequence for eNpHR with a synapsin promoter was infused into the LHb of Sprague-Dawley rats, and eNpHR expression was verified with confocal microscopy. Following viral incubation, the LHb was optically stimulated while recording from brain slices. Our results show that viral infusion into the LHb successfully transfected both the RMTg and VTA pathways and that optical stimulation produced robust hyperpolarization of LHb glutamate cells. Preliminary behavioral results revealed an attenuation of open arm entries on the elevated plus maze following inhibition of efferents to the VTA, while open arm entries increased following inhibition of efferents to the RMTg. Additionally, these changes occurred independent of general locomotor activity, suggesting LHb/RMTg/VTA pathway selectivity. These results demonstrate that optogenetic approaches can be utilized in virally transfected cells in the LHb/RMTg/VTA pathway of rats, offering unique possibilities for future exploration of the role of this critical neural circuit. NIH DA010462

165 Proteomic Analysis Of Cerebral Spinal Fluid Reveals Candidate Biomarkers Of Domoic Acid Toxicosis In California Sea Lions. Benjamin A Neely, Jennifer Soper, Frances M D Gulland, John M Arthur, Michael G Janech; 1Nephrology, MUSC, 2The Marine Mammal Center, 3Research Service, Ralph H. Johnson VA Medical Center, Charleston, SC.

Domoic acid toxicosis (DAT) is a major cause of California sea lion (Zalophus californianus) strandings along the west coast of the United States. Domoic acid is a potent neurotoxin produced by some marine diatoms, which causes hippocampal atrophy and necrosis as a result of excessive stimulation of AMPA-kainate and NMDA receptors, and is rapidly cleared from the body. DAT is classified as acute or chronic, with the former recovering over time and the latter progressing to status epilepticus. Currently markers of DAT are limited and inconclusive; therefore by developing markers of DAT, diagnosis and treatment could be greatly facilitated. For this reason we evaluated whether protein differences exist in the cerebral spinal fluid (CSF) that could be utilized as markers of DAT. CSF samples from 11 sea lions [3 without DAT, 2 diagnosed with acute-DAT and 6 with chronic-DAT] were acquired from The Marine Mammal Center and proteins were digested with trypsin for analysis by tandem mass spectrometry. Data were searched using Mascot against a mammalian database, with identifications supported by Scaffold. We identified 182 experiment-wide proteins with a protein false discovery rate of <0.1%. Relative protein abundance was estimated for comparison by spectral counts across all samples and differences were detected using a Wilcoxon rank-sum test. Six proteins were significantly different (p<0.05) between non-DAT and DAT animals, five of which were higher in animals with DAT. Interestingly, Dickkopf-3 and Gelsolin were elevated in sea lions with DAT. Both of these proteins have been implicated in the progression of Alzheimer’s...
Disease, suggesting that DAT and Alzheimer's may share common features. Future studies to qualify these proteins as markers of DAT are ongoing. ONR N00014-08-1-0341

166 β-blockade Prevents P21-activated Kinase 1 (Pak1) Activation in an in Vitro Model of Cardiac Hypertrophy, Grace Wallenborn, Guangmao Cheng, Dhandapani Kuppuswamy, George Cooper; Medicine, Cardiology, MUSC.

During pathological, but not physiological cardiac hypertrophy a dense microtubule network is formed, impeding contractile function and intracellular transport, which in turn impairs the growth response and leads to heart failure. Previously we have linked this densification to a pathway beginning with activation of the kinase Pak1, leading to activation of the phosphatase PP2A, which dephosphorylates microtubule associated protein MAP4, giving it a higher affinity to bind to, and stabilize microtubules. A hallmark of deteriorating cardiac function is increased and persistent β-adrenergic signaling, β-blockers are a current heart failure therapy. Recently Pak1 activation has been linked to β-agonism. The overarching hypothesis of this study is that the etiology of microtubule densification is β-adrenergic signaling, via Pak1-PP2A-MAP4 dephosphorylation. Specifically, we hypothesize that Pak1 is activated via β-adrenergic stimulation, mainly via cAMP mediated signaling, and that this activation is blocked by pre-treatment with the nonselective β-blocker propranolol. Isolated adult feline quiescent ventricular cardiomyocytes were treated with 100nM of the β-agonist isoproterenol for 30 minutes or 48 hours. Isoproterenol increased Pak1 activity, measured by Western blot with a phospho-T423 Pak1 antibody. 15 minutes pretreatment with 20μM propranolol blocked this effect. Raising intracellular levels of cAMP independently of β-receptors via forskolin similarly increased Pak1 activity, supporting the dependence of Pak1 activity on cAMP signaling. Furthermore, pretreatment with 300nM of the β2-selective antagonist ICI-118,551 did not affect the isoproterenol-induced increase in Pak1 activity, but pretreatment with 300nM of the β1-selective antagonist CGP-20712 did, suggesting that isoproterenol-induced Pak1 activation is mediated mostly via the β1-receptor. These data provide a specific etiology of the dense microtubule network found in pathological cardiac hypertrophy, as well as a specific remedy. In a clinical context, these data support the notion that if instituted early, β-blockade may delay or prevent microtubule densification which itself is one cause of heart failure. NIH T32HL07260

167 Anxiogenic Effects of Cocaine Withdrawal in Rats, Kyle T Brown, Parrish R Waters, Ronald E See; Psychology, CofC.

Drug addiction is a chronic relapsing disorder associated with compulsive drug taking behavior and the subsequent impairment of social and occupational functioning. In individuals with a compulsive substance abuse disorder, drug relapse is hypothesized to be motivated by an aversive affective state that increases the probability that an addict will seek out substances of abuse in order to temporarily remove unpleasant feelings associated with withdrawal. In this study, the transition to compulsive cocaine abuse was modeled using rats on extended access, cocaine self-administration. Subjects exhibited an escalation in drug taking behavior as the trials progressed. In particular, an escalation in the amount of cocaine infusions was found in the first hour of self-administration trials. Following acute withdrawal, anxiety-like behavior was measured in the subjects using the elevated plus maze. Behavioral measures indicate a statistically significant increase in anxiety-like behavior among subjects undergoing withdrawal from cocaine compared to control subjects. NIH P20 RR-016461

168 Structure-function Relationships in the Brain Using Imaging Across Multiple Spatial Scales, Grace Margaret A Dion, Zhongyang Lu, Manuel Levy, Prakash Kara; Neuroscience, MUSC.

The neocortex accounts for more than 80% of brain volume. The most common neuron in all cortical regions is the layer 2–3 pyramidal cell, which receives thousands of synaptic inputs from other cortical neurons on its apical and basal dendrites. However, the function of apical vs. basal dendrites in sensory signal processing is largely unknown—because the organization of cortical dendrites was previously studied in artificial brain slices. Zhongyang Lu labeled single pyramidal neurons in the primary visual of the neocortex in vivo using two-photon microscopy such that the entire dendritic tree was visualized. Thus, we examined the organization of apical and basal dendrites relative to the boundaries of a functional map that represents the orientation of different sensory stimuli. Using the in vivo data, I have been performing detailed morphometric analyses on the dendrites of individual neurons. Using Neuroulucida software, I have thus far traced the dendrites of ten neurons from 23. To eliminate bias, I am performing these single-neuron reconstructions 'blind' until all reconstructions are completed. I have no knowledge of the domains in which these neurons reside. In the pyramidal neurons thus far examined, apical dendrites had more branch points than basal dendrites. Summing all branches, apical dendrites also had a longer total dendritic length. Finally, apical dendrites had higher branch orders. All values are cited as mean ± standard deviation. Dependence of these branch morphometrics on the location of neurons in the functional map will be determined once all reconstructions are completed. Specific sub-domains of the functional map for stimulus orientation have been postulated to play an important role in experience-dependent development.
and learning. This first morphometric analysis of dendrites across specific sub-domains of the map provides a necessary blueprint for all future work examining how dendrites change at different phases of development and learning.

169 Evaluating an Intervention to Increase Cancer Knowledge in Racially Diverse Communities in South Carolina. CoDanielle Green\(^1\), Marvella E. Ford\(^2\), \(^1\)SC State University, \(^2\)MUSC.

Objective. To conduct a cancer education intervention with racially diverse communities in South Carolina. Then, to assess the impact that the cancer knowledge intervention is having on the cancer prevention activities of the residents. Methods. The study was conducted at eight different sites in six counties in SC. The intervention included a 3-hour general cancer knowledge and 30-minute prostate cancer knowledge component. Pre- and post-intervention surveys were administered. Maximum scores were 31, 10 and 5 for the general cancer knowledge, prostate cancer knowledge and perceived self-efficacy in patient-physician interaction instruments, respectively. In addition to evaluating changes in cancer knowledge, the impact of the intervention on behavioral outcomes associated with cancer incidences was also assessed. The behavioral outcomes were evaluated using data from the Behavioral Risk Factor Surveillance System (BRFSS). The behavioral outcomes assessed were alcohol consumption, tobacco use, physical inactivity, prostate specific antigen (PSA) tests, mammograms, pap tests, and sigmoidoscopies or colonoscopies. Results. The study sample consisted of 164 predominantly African American participants (n=159). Most of the 160 participants who reported age were 50+ years (62.5%). Among those who reported income (n=154), 46.1% had an annual household income < $40,000. The mean general cancer knowledge pre-test score was 26.2 (standard deviation (SD) 3.7) with a mean post-intervention increase of 2.04 points (p<0.01). The mean pre-test prostate cancer knowledge score was 7.3 (SD 2.0) with a post-intervention increase of 0.48 points (p<0.01). Perceived self-efficacy in patient-physician interaction scores had a ceiling effect. The intervention had a significant impact on colorectal screening. Unfortunately, the intervention did not have a significant impact on the other cancer prevention behaviors and activities investigated. Conclusions. General cancer knowledge and prostate cancer knowledge scores increased following the intervention. The intervention had little association with improved cancer prevention behaviors and activities with one major exception. DOD HBCU Collaborative Summer Undergraduate Research Training Program.

170 Pilot Study: Maternal Infant Neurobiology. Courtney H Marsh\(^1\), Amy Wahlquist\(^2\), Paul Nitert\(^2\), Carol Wagner\(^2\), Eve G Spratt\(^2\), 1Medicine, MUSC, 2Pediatrics and Psychiatry, MUSC.

Maternal well-being can influence infant neurodevelopment. Oxytocin is capable of moderating behavioral responses to various stressors as well as the reactivity of the hypothalamic–pituitary–adrenal (HPA) axis (Carter, 2003). This pilot study examined 42 mother-infant dyads recruited for a Vitamin D study. Both infant and mom provided a sample of saliva to measure cortisol pre and post a blood draw stressor. Simple descriptive statistics (mean, standard deviation, median, min, and max) were used to describe the outcomes of interest (cortisol and change in response) by gender, breast feeding vs. bottle feeding, and whether mom was present at time of blood draw. Results: Baseline cortisol levels did not differ significantly between genders (p=.5085). Girls had a larger increase in cortisol than boys (0.36 and -0.06, respectively), after adjusting for baseline cortisol values (p=0.0452). Girls had higher increase in cortisol levels than boys (p=.0020). Increasing baseline cortisol measures for mom was related to increasing baseline cortisol measures for babies (p= <0.001). As mom’s baseline cortisol increases, the change in the infant’s cortisol level increases, as well (p=0.0700). Conclusions: Mothers who breastfed had higher salivary and plasma oxytocin levels. Infants whose mothers were present at the time of the blood draw did not have lower cortisol levels than infants whose mothers were present at the time of the blood draw. Baseline cortisol patterns resembled those of the mother. Symptoms of depression and anxiety did not explain the findings. Future research in this area may help us better understand mechanisms associated with stress, attachment and post partum depression. An improved understanding of neurobiologic markers may help. K23MH -63111, MUSC DART, and SCTR.

171 Importance of Lymph Node Metastasis in Head and Neck Sarcomas. Lewis J Overton, Valerie A Smith, Eric J Lentsch; Otolaryngology, MUSC.

Head and neck soft tissue sarcomas (HN-STS) are exceedingly rare neoplasms and it is unclear whether they are distinct from STS in other anatomic regions. Although hematogenous dissemination and local invasion occur commonly, lymph node metastasis is rare and its prognostic significance is not well understood. It’s currently unclear whether disease-positive lymph nodes serve as a nidus for systemic spread, or whether they are a marker of distant disease. Our objective is to determine how nodal metastases affect disease-specific survival (DSS) in (HN-STS), and whether the effect is the same in comparison to STS in non-head and neck regions (NHN-STS). The Surveillance Epidemiology and End Results (SEER) database (a program of coordinated population-based cancer registries sponsored by the National Cancer Institute) was queried for patients diagnosed with STS and histopathologically confirmed...
lymph node status. Patients were grouped according to tumor location in the head and neck region or elsewhere, and further classified by histologic subtype for subsequent analysis. Kaplan-Meier survival analysis was performed and DSS curves were compared between node-negative and node-positive patients using the logrank test. Of the 842 patients with STS and histopathologically-confirmed lymph node status who were identified, 115 (13.7%) had HN-STS. Although nodal metastasis was significantly associated with poorer DSS in NH-ST (overall, fibromatous, and undifferentiated variants, p<0.001), node positivity was not predictive of worse DSS in HN-STS (p>0.5). Node metastases did not affect survival for any patients with myomatous neoplasms, regardless of tumor location (p>0.2). Lymph node metastasis does not appear to significantly impact DSS in HN-STS. The reason for differences between HN-STS and NHN-STS is uncertain. However, this effect may be explained by a higher propensity for hematogenous metastasis and local recurrence in the head and neck.

172 Using a Community-Based Participatory Research Approach to Create and Test a Culturally Sensitive Oral Health Educational Handbook—Hollywood Smiles Handbook, Christine M Hudson¹, Lynn J West¹, Elizabeth Carpenter², Renata Leite¹; ¹Center for Oral Health Research, MUSC, ²Hollywood, SC, Mayor’s Office.

Despite national improvements in oral health (OH) status over the past decade, profound disparities remain in some populations as classified by income, age, gender, race/ethnicity, and geographical location. The reasons for disparities in oral health are complex, and traditional main-stream OH interventions are not effectively reaching these disparate groups. Hollywood is a rural town in Charleston County, South Carolina, consisting primarily of African American Gullah residents. Our previous clinical interactions with the Gullah community have revealed that the predominant dental treatment received is tooth extraction, usually due to late diagnosis of dental/oral pathology. With the support of Hollywood’s mayor’s office, we have developed a unique academic-community partnership model to identify the perceived health issues and feasible solutions to address the OH disparities in this community. Through our formative research, we have identified reasons for not seeking earlier or preventive care (i.e., fear, lack of access to dental care, cultural beliefs, lack of transportation, lack of trust, lack of dental insurance, and/or decreased oral health literacy) and potential solutions to improve OH outcomes (multi-level approach in faith-based settings). The Hollywood Smiles (HS) project proposes to use a community-based participatory research (CBPR) approach to design and test a multi-level intervention including church level strategies, group based education, and community-based oral health promoters. Objectives: To develop and test the written material (HS handbook) to be used in the group education/behavioral intervention, integrating the community in the process. Methods: Initial drafts of the HS handbook encompassing the importance of good oral hygiene (OHy), understanding the risks of poor OHy, and tools for keeping good OHy and staying healthy, will be created and will undergo in-depth review and comment by community participants, through focus group (FG) sessions. Participants will be presented with at least two options for each session of the handbook and will be asked not only to pick and choose between the different options, but also the reasoning behind it, so we can further develop a culturally sensitive and effective adjunct material for the proposed multi-level intervention. Once a final draft of the handbook is developed, it will be pilot tested using FG sessions. In these sessions, participants will be asked probing questions about the material presented in the handbook, indicating their understanding and comprehension of the presented subject. Participants will also be given an opportunity to make suggestions on how to improve the handbook.

Results: Participants reported that they liked the layout and content of the HS handbook overall, however, age differences in the participants appeared to be a factor in the preference of a religious themed handbook as opposed to a neutral handbook. There was a strong preference for more pictures and less words on the pages, along with realistic, graphic pictures of dental procedures and conditions. Participants were also in favor of a break-down of compact pages into more pages with less content per page. Conclusion: Preferences and needs of the community will be addressed and used to further design the HS handbook. New amendments of the handbook will be further tested through focus groups to ensure the community’s understanding of oral health concepts. The acceptability and efficacy of the handbook will be further tested during the Hollywood Smiles multi-level intervention.

SC COBRE for Oral Health; and MUSC SCTR

173 A Unique Case of Anton’s Syndrome, Elizabeth M Quattlebaum¹, Robert J Adams¹, Nolan Williams², Mark T Wagner³; ¹Neurosciences, MUSC, ²Psychiatry and Neurosciences, MUSC, ³Neuropsychology, MUSC.

Abstract not available.

174 Selective MicroRNA Suppression in Thoracic Aortic Aneurysm: Relationship of MiR-29a to Aortic Size and Proteolysis, Charlotte R Ivey¹, Jeffrey A Jones², Elizabeth C O’Quinn¹, John A Elefteriades¹, Robert E Stroud², Francis G Spinale², John S Ikonomidis²; ¹Medicine, MUSC, ²Surgery, MUSC.

Thoracic aortic aneurysms (TAAs) develop as a result of dysregulated extracellular matrix remodeling mediated in part by a family of matrix
Nkx2.5 Regulates Hoxb4, MiR-10a, and Jarid2 Expression in the Developing Heart, Aaron M Blackshaw\(^1\), Kyu-Ho Lee\(^2\); \(^1\)CofC, \(^2\)MUSC Pediatric Cardiology.

The right ventricle, pulmonary arteries, and aorta are all derived from cells that originate from a subdivision of the developing heart, the second heart field (SHF). Nkx2.5 is an important transcription factor for many genes expressed in the SHF; in-fact Nkx2.5 null embryos experience lethal heart malformations. In-situ data from our lab shows that Hoxb4 is also expressed in the heart and in the SHF. In this study, we expand upon the finding that Nkx2.5 positively regulates Hoxb4 expression. Interestingly, just 5′ of the Hoxb4 coding locus is a transcriptional start site for microRNA-10a (miR-10a). One of the predicted targets of miR-10a is Jarid2, which previously has been shown to be down-regulated by Nkx2.5 in a paper by Dr. Kyu-Ho Lee. This data led us to our hypothesis that Nkx2.5 concurrently increases expression of Hoxb4 and miR-10a. MiR-10a then continues on to secondarily decrease Jarid2 mRNA levels. MUSC's Summer Undergraduate Research Program (SURP) 2010-11

176 Comparative Transcriptome Analysis to Identify Genes Regulating Elastogenesis, Sharon L Guffy\(^2\), Erin L Pardue\(^1\), Jeremy L Barth\(^1\), Kathleen R Braun\(^1\), Thomas N Wight\(^2\), W Scott Argraves\(^1\);
\(^1\)Regenerative Medicine and Cell Biology, MUSC, \(^2\)Benaroya Research Institute.

Elastin-containing fibers and lamellae are important to the mechanical performance of many tissues. The underlying mechanisms of the assembly of these structures (elastogenesis) remain ill defined. Arterial smooth muscle cells (SMCs) produce significant quantities of elastin fibers when transduced to express the V3 variant of the proteoglycan versican. Furthermore, V3 promotes elastogenesis and improves the structural and functional properties of engineered vascular constructs. To identify changes in gene expression that may underlie V3 induced elastogenesis, we used microarray expression analysis and qPCR to measure mRNA changes accompanying overexpression of V3 in SMCs. Compared to controls, V3 upregulated the expression of tropoelastin as well as a number of genes previously shown to be critical for elastogenesis. We next sought to refine the set of V3 influenced genes through analysis of their expression in two other models of elastogenesis, namely a model of mouse lung repair after naphthalene injection and a model of mouse skin repair after a punch biopsy. As a result, a subset of twenty-nine genes, including those encoding tropoelastin, fibulin-2, neuraminidase-1, ADAMTS9, tenascin-C and decorin, was consistently either upregulated or downregulated in all three models, suggesting the importance of these genes in the process of elastic fiber formation. This potential involvement was further assessed by defining their expression profile during postnatal lung development at stages before, during and after periods of active elastogenesis. In summary, we have identified a group of genes whose expression correlates in multiple models of elastin formation. Many of the genes identified through this approach have not previously been associated with elastogenesis and thus may represent novel players in the process. NIH HL095067; NSF EPSCoR EPS-0903795; and SC EPSCoR NNX10AM76H

177 The Effect of Cytokines on T Cell Antioxidant Capacity, Jazzmine Clemons\(^1\), Shikhar Mehrotra\(^2\); \(^1\)Clafflin University, \(^2\)MUSC.

Introduction: Persistence of effector cytotoxic T lymphocytes during an immunological response is critical for successfully controlling a viral infection or
tumor growth. Various cytokines are known to play an important part in regulating the immune response and are known to function as growth and survival factors for antigen-experienced T cells. Based on previous work in our laboratory, we hypothesized that cytokines would differentially affect the antioxidant capacity of T cells. Methods: Experiments were conducted using the pmel-1 transgenic mouse model. Results: IL-12 and IL-21 favored the generation of central memory-like T cells, as evidenced by the upregulated expression of CD62L. Importantly, we found that T cells cultured in the presence of these cytokines expressed increased levels of intracellular glutathione. In contrast, IL-2 did not affect any of the above parameters. Conclusions: Our results suggest that IL-12 and IL-21 could increase the antioxidant capacity of T cells, potentially becoming a more successful tool for T cell immunotherapy. DOD SE VIEW

178 Neurotransmitters Effected By Cocaine Addiction, Catherine M Claro, Parrish R Waters, Ronald E See; Neuroscience, MUSC.

Cocaine addiction prompts a variety of adverse effects on to the human body and brain. In particular, anxiety levels tend to be a significant issue that develops with cocaine addiction. Recent evidence has shown that brain levels of oxytocin and vasopressin may influence this anxiety, specifically during a period of withdrawal. To investigate this relationship, we used an animal model of cocaine addiction, and measured anxiety levels following a short period of withdrawal. We also measured levels of vasopressin and oxytocin in the central amygdala during withdrawal using ELISA), an immunological peptide quantification technique. Preliminary evidence suggests that an acute cocaine withdrawal increases anxiety levels, and that changes in levels of these neurotransmitters may influence this behavioral effect. NIH P20 RR-016461

179 MBD4 DNA Repair in Prostate Cancer, Sierra S Brooks1, David Turner2, 1Voorhees College, 2MUSC.

Introduction: Increased glycation is associated with increased DNA mutation which promotes the cancer phenotype. Most obese men are twice as likely to die of prostate cancer. Over 30% of SC African American men are overweight. AGE content in Western diets has greatly increased there are low income or poor eating habits that promote AGE production. These factors provide a compelling reason for examining AGE levels as a possible mechanism promoting racial disparity in prostate cancer. Therefore, the goal of this study was to analyze the expression and functional activity of anti-glycation repair protein in human prostate cancer tissue. This aim defines if MBD4 protein can go in and repair tissues that have been affected due to prostate cancer. The MBD4 protein can be added to repair the tissues or control the activity of the prostate from growing or going to a different region of the body. Methods: To examine if MBD4 RNA and protein levels are reduced in prostate cancer cell lines, we cultured a series of LNCAp prostate cancer cells which represented human prostate cancer progression. RNA and protein were extracted using established protocols and RNA levels were examined by Real Time PCR and protein levels by western blot analysis. Also Isopropyl b-D-1 thiogalactopyranoside (IPTG) was used as molecular reagent. It turns on vector creating proteins. Results: MBD4 protein was successfully purified using bacterial expression system. MBD4 has potential to be able to bind to the AGE CeDG in vitro. Decreased MBD4 protein levels associated with increased aggression in LnCap prostate cancer progression model. African American’s low grade prostate cancer patients may have lower levels of MBD4 than European Americans. Conclusion: The data provided initial evidence that MBD4 may repair DNA associated AGE’s and its reduced expression may be a mechanism promoting racial specific prostate cancer. Liberty Life Insurance

180 Thioredoxin 1 As a Therapeutic Target in Advanced Prostate Cancer, DeAngelo Dinkins1, Christina Voelkel-Johnson2, 1SC State University, 2MUSC.

Introduction: Thioredoxin is a redox-regulating protein that plays a central role in regulating cellular redox and preventing cell death. There is a high expression of thioredoxin in cancer cells because the tumor environment is usually under either oxidative or hypoxic stress and both stresses are known to be up-regulators of thioredoxin expression. Prostate cancer is the 2nd leading cancer in men after lung cancer. Indolent disease can be treated fairly well and progresses slowly. However, the more aggressive form of prostate cancer spreads throughout the body and there are no curative treatments. Hypothesis: We tested the hypothesis that increased expression of redox proteins is an underlying cause for the aggressive, therapy-resistant prostate cancer phenotype. Methods: In our project we looked at the expression of redox proteins and susceptibility to chemotherapy in ARCaPm cells. Using western blot methods and Image J we were able to quantify the expression of thioredoxins. Susceptibility to chemotherapy was tested in a viability assay. Results: Western blot analysis indicated increased expression of the redox proteins such thioredoxin 1 and thioredoxin 2 in ARCaPm cells when compared to ARCaPm cells. Early results show that taxotere is highly effective in concentrations over 100 nM/ml. Conclusion: We found that ARCaPm cells do have an increased expression of redox proteins. Therefore they are more resistant to cancer treatments, such as taxotere and px-12. DOD HBCU Summer Collaborative Research Grant
181 Pilot Study: Tolerability and Functionality of Two High-Fiber, Weight Loss Diets, William D Strickland1, O’Neil M Patrick2, Tonya Turner2; 1Medicine, MUSC, 2Psychiatry, MUSC.

Abstract not available.

182 Prevalence of Vitamin D Deficiency in Obese Children and Adolescents, Jennifer N Paige, Janet Carter, Melissa Henshaw; Medicine, MUSC.

Background: Vitamin D deficiency and obesity are becoming increasingly prevalent in the United States. Obesity has been identified as a risk factor for developing Vitamin D deficiency. Objective: To examine an obese pediatric population for the prevalence of Vitamin D deficiency. Methods and Procedures: 157 participants, ages 4-21, were consented and evaluated via the IRB-approved Pediatric Metabolic Syndrome Study (HR 19375). Each participant completed the Block Kids Food Frequency Questionnaire with a registered diettian, to determine usual dietary consumption of food groups and various nutrients. Participants also supplied blood samples to calculate serum levels of 25(OH) Vitamin D. Deficiency = <20 ng/mL, Insufficiency = ≥20 ng/mL <30 ng/mL and Sufficiency = ≥30 ng/mL. Results: 63% of Black participants were found to be deficient compared to 11% of White participants. Less than 1% (2/38) of White girls were 25 (OH) deficient. Only 6% of the black participants contained sufficient amounts of serum 25(OH) Vitamin D compared to 39% sufficiency in the White participant pool. Discussion: Our study suggests that a vast majority of obese children and adolescents are not getting enough Vitamin D through their diet nor through sun exposure. African-Americans had notably higher instances of Vitamin D deficiency. SCTR Institute, NIH

183 Predictors of Adequate Health Literacy In a Diverse Primary Care Sample with Type 2 Diabetes, Julie Teuber, Sujeet S Bains, Joni L Strom, L E Egede; Medicine, MUSC.

Background: Diabetes disproportionately affects minorities and populations with lower levels of education and socioeconomic status. Among diabetics, inadequate health literacy is common and has been associated with poor disease knowledge and self-management. The objective of our study was to determine the sociodemographic predictors of health literacy in a minority diabetic population. Methods: 674 type 2 diabetes patients were recruited from three medicine clinics. A validated survey and screenner was used to assess sociodemographics and health literacy. Health literacy status was dichotomized into inadequate and adequate health literacy. Health literacy status was compared by demographics using chi-squared statistics. Logistic regression models were used determine independent predictors of health literacy. Results: 66% of the sample were African American, 39% were 65+ years, 24% had less than a high school education, and 75% percent of our sample had adequate health literacy. There were significant differences in health literacy by demographic characteristics. Among those with adequate literacy, it was higher among white race (Whites 80%, Blacks 72%; p<0.02), married status (78% married, 71% unmarried;p<0.05), higher education (92% college +, 60% < high school; p=0.001), those employed (89% employed, 70% unemployed; p=0.001), those insured (83% private insurance, 77% noninsured;p=0.02), and higher income (92% > $35,000, 64%<$10,000; p<0.001). In the our logistic regression model, independent correlates of adequate health literacy were higher education (p=0.02), being employed (p=0.006), and higher income (p<0.001). Hispanic/other race was associated with inadequate health literacy (p=0.03). Conclusions: In our sample, health literacy status varied by sociodemographics. Independent predictors of adequate health literacy included higher educational status, being employed, and higher income. Further research should be implemented to identify the mechanism by which these sociodemographic characteristics relate to health literacy in this population. Also, further studies should identify strategies to increase health literacy in minority groups at risk. MUSC Center for Health Disparities

184 Multiple Cardiovascular Risk Factor Control (MCRFC) Across Sites of Care in Type 2 Diabetes, Jacob C DeWeerth, Clara E Dismuke, Joni L Strom, Leonard E Egede; Medicine, MUSC.

Background: Diabetes affects 8.3% of the US population. Glicemia (HbA1c), Low-density Lipoprotein (LDL) cholesterol and blood pressure (BP) control are the main cardiovascular risk factor targets for clinicians in managing diabetes. There is little evidence regarding the association of facility type with diabetes outcomes. We examined the association of facility type with single and a multiple measure of control of cardiovascular risk factors (MCRFC).Methods: 534 individuals with type 2 diabetes were recruited from a private hospital affiliated clinic (MUSC), a Federally Qualified Health Center (FQHC) and a VA facility. We created MCRFC which took the value of 1 if all three factors under control. We performed chi2 to examine socioeconomic, separate risk factors and MCRFC by facility. We estimated the independent association of facility type with each risk factor and MCRFC, adjusting for covariates in logistic regression.

Results: At FHQC, individuals were predominantly Black (84.83%), female (65.56%), 50-64 (52.81%), unmarried (70.06%), high-school graduates (43.75%), unemployed (72.30%), uninsured (45.76%) with less than $10,000 income (54.34%). At VA, individuals were predominantly Black (51.88%), male (97.51%), 50-64 (46.47%), married (52.08%), some college (47.48%), unemployed (79.17%), government insured
(75.00%), had $35,000 plus income. At MUSC, individuals were predominantly Black (65.13%), female (66.41%), 65 plus (42.15%), unmarried (59.5%), equally less than high school (30.23%) and high school (30.23%) educated, unemployed (75.38%), government insured (74.71%), had $35,000 plus income. In an unadjusted analysis, at FQHC, 38.89% had BP, 51.63% LDL, 10.43% MCRFC control. At VA, 57.74% had BP, 74.15% LDL, 19.17% MCRFC control. At MUSC, 37.35% had BP, 64.37%, 7.34% MCRFC control. After adjustment, MUSC associated with 57% lower MCRFC (OR 0.428, 95% CI 0.187:0.978), male with 277% higher MCRFC, Black with 44% lower MCRFC. Conclusion: After adjusting for socio-economic factors, VA facilities are associated with better MCRFC in individuals with diabetes.

**185 Effect Of Delayed Discounting On Multiple Diabetes Outcomes In Adults With Diabetes.** Adam H Fox, Clara E Dismuke, Joni L Strom, Leonard E Egede; Medicine, MUSC.

Background: Diabetes affects 8.3% of the US population. Glycemia (HbA1c), Low-density Lipoprotein (LDL) cholesterol and blood pressure (BP) control are the main cardiovascular risk factor targets for clinicians in managing diabetes. Delayed discounting (DD) is a measure of an individual’s impulsivity based on willingness to forgo benefits today to receive a higher amount in the future. It is being increasingly considered as a barrier to patient adherence. We examined the association of DD rates with BP, HbA1c and LDL. Methods 534 individuals with type 2 diabetes were recruited from MUSC a private hospital affiliated clinic, VA and the Franklin C. Fetter Federally Qualified Health Center (FQHC). We used the 1996 Kirby model of delayed discount rate to estimate an individual’s level of impulsivity on a scale of 1-9 with 1 representing the lowest impulsivity and 9 representing the highest impulsivity levels. We estimated Pearson correlations of DD and impulsivity with BP, HbA1c and LDL. We estimated independent association of DD with each diabetes outcome adjusting for covariates. Results: Our sample was predominantly Black (65.63%), 50-64 (44.85%), male (56.37%), unmarried (59.50%), unemployed (76.18%), government insured (66.52%), less than $10,000 income (35.37%) and better or same health status as previous 12 months (71.99%). Unadjusted correlation showed no association between DD, impulsivity and diabetes outcomes. Adjusted analyses showed that each additional point in DD rate was associated with 1.89 lower systolic BP (95% CI -33.73:-2.05) BP. In same model, Black was associated with 9.67 higher systolic BP relative to White, private insurance 7.07 lower, and government insurance 5.72 lower, relative to uninsured. VA was associated with 7.88 lower, and MUSC 5.76 lower systolic BP relative to FQHC. Conclusion: In adjusted models, DD rate is associated with lower systolic BP. DD rates may have implications for clinical management of BP in individuals with diabetes. NIH/NIDDK T35 DK007431-26 (09012151)

**186 Differential Inflammatory Response Could Contribute To The Disparity Of Barrett's Esophagus and Esophageal Adenocarcinoma In European Versus African Americans.** Jason B Wheeler, Dennis K Watson, Elizabeth Garrett-Mayer, Carolyn E Reed; MSCR, MUSC, Pathology, MUSC, Biostatistics, MUSC, Surgery, MUSC.

Abstract not available.

**187 Does Completion Lymphadenectomy Improve Survival for Patients with Sentinel Node-Positive Cutaneous Melanoma of the Head and Neck? Experience From The SEER Database, Valerie A Smith, Joan E Cunningham, Eric J Lentsch; Otolaryngology-Head and Neck Surgery, MUSC, Biostatistics and Epidemiology, MUSC.

It is unclear whether completion lymph node dissection (CLND) improves outcomes in patients with sentinel lymph node (SLN) positive cutaneous melanoma of the head and neck (CMHN). Given the risk of morbidity associated with CLND in the head and neck, it is important to understand this procedure’s impact on survival. Hence, our objective was to determine the effect of CLND on survival in SLN-positive CMHN patients. We used the Surveillance Epidemiology and End Results database to identify patients with SLN-positive CMHN (n=350). Clinicopathologic data and 5-year disease-specific survival (DSS) were examined for patients who underwent sentinel lymph node biopsy (SLNB) alone (n=140) vs. SLNB+CLND (n=210). Patients in the SLNB-only group were significantly older (median age 62 vs. 53 years, p<0.0001). Overall, DSS was similar among patients in the SLNB+CLND and SLNB-only groups (p=0.7). On subsequent subgroup analyses, CLND did not improve survival for patients with thick (>2mm) or ulcerated tumors, or those greater than or equal to age 60 regardless of tumor characteristics. However, CLND was associated with improved DSS for a subgroup of patients less than age 60 with thin (≤2mm), non-ulcerated tumors (p=0.03). Thus, with the exception of this subgroup of patients with low risk tumor characteristics, CLND does not appear to improve survival for the majority of patients with CMHN. Still, our study is the first to demonstrate any survival benefit associated with CLND in SLN-positive melanoma. Our results support the notion that increasing tumor depth, tumor ulceration, and nodal metastases denote a more invasive metastatic property of melanoma that is not likely to be overcome by achieving regional disease control. Also, age appears to be a significant factor in CMHN that is related not only to prognosis, but to treatment outcomes as well.
differ in alkyl chain length and desaturation. Synthesis of quinolones requires the enzymes encoded by the first four genes of the pqsABCDE operon and pqsH. PqsD is a condensing enzyme homolog that condenses the anthraniloyl moiety with a malonyl-CoA to form 2,4-dihydroxyquinoline (DHQ) or a 3-oxo-fatty acid to form an alkylquinolone. Thus, PqsD is a crucial gatekeeper catalyzing the reactions at the branching point of quinolone biosynthesis in Pa. We examined the catalytic activity of PqsD using 3-oxo-fatty acids of various chain lengths in vitro. The results revealed that PqsD required a minimum chain length of ten carbons to perform a condensation reaction, suggesting that the chain length of fatty acid substrate is critical in positioning the carboxylic group for efficient catalysis. Further analyses of the kinetics and catalytic mechanisms of PqsD showed that malonyl-CoA was the preferred substrate of PqsD in vitro. Alanine mutants of the active site triad (Cys112, His257, and Asn287) were constructed and purified to determine the residues required for PqsD activity. We found that Cys112, His257, and Asn287 were all necessary for condensation, whereas Asn287 was not required in the formation of anthraniloyl-PqsD intermediate. Finally, we identified inhibitors of PqsD based on its structure using a flexible docking program to virtually screen the ChemBridge’s DIVERSet compound library. The top-scored virtual hit compounds were assessed for their effects on PqsD activity in vitro and the production of quinolone-dependent virulence factors in vivo. 

190 Severe Hunter Syndrome (Mucopolysaccharidosis II) Phenotype Secondary to Large Deletion in the X Chromosome

Introduction: We present a two-year-old Honduran male with severe infantile global neurodevelopmental delays, macrocephaly with a prominent forehead, coarse facial features with clear corneas, chronic congestion with snoring, wide-spaced teeth, hepatomegaly, inguinal hernia, early claw-hand deformities, and severe generalized hypotonia of his trunk and extremities. Initially, urine glycosaminoglycan testing showed increased dermatan and heparan sulfate and iduronate-2-sulfatase activity was deficient, consistent with the diagnosis of Hunter syndrome. Because of his markedly severe clinical presentation, additional genetic testing revealed that all IDS coding exons failed to amplify via polymerase chain reaction and multiplex ligation-dependent probe amplification analysis confirmed a deletion of all nine exons of the IDS gene. Methods: Oxford Gene Technology chromosome X microarray was performed. Results: X...
chromosome microarray revealed a large 3.2 Mb deletion encompassing the genes IDS, FMR1 and FMR2. Along with the original diagnosis of Hunter syndrome, deletion of FMR1 adds an additional diagnosis of classic Fragile X syndrome. Deletion of FMR2 results in mild neurodevelopmental delays without the typical clinical features of Fragile X syndrome. Many of the clinical features associated with both Hunter and Fragile X syndrome progress and become more clinically evident as the patient ages. It is difficult to determine which deleted gene (IDS, FMR1, FMR2) is the primary causative agent for our patient’s severe neurodevelopmental delays. We compare our patient to other cases reported in the literature, only one of those a male. Conclusion: This case demonstrates that advancing technology, such as X chromosome microarray, provides additional resources to better understand the underlying etiology for individuals with neurodevelopmental disabilities. This case is also a reminder to clinicians that further diagnostic testing is warranted if there is concern that a patient’s phenotype is more severe or complex than would be expected for the initial neurogenetic diagnosis.

191 The Role of Complement Peptides, C3a, in Host Defense Against Candida, a Human Fungal Pathogen, Geoff Bloomquist¹, Caroline Westwater²; ¹College of Dental Medicine, MUSC, ²Craniofacial Biology, MUSC.

Abstract not available.

192 RPE65 Protein is Present Within Human Cones to Enhance Photopigment Regeneration for Vision, Peter H Tang¹, Mona Buhusi¹, Rosalie K Crouch²; ¹Neuroscience, MUSC, ²Ophthalmology, MUSC.

RPE65 is an abundantly expressed protein within the retinal pigment epithelium (RPE) of the eye that is required for retinoid metabolism to support vision. Its genetic mutations are linked to the congenital disease Leber congenital amaurosis Type 2 (LCA2) characterized by the early onset of central vision loss. Current gene therapy trials have targeted restoration of functional RPE65 within the RPE of these patients with some success. Recent data show RPE65 is also present within mouse cones to promote function. In this study, we evaluated the presence of RPE65 in human cones and investigated its potential mechanism for supporting cone function in the 661W cone cell line. We found that RPE65 was selectively expressed in human green/red cones but absent from blue cones and mediated ester hydrolysis for photopigment synthesis in vitro. These data suggest that cone RPE65 supports human diurnal vision, potentially enhancing our strategies for treating LCA2. NIH R01 EY04939; C06 RR015455; Foundation Fighting Blindness, Inc.; and Research to Prevent Blindness

193 Melatonin Attenuates Oligodendrocyte Cell Death and Myelin Loss, Okwuchukwu G Obi¹, Arabinda Das², Narendra L Banik²; ¹Medicine, MUSC, ²Neuroscience, MUSC.

Studies have shown that melatonin (MEL) has neuroprotective properties that confer efficacy in the treatment of spinal cord injury (SCI). These studies show that MEL attenuates SCI induced cell death in neurons and astrocytes by attenuating expression and activities of pro-apoptotic proteins. However, whether melatonin protects oligodendrocytes following SCI remains unknown. Because oligodendrocytes are essential for proper myelination of axons within the spinal cord, their preservation following injury may promote functional recovery. We therefore studied the neuroprotective effects of MEL following SCI with emphasis on oligodendrocytes. Rats were divided into 4 groups: sham+vehicle; sham+MEL, injury+vehicle and injury+MEL. Sham rats received laminectomy only. SCI was induced in animals using a standard weight drop method (40 g, cm force) at T10. Injured animals were treated with either 45 mg/kg MEL (dissolved in dimethyl sulfoxide, DMSO) or vehicle via ip injection 15 minutes post injury and were sacrificed at 48hrs. Western blotting was used to quantify expression of pro-apoptotic proteins (Bax and Caspase-3), anti-apoptotic factors (Bcl-2) and melatonin receptors (MT1 and MT2). The effect of MEL in oligodendrocytes was investigated using cell specific antibodies (mab328), mCalpain, myelin basic protein (MBP) and cell death was evaluated by TUNEL staining. Results obtained indicate that there is a significant decrease in the expression of Bax and Caspase-3 in MEL treated animals. The neuroprotective effects of MEL were also associated with increased expression of Bcl-2 and melatonin receptors, indicating that MEL may act via receptor mediated pathways. Immunoﬂuorescent labeling demonstrated a pattern of increased MBP and mab328 with a concurrent decrease in TUNEL and mCalpain expression in MEL treated animals. These results validate previous studies that melatonin prevents neuronal and glia apoptosis in acute SCI. Furthermore, our data indicate that MEL reduces oligodendrocyte death and maintains myelin integrity. Minority Medical Students in Cardiovascular Research

194 The Role of the Prrx-1 Gene in Cell Proliferation During Secondary Palate Development, Charles Moore¹, Michael Kern², Christine Kern²; ¹Dental Medicine, MUSC, ²Regenerative Medicine and Cell Biology, MUSC.

The Prrx-1 gene is a homeobox transcription factor, the absence of which causes craniofacial malformations in mouse models. One of the malformations shown in Prrx-1 -/- mice is a cleft palate. In this study we use immunohistochemistry to examine the difference in size of the palatal shelves.
and the relative amounts of cell proliferation and cell death that occur among mesenchymal cells within the palatal shelves. Our results showed a statistically significant difference between the wildtype (WT, Prx-1+/+) and knockout (KO, Prx-1 -/-) with regard to total cell number and the number of actively proliferating cells in the palatal shelves at embryonic age 13.5, however the ratio of dividing cells to total cells remained similar in both the WT and KO. There was also no difference in the amount of apoptosis occurring in the shelves at the same age. These results suggest that the size difference of the palatal shelves seen in the Prx-1 -/- mice is not caused by a change in cell proliferation or cell death at E13.5. The size difference could, however, result from a difference in proliferation earlier in embryonic development and needs further evaluation.

**195 Expression of Nucleobindin-2/Nesfatin-1 in Bone Tissue**, Tejas Doshi, Lauren Ball, Alexis Nagel; Pharmacology, MUSC.

Nesfatin-1 is a recently discovered hormone that has been found to have an anorexic effect by acting on the hypothalamus. It is cleaved from the prohormone Nucleobindin-2 (NUCB2) by prohormone convertases. NUCB2 is found in many tissues of the body, including bone tissue, which allows for release of Nesfatin-1. Recently, bone tissue has been found to have some endocrine function in regulating blood glucose levels by communicating with pancreatic islet beta cells. Few studies have been conducted on NUCB2 and Nesfatin-1 protein expression in bone tissue. NUCB2 and Nesfatin-1 may aid in the endocrine function of bone tissue. Previous studies have indicated that NUCB2 expression and secretion increases as adipocytes differentiate and when they are stimulated by insulin. Based off of those studies we hypothesize that NUCB2 expression will increase as osteoblasts differentiate and when they are stimulated by insulin. In this study we observe the effects on increasing concentrations of insulin (10nM, 100nM) on the protein expression of NUCB2 after 3 days of osteoblast differentiation in mouse osteoblast cells (MC3T3E1). Then the cells underwent an overnight starve and were stimulated by different concentrations of insulin for twenty-four hours. Compared to the untreated and starve only treatments, we found the protein expression of NUCB2 decreased as the insulin concentration increased over the 3 day period. In the future we would like to repeat this experiment and conduct it over a longer time course. Future studies may determine if NUCB2/Nesfatin-1 may be able to be used for treatment in obese individuals and those with diabetes.

**Summer Health Professionals**

**196 Mitochondrial Dysfunction in Degenerative Pathologies**, Danielle M Desjardins1, Craig Cano Beeson2; 1MUSC, 2Pharmaceutical & Biomedical Sciences, MUSC.

**197 The Effect of IRS-1 Modification By N-acetyl Glucosamine (O-GlcNAc) on the Insulin Response**, Tabatha B Davis1, Katherine Robinson1, Maria G Buse1, Lauren Ball2; 1Endocrinology, MUSC, 2Pharmacology, MUSC.

Abstract not available.

**198 Imbalance in Histone Acetyl Transferase and Histone Deacetylase Activity During Hypertrophy**, Christopher R Smith1, Mona S Li1, Olga Chernysh1, Elizabeth S Inks2, James C Chou2, Santhosh K Mani1, Donald R Menick1; 1Cardiology, MUSC, 2Pharmaceutical and Biomedical Sciences, MUSC.

The high rate of morbidity in patients with diastolic heart failure, along with the 62 million people in the US annually diagnosed with some form of cardiovascular disease emphasizes the need for alternative means of therapy to treat heart failure. Previous work has demonstrated that inhibition of histone deacetylase (HDAC) activity has protective properties and significantly decreases symptoms associated with pressure-overload induced hypertrophy. This suggests that the natural equilibrium at which histone acetyl transferase (HAT) and HDAC enzymes are maintained in healthy heart tissue could be shifted in diseased myocardium. However, no one has measured HAT or HDAC activities in the normal or hypertrophic heart. We hypothesize that the normal balance of enzymatic HAT/HDAC activity is disrupted under pathological hypertrophic conditions. To investigate, feline myocardium were subjected to Pulmonary Artery Banding (PAB) to cause pressure overload induced hypertrophy for periods of 2 weeks, 4 weeks, and 8 weeks, and then examined for HAT activity to support previous findings of HDAC activity. Results indicated a decrease in HAT activity after 2 weeks and an even more pronounced decrease in the 4th week of pressure overload. HAT activity was still significantly decreased after 8 weeks of pressure overload, in comparison to the non-banded feline myocardium. HAT and HDAC activity in isolated adult cardiomyocytes and cardiac fibroblast was much lower than what is seen in other cell types. These results suggest that there is a disruption in the normal balance of HAT/HDAC activity in pathological hypertrophy. Inhibition of HAT/HDAC enzyme activity may be a potential therapeutic target for the treatment of heart failure.

**NIH Grant for Minorities**

**199 Interstitial Trafficking of MicroRNAs Within the Human Myocardium Following Ischemia-Reperfusion**, Ashley B Arana, Robert E Stroud, Risha Patel, Jeffery Jones, Francis G Spinale; Cardiothoracic Surgery, MUSC.

MicroRNAs (miRs) comprise a large family of short nucleotide sequences that have been recently...
identified to influence a large majority of biological processes through regulation of post-transcriptional events. For example, basic studies have revealed that certain miRs regulate myocardial growth and survival pathways critically involved in the response to ischemia/reperfusion (I/R). However, whether the interstitial space between cells may serve as a reservoir for miRs and whether and to what degree intracellular trafficking of miRs may actually occur within the human myocardium remains unknown. This project tested the central hypothesis that a large array of miRs reside within the human myocardial interstitial space which dynamically change following a period of I/R. Myocardial interstitial fluid (MIF) was collected through the placement of microdialysis probes (0.77 mm OD, 20kDa, cutoff) into the left ventricular midmyocardial wall in patients undergoing elective coronary artery bypass surgery (66± 3 yrs, n=7, informed consent) requiring a period of cardioplegic myocardial arrest followed by reperfusion (I/R). RNA was extracted from the MIF (extraction efficiency of 76± 1%, CV= 2.2%) and then subjected to a miR superarray (352 miRs) under steady-state, baseline conditions and following I/R (conventional established threshold of >2 fold change considered significant). Within the MIF, 325/352 miRs were detectable under baseline conditions, and 59 miRs significantly changed within the MIF following I/R; whereby 42 miRs increased (suggesting increased cellular export) and 17 miRs decreased (suggesting cellular import). Using a bioinformatics approach regarding miR targets (TargetScanHuman) and clustering analysis (Database for Annotation, Visualization and Integrated Discovery;DAVID), miRs that changed dynamically after I/R were predominantly in functional classes related to transcription, macromolecular biosynthesis, DNA binding, RNA Polymerase II regulation, and RNA metabolic processes. This study demonstrated for the first time, that within, a detectable and diverse portfolio of miRs exists within the human myocardial interstitium, which dynamically changes with a physiological stimulus such as I/R. Thus the interstitium likely serves as an important reservoir for miRs, which are imported and exported from myocardial cells. Moreover, miR trafficking within this extracellular space may be an important form of cell-to-cell regulation and communication. NIH Cardiovascular Summer Fellowship

**200 Progression of Arterial Stiffness and Coronary Atherosclerosis: Longitudinal Evaluation By Cardiac Computed Tomography**

By Cardiac Computed Tomography, Shane Oberoi, U Joseph Schoepf, John Nance; Radiology, MUSC.

Abstract not available.

**201 Radiation Dose and Image Quality At High-Speed CT Angiography of the Aorta: Intra-Individual and Inter-Individual Comparison with Conventional CT Angiography**

E Lexworth Hanna¹, Paul Apfaltrer¹, J. Reid Spears¹, Garrett W Rowe¹, Daniel Harris¹, Stefan O Schoenberg², Rozemarijn Vliegenthart¹, U Joseph Schoepf¹; ¹Radiology, MUSC, ²Clinical Radiology and Nuclear Medicine, University Medical Center Mannheim.

We evaluated the radiation dose and quantitative image-quality parameters at high-speed CT angiography (CTA) of the thorax and abdomen/pelvis, with comparison to conventional CTA. We searched PACS for all patients who underwent CTA of the thorax and abdomen/pelvis to evaluate the aorta between September 2009 and March 2011. This retrospective study included 110 patients (65 male, mean age 64±15 years), of which 50 had undergone high-speed CTA on a 2nd generation dual-source CT system. Selection of the high-pitch scan protocol was based on patient size (≤30 kg/m2 body mass index). Main indications were suspected aortic syndrome (n=12), follow-up of aneurysm (n=37) or dissection (n=20), or post aortic repair (n=35). For quantitative analysis we calculated the mean arterial attenuation, contrast-to-noise ratio (CNR), and figure of merit (FOM) at multiple aortic levels. In addition to this, radiation dose exposure was compared between the two groups. All scans were considered of diagnostic quality for their indication. At high-speed CTA, mean kV and mAs were 118±7 and 197±78, respectively, compared to 120±1 and 258±78 for conventional CTA (p<0.05). Mean volume CT dose index (CTDvol), Dose Length Product (DLP), and effective dose (ED) were 8.1±2.4 mGy, 561±179 mGy*cm, and 9.6±3.0 mSv at high-speed CTA versus 18.3±7.7 mGy, 1163±480 mGy*cm, and 19.8±68.2 mSv at conventional CTA (p<0.001). Aortic enhancement was not significantly different between the two groups, while significantly less iodine contrast medium was injected for high-speed CTA (87.3±16 mL vs. 97.9±16 mL, p<0.01). There was significantly less SNR and CNR in the conventional CTA group (<0.01), while differences in FOM were non-significant. In 20 patients who had undergone both high-speed and conventional CTA, radiation dose was reduced by 45% (p<0.001), while differences in contrast medium volume and enhancement were non-significant. High-speed CTA of the aorta provides low radiation exposure while maintaining excellent image quality. Summer Health Professionals Research Grant
202 Stimulation of Human Aortic Endothelial Cells (HAEC) with OxLDL-IC Stimulates Fc Gamma Receptor Expression and Endothelial Dysfunction, Katalina Romero, Yanchun F Li, Gabriel Virella, Maria Lopes-Virella, Medicine, MUSC, Endocrinology, Diabetes & Medical Genetics, MUSC, Microbiology & Immunology, MUSC.

The initial step in the cascade of events that leads to vessel wall inflammation and atherosclerosis is believed to be endothelial dysfunction. Circulating LDL transmigrates through the endothelial wall and undergoes modification. Oxidized LDL (oxLDL) has pro-inflammatory properties mediated by macrophage activation, which leads to increased expression of Fc and other receptors and release of pro-inflammatory cytokines. OxLDL can diffuse back across the endothelium into circulation, eliciting the formation of autoantibodies. OxLDL autoantibodies can form antigen-antibody complexes (immune complexes, IC) and those IC are able to activate phagocytic cells more strongly than oxLDL alone as a consequence of the interaction and cross-linking of Fcγ receptors (FcγR). Mesangial cells, which in their resting state do not express FcγR, do so after incubation with IC containing oxidized LDL (oxLDL-IC), but not if incubated with oxLDL alone. In this study, we have studied the effect of oxLDL-IC on FcγR and E-selectin expression by human aortic endothelial cells. We found that OxLDL stimulated the expression of FcγRI and E-selectin. The timing sequence suggests that the activation of FcγRI expression is mediated by engagement of LDL scavenger receptors, while the expression of E-selectin is mediated by the interaction of IC with FcγRI. NIH Summer Fellowship for Minority Students

203 Kaposi’s Sarcoma-Associated Herpesvirus Induced Expression Of Emmprin On The Cell Surface Following De Novo Infection Of Endothelial Cells, Paul A Bomar, Christopher Parsons, Infectious Disease, MUSC.

Abstract not available.

204 Mammary Gland Laterality in Normal and Neoplastic Development, Jacquelyn P Robichaux, Joan E Cunningham, Demetri D Spyropoulos, Regenerative Medicine and Cell Biology, MUSC, Biostatistics, Bioinformatics and Epidemiology, MUSC, Pathology and Laboratory Medicine, MUSC.

According to the American Cancer Society, approximately 230,500 new cases of invasive breast cancer will be diagnosed this year in the U.S. Our work addresses a virtually unstudied feature of the disease: the left-sided prevalence of tumors. Although the left-sided bias is modest (5-7% increase), it nevertheless is a consistent finding in epidemiological studies performed with worldwide databases spanning several decades. We hypothesize that the increased incidence of left-sided breast cancer reflects differential susceptibility of the left and right mammary glands to tumor initiation and/or progression. To test this, we are investigating whether the left and right-sided mammary glands of pubertal stage mice are equally responsive to high-dose estrogen exposure—a well-documented primary risk factor for breast cancer. Ongoing experiments involve injecting female FVB mice with high or low doses of estrogen for five days following birth. Mammary glands are then harvested at postnatal days 25-29 for morphometric analysis, including the area of the ductal network, number of branch points, and number of terminal end buds. Preliminary results suggest that high dose (35 µg), but not low dose (2 µg), estrogen treatment promotes L-R asymmetric growth of the thoracic mammary glands compared to non-estrogen treated mice, which have symmetric ductal network development. To identify genes that may drive L-R asymmetric ductal network growth, studies are underway to examine embryonic expression of nodal, a TGFβ family member that regulates L-R axial patterning, during normal embryonic mammary gland development. The lateral plate mesoderm and overlaying ectoderm asymmetrically express nodal during early development and also give rise to the mammary glands as well as other tissues. We hypothesize early asymmetric expression of nodal cause mammary glands to have a differential susceptibility to neoplastic conditions. NIH R21HD068993

205 Identifying Cancer-Associated Inflammatory Genes: A Data-Mining Approach, Saleh M Rachidi, Tingting Qin, Jim Zheng, Zihai Li, Microbiology and Immunology, MUSC, Biochemistry and Molecular Biology, MUSC.

An intricate relationship exists between cancer and the immune system. As transformed cells display “non-self” antigens, they become subject to immune-surveillance which halts tumor progression. However, some cells eventually acquire an immune-suppressive phenotype and evade adaptive immunity. In fact, cancer hijacks the immune system and uses its machinery to nourish and invade. This warranted immunological interventions in multiple cancer types. To point out conserved inflammatory patterns in the process of carcinogenesis, we decided to look for aberrantly regulated inflammatory genes in seven epithelial cancer types: Breast, prostate, lung, colon, gastric, pancreatic and oral cancers. Using microarray gene expression data from 555 human samples among the seven cancer types, we identified 96 genes which are consistently differentially expressed (Fold change > 2, p < 0.05) between cancer and normal tissue. To check for the expression of these genes on the protein level, data from microarray analysis was verified by immunohistochemistry (IHC). Using Human Protein Atlas (HPAT) database, IHC results were
obtained for the 96 genes on normal and cancer tissue from 6 out of the 7 cancer types. Most of the identified genes showed differential expression at the protein level as well. To determine whether these conserved genes have any clinical significance, we identified clinical correlations with most of these genes in terms of tumor grade, stage, recurrence and patient survival. Moreover, we mapped these genes into a few pathways and networks, highlighting certain inflammatory signaling machinery in the process of cancer initiation and progression. This work sheds light on conserved inflammatory profiles in epithelial cancers. These genes could serve as potential targets in cancer immunological therapy and/or predictive indicators to identify patients who could benefit from immunological interventions.

**206 NAVIGATE: A Trial to Increase Patient Enrollment in Thoracic and Esophageal Cancer Clinical Trials**, Kathleen B Cartmell1; Marvella E Ford2; Nestor F Esnaola3; Tricia A Adrales-Bentz4; Terri L Matson5; Carolyn E Reed6; Debbie C Bryant7; Anthony J Alberg8; Lauren A Smith1; James D Bearden9; Howard A Zaren7; Anita L Harrison4; Anthony J Alberg1,3; Lauren A Smith1; James D Bearden9; Howard A Zaren7; Anita L Harrison4

Discovery of effective cancer treatments is limited by challenges recruiting patients in cancer clinical trials (CTs). Approximately 49% of patients invited to participate in a CT do not participate. One reason for low trial participation is due to barriers faced by patients related to trial participation, such as poor trial understanding, communication issues with the clinical team and logistical barriers. The few trials that have tested patient interventions to improve trial enrollment examined brief interventions (e.g. simplified consents, videos), none of which improved trial enrollment. Due to the barriers faced by patients and the complexity of the CT decision, it is likely that more intensive interventions are needed. We conducted a single arm pilot trial to determine if adding a lay navigator to the multidisciplinary thoracic and esophageal care team could improve trial enrollment. The study was conducted at three cancer centers, each of which recruited a lay navigator with a non-nursing background from the minority community. If a patient was deemed potentially eligible for a therapeutic trial and consented to navigation, navigators linked them to educational and support services, provided counseling about CTs, and facilitated communication between the patient and clinical team. The NCI Clinical Trials Video was utilized as a patient teaching tool to open discussions about the CT option. Of the 38 navigation trial participants, 84% agreed to participate in a CT, compared to 49% documented in the literature. African American (AA) patients who received navigation were 30% more likely to participate in CTs than Caucasians who were navigated. The number of AA patients who participated in a CT increased from 1 AA patient in the year preceding the trial to 8 AA patients in the intervention year. These results suggest that navigation can impact CT enrollment and that the intervention effect is greatest for AA patients. NCI 1P30CA138313-01

**207 MKP-1 Deficiency Enhances Epithelial Neoplasia in a Murine Oral Cancer Model**, Xiaoyi Zhang, Hong Yu, Keith L Kirkwood; Craniofacial Biology, MUSC.

Head and neck cancer accounts for approximately 6% of diagnosed malignancies in the United States, the most common form being head and neck squamous cell carcinoma (HNSCC). Despite research efforts, survival rates remain lower than other more common malignancies. Cytokines and pro-inflammatory factors have been shown to have a critical role in various steps of malignant transformation, including tumor growth, survival, invasion, angiogenesis, and metastasis. Many of these diverse cellular processes are regulated by mitogen-activated protein kinases (MAPK), such as p38, JNK, and ERK. These kinases are negatively regulated by MAPK phosphatases (MKPs), the founding member of this class being mitogen-activated protein kinase phosphatase-1 (MKP-1). Initial studies revealed significant over-expression of MKP-1 in a range of human epithelial tumors, seen in the early phases of disease with levels of MKP-1 expression falling progressively in tumors of higher histological grade and in metastases. We hypothesize low levels of MKP-1 in HNSCC generate high levels of inflammation which promote tumor development and progression. To address how MKP-1 signaling and regulation of inflammatory cytokine expression via MAPK activity may affect HNSCC development and progression, MKP-1 deficient and wild-type mice were treated with 4-nitroquinoline 1-oxide, a surrogate for tobacco exposure, for 16 weeks and monitored an additional 16 weeks. In the absence of MKP-1, animals show a significant increase in tumor development, characterized by onset of disease, tumor size, histological grade, and inflammation. In addition, isolated tissues demonstrate increased levels of inflammatory cytokines and receptors by qPCR and altered MAPK activity by immunoblot analysis. Ongoing work will be conducted to assess how MKP-1 regulates expression of these inflammatory targets and their impact on tumor development and progression. Elucidating the regulation of inflammatory mediators in the tumor microenvironment may reveal critical tumor suppressive interactions mediated by MKP-1 that are lost during cancer initiation and progression. MUSC MSTP; R01DE018290; P20 RR017696; and SCE&G Fellowship
208 The Role of Bone Morphogenetic Protein 4 in the Developing Inflow and Outflow Regions of the Heart, Laura Briggs, Jayant Kakarla, Aimee Phelps, Andy Wessels; Regenerative Medicine and Cell Biology, MUSC.

Although it will eventually assume a four-chambered conformation, the heart initially develops as a tube consisting of little more than an outer ring of myocardium and an inner layer of endocardium. Blood flows through this linear tube in one direction only, entering at a region termed the inflow (arterial pole) and exiting through the venous pole. While the initial tube is derived from a precursor population of cells termed the primary heart field, additional components are added at inlet and outlet extremities by cells of the second heart field. Eventually, a four-chambered organ results, with cells of the primary heart field contributing primarily to the left ventricle and second heart field cells forming the right ventricle and the outflow tract. Prior studies have indicated that the growth factor Bone Morphogenetic Protein 4 (BMP4) is essential for proper heart development, possibly by playing a role in neural crest migration and epithelial-to-mesenchymal transformation. In order to determine the role BMP4 plays in the formation of both the arterial and venous poles of the heart, we have utilized a cre-lox strategy to conditionally delete the BMP4 receptor Alk3 from the second heart field. Further illustrating the importance of this growth factor in the development of the heart, we have found both inflow and outflow abnormalities in mutant mice. Here, we will histologically and immunohistochemically describe these mutants and further characterize the role of BMP4 in the developing heart.AHA 11PRE7310036

209 Does Acetylation Regulate MiRNA Expression in Myocardial Infarction? Ludivine Renaud1, Harinath Kasiqanesan1, Santhosh K Mani1, Erhe Gao2, Jeffrey A Jones3, Robert E Stroud3, Donald R Menick2; 1Cardiology, MUSC, 2Center for Translational Medicine, Thomas Jefferson University, 3Surgery, MUSC.

Cardiovascular diseases are one of the leading causes of morbidity and mortality in the world, underlining the need for innovative therapies and diagnosis for heart disease. MicroRNAs (miRNAs) have been identified as central players in regulating gene expression. miRNAs are noncoding RNAs that bind to target mRNAs and reduce their expression. Several recent reports have demonstrated that some miRNAs are aberrantly expressed in cardiac arrhythmia, hypertrophy, fibrosis, ischemia, vascular atherosclerosis and heart failure. Histone deacetylase (HDACs) are a class of enzymes that affect the transcriptional regulation of genes during pathological conditions. Previous studies in our laboratory demonstrated that 1) class I and class II HDACs play an important role in the basal expression and upregulation of the sodium calcium exchanger (Ncx1) gene in adult cardiomyocytes and 2) treatment with HDAC inhibitor trichostatin (TSA) improved ventricular function by suppressing MMP9 gene expression in MI. SAHA inhibits class I and class IIA HDACs specifically and is currently FDA approved for T-cell lymphoma treatment. We hypothesize that SAHA treatment will ameliorate the shift in expression of some of the miRNA which are misregulated in MI. We utilized a novel coronary artery ligation to induce MI. Mice were divided into 5 treatment groups: SHAM control, MI-7days, MI-7days+SAHA-day0, MI-7days+SAHA-day1. We examined the expression level of miRNAs that have been shown previously to be aberrantly expressed in MI by RT-PCR. We show that miR-1, miR-29a, miR-133a, miR-208a and miR-486 are decreased 7 days post-MI, miR-760 remains constant and miR-21 is increased by 10 fold. Interestingly, SAHA treatment only significantly attenuated the abnormal expression of miR-21. miR-21 was previously shown to contribute to myocardial disease. Our preliminary data confirm this finding and introduce the novel idea that inhibition of HDAC by SAHA treatment could improve cardiac remodeling post MI and provide a potential therapy. NIH HL066223, AHA Grant in Aid 09GRNT2020202
and efficient healthcare system among Sickle Cell patients because it will allow each patient's primary care physician (PCP) to be alerted when a hospitalization or ED visit is likely to occur. This will prompt the PCP or PCP's nurse to contact the patient and ask patient-care questions and if necessary, schedule a timely clinic visit. This risk stratification model will benefit both the Sickle Cell patient and the hospital in terms of quality care and finances.

211 Natriuretic Peptides Protect the RPE From Advanced Glycation End Products-Induced Barrier Breakdown, Mohammad Dahrouj, Zsolt Ablonczy, Craig E Crosson; Ophthalmology, MUSC.

A central component of vision loss in diabetic retinopathy is the development of macular edema. Macular edema develops when the ability of retinal pigment epithelium (RPE) to actively remove fluid cannot compensate for the fluid entry from the retinal vasculature. Natriuretic peptides (NP) (atrial, brain, and C-type) play an essential role in cardiovascular homeostasis and the receptors for these peptides are expressed in the retina. However, their role in regulating retinal vasculature and the development of macular edema in response to the activation of the receptor for advanced glycation end products (RAGE) has not been investigated. We used transepithelial resistance (TER) to assess the barrier function of adult RPE (ARPE19) and primary human fetal RPE (hRPE) monolayers cultured on Transwell filters following human glycated albumin (RAGE agonist) treatment in the absence or presence of different concentrations (1pM to 100nM) of ANP, BNP or CNP. Immunohistochemistry and immunoblotting were used to test the expression and localization of the NPR in cultures. Initial data demonstrated that RAGE activation disrupts RPE barrier function. This response was concentration-dependent (EC50=2.3 µg/ml) with a maximal reduction in TER of 40±2% for ARPE-19 and 27±7% for hRPE at 100µg/mL. One hour pretreatment with ANP, BNP or CNP blocked this effect. The rank-order of agonist potency of natriuretic peptides was CNP (IC50=9.5 pM)>BNP(IC50=0.9 nM)>ANP(IC50=2.5 nM). The inhibitory response of NPs was reversed by the non-selective NPR inhibitor isatins (100µM). Immunohistochemistry and immunoblotting demonstrated the presence of NPR2 and NPR3. Our data demonstrate that NPs can reverse the increase in permeability in RPE monolayers induced by RAGE activation and that the NPR2 is the primary receptor that mediates this response. Taken together, these studies support the idea that NP agonists may be useful in the treatment of diabetic macular edema. EY019065

212 Valproic Acid (VPA) Reduces Retinal Ganglion Cell (RGC) Degeneration in a Rat Model of Ocular-Hypertensive Injury, Oday Alsarraf, Phillip W Yates, Craig E Crosson; Ophthalmology, MUSC.

Purpose: The dysregulation of protein acetylation is an integral event in the pathogenesis of cancer, inflammatory disorders and neurodegenerative diseases, including those of the retina. The current studies investigate if reduced histone deacetylase (HDAC) activity via administration of VPA can limit ocular-hypertensive retinal injury. Methods: Intraocular pressure (IOP) was elevated unilaterally in Brown Norway rats by hypertonic saline injection, and the rats divided into vehicle and VPA (100 mg/kg) treatment groups. VPA or vehicle was administered (i.p.) twice-daily for 28 days. At the end of the treatment period, RGC function and number was assessed by pattern electroretinogram (pERG) and retrograde FluoroGold-labeling. Contralateral eyes served as controls. Results: Hypertonic saline injections increased IOPs by 8-14 mmHg in ipsilateral eyes. In vehicle-treated animals, mean pERG amplitudes from hypertensive eyes were significantly reduced by 31% when compared to contralateral values. In rats treated with VPA, pERG amplitudes in hypertensive eyes were significantly increased when compared to corresponding eyes of vehicle treated animals. Analysis of FluoroGold labeled flat-mounts from vehicle-treated animals revealed a mean RGC density of 1964 ±60 cells/mm2 for contralateral control eyes and a significant decrease to 1155 ±49 cells/mm2 for hypertensive eyes. Whereas, in VPA treated animals, mean densities were 2049 ±64 and 1746 ±95 cells/mm2, in contralateral control and hypertensive eyes, respectively. There was a significant increase in labeled cells in hypertensive eyes from rats receiving VPA compared to vehicle-treated animals, but not between the contralateral eyes in the two groups. Administration of intraperitoneal VPA demonstrated an increase in acetylation levels in all retinal layers. Conclusions: These studies provide evidence that VPA provides structural and functional protection to RGCs during ocular-hypertensive stress. This protective action appears to be associated with the inhibition of retinal HDAC activity, providing a basis for development of HDAC inhibitors in the treatment of optic neuropathies. NIH/NEI EY-009741

213 Globin Regulatory Proteins As Components Of The Molecular Response To Hypoxia In Alveolar Epithelial Type II Cells, Robyn G Lottes¹, Danforth A Newton², Demetri D Spyropoulos³, John E Baatz²; ¹Molecular and Cellular Biology and Pathobiology, MUSC, ²Pediatrics and Neonatology, MUSC, ³Pathology and Laboratory Medicine, MUSC.

Severe hypoxic conditions in lung tissues are associated with a variety of human respiratory diseases including respiratory distress syndromes and
chronic obstructive pulmonary disease; however, the molecular response of alveolar cells to low oxygen tension is largely undefined. Determining the molecular basis of hypoxic response in alveoli has important implications for understanding the progression and outcome of these disease states, in addition to delineating the poorly-characterized mechanisms driving lung development. Previous work established that hemoglobin is expressed in alveolar epithelial type II cells (ATII) and is dramatically up-regulated in hypoxia. Here, we present findings indicating that hemoglobin-associated factors classically known to govern erythroid development, specifically GATA1 and HIF2α, are also involved in the response to hypoxia in ATII. shRNA transfection generated GATA1 and HIF2α knockdown in a mouse lung epithelial cell line. 2-dimensional gel electrophoresis, qPCR, and classical western blotting identified protein-level responses to hypoxia. Cumulatively, these studies suggest that globins and associated proteins are involved in an oxygen-sensitive pathway that governs hypoxia-induced shifts in cellular functions including metabolism, secretion, and apoptotic pathways. In stark contrast to humans, lungs of deep-diving marine mammals are subjected to severe, prolonged hypoxia without sustaining cellular damage. Mammals like the Pygmy Sperm Whale (PSW[Kogia breviceps]) collapse their lungs while diving, creating an alveolar environment of extremely low oxygen tension that would cause significant damage to pulmonary tissues in terrestrial species. Dissecting the means through which alveoli of diving mammals survive hypoxia has implications for treating human disease, but the molecular mechanisms behind their resilience are not understood. To this end, we have developed a line of ATII derived from PSW induced-pluripotent stem cells to be used for functional comparison to mouse ATII. Planned study employs knockdown and proteomics-based techniques to investigate differences in terrestrial and diving mammalian alveolar cell responses to hypoxia. 

Graduate Assistance in Areas of National Need (GAANN), Hollings Marine Laboratory Consortium for Research Training in Oceans and Human Health

214 A Comparison of the Differentiative Capacities of Induced Pluripotent Stem Cell (iPSC)-Derived Fibroblasts and Other Primary Fibroblasts in Hypoxia, Emily M Allen1, Demetri D Spyropoulos2, John E Baatz3; 1Marine Biomedicine and Environmental Science, MUSC, 2Pathology, MUSC, 3Pediatrics, MUSC.

Induced pluripotent stem cells (iPSCs) hold great promise in regenerative medicine and cell-based therapies. To utilize iPSCs in a clinical setting, it is crucial to demonstrate their potency (stable self-renewal and differentiative capacities). Through activation of 4 stem cell factors, we have established iPSCs from lung fibroblasts of the pygmy sperm whale (PSW), a deep diving mammal. PSW iPSCs provide a novel platform to study potency under very low oxygen tensions. We hypothesize that PSW iPSC-derived cells will demonstrate novel mechanisms to maintain differentiative capacities under hypoxic conditions. To first validate our PSW iPSC system, we tested for the expression of genes indicative of “stemness” (e.g. NANOG, DNMT3B, and c-Kit) as well as for the absence of differentiation markers (e.g. fibroblast procollagen). We have documented potency by differentiating the iPSCs to several lung cell types (i.e. ATIIs, Clara cells). However, adipogenic differentiation, which can be stimulated by oxidative stress, is a generally more accepted approach to assess differentiation. We used terrestrial and marine-derived fibroblasts to compare adipogenesis under hypoxic conditions (1.5% O2). Included in our study are phylogenetically comparable pig lung fibroblasts and NOX4-deficient mouse lung fibroblasts. Under hypoxic conditions, we observed that the PSW iPSC-derived fibroblasts accumulate lipid vesicles and are highly glycolytic, characteristics not representative of pig and mutant/wild type mouse fibroblasts. Results of this study will be presented and discussed in relation to human disease states involving adipocyte dysfunction. Adipocyte dysfunction involves NADPH accumulation in response to hypoxia and oxidative stress, and is also a major cause of obesity-related metabolic diseases, including insulin resistance, cardiovascular disease, and chronic inflammation. 

Graduate Assistance in Areas of National Need (GAANN) Fellowship; NSF Graduate Research Fellowship Program (GRFP)

215 Pseudomonas Aeruginosa: Utilizing Two Guns of Virulence - Swarming Motility and Biofilm Formation, Jordon D Gruber, Souzan Abdel-Samie, Yong-Mei Zhang; Biochemistry, MUSC.

Motility has been strongly implicated in bacterial pathogenesis for colonization and biofilm formation. Swarming motility forms tendrils in radial patterns and requires functional flagella and biosurfactant rhamnolipids in Pseudomonas aeruginosa, a versatile human pathogen that causes infections in burn and diabetic wounds, urinary tracts, and lungs of cystic fibrosis patients. PAO1 and PA14 are two common laboratory strains of P. aeruginosa. Although these strains share >90% sequence identity, PA14 exhibits higher virulence in various infection models. In this study, we examined the two strains for a panel of virulence phenotypes to determine the underlying mechanism for the increased virulence of PA14. On M9 medium, PA14 exhibited robust swarming motility whereas PAO1 did not swarm. The conditioned medium of both PAO1 and PA14 facilitated the swarming of PAO1 on M9 plates. PAO1 exhibited avoidance phenotype and did not cross paths with swarms of neither PAO1 nor PA14. In contrast, the swarming tendrils of PA14 were attracted to the PAO1.
swarm. Because the avoidance phenotype of swimming is mediated by rhamnolipids, we determined the concentration and composition of rhamnolipids of PAO1 and PA14. No significant difference in the concentration of rhamnolipids was detected, whereas the composition of rhamnolipids exhibited distinct patterns. Since rhamnolipid production is also important for biofilm formation, we studied the biofilm formation by PAO1 and PA14. The amount of biofilms of PA14 was about 50% of the PAO1; however, co-cultures with PA14 as the dominant strain in the inoculum exhibited 150% increase in biofilm formation compared to PAO1 alone. Further experiments with mutants of PA14 defective in rhamnolipid synthesis indicated that the HAA and mono-rhamnolipid components were important for increased biofilm formation in co-culture conditions. This research underscores the distinct abilities of P. aeruginosa lab strains in promoting virulence in response to extracellular metabolites using similar genetic machinery. NIH P20 RRO172766

216 Regulation of Sphingosine Kinase 1 By P53-Dependent Proteolysis, Brittany L Carroll, Linda A Heffernan-Stroud, Lina M Obeid; Biochemistry, MUSC. Bioactive sphingolipids have been implicated as important stress signaling molecules. Ceramide and sphingosine are thought to be involved in inducing apoptosis and cellular senescence, while sphingosine-1-phosphate (S1P) is a signaling molecule that induces cell proliferation and survival. Within the cell, the two isoforms of sphingosine kinase (SK), sphingosine kinase 1 (SK1) and sphingosine kinase 2 (SK2), are responsible for converting sphingosine into S1P. Once produced, S1P acts extracellularly on the G-protein coupled receptors S1P1-5 to induce many of its effects. SK1 levels are known to be elevated in several types of cancers that also have altered p53 status. We have found through the use of several DNA damaging agents, that p53 induction corresponds with SK1 degradation and subsequent decreases in S1P and increases in ceramide. This p53-dependent decrease in SK1 appears to be mediated by proteolysis. Through various cell studies we are in the process of defining the protease(s) involved in p53-dependent SK1 degradation. Our preliminary data implicate that Caspase 2 may be responsible for p53-dependent SK1 degradation. This regulation of SK1 and of bioactive sphingolipids by p53 has important implications to p53-mediated cancers and also could define a novel regulatory mechanism of bioactive sphingolipids by Caspase 2.

217 The E3 Ubiquitin Ligase EDD Regulates Platinum Resistance and is a Novel Therapeutic Target for Epithelial Ovarian Cancer, Amber T Bradley¹, Hui Zheng¹, Angela Ziebarth², Wayne Sakati³, Gabriel Lopez-Berestein³, Anil K Sood³, Charles N Landen², Scott T Eblen¹; ¹Cell and Molecular Pharmacology and Experimental Therapeutics, MUSC, ²Obstetrics and Gynecology, University of Alabama Birmingham, ³Gynecologic Oncology, University of Texas MD Anderson Center.

Ovarian cancer is treated with a combination of surgery and chemotherapeutics, including taxol and platinum agents. A major difficulty in eradicating these tumors is the selection of drug resistant cells. EDD (E3-ubiquitin ligase identified by Differential Display) is a p53 induced apoptosis in ovarian cancer cell lines, as evidenced by flow cytometry analysis of DNA content and western blotting for PARP cleavage. EDD siRNA-mediated knockdown resulted in loss of expression of the anti-apoptotic proteins Mcl-1 and Bcl-XL. Knockdown of Mcl-1, but not Bcl-XL, induced apoptosis equivalent to that seen with EDD siRNA and stable overexpression of Mcl-1 inhibited apoptosis induced by EDD knockdown. To separate EDD functions in basic cell survival from possible roles in cisplatin resistance, we generated EDD shRNA stable cell lines. These cells represent that portion of the population that can survive initial EDD knockdown. Three separate ovarian cancer cell lines with stable EDD knockdown demonstrated increased cisplatin sensitivity compared to cells expressing control shRNA. Importantly, EDD overexpression in COS-7 cells was sufficient to protect from cisplatin-induced apoptosis and the induced resistance was dependent upon EDD ubiquitin ligase activity. In vivo, mice treated with EDD siRNA by nanoliposomal delivery (DOPC) had a trend towards less tumor than those treated with control siRNA (27.7% reduction in ES2, 42.5% in A2780ip2). Mice treated with combined EDD siRNA and cisplatin had significantly less tumor than controls (77.9% reduction in ES2, 75.9% in A2780ip2) and cisplatin alone. Our results demonstrate that EDD is a viable therapeutic target for the treatment of ovarian cancer.

218 Development Of A Clinically Relevant Murine Model Of Pancreatic Cancer, Clayton S Lewis, Jody T Mack, Charles D Smith; Pharmaceutical and Biomedical Sciences, MUSC.

Pancreatic cancer is one of the most devastating cancers known. Among those diagnosed with pancreatic cancer, 74% will die within the first year and only 5% live beyond five years past diagnosis. The onset of metastasis, secondary to pancreatic cancer, typically results in a continuing life span of three to six months. Our lab is developing a murine model that more accurately represents the most common pancreatic cancer phenotype seen in humans. Current
models fail to take into account the large inflammatory and fibrotic responses seen in most cases of human pancreatic cancer. In order to recapitulate this inflammatory element of pancreatic cancer, our lab is developing a murine model based in the immunocompetent C57/Bl6 strain which includes orthotopic injection of luciferase expressing pancreatic cancer cell lines followed by subcutaneous injections of caerulein, a decapeptide analog of the potent pancreatic secretagogue cholecystokinin, which results in acute pancreatitis. Repeated administrations of caerulein leads to the more chronic pancreatitis phenotype seen in approximately 50% of human pancreatic cancer cases. Combining the orthotopic injection of luciferase expressing pancreatic cancer cells of C57/Bl6 origin (along with repeated acute occurrences of pancreatitis in an immunocompetent C57/Bl6 mouse) will provide an orthotopic, syngeneic model of pancreatic cancer who’s progression can be regularly monitored through bioluminescence imaging. The development of this model will be invaluable in our continued understanding of pancreatic cancer and in the development of therapeutics to treat this disease. NIH CA122226

219 Defining the Role of FLI1 in Breast Cancer, Melissa N Scheiber¹, Patricia M Watson², Victoria J Findlay¹, Tihana Rumboldt¹, Dennis K Watson¹; ¹Pathology, MUSC, ²Medicine, MUSC.

Breast cancer is the second most common cancer-related death among women in the US. The majority of the breast cancer-related deaths are due to tumor progression. A multitude of changes in gene expression are required for the cancer cell to acquire the ability to invade and migrate. The transcriptional activation or repression of these cancer-associated genes is not clearly understood, however many ETS family members have been considered good candidates. Friend leukemia virus integration 1 (FLI1) is an ETS protein that is aberrantly expressed in retrovirus-induced hematological tumors, and is found to be rearranged in Ewing’s sarcoma and related primitive neuroectodermal tumors characterized by a t(11;22)(q24;q12) translocation. Limited attention has been directed towards elucidating the potential role of FLI1 in epithelial-derived cancers, including breast cancer. Our preliminary immunohistochemical analyses show that FLI1 protein is decreased in human invasive breast tumors compared to normal breast tissue. A decrease of FLI1 mRNA and protein was also demonstrated in breast cell cancer cell lines through Real Time RT-PCR and western blot, respectively. We used adenovirus to examine the effects of FLI1 expression in an invasive breast cancer cell line (MDA-MB-231). Re-expression of FLI1 inhibited cell growth, mainly due to a decrease in cellular proliferation. FLI1 expression also inhibited the motility and invasiveness of the breast cancer cell line, determined by the use of Transwell inserts coated with fibronectin or Matrigel, respectively. We hypothesize that the loss of FLI1 is a critical step for breast cancer progression. Loss-of-function studies using shRNA are being performed in two non-transformed, immortalized human mammary epithelial cell lines (MCF-10A and MCF-12A) to complement the above gain-of-function studies. Future studies will investigate potential downstream targets of FLI1. Inhibiting the reduction of FLI1 or regulating its downstream targets may be to be unique targets of breast cancer therapy. NIH P01CA78582

220 Regulation of Telomerase By Sphingosine Kinase 2/Sphingosine-1-Phosphate Signaling in Lung Cancer, Shanmugam Panneer Selvam¹, Yuri K Peterson², Christopher R Gaul³, Lina M Obeid³; Jennifer S Isaacs⁴, Sarah Spiegel⁵, Charles D Smith⁶; Besim Ogetmen¹; ¹Biochemistry and Molecular Biology, MUSC, ²Pharmaceutical Sciences, MUSC, ³Medicine, MUSC, ⁴Pharmacology and Experimental Therapeutics, MUSC, ⁵Biochemistry and Molecular Biology, VCU.

Acid ceramidase is an important modulator of the cellular balance between ceramide, sphingosine, and sphingosine-1-phosphate. These bioactive sphingolipids have diverse, powerful, and often oppositional impacts on cell signaling, including the activation status of the oncogenic kinase Akt. Our studies show that acid ceramidase overexpression activates Akt in PTEN positive and PTEN negative cells. Interestingly, we observed that acid ceramidase promotes an increased cytoplasmic:nuclear PTEN ratio in diverse cell types with endogenous as well as exogenously expressed PTEN. Treatment with exogenous sphingosine 1-phosphate also promotes PTEN nuclear egress, thus suggesting sphingosine 1-phosphate mediates acid ceramidase induced PTEN nuclear egress. We have previously found that acid ceramidase is overexpressed in >85% of prostate tumors vs. normal adjacent tissue and that acid ceramidase overexpression in prostate cancer cell promotes cell proliferation. These observations open the door to many exciting possibilities for the role of acid ceramidase in cancer pathogenesis and progression through multi-faceted modulation of the Akt oncogene and the PTEN tumor suppressor. DoD PC101962
Cardiac valvulogenesis is dependent on heparin binding epidermal growth factor (HB-EGF) signaling via the receptor, ErbB1. This is evident in mice deficient in HB-EGF or ErbB1 which display hypercellularity of progenitor valve structures, endocardial cushions, as well as hyperplastic valves. Fibulin-1 (Fbln1) is a component of the extracellular matrix (ECM) of endocardial cushions and adult cardiac valves, but its function in the process of cardiac valvulogenesis is not known. Analysis of the hearts of Fbln1 null embryos reveals hypercellular endocardial cushions and increased levels of proliferation in developing valves. Mechanistically, the basis for these abnormalities may relate to the findings that Fbln1 binds both HB-EGF and ErbB1 and that it can promote HB-EGF stimulated activation of Erk1/2. Taken together, the findings highlight a critical role for fibulin-1 in valve morphogenesis and point to it possibly serving as a positive regulator of HB-EGF or ErbB1 signaling, which is required to prevent hypercellularization of endocardial cushions and consequential effects on valve formation. NIH HL095067

224 An Integrated Bioinformatic and Biochemical Approach to Identifying Caspase Activity During the Aging Process of Karenia Brevis, Jillian G Johnson, Frances M Van Dolah; Marine Biomedicine and Environmental Sciences, MUSC.

The induction of caspase activities during cell death has provided a new framework for understanding the evolutionary and ecological contexts of programmed cell death for a diverse group of phytoplankton species. However, the role of caspase activity during the chronological aging process has remained largely unexplored, and thus its impact on environmental processes remains unknown. In addition, the enzymes responsible for caspase activity in phytoplankton remain controversial. To identify the role caspase activity may play in the chronological aging process and identify the upstream and downstream pathway constituents of caspase – specific activities in K. brevis, a combination of biochemical cleavage analysis and in silico EST sequence data mining was employed. Quantification of caspase activities (caspase 1, 3, 6, 7, 8, and 9), determined by specific cleavage of fluorogenic canonical substrates, were assessed over the growth curve to gain an understanding of the presence, timing, and magnitude of K. brevis caspase activities during chronological aging. An induction of caspase activities was observed at the transition into and maintenance of stationary phase suggesting an active role for caspase-like enzymes in mediating the shift into quiescence, as opposed to during cell death as caspase activities decreased by the end of late stationary phase and culture demise was not observed. Targeted in silico bioinformatic mining for enzymes potentially responsible for the activities observed were next
identified from a K. brevis EST library. Finally, computational prediction of downstream caspase substrates using substrate sequence context and predicted secondary structure parameters identified proteins involved in a wide range of biological processes including regulation of protein turnover, cell cycle progression, lipid metabolism, coenzyme metabolism, apoptotic death, and autophagic death. Together, these results lend new insight into the diversity of processes involved in the modulation of aging and execution of death in dinoflagellates. NOAA

225 SPARC and the Collagenous Extracellular Matrix of the Periodontal Ligament, Jessica M Trombetta-eSilva1, Amy D Bradshaw2; 1Dental Medicine, MUSC, 2Medicine, MUSC.

In periodontal disease, there is inflammation to eradicate infection. This inflammation also causes destruction to the periodontal ligament (PDL) and alveolar bone. Currently, there are no therapies to promote regeneration of the PDL. Without regeneration of the PDL, periodontal disease patients eventually lose their teeth due to complete loss of attachment. PDL is primarily composed of collagen type I and fibroblasts. The mechanism of collagen secretion and extracellular assembly is not understood and involves many proteins. One such protein, SPARC, is a collagen binding protein that is ubiquitously expressed. We have previously demonstrated SPARC is expressed in the PDL at various ages, although most highly in 1-month and >18-month mice. SPARC-null mice have significantly less collagen in the PDL, indicating SPARC is essential to maintain collagen homeostasis in PDL. In addition, in a model of periodontal disease using the bacterial endotoxin lipopolysaccharide, SPARC-null mice had significantly more alveolar bone and PDL collagen loss despite a decreased inflammatory response as compared to similarly treated WT mice. Interestingly, after recovery time, WT and SPARC-null mice restored alveolar bone and PDL collagen to levels similar to that of uninjured. We conclude that SPARC is essential to maintain PDL ECM, as without SPARC the PDL is more susceptible to disease. NIH T32DE017551; R01DE018290; and P20 RR017696

226 MKP-1 is Required for Canonical 1,25(OH)2D3-signaling and Osteoclastogenesis. Alfred C Griffin, Keith K Kirkwood; Craniofacial Biology, MUSC.

Vitamin D3, and its most active form 1,25(OH)2D3, are well known to stimulate osteoclastogenesis through stromal cell induction of the receptor activator of nuclear factor kappaB (NF-kappaB) ligand (RANKL). Mitogen activating protein kinase phosphatase-1 (MKP-1) is a phosphatase classically known to negatively regulate the innate immune response through dephosphorylation of p38, ERK, and JNK activity. Here we describe a new, novel function of MKP-1 in permitting genomic 1,25(OH)2D3 signaling and downstream osteoclastogenesis through RANKL. Initially, qRT-PCR and immunoblot analysis comparing BMSCs revealed that 1,25(OH)2D3-induced VDR, CYP24a1 and RANKL mRNA expression and protein were significantly attenuated or absent in MKP-1/-/ BMSCs. When stable RANKL-BAC reporter UAMS-32 stromal cells containing the entire RANKL gene with 120kb of 5’ flanking region including 5 validated VDREs were treated with MKP-1 siRNA or control siRNA, we found MKP-1 siRNA treated UAMS-32 stromal cells had a 4.79-fold decrease in RANKL reporter activation and a 3.22-fold decrease in VDR mRNA induction in the same cell line. BMSCs from tibias and femurs of MKP-1/-/- mice treated with 1,25(OH)2D3 and co-cultured with RAW 264.7 cells had a 91% decrease in osteoclastogenesis (TRAP+, ≥3 nuclei) compared with WT co-cultures (p<.0001). Immunoblot analysis from cellular fractions of WT and MKP-1/-/- BMSCs stimulated with 10-7M 1,25(OH)2D3 for 1 hr revealed that RXRα nuclear import was impaired in MKP-1/-/- BMSCs, while VDR import was not affected. Duolink experiments addressing VDR-RXRα heterodimer translocation revealed that while baseline levels were unchanged, 1,25(OH)2D3-induced nuclear translocation of VDR-RXRα heterodimers was significantly decreased in MKP-1/-/- BMSCs. These results reveal an unexpected and highly novel role for MKP-1 in permitting canonical 1,25(OH)2D3 signaling via VDR-RXRα heterodimer nuclear import and downstream osteoclastogenesis through stromal cell RANKL expression. NIH T32DE017551; R01DE018290; and P20 RR017696

227 The Contribution of Fatty Acid Amides to Pyrnesium Parvum Toxicity, Matthew J Bertin1, Paul V Zima2, Kevin R Beauchesne2, Kevin M Hunicck3, Peter Moeller3; 1Marine Biomedicine and Environmental Sciences, MUSC, 2Center for Coastal Studies, Texas A&M University-Corpus Christi, 3Hollings Marine Lab, NOAA.

Abstract not available.

228 Estrogen Receptor Agonists Protect Against Glutamate Excitotoxicity In Spinal Cord Slice Cultures, Joshua A Smith1, Arabinda Das1, Gerald C Wallace1, Swapan K Ray2, Naren L Banik1; 1Neurosciences, MUSC, 2Pathology, Microbiology, & Immunology, USC School of Medicine.

Glutamate excitotoxicity is an important mediator of secondary damage to neurons and glial cells following spinal cord injury (SCI). Thus, development of therapies targeting glutamate-induced cell death may protect the injured spinal cord and improve functional recovery in SCI. Recent studies indicate estrogen is an agent of interest in treatment of SCI due to its neuroprotective actions as an anti-apoptotic, anti-inflammatory, and anti-oxidant steroid hormone. Despite recent progress in elucidating the mechanisms...
by which estrogen mediates neuroprotection, little is known about the individual contributions of estrogen receptor (ER) subtypes ERα and ERβ to this process. To further elucidate the roles of ERα and ERβ, we examined the effects of PPT (an ERα agonist), DPN (an ERβ agonist), and estrogen itself on apoptotic cell death in rat spinal cord slices following glutamate insult. Exposure to glutamate (L-glutamic acid; 500 μM) for 4 hrs resulted in increased intranucleosomal DNA fragmentation suggesting apoptotic death in spinal cord slices. Apoptosis following glutamate excitotoxicity was also confirmed by an increase in the ratio of Bax (pro-apoptotic protein) to Bcl-2 (anti-apoptotic) at the mRNA and protein levels as indicated by real-time polymerase chain reaction (RT-PCR) and Western blot analysis, respectively. Glutamate exposure was also associated with up-regulation of the neutral protease calpain and down-regulation of its endogenous inhibitor calpastatin. Treatment of spinal cord slices with PPT (100 nM), DPN (100 nM), or estrogen (250 nM) attenuated glutamic acid-induced apoptosis and reversed biochemical changes associated with cellular degeneration. The ER antagonist IC182,780 significantly reduced the ability of PPT, DPN, and estrogen to prevent cell death, indicating that estrogen and ER agonists may provide neuroprotection via receptor-mediated pathways involving multiple ER subtypes. Overall, these findings also suggest that estrogen receptor agonists may have potential as novel therapeutics to improve outcomes in SCI patients. NIH-NINDS NS031622, NS045967, State of South Carolina Spinal Cord Injury Research Fund (SC-SCIRF)

229 Changes in Prefrontal Cortex Catecholamine and Glutamate Levels During Cued Vs. Drug Primed Reinstatement of Methamphetamine-seeking in Rats, Aram Parsegian, Ronald E See; Neurosciences, MUSC.

Methamphetamine (meth) addiction is a costly and devastating disorder, and has risen dramatically across the US and the world over the last decade. Increased understanding of the neurobiological substrates in relapse to meth-taking will help guide the development of effective treatments. Meth addicts commonly exhibit enduring cognitive and motivational abnormalities that likely reflect a dysregulation of prefrontal cortex (PFC) and nucleus accumbens (NAc) function. Previous studies in animal models of self-administration and relapse have shown that glutamatergic projections from the PFC to the NAc critically mediate reinstatement of drug-seeking produced by drug-paired cues, drug-priming, or stress. Although catecholamines modulate these signals, little is known of their role in the dorsomedial PFC (dmPFC) during reinstatement. Further, while NAc glutamate (GLU) homeostasis has a critical role in cocaine-seeking, the impact of meth on GLU homeostasis within the PFC remains unknown. To address these questions, we implanted rats with a jugular catheter and two separate guide cannulae aimed at the dmPFC and contralateral NAc core in order to simultaneously measure changes in GLU and catecholamine levels in vivo during reinstatement of meth-seeking. During reinstatement, GLU significantly increased in the dmPFC under all reinstatement conditions (cued, meth-primed, or both) in animals with a history of meth but not in yoked-saline controls. Extracellular levels of dopamine and norepinephrine showed substantial increases in the dmPFC during cued or cued+primed reinstatement in meth rats as compared to yoked-saline controls. These data are the first to demonstrate that the dmPFC exhibits dynamic changes in GLU and catecholamine function during relapse after chronic meth. These data also indicate that meth alters GLU activity upstream of GLU release in the NAc. Further investigation will be directed at the concurrent changes in catecholamine and GLU levels in the NAc, as well as the relationship of these changes to meth-seeking behavior. NIDA P20 DA022658; INRSA 2T32D007288-17; and Ruth L. Kirschstein NRSA F31 DA020931-01A1

230 A Novel Function of Bves Revealed By Bimolecular Interaction Studies, Claire L Hinsch, Jagadish Kummetha-Venkata, Vincent Dammai; Pathology and Laboratory Medicine, MUSC.

Blood vessel/epicardial substance (Bves) is the founding member of the three related proteins of the popdc family. The Bves protein is highly conserved (80%) across vertebrate species. Prior studies from two prominent groups have proposed Bves role in cell adhesion, cell motility, and vesicular transport. However, mouse bves homozygous knockouts are viable and normal other than exhibiting defects in muscle regeneration after experimental injury. Therefore, the molecular function of Bves and its significance to organism biology remains a mystery to date. In an effort to uncover novel Bves functions, we independently conducted a yeast two-hybrid interaction screen using four different segments of the Bves coding sequence against two different pools of human cDNA library (fetal brain and kidney). A total of 150 positive clones representing 35 different proteins were confirmed as bona fide interacting partners of Bves. These interactions suggested that Bves could be involved in biological pathways critical to cell division. We observe that protein localization of Bves is cell cycle regulated and influenced by its binding partners. Shuttling of the Bves protein between two distinct sub cellular compartments is observed during transition into mitosis. Co-localization of Bves, using live cell imaging and immunofluorescence, show specific association with the interacting partners through multiple stages of cell cycle. We present evidence of Bves role in cell cycle and suggest that Bves regulates its partners to influence mitotic exit,
with links to ER stress, which is dysregulated in cancers and is physiologically relevant in cardiac functions as well, and therefore of clinical significance. We anticipate the knowledge gained will be useful for regeneration after cardiac injury. NIH/NCI RO1 CA128002

231 Endogenous Opioids Mediate Left Dorsolateral Prefrontal Cortex RTMS-Induced Analgesia, Joseph J Taylor¹, Jeffrey J Borckardt², Mark S George³; ¹Neuroscience, MUSC, ²Psychiatry, MUSC.

Abstract not available.

232 Interleukin-10 And Kupffer Cells Protect The Fatty Liver From Ischemia And Reperfusion Injury, Alton Sutter¹, Justin Ellett², Kenneth Chavin²; ¹Microbiology and Immunology, MUSC, ²Surgery, MUSC.

Steatotic donor organs are routinely rejected for transplantation because of their increased rate of primary nonfunction. These grafts are more sensitive to ischemia/reperfusion (I/R) during transplantation. TLR4 KO improved survival and liver function in Leptin KO (ob/ob) and high fat diet animals, implicating TLR4 as a mediator of steatotic graft failure after I/R. In the normal, or lean, livers, Kupffer Cells (KC) are protective after total I/R with associated bowel congestion, and are not deleterious as previously thought. This protection appears to be due to KC secretion of the potent anti-inflammatory cytokine Interleukin-10 (IL-10). However, KC of ob/ob mice are incapable of sufficiently regulating an increased TLR4 dependent inflammatory response occurring in steatotic livers after I/R, resulting in more severe injury. We hypothesized that pretreatment with exogenous IL-10 would protect these mice from inflammatory over-activation and injury. Methods: lean and ob/ob mice were pretreated with either IL-10 or the liposomally encapsulated bisphosphonate Clodronate (shown to deplete Kupffer cells). Animals were then subjected to either 15 minutes total warm hepatic ischemia or sham manipulation, followed by 1, 6, or 24 hours reperfusion. IL-10 pretreatment resulted in significantly improved survival of ob/ob animals (100% vs. 33% in control animals). ALT levels were elevated at 6 hours in the macrophage-depleted group (1880±162 IU/L), above all other groups, including the untreated ob/ob group (852±336). IL-10 pretreatment of ob animals resulted in decreased ALT levels at 6 hrs (564±71), and normalization at 24 hrs reperfusion (156±162 vs. 197±123 in sham operated animals). Furthermore, qRT-PCR showed IL-10 pretreatment suppressed expression of the inflammatory cytokine IL-1b after reperfusion, and elevated IL-10 mRNA expression. This data indicates IL-10 protects steatotic livers undergoing I/R. Increased I/R injury was also observed in the setting of obesity when animals were pretreated with Clodronate to deplete KC. This indicates a hepatoprotective role played by phagocytically active KC in the steatotic environment, and the possibility that modification of Kupffer cell inflammatory responses may protect fatty livers in transplantation. NIH 1R01DK069369

233 The Role of Acid Ceramidase in the Failure of Radiation Therapy for Prostate Cancer, Joseph C Cheng¹, S Tucker Marrison¹, Thomas H Beckham¹, Thomas E Keane², David T Marshall³, Xiang Liu⁴, James S Norris¹; ¹Microbiology & Immunology, MUSC, ²Urology, MUSC, ³Radiation Oncology, MUSC.

Abstract not available.

234 Elevation of CerS6 Expression Triggers Compensation Via the Ceramidase Pathway in Colon Cancer Cells, Tejas S Tirodkar, Christina Voelkel-Johnson; MCBP, MUSC.

Ceramide synthase 6 (CerS6) is a key enzyme in the sphingolipid metabolism pathway that preferentially generates C16-ceramides. Previously we have shown that modulation of CerS6 expression affects susceptibility to apoptosis in human colorectal cancer cells (White-Gilbertson et al, Oncogene 28:1132). In this study we investigated the effects of acute and chronic upregulation of CerS6 in the SW620 and HT29 colon cancer cells. Transient overexpression of CerS6 using an adenovirus specifically increased C16-ceramide and C16-dihydroceramide levels, suggesting that increased CerS6 expression stimulated both the de novo and the salvage pathways of ceramide synthesis. Increased generation of C16-ceramides occurred at the expense of very long chain ceramides and was also accompanied by a decrease in sphingosine. Interestingly, stable expression of the same CerS6 cDNA in HT29 cells did not result in increased C16-ceramide. Instead we detected an increase in sphingosine levels, suggesting activation of a compensatory pathway. Analysis of ceramidases, which convert ceramides to sphingosines, indicated that the expression of acid ceramidase was increased upon forced expression of CerS6. To test the relevance of these results in vivo, we analyzed human normal and tumor tissues of the colon for sphingolipids. Similar to the observation in CerS6 stable transfectants, the sphingolipid profile revealed increased sphingosine levels in the tumor compared to normal tissues. Collectively, our data suggest that human colon cancer cells compensate for CerS6 expression or activation by inducing acid ceramidase expression in order to prevent accumulation of intracellular C16-ceramides. MUSC interim funds
Identification and Characterization of PP2C Activation By Ceramide, David M Perry1, Kazuyuki Kitatani1, Patrick Roddy1, Mohamad El-Osta1, Yusuf Hannun2;1, Biochemistry, MUSC, 2Tottori University.

Sphingolipids are an enigmatic class of lipids implicated as mediators in several biological processes. Ceramide, the central sphingolipid, metabolically, has been well studied for its roles in apoptosis, differentiation, and inflammation. Despite this, a correspondingly clear, mechanistic understanding has not been elucidated. Previous work form our lab has shown that PP1 and PP2A of the PPP family of phosphatases are activated by ceramide in a selective and sterosepecific manner. Biological targets of ceramide-activation of these phosphatases include Rb, ERM, SR, and p38. However other serine/threonine phosphatases have not been ruled out as ceramide-activated. From this work, PP2C was discovered to be a novel ceramide-activated protein phosphatase (CAPP). Using A549 human lung adenocarcinoma cells or rat brain as sources of soluble lysate, a fraction containing an unknown phosphatase, from a MonoQ anionic exchange column, with relatively low basal activity and devoid of known CAPPs, was activated by C6-ceramide, which was later identified by LC/MS/MS to be PP2Cgamma. In order to further study this interaction the canonical PP2C isoform, PP2Calpha/PPM1A was used. Both PP2Cgamma and PP2Calpha were activated by C6-ceramide delivered in ethanol. C16-ceramide resulted in a robust increase in catalytic activity of PP2Calpha, where this activation was stereospecific. Lastly, C16-ceramide induced the dephosphorylation of p38delta by PP2Calpha demonstrating this effect using a physiological substrate with potential biological implications for regulation of p38 signaling.

236 The Role of the Cancer-associated Sm-like Oncogene on Apoptotic Messages and Chemotherapeutic Sensitivity in Pancreatic Cancer, Elizabeth C Little1, Ernest R Camp2, Cindy Wang2, Dennis K Watson3, Patricia M Watson2, David J Cole2;1, Microbiology and Immunology, MUSC, 2Surgery, MUSC, 3Pathology, MUSC.

Evaluating the genetic alterations behind neoplastic progression can enhance understanding and lead to development of novel therapeutics. The Cancer associated Sm-like (CaSm) oncogene is overexpressed in 87% of human pancreatic tumor samples and its expression is necessary for in vivo tumor formation. Evidence supports the notion that altered CaSm expression modulates mRNA decapping and degradation. CaSm overexpression in breast cell lines altered several gene pathways including cell cycle, cytokine-signaling, and apoptosis. Our previous studies have shown that reduced CaSm RNA increased apoptosis in human AsPC-1 and Panc1 cell lines in vitro and enhanced the therapeutic effects of gemcitabine in a xenograft model of pancreatic cancer. We hypothesize that CaSm overexpression alters apoptotic gene expression, promoting an anti-apoptotic phenotype to decrease chemotherapeutic sensitivity. Using the Clontech Retro-X doxycycline inducible system, we overexpressed human CaSm in Panc1 cells (tet-on CaSm Panc1) and performed real-time PCR-based microarrays to identify genes that are altered upon induced CaSm expression compared to the tet-on Panc1 driver controls. Changes in expression were observed among several genes — notably apoptotic genes Bad, Bcl-XL, and E2F1 which have reported roles in gemcitabine resistance. Alterations in mRNA were confirmed with real-time PCR and Bad protein knockdown confirmed with western blot analysis. Using SRB assays to evaluate cell growth, tet-on CaSm Panc1 cells demonstrated increased resistance to gemcitabine, exhibiting significantly higher cell numbers at all concentrations (0.1-100uM, P<0.05). Cell cycle analysis confirmed significantly decreased apoptosis (sub-G1 DNA content) after treatment with 200nM gemcitabine in the tet-on CaSm Panc1 cells compared to the tet-on Panc1 driver cells (P<0.05). In summary, induced CaSm expression results in altered expression of apoptotic genes and decreased gemcitabine-induced apoptosis. Future studies will investigate whether the CaSm-mediated alterations in apoptotic gene expression are due to increased decapping and message destabilization and whether CaSm expression confers drug resistance in vivo. NIH R01CA123159-05

237 Transcriptional Regulation of Cartilage Link Protein in the Developing Heart, Marie M Lockhart1, Elaine Wirrig2, Aimee Phelps1, Andy Wessels1;1Regenerative Medicine and Cell Biology, MUSC, 2University of Cincinatti.

Previous studies by the Wessels lab have demonstrated that Hyaluronic and Proteoglycan binding Link Protein 1 (Hapln 1 or cartilage link protein 1/Crtl1) is involved in heart development. Crtl1 is an extracellular matrix (ECM) protein that stabilizes the interaction between hyaluronan and versican and is expressed in endocardial and endocardially derived cells in the developing heart, including cells in the atrioventricular (AV) and outflow tract (OFT) cushions. Crtl1 knockout mice have a range of cardiovascular malformations such as thin myocardium, atrioventricular septal defects (AVSD), and decreased trabeculation. Histological analysis of Crtl1 knockout mice reveals there is decreased expression of the Crtl1 binding-partners versican and hyaluronan and that reduced expression of these ECM proteins may contribute to the cardiovascular malformations observed. Investigations into the transcriptional regulation of the Crtl1 gene have resulted in the finding that the cardiac transcription factor Mef2c may bind to the Crtl1 promoter to regulate its expression in the
ventricular endocardium, while the SRY-box transcription factor Sox9 regulates Crt1 expression in OFT and AV cushion mesenchyme. NIH 5T32HL007260-34; NIH-NHLBI R01HL084285; AHA 09GRNT2060075

238 Cubilin is Essential for Maintaining Blood HDL Levels, Obaidullah Aseem, Brian T Smith, Marion A Cooley, W Scott Argraves; Regenerative Medicine and Cell Biology, MUSC.

Cubilin is a multiligand receptor capable of mediating the endocytosis of the HDL apolipoprotein, apoA-I. The significance of cubilin-mediated apoA-I endocytosis to blood HDL homeostasis has not been established. Through study of mice heterozygous for targeted cubilin gene deletion, we show that cubilin haploinsufficiency results in 25% decrease in blood levels of HDL. While cubilin is not expressed in liver, the major site of HDL biogenesis involving the transporter Abca1, it is expressed in two other tissues, the kidney and intestine, both capable of HDL biosynthesis. In addition, the kidney proximal tubules mediate the uptake of apoA-I from the glomerular filtrate by cubilin-mediated endocytosis. Thus, the decreased blood levels of HDL observed in cubilin heterozygous mice may be due to decreased biosynthesis of HDL in the intestine and kidney or decreased salvage of apoA-I/HDL in the kidney. We observed no significant change in the levels of apoA-I and Abca1 protein or mRNA extracted from liver, kidney or intestine of cubilin heterozygous mice as compared to wild type. In contrast, cubilin heterozygous mice displayed an increase in urinary loss of apoA-I, which inversely correlated with blood levels of apoA-I. Furthermore, the fractional clearance of smaller HDL particles (d>1.13 g/mL) from the blood was significantly increased in cubilin heterozygous mice, whereas there was no significant change in the fractional clearance of larger HDL2 particles, which are not filtered through the glomerulus. These observations indicate that the cubilin heterozygous mice have reduced salvage of apoA-I from the glomerular filtrate back to the blood. Therefore, we hypothesize that renal cubilin-mediated endocytosis plays a significant role in maintaining blood HDL levels by salvaging apoA-I from the glomerular filtrate leading to its transfer back to the blood. NIH HL061873 and AHA 10PRE3870038

239 Phosphoregulation of the Cx43 Carboxyterminus in Cardiac Injury, Joseph A Palatinus, Robert G Gourdie; Regenerative Medicine and Cell Biology, MUSC.

Abstract not available.

240 pGlcNAc Nanofibers From a Marine Diatom Stimulate a Scarless Wound Healing Program, Hailey B Lindner, Aiguo Zhang, Juanita Eldridge, Arun Seth, Rick Visconti, Amy Bradshaw, John Vournakis, Robin Muise-Helmers; Regenerative Medicine and Cell Biology, MUSC, Sunnybrook Research Institute, University of Toronto, Medicine, MUSC, Marine Polymer Technologies.

Our published findings show that treatment of cutaneous wounds with poly-N-acetyl-glucosamine nanofibers (pGlcNAc), a novel polysaccharide material derived from a marine diatom, results in an increased kinetics of wound healing and in innate immune responses. These fibers bind to and stimulate integrin mediated signal transduction that is, at least in part, dependent on Akt1. Our preliminary data indicates that a single treatment of cutaneous wounds with these nanofibers results in decreased scar formation. To determine whether decreased scar formation correlated with changes in tensile strength, skin samples from treated, untreated or unwounded normal control skin were trimmed to 7mm in width and 15 mm in length, to insure even tension. Skin was loaded onto an Instron instrument and tensile strength and elasticity measurements were taken. Animals treated with pGlcNAc showed increased tensile strength compared to untreated animals, a similar tensile strength to untreated controls. Masson trichrome staining suggests that untreated wounds have higher collagen content as indicated by more intense blue staining and a marked difference in collagen organization. In the untreated wounds the collagen is unorganized layed down in a vertical direction. In pGlcNAc treated wounds the collagen fibrils are organized similar to normal, unwounded skin suggesting a “scarless” wound healing program. In whole transcriptome analysis, many genes up-regulated in response to pGlcNAc are involved in the innate immune response. We tested whether Epithelial Stromal Interaction Protein 1 (EPST1), a gene strongly up-regulated in vitro, was controlled by pGlcNAc treatment in vivo. Immunofluorescence shows that EPST1 is strongly up-regulated by pGlcNAc treatment in an Akt1-dependent manner. Taken together pGlcNAc stimulates wound healing via a scarless wound healing mechanism that results in increased tensile strength and decreased scarring due to proper alignment of collagen. The potential role of EPST1 in the regulation of fibroblast alignment will be discussed.

241 Histone Deacetylase Inhibitor Suberoylanilide Hydroxamic Acid Normalizes the Levels of Very Long Chain Fatty Acids in Human Skin Fibroblasts From X-Adrenoleukodystrophy Patients, Jaspreet Singh, Mushfiquddin Khan, Inderjit Singh; Pediatrics, MUSC.

X-Adrenoleukodystrophy (X-ALD) is a peroxisomal metabolic disorder, caused by mutations in the ABCD1 gene encoding the peroxisomal ABC transporter adrenoleukodystrophy protein (ALDP). The consistent metabolic abnormality in all forms of X-ALD is an inherited defect in the peroxisomal β-oxidation of very
long chain fatty acids (VLCFA>C22:0) and the resultant pathognomonic accumulation of VLCFA. The accumulation of VLCFA leads to a neuroinflammatory disease process associated with demyelination of the cerebral white matter. The present study underlines the importance of a potent histone deacetylase (HDAC) inhibitor suberoylanilide hydroxamic acid (SAHA) in inducing the expression of ABCD2 (ALDRP), and normalizing the peroxisomal β-oxidation as well as the saturated and monounsaturated VLCFAs in cultured human skin fibroblasts of X-ALD patients. The expression of ELOVL1, the single elongase catalysing the synthesis of both saturated VLCFA (C26:0) and mono-unsaturated VLCFA (C26:1), was also reduced by SAHA treatment. In addition, using Abcd1/Abcd2-silenced mouse primary astrocytes we also examined the effects of SAHA in VLCFA-induced inflammatory response. SAHA treatment decreased the inflammatory response as expression of inducible nitric oxide synthase, inflammatory cytokine, and activation of NF-kB in Abcd1/Abcd2-silenced mouse primary astrocytes was reduced. The observations indicate that SAHA corrects both the metabolic disease of VLCFA as well as secondary inflammatory disease; therefore, it may be an ideal drug candidate to be tested for X-ALD therapy in humans. NIH NS-22576; NS-37766; C06 RR018823; C06 RR015455; and VA BX1072-01

242 Regulation of Mitochondrial Protein Biosynthesis By Formylation and Deformylation of Methionyl-tRNA, Kyle C Strickland, Sergey A Krupenko; Biochemistry, MUSC.

In mammalian cells, there are two distinct species of methionyl-tRNA, one used in initiation and the other in elongation during the translation of nuclear DNA encoded proteins. In mitochondria, however, there is only one methionyl-tRNA, which is used in both initiation and elongation during translation of mitochondrial DNA-encoded proteins. To initiate translation, the mitochondrial methionyl-tRNA is formylated by the action of the formylmethionyl-tRNA transferase (FMT) using 10-formyltetrahydrofolate as the formyl-group donor. This process is similar to the initiation of translation in bacteria. While it has been recently shown that mutations of FMT might cause defects in mitochondrial translation in humans, the absolute requirement for formylation in the initiation step is still debatable. Moreover, excessive formylation would limit the level of non-formylated methionyl-tRNA thus suppressing the elongation and translation in general. While the bacterial polypeptide deformylase (PDF) can deformylate the initiator in vitro, a homologous human enzyme deformylates N-terminal amino acid of synthesized polypeptides, but its ability to deformylate formylmethionyl-tRNA in human mitochondria has not yet been demonstrated. To sort out the role of FMT and PDF in mitochondrial translation in humans, we studied the effects of FMT over-expression and silencing in cultured cells. Using recombinant FMT and PDF we have further reconstituted the in vitro formylation of methionyl-tRNA and demonstrated that it can be deformylated by human PDF. Overall, our results demonstrate that (i) mitochondrial translation in human cells can proceed in the absence of FMT; (ii) the excessive FMT activity can inhibit mitochondrial translation; and (iii) mammalian PDF acts as formylmethionyl-tRNA deformylase. Based on these findings, we propose that FMT and PDF act in concert to regulate the use of methionyl-tRNA in the initiation and elongation processes of mitochondrial translation. NIDDK F30 DK083215; and NIDDK R01 DK054388

243 Biased Agonism of the Angiotensin AT1 Receptor Induces the Akt-mediated Activation of the Mammalian Target of Rapamycin, Ryan T Kendall, Louis M Luttrell; Medicine, MUSC.

Biased agonism of G protein-coupled receptors is a recently characterized form of pharmacology, and the significance of this phenomenon is not fully understood. Here we test the hypothesis that a beta arrestin pathway-directed biased agonist of the angiotensin AT1 receptor activates an Akt-mediated cellular growth response. The AT1 receptor is a G protein-coupled receptor that regulates blood pressure and cardiac function in response to the hormone angiotensin II. Chronic AT1 receptor stimulation promotes atherosclerosis and a pathological form of cardiac hypertrophy resulting in heart failure therefore, angiotensin receptor blockers (ARBs) are commonly used as treatments of these disorders. These responses are largely thought to be mediated by heterotrimeric G protein-mediated signaling pathways. The AT1 receptor biased agonist, [Sarcosine1, Isoleucine4, Isoleucine8]angiotensin II (SII), stimulates receptor internalization and beta arrestin-dependent activation of the signal transduction nodes ERK1/2 and Akt—without activating G proteins. Such pathways represent a separate signal from these receptors; however, it is unknown what physiologic roles such beta arrestin-mediated signaling pathways serve. Moreover, beta arrestin scaffolded signaling molecules are often observed to display restricted access to select substrates. Whereas SII-induced Akt activation does not appear to activate the known Akt effector system beta catenin in HEK 293 cells, SII does activate the mammalian target of rapamycin (mTOR)-dependent ribosomal S6 kinase (p70/p84 S6K). This pathway is dependent on both ERK1/2 and Akt kinases. Such unique receptor-coupled G protein-independent signal transduction networks could represent a druggable target—or pathways to avoid—in the rational design of more effective AT1 receptor-targeted therapies. NIH K12GM081265, DK55524, and Veterans Affairs Research Enhancement Award Program
Systemic lupus erythematosus (SLE) patients display impaired endothelial nitric oxide synthase (eNOS) function required for normal vasodilatation. SLE patients express increased compensatory activity of inducible nitric oxide synthase (iNOS) generating excess nitric oxide that may result in inflammation. We examined the effects of genetic deletion of NOS2 and NOS3, encoding iNOS and eNOS respectively, on accelerated vascular disease in MRL/lpr lupus mouse model. NOS2 and NOS3 knockout (KO) MRL/lpr mice had higher plasma levels of triglycerides (23% and 35%, respectively), ceramide (45% and 21%, respectively), and sphingosine 1-phosphate (S1P) (21%) compared to counterpart MRL/lpr controls. Plasma levels of the anti-inflammatory cytokine interleukin 10 (IL-10) in NOS2 and NOS3 KO MRL/lpr mice were lower (53% and 80%, respectively) than counterpart controls. Nodule-like lesions in the adventitia were detected in aortas from both NOS2 and NOS3 KO MRL/lpr mice. Immunohistochemical evaluation of the lesions revealed activated endothelial cells and lipid-laden macrophages (foam cells), elevated sphingosine kinase 1 expression, and oxidized low-density lipoprotein immune complexes (oxLDL-IC). The findings suggest that advanced vascular disease in NOS2 and NOS3 KO MRL/lpr mice may be mediated by increased plasma triglycerides, ceramide and S1P; decreased plasma IL-10; and accumulation of oxLDL-IC in the vessel wall. The results expose possible new targets to mitigate lupus-associated complications. NIH HL079274; NIH (ARRA) R01 HL079274-04S1; NIH P20 RR17677; NIH P20 RR016434; NIH K08AR002193; NIH AR045476; and NIH/NHLBI R25 HL092611

246 Prognostic Importance of Age, Gender, and Subtype in Differentiated Thyroid Cancer, Samuel L Oyer1, Valerie A Smith2, Eric J Lentsch1; 1Otolaryngology, MUSC, 2Medicine, MUSC.

Introduction: Differentiated thyroid cancer (DTC) consists of papillary (PTC) and follicular (FTC) subtypes. Patient age > 45 is associated with worse survival in DTC, and is included in the cancer staging system, but alternative age cutoffs have been proposed. Male gender is considered a poor prognostic indicator in DTC but is not part of the staging system. FTC is consistently reported to have a worse prognosis than PTC but both subtypes are currently staged identically. Objectives: Determine the prognostic importance of patient age, gender, and tumor subtype in disease specific survival (DSS) among DTC. Materials/Methods: The Surveillance Epidemiology and End Results (SEER) database was searched to identify adults diagnosed with DTC between 2004-2008. Patients were categorized by age, gender, tumor subtype, cancer stage, and survival. Age was stratified by decade beginning with 18-24, 25-34, 35-44 and so on up to age > 85. Kaplan-Meier analyses were performed to estimate DSS for each patient age group with significance set at p<0.05. Results: There were 38,221 patients identified: 35,858 with PTC and 2,363 with FTC. Each decade of increasing age was associated with a sequentially worsening survival starting at age 45 for PTC and 55 for FTC (p<0.0001). Male patients with DTC presented with more advanced tumors than females (p<0.001), but there was no difference in survival between males and females when controlled for overall stage in any age group (p>0.05). FTC had significantly worse survival than PTC based on individual tumor, node or metastasis stage, but there was no difference in survival based on overall cancer stage (p>0.05). Conclusions: Patient age greater than 45-55 has a negative impact on survival in DTC but gender does not. There is no difference in survival between PTC and FTC when compared by overall stage and these subtypes should be staged identically.

247 Use of Hybrid Torque+Position Controller Towards More Realistic Movement Profiles of Neurally Controlled Devices, Pratik Y Chhatbar, Joseph T Francis; SUNY Downstate Medical Center.

Current state-of-the-art technology of brain-machine interfaces achieves movement profiles by using neural activity to predict kinematic values like position or velocity. Real-life reach-to-grasp actions heavily involve forces and joint torques towards successful movements, but neural predictions of such dynamic parameters have not been demonstrated to drive computer cursor or robotic arm in real-time. Offline predictions of torques/forces has been shown and that such predictions improve when provided with limb state information. Here we demonstrate combined use of dynamic and kinematic predictions towards achieving real-time control of movements. Movements thus made using such hybrid torque+position predictions look more natural when compared with pure kinematic predictions-based movements. We observed that with relatively low position prediction contribution the stiffness/impedance decreases and vice versa. By giving neural control to toggle such
individual prediction influence at individual joint of the prosthetic arm, the user can attain more comprehensive control of movements. That is, the user can determine the stiffness/impedance of individual joints in a task and environment-dependent manner. We adapted non-human primate model (bonnet macaque, M. radiata) because of its human-like reach-and-grasp movements. We implanted floating 10x10 intracortical microelectrode array (UIEA, Blackrock Microsystems) after the animal is proficient in random target pursuit task while the arm is attached on 2-DOF exoskeletal robotic arm (Kinarm, BKin Technologies) under different force/torque field environments. We then put the animal on brain-control mode where the visual feedback cursor, representing the animal arm + robotic manipulandum, is directly controlled by neural predictions of behavioral parameters. Predictions of torque and position were made using multiple linear regression and individual contribution of each towards final movement was changed to determine the behavior of the brain-controlled cursor representing virtual arm. NYS SCIRBs #C022048; and DARPA N66001-10-C-2008

248 The SR Protein Kinase Ctk1 Phosphorylates SPF45 and Regulates Its Degradation and Splice-Site Selectivity, Yuying Liu, Adnan Al-Ayoubi, Hui Zheng, Jennifer Bethard, Scott T Eblen; Cell & Molecular Pharmacology & Experimental Therapeutics, MUSC.

Abstract not available.

249 High Throughput Antifungal Drug Screening, Visesato Mor, Erika Bullesbach, Maurizio Del Poeta; Biochemistry, MUSC.

During the last two decades, the opportunistic fungal infections have significantly increased due to the increase of immunocompromised patients. Current antifungal drugs are often inadequate, toxic and becomes quickly ineffective due to the development of resistant strains. Thus, new antifungal compounds are needed. We utilized the Chembridge DIVERset compound library to screen for small molecules that would inhibit growth of Cryptococcus neoformans under physiological conditions (alkaline pH, 370C and 5% CO2). We screened 49,120 compounds against C. neoformans wild-type H99 strain and found 18 compounds that inhibit growth by more than 80% at alkaline pH. We further tested these 18 compounds and found two compounds to significantly inhibit the synthesis of fungal but not mammalian glucosylceramide. The 2 compounds are N’-(3-bromo-4-hydroxybenzylidene)-2-methylbenzohydrazide (BHBM) and its derivative N’-(3-bromo-4-hydroxybenzylidene)-3-bromobenzohydrazide (BHBB). The minimal inhibitory concentration (MIC) is 1 µg/mL for BHBM and 0.3 µg/ml for BHBB. Both BHBM and BHBB exhibit fungicidal activity and up to 80% killing was observed with 4 µg/mL BHBM and 2 µg/mL BHBB in 24 hours. BHBM and BHBB possess synergistic effect when combined with fluconazole. Interestingly, using 3H-palmitate labeling, cell treated with BHM showed a significant decrease in glucosylceramide production in a dose dependent manner, suggesting that BHBM affects the “de novo” synthesis of GlcCer. BHBM showed no toxicity on primary alveolar macrophage as well as macrophage like murine cell line using 10X the antifungal inhibitory concentration. Upon injecting 20 µg of BHBM in mice intraperitoneally, approximately 1 µg/ml was present in the serum after 24 hours of the injection. Of interest, this serum concentration of BHBM inhibits >80% of fungal growth. These studies highlight how drug screening may lead to promising antifungal compounds. NIH AI56168; and AI71142

250 Chromosomal Instability and Virulence: A Study with Cryptococcus Neoformans, Narendra K Bairwa, Visesato Mor, Maurizio Del Poeta; Biochemistry, MUSC.

Sphingolipids are key biomolecules in the cell and they play a major role in the regulation of both Structural membrane organization and cell signaling. Mutations of key genes of the sphingolipid metabolic pathway have been implicated in promoting various diseases including cancer whose hallmark has been genome instability. It has been well established in our and others laboratory that mutations in sphingolipid metabolic pathway genes leads to loss of virulence of the human fungal pathogen Cryptococcus neoformans. Here we hypothesized that sphingolipids may play a role in the regulation of fungal pathogenesis through genome stability. Thus, we analyzed the genome instability phenotype of several C. neoformans mutants in the sphingolipid pathway using karyotype analysis by CHEF-PFGE. We observed that deletion of C. neoformans inositol sphingophospholipid phospholipase C 1 (ISC1) gene leads to altered karyotype in comparison to wild-type. The deletion of C. neoformans ISC1 leads to loss of virulence of Cryptococcus neoformans. This phenotype was not observed when other mutants of the sphingolipid pathway were analyzed. This study highlight for the first time that genome instability is controlled by specific sphingolipids and it may regulate virulence in C. neoformans.

251 The Sphingolipid Delta 8 Desaturase SLD8 is Involved in the Pathogenesis of Cryptococcus Neoformans, Shriya Raj, Maurizio Del Poeta; Biochemistry & Molecular Biology, MUSC.

The opportunistic fungus Cryptococcus neoformans is the leading cause of meningoencephalitis in immunocompromised patients. Studies from our laboratory have highlighted the role of sphingolipids as critical regulators of cryptococcal growth and pathogenesis. In particular, deletion of glucosylceramide synthase 1 (Gcs1) produced a strain...
that failed to survive within the alveolar spaces of the lung. Lipid analysis revealed that delta-gcs1 lacked GlcCer but accumulated methylated ceramide. To further investigate the role of the sphingolipid biosynthetic pathway in the pathogenesis of C. neoformans, we analyzed the antepenultimate enzyme within the pathway, delta 8 desaturase (Sld8) that desaturates the alpha-OH-delta 4-ceramide by introducing a double bond at the carbon-8 position of the sphingosine backbone. This is necessary for subsequent methylation at carbon-9 by the C9 methyltransferase and glycosylation by Gcs1, producing GlcCer. We generated mutants that were deleted for the SLD8 gene (delta-sld8) or reconstituted back at its genomic locus. The lipid profile of delta-sld8 revealed accumulation of alpha-OH-delta 4-ceramide and modest amounts of alpha-OH-delta 4-GlcCer with a concomitant absence of GlcCer or methylated ceramide. As expected, wild type (WT) and the reconstituted strains showed similar levels of GlcCer, with barely detectable levels of alternative ceramides. Interestingly, in contrast to delta-gcs1, the delta-sld8 mutant exhibited no significant defect when assayed for growth in DMEM medium pH 7.4 at 37°C in the presence of physiologic 5% CO2. The delta-sld8 mutant exhibited a significant virulence defect in CBA/J immunocompetent mice (survival >90 days) while mice infected with the WT strain succumbed by 25 days. Analysis of major organs recovered cells only from the lungs (~500-fold decrease in initial inoculum). The delta-sld8 mutant was also significantly inhibited in its ability to grow inside J774.16 peritoneal macrophages when compared to WT. This study provides new insights into the role of GlcCer pathway on pathogenicity of C. neoformans.

253 Cellular Morphogenesis Under Stress is Influenced By the Sphingolipid Pathway Gene ISC1 and DNA Integrity Checkpoint Genes in Saccharomyces Cerevisiae, Tripathi Kaushlendra, Nabil Matmati, W Jim Zheng, Yusuf A Hannun, Bidyut K Mohanty; Biochemistry & Molecular Biology MUSC.

In Saccharomyces cerevisiae, replication stress induced by hydroxyurea (HU) and methyl-methane sulfonate (MMS) activates DNA integrity checkpoints; in checkpoint-defective yeast strains, HU treatment also induces morphological aberrations. We find that the sphingolipid pathway gene ISC1, the product of which catalyzes the generation of bioactive ceramides from complex sphingolipids, plays a novel role in determining cellular morphology following HU/MMS treatment. HU-treated isc1Δ cells display morphological aberrations, cell-wall defects, and defects in actin depolymerization. Swe1, a morphogenesis checkpoint regulator, and the cell cycle regulator Cdk1 play key roles in these morphological defects of isc1Δ cells. A genetic approach reveals that ISC1 interacts with other checkpoint proteins to control cell morphology. That is, yeast carrying deletions of both ISC1 and a replication checkpoint mediator gene including MRC1, TOF1, or CSM3 display basal morphological defects, which increase following HU treatment. Interestingly, strains with deletions of both ISC1 and the DNA damage checkpoint mediator gene RAD9 display reduced morphological aberrations irrespective of HU treatment, suggesting a role for RAD9 in determining the morphology of isc1Δ cells. Mechanistically, the checkpoint regulator Rad53 partially influences isc1Δ cell morphology in a dosage-dependent manner. NIH P20 RR17677; ACS-IRG IRG 97-219-08; and PhRMA Foundation.
Head and neck squamous cell carcinomas (HNSCC) are the most common malignant neoplasm estimated to be greater than 40,000 cases annually in the US. Oral squamous cell carcinoma (OSCC), which contributes to >40% of all HNSCC, is associated with mucosal surfaces of the oral cavity and oropharynx. We recently reported OSCC tumor invasion of bone and osteolysis in mice. Autophagy is a cellular self-consumption process for degradation of damaged/dysfunctional cellular organelles, protein aggregates and plays an important role in malignant tumor progression and resistance to anti-cancer therapies. We showed OSCC cells express high levels of RANK ligand (RANKL), a potent osteolytic factor; however a functional role for RANKL in autophagy is unknown. We demonstrated RANK expression in OSCC tumor cells by confocal and histochemical analysis. Formation of autophagosomes involves autophagy proteins (Atg) and conversion of cytoplasmic microtubule-associated protein 1 light chain 3 (LC3-I) into the membrane form of LC3-II. We identified high levels of LC3-II expression in OSCC tumor cells (SCC-1, SCC-12 & SCC-14a) compared to normal human epithelial (RWPE-1) cells. Further, we showed increased levels of LC3-II and Atg5 expression in OSCC tumor specimens from human subjects and OSCC tumors on calvaria from athymic mice by immunohistochemistry. Interestingly, Western blot analysis of total cell lysates obtained from OSCC cells stimulated with RANKL (0-100 ng/ml) for 24 h demonstrated a dose dependent increase in LC3-II and RANKL expression which indicates an autoregulation of RANKL expression and autophagosome formation in OSCC cells. Thus our results implicate a novel function for RANK-RANKL signaling that may play an important role in autophagy modulation of OSCC tumor progression/osteolysis.

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