The Perry V. Halushka
MUSC Student 2009
Research Day

Program and Abstracts

Friday, November 6th 2009

http://srp.musc.edu
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 7:00 am on Friday, November 5th, 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 SRD2009 Chairman, Steve Kubalak, know by email (at <kubalaks@musc.edu>) 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:
All oral sessions will be in the College of Health Professions Building A at 151-A Rutledge Avenue. This 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 SRD2009 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 6th. 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 13th in the Graduate Studies office on the 1st floor of the Basic Sciences Building. Any evaluation sheets not collected by November 20th will be sent out by campus mail 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, Interprofessional 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 Basic Science 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; Leigh Manzi, MUSC Development Office; Maralynne Mitcham, College of Health Professions; Susan Reed, College of Dental Medicine; Mike Schmidt, College of Medicine; Debbie Shoemaker, College of Graduate Studies; Linnea Freeman, Elizabeth Little and Vondina Brown, Student Representatives; Thomas Waldrep, Center for Academic Excellence; Steven Kubalak, College of Graduate Studies (Chair); Eric James, (Chair Emeritus).
SRD2009 – SCHEDULE

FRIDAY, NOVEMBER 6th – 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: 12:00 am – 3:15 pm

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Keynote Address: Basic Science Auditorium, 4:00 – 5:00pm

"A Life in Science"

By:

Dr. Peter Agre
University Professor and Director
Recipient of The Nobel Prize in Chemistry 2003
Johns Hopkins Malaria Research Institute
Department of Molecular Microbiology and Immunology
Bloomberg School of Public Health
Baltimore, MD.

SATURDAY, NOVEMBER 7th – Careers Workshop XIX

‘Job Searching and Career Development’

Gazes Cardiac Research Institute, Rm 125, 10:00 am – 12:00 noon

for Graduate Students and Postdocs

Presented by College of Graduate Studies / Graduate Studies Alumni Association

Panelists: Terra Gibbs (’01), US Patent and Trademark Office; Michael Janech (’03), Assistant Professor MUSC; Christine Keogh (’08), Harrison and Star, Healthcare Communications; Sean Norman (’99, ’03), University of South Carolina; Paula Acierno Pellissier (’02), UCB, Inc; Andy Whitlock (’03), Lexicon Pharmaceuticals
LOCATION OF ORAL PRESENTATIONS – SESSIONS 11-17

College of Health Professions, Building-A, 151-A Rutledge Avenue, 2\textsuperscript{nd} floor

Access either:
a) from the Children’s Hospital-Rutledge Tower crosswalk over Ashley Avenue at the 2\textsuperscript{nd} floor level, or
b) through the Ashley Avenue Parking Garage to Rutledge Avenue to the main entrance on Rutledge.
POSTER PRESENTATIONS

Harper Wellness Center Gym

8:30 am - 12:00 noon

Session 1: Undergraduate – I #001-007
Session 2: Clinical Prof/Masters – I #008-018
Session 3: Clinical Prof/Masters – II #019-033
Session 4: Clinical Prof/Masters – III #034-043
Session 5: Clinical Prof/Masters – IV #044-053
Session 6: PhD – I #054-070
Session 7: PhD – II #071-083
Session 8: PhD – III #084-096
Session 9: Postdocs/Residents/Fellows – I #097-105
Session 10: Postdocs/Residents/Fellows – II #106-114

ORAL PRESENTATIONS

College of Health Professions, Building-A - 2nd Floor

Session 11: Undergraduates – III CHP 204 12:15-3:00 #115-124
Session 12: Clinical Prof/Masters – V CHP 201 12:00-3:00 #125-135
Session 13: Clinical Prof/Masters – VI CHP 202 12:15-3:15 #136-147
Session 14: PhD – VI CHP 205 12:30-2:30 #148-154
Session 15: PhD – VII CHP 206 12:00-3:15 #155-166
Session 16: PhD – VIII CHP 207 12:00-3:15 #167-178
Session 17: Postdocs/Residents/Fellows – III CHP 203 12:00-3:15 #179-190
POSTER PRESENTATIONS: Harper Center Gym – 8:30 – 12:00pm

Session 1: Undergraduate I

001 2-Hydroxypropyl-Beta-Cyclodextrin Removes All-Trans Retinol From Frog Rod Photoreceptors in a Concentration-Dependent Manner, Daniel Johnson¹, Chunhe Chen², Yiannis Ko³; ¹Physics, College of Charleston, ²Ophthalmology, Neurosciences, MUSC.

002 X-ray Tube Current Modulation and E/DLP Conversion Factors in CT, Dennise M Magill¹, Wenjun He², Emily Tavrides³, Hai Yao⁴, Walter Huda⁵; ²Radiation Health Physics, Oregon State University, ²Bioengineering, Clemson, ³Radiology and Radiological Science, MUSC, ²Bioengineering, Clemson.

003 Differences in Cortico-Limbic Activation in Patients Receiving Three Weeks of Real or Sham RTMS, Dakota Hadley¹, Samet Kose², Li Xingbao², Paul Morgan², Berry A Anderson², Kevin Johnson², Ziad A Nahas², Mark A George³; ¹College of Charleston, Brain Stimulation Lab, MUSC, ²Brain Stimulation Lab, MUSC, ³Brain Stimulation Lab, MUSC, Ralph H. Johnson VA Medical Center.

004 Seizure Detection System for Scalp EEG Monitoring, Rebecca L Wilson¹, Jonathan Halford²; ¹College of Charleston, ²Neurosciences, MUSC.

005 CRF Reduces GABA Release Onto VTA Dopamine Cells: Neuroadaptations After Chronic Cocaine Self-Administration, Courtney L Williams¹, Arthur C Riegel²; ¹Biology, College of Charleston, ²Neuroscience, MUSC.

006 Altered Versican Processing in Mouse Models of ADAMTS5 Deficiency Leads to Severely Hypertrophic Semi-lunar Valves, Alexandria C Bahan¹, Suneel S Apte², Christine B Kern³; ¹Cardiovascular Developmental Biology Center, MUSC, Honors College, College of Charleston, ²Lerner Research Institute, Biomedical Engineering, Cleveland Clinic, ³Cardiovascular Developmental Biology Center, MUSC.

007 Immunohistochemical Analysis of Mechanisms Mediating Accelerated Vascular Disease in a Lupus Mouse Model Lacking the Inducible Nitric Oxide Synthase Gene, Jashalynn C German¹, K J Smith², Ann Hofbauer³, James C Oates³, Samer Hammad²; ¹Spelman College, ²Medicine, Regenerative Medicine and Cell Biology, MUSC, ³Rheumatology and Immunology, MUSC.

Session 2: Clinical Prof/Masters I

008 Aphasia in the United States: A Ten Year Review (1997-2006), Amanda Kinnamon¹, Meredith Crum¹, Kathryn Edwards¹, Laura B Branan¹, Meryl Hughes¹, Launa Fuhrman¹, Clara Dismuke², Charles Ellis¹; ¹Health Professions, Communication Sciences and Disorders, MUSC, ²Pharmacy, Clinical Pharmacy and Outcomes Sciences, MUSC.

009 Understanding the Evidence in Adult Neurogenics: The Importance of Effect Size, Jennifer Tate, Samantha Martin, Whitney Sheppard, Rachel Engle, Samantha Conner, Charles Ellis; Health Professions, Communication Sciences and Disorders, MUSC.

010 Aphasia in the Stroke Belt, Elizabeth McCutchen¹, Nicole Simpson¹, Carly Georgiades¹, Ann Weber¹, Sunshine Evans¹, Clara Dismuke², Charles Ellis¹; ¹Health Professions, Communication Sciences and Disorders, MUSC, ²Pharmacy, Clinical Pharmacy and Outcomes Sciences, MUSC.
011 The Effects of an Oral Motor Protocol on the Feeding Skills of Infants Born With Congenital Heart Defects, Laura R French, Jennifer L Biro, Jamie D Lee, Debra M Martin, Kerry E Mitchum, Chau M Nguyen, Kathryn Williams, Patricia Coker; Health Professions, Occupational Therapy, MUSC.

012 Sociodemographic Predictors of Diabetes Fatalism in Primary Care Adults with Type 2 Diabetes, Julius E Hamilton, Leah A Bonaparte, Emma G Carter, Joni Strom, Leonard E Egede; College of Medicine, MUSC; Ralph H. Johnson VAMC.

013 Effect of Ethnicity and Health Literacy on Medication Adherence, Blood Pressure and Glycemic Control in Adults with Type 2 Diabetes, Leah A Bonaparte, Julius E Hamilton, Emma G Carter, Joni Strom, Leonard E Egede; College of Medicine, MUSC; Ralph H. Johnson VAMC.

014 The Effect of Unemployment and Low Cost Prescription Generic Plans on Healthcare, Andre S Dyer¹, Andrea D Boan², Samuel Conyers², Daniel T Lackland²; ¹College of Medicine, MUSC, ²Biostatistics and Epidemiology, MUSC.

015 Knowledge and Education of MUSC Health Professions Students Pertaining to the Prevention, Diagnosis and Treatment of Oral, Head and Neck Cancer, Julian L Rinehart¹, Terry A Day², Susan G Reed³, Katherine R Sterba⁴; ¹College of Medicine, MUSC, ²Otolaryngology - Head and Neck Surgery, MUSC, ³CDM, Stomatology, MUSC, ⁴Biostatistics & Epidemiology, MUSC.

016 A Survey of the Driving Curricula of Accredited Occupational Therapy Programs in the United States, Stacie Barber¹, Megan Crawford², Nikki Oder³, Amanda Urowsky², Hon Yuen²; ¹Health Professions, MUSC, ²MUSC.

017 A Survey of Important Criteria in Driving Rehabilitation, Cristopher M Deluna, Jessica R Emerson, Katherine J Falkiewicz, Amanda M Holman, Allison J DuBois, Hon K Yuen; Health Professions, Occupational Therapy, MUSC.

018 What Are the Potential Benefits of a Laptop Computer Ergonomics Educational Session?, Allison K Strock¹, Emily K Chaka¹, Rebecca A Harley¹, Alyssa V Harris¹, Rachel C Miron¹, Brianna L Bailey¹, Peter Bowman²; ¹CHP, Occupational Therapy, MUSC, ²OTD, OTR/L, CHP, Occupational Therapy, MUSC.

Session 3: Clinical Prof/Masters II

019 Differences in Tooth Morphogenesis of Orpk Mutant Mice, Vatsal Suthar¹, Courtney Haycraft²; ¹College of Dental Medicine, MUSC, ²College of Medicine, MUSC.

020 The Effects of Hydrogel Construction on Pancreatic Beta Cell Phenotype, John F Wiles¹, Xiaowei Li², Xuejun Wen³; ¹College of Medicine, MUSC, ²College of Graduate Studies, Clemson-Musc Bioengineering Program, MUSC, ³Clemson-Musc Bioengineering Program, Bioengineering, MUSC.

021 Tendon Graft Ossification in a Bone Tunnel: Growth Factor-Loaded Hydrogel and Release Assay, Daly A Daly¹, Xiaowei Li², Xuejun Wen³, Qian Kay Kang³; ¹Medicine, MUSC, ²Bioengineering, MUSC/Clemson, ³Medicine, Orthopaedic Surgery, MUSC.
022 Prenatal Vitamin D Supplementation and the Innate Immune System: Vitamin D As an Inducer of MCP-4/CCL13 During Pregnancy, Joseph A Hutson¹, John E Baatz², Myla Ebeling³, Thomas C Hulsey³, Carol L Wagner²; ¹Medicine, MUSC, ²Pediatrics, Neonatology, MUSC, ³Pediatrics, Pediatric Epidemiology, MUSC.

023 Regulation of HIF-1α in Adult Cardiocytes, Crystal N Johnson¹, Paul J McDermott²; ¹College of Medicine, MUSC, ²College of Medicine, Cardiology, MUSC.

024 Characterizing the Role of Distinct ECM Proteins in Remodeling of the ECM with Cardiac Hypertrophy, Kelly E Pace³, Amy Bradshaw⁴; ³Medicine, MUSC, ⁴Medicine, Cardiology, MUSC.

025 Myeloperoxidase and Periostin: What's the Connection?, Katherine S Bristow¹, David P Lebel², Titus A Reaves²; ¹College of Medicine, MUSC, ²Regenerative Medicine and Cell Biology, MUSC.

026 Role of Periostin in Epithelial Injury, Jarod L Suber¹, David P Lebel², Titus A Reaves²; ¹College of Medicine, MUSC, ²Regenerative Medicine and Cell Biology, MUSC.

027 Prdx Inhibits Akt Activity Via Regulating Akt Phosphatases, Rebecca Weber¹, Brittany Turner², Juxiang Cao², Jennifer Schulte², Carola Neumann²; ¹College of Medicine, MUSC, ²Pharmacology, MUSC.

028 Immunotherapy of Oral and Pharyngeal Cancer, Isaac F Dingle¹, Brian D Hoei², Semyon Rubinchik², Wei Sun³, M Boyd Gillespie³, Natalia A Sutkowski³; ¹College of Medicine, Otolaryngology - Head and Neck Surgery, MUSC, ²Microbiology and Immunology, MUSC, ³Otolaryngology - Head and Neck Surgery, Hollings Cancer Center, MUSC, ⁴Microbiology and Immunology, Hollings Cancer Center, MUSC.

029 Determining the Role of the E3 Ubiquitin Ligase EDD in Cisplatin Resistant Ovarian Cancer: Regulation By ERK2 Phosphorylation, Danielle W Clark, Hui Zheng, Jennifer R Bethard, Scott T Eblen; Cell and Molecular Pharmacology and Experimental Therapeutics, MUSC.

030 Pure Intraductal Papillomas (IDP) of the Breast: Differential Effect of Histologic Variants on Core Needle Biopsy As Demonstrated in Final Surgical Excised Pathology, Kristen N Arnold¹, Steven D Trocha², Garrett Rowe³, Stephen Mitchell⁴, David P Schammel⁴, Brian P McKinley²; ¹College of Medicine, MUSC, ²Surgery, Greenville Hospital System, ³Clemson University, ⁴Pathology Associates.

031 Combination of Low Dose Estrogen and VEGF Protects C6 Astroglia From Glutamate and TNF-α Induced Apoptosis, Rebecca G Lopez, Arabinda Das, Joshua A Smith, Abhay K Varma, Narendra L Banik; College of Medicine, Neuroscience, MUSC.

032 Methamphetamine Preconditioning: Protective Effects on the Monoaminergic Systems in the Brain, Onica L Washington¹, Marcelo Llanos¹, Amber Hodges², Bruce Ladenheim², Michael T McCoy², S Lud Jayanthi², Jean Cadet², Irina Krasnova²; ¹College of Medicine, MUSC, ²National Institute on Drug Abuse, Molecular Neuropsychiatry Branch.

033 The Effects of PEPA, an AMPAkin, on Activity and BDNF Expression in Rats Following an Acute Administration of Amphetamine, Laura E Briggs, Sarah E Eisenstein, Timothy W Whitfield, Adrian M Gomez, Jacqueline F McGinty; Neurosciences, MUSC.
Session 4: Clinical Prof/Masters III

034 Benefits of a Tracheostomy Team: Four-Year Pre and Post Statistics, Elaina L Simpson, Danielle A Gill, Amy H Dickson, Laurel H Hays; CHP, Communication Sciences & Disorders, MUSC.

035 Videofluoroscopic Swallow Study Practices in Pediatric Dysphagia, Shannon A Torres, Katherine C Viars, Laura E Draize, Amy M Hartenburg, Kate W Humphries, Kelly C MacDonald, Bonnie Martin-Harris; Health Professions, Communication Sciences and Disorders, MUSC.

036 Does Reporting Race Matter in Occupational Therapy Research?, Yolonda J Stuckey, Molly L Chapell, Christina L Eulau, Hazel L Breland; College of Health Professions, Occupational Therapy, MUSC.

037 The Level of Evidence of Stroke Research in Occupational Therapy, Samantha Maslyn, Claudia Cassell, Elise Gardner; Occupational Therapy, MUSC.

038 The Effect of Occupational Therapy Research: Does It Really Matter?, Katherine L Lancaster, Harriet P Gallivan, Jessica L Prescott; College of Health Professions, Occupational Therapy, MUSC.

039 Can We Decrease Energetic Cost During Walking By Consciously Reducing Muscle Activity?, Emily C Hendrix, Lindsay C Hunter, Jesse C Dean; College of Health Professions, Health Professions, Physical Therapy, MUSC.

040 Muscle Plasticity of the Quadriceps in Response to Velocity-Enhanced Resistance Training in a Teenager with Cerebral Palsy Improves Muscle Performance and Quality of Life: a Case Report, Catherine J VanDerwerker, Katy D Holthaus, Noelle G Moreau; College of Health Professions, Physical Therapy, MUSC.

041 Ethnic Differences in Diabetes Knowledge, Self-Care, and Glycemic Control in Adults with Type 2 Diabetes, Emma G Carter¹, Julius E Hamilton², Leah A Bonaparte², Joni Strom², Leonard E Egede²; ¹College of Medicine, MUSC; Ralph H. Johnson VAMC, ²College of Medicine, MUSC.

042 Left Prefrontal Transcranial Magnetic Stimulation Effects on Pain Perception: A Functional Magnetic Resonance Imaging Study, Laura Y Martin¹, Jeffrey J Borckardt², Mark S George³; ¹College of Medicine, MUSC, ²Psychiatry and Behavioral Sciences, College of Medicine, MUSC.

043 Predicted Versus Actual: Participant Accrual in a Feasibility Study, Christopher T Carter¹, Paul Goforth¹, Joan E Cunningham², Michael J Wargovich³, Jeffrey E Korte², Jay Morris³, Dayan G Ranwala⁴, Susan G Reed¹; ¹College of Dental Medicine, Craniofacial Biology, MUSC, ²College of Medicine, Biostatistics and Epidemiology, MUSC, ³College of Medicine, Cell and Molecular Pharmacology and Experimental Therapeutics, MUSC, ⁴Costal Research and Education Center, Clemson University.

Session 5: Clinical Prof/Masters IV

044 The Immediate Effect of Xylitol Gum and Mouthrinse on Salivary Levels of Mutans Streptococcus Bacteria, Justin M DeGarmo¹, Caroline Westwater³, Hon K Yuen¹; ¹College of Dental Medicine, MUSC, ²College of Health Professionals, MUSC.

045 Mandible Growth in Late Teen Caucasian Males, Nathen D Head¹, Paul Nietert², Jing Zhou³; ¹Dental Medicine, MUSC, ²Biostatistics & Epidemiology, Medicine, MUSC, ³Dental Medicine, Orthodontics, MUSC.
046 CT Signs of Right Ventricular Dysfunction: Prognostic Role in Acute Pulmonary Embolism, J M Barraza, D K Kang, C Thilo, A M Armstrong, P Costello, U J Schoepf; 1College of Medicine, MUSC, 2Radiology, Visiting Scholar, 3Radiology, MUSC.

047 Detection of Coronary Artery Anomalies Using Non-Contrast Coronary Artery Calcium Scoring Studies, P Tim Maddux, Doo Kyong Kang, Joseph Abro, Christian Thilo, U Joseph Schoepf; Radiology and Radiological Sciences, MUSC.

048 Short-Term Effects of Repetitive Transcranial Magnetic Stimulation on Cerebral Blood Flow to Limbic System Structures, Daniel Pasko, Tal Herbsman, Kevin Johnson, Paul Morgan, Ziad Nahas, Mark George; 1Medicine, Psychiatry & Behavioral Sciences, MUSC, 2Psychiatry, University of Wisconsin-Madison, 3Neurosciences, MUSC, 4Radiology, MUSC, 5Psychiatry & Behavioral Sciences, MUSC.

049 Reliability of Stroke Diagnosis and Outcomes of TPA Treatment Using the REACH MUSC Stroke Program, Karon N Hammonds, Robert J Adams; Neurosciences, MUSC.

050 Behcet's Disease with Recurrent Erythema Multiforme in a 20-Year-Old African American Male, Julie A Jefferson, Ross B Pollack; 1College of Medicine, MUSC, 2Dermatology and Dermatologic Surgery, MUSC.

051 Prevalence and Correlates of Helminth Co-Infection in Kenyan HIV-1 Infected Adults, Barclay T Stewart, Judd L Watson, Laura Sangare, Loice Mbogo, Phelgona Otieno, Benjamin KS Piper, Barbara Richardson, Grace John-Stewart; 1Medical University of South Carolina, 2University of Washington, 3Centre for Clinical Research, Kenya Medical Research Institute.

052 Hemophagocytosis Lymphohistiocytosis: Description of Clinical and Associated Genetic Findings in 16 Patients, John T Lucas, Munira Shabbir, Adnan Alayoubi, Keisuke Shirai, Charles Greenberg, John Lazarchick; 1Pathology, MUSC, 2Hematology/Oncology, MUSC, 3Cellular and Molecular Pharmacology and Experimental Therapeutics, MUSC.

053 Importance of Long-term Video Electroencephalography to Differentiate Epilepsy From Non-Epileptic Events in Children: MUSC Four-Year Experience, Annie W Chen, Robert P Turner; 1College of Medicine, MUSC, 2Pediatric Neurology, MUSC.

Session 6: PhD I

054 How Does Patient Size Affect Radiation Doses in Cardiac NM Imaging?, Eugene Mah, Samir Tipnis, Leonie Gordon, David Davison, Walter Huda; MUSC.

055 The Role of Cubilin in HDL Homeostasis, Obaidullah Aseem, Jeremy L Barth, Marion A Cooley, Sandra C Klatt, W Scott Argraves; Medicine, Regenerative Medicine and Cell Biology, MUSC.

056 Poly-N-Acetyl Glucosamine Nanofibers From a Marine Diatom Promote Wound Healing and Defensin Expression Via an AKT1/ETS1-Dependent Pathway, Haley Buff, Elizabeth Perkins, Aiguo Zhang, Juanita Eldridge, Marina Demcheva, Arun Seth, John Vournakis, Robin Muise-Helmericks; 1Regenerative Medicine and Cell Biology, Hollings Cancer Center, MUSC, 2Sunnybrook Research Institute, 3Marine Polymer Technologies, Inc.

057 Effect of Mechanical Conditioning and Elastogenic Factors on Elastin Regeneration in 3-D Tissue Constructs, L Venkataraman, A Ramamurthi; Clemson-MUSC Bioengineering.
058 Modulating Effects of PMNs on Induced Elastin Regeneration in Proteolytically-injured Vascular Smooth Muscle Cell Cultures, Emily L Ongstad, Anand Ramamurthi; Clemson-MUSC Bioengineering.

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

060 Fli-1 Transcription Factor is Involved in Cytokine Production and the Inflammatory Response Through TLR4 Stimulation, Emmanuel O Reyes-Cortes¹, Sarah K Williams², Gary S Gilkeson², Dennis K Watson³, Xian K Zhang³; ¹Graduate Studies, Medicine, MUSC, ²Rheumatology & Immunology, Medicine, MUSC, VA, ³Pathology & Laboratory Medicine, MUSC.

061 Administration of a Vaccine Composed of a Immortalized Dendritic Cells Pulsed with Premalignant Oral Lesion Lysate Results in an Increase in CD4+ and CD8+ T Cells in the Tongue, Anna-Maria A Clark¹, Rita I Young²; ¹Graduate Studies, Microbiology and Immunology, MUSC, ²Otolaryngology, MUSC.

062 Acid Ceramidase Upregulation Following Radiation Therapy Desensitizes Cancer Cells to Taxol, Thomas H Beckham¹, Joseph C Cheng¹, Ayman E Mahdy², Xiang Liu², James S Norris²; ¹Graduate Studies, Microbiology and Immunology, MUSC, ²Microbiology and Immunology, MUSC.

063 The Isolation and Structural Characterization of Novel Toxins From the Harmful Algae, Prymnesium Parvum, Matthew J Bertin¹, Paul V Zimba², Kevin R Beauchesne³, Peter Moeller⁴; ¹Marine Biomedicine and Environmental Sciences Center, MUSC, Hollings Marine Laboratory, ²Center for Coastal Studies, Texas A&M University, Corpus Christi, TX, ³JHT in support of the Hollings Marine Laboratory, NOAA, Charleston, SC, ⁴Marine Biomedicine and Environmental Sciences Center, MUSC, Hollings Marine Laboratory, Charleston.

064 Virtual Screening for Novel Inhibitors of Pbp2 From Neisseria Gonorrhoea, a Critical Enzyme in Penicillin Resistance, Richard E Trager, Alena Fedarovich, Christopher Davies; Graduate Studies, Biochemistry and Molecular Biology, MUSC.

065 Role of C18-Pyridinium Ceramide in Autophagy Induced Cell Death in Human Head and Neck Squamous Cell Carcinomas (HNSCC), David Sentelle, Besim Ogretmen, Yusuf Hannun; CGS, BMB, MUSC.

066 MKP-1 is Required for Maximal 1,25(OH)2D3-Induced RANKL Expression and Osteoclastogenesis, Alfred C Griffin, Carlos Rossa, Keith L Kirkwood; Craniofacial Biology, MUSC.

067 SPARC Has a Critical Role in Collagen Fiber Morphology of the Periodontal Ligament, Jessica Trombetta, Amy Bradshaw; MUSC.

068 Oxidative Stress MRNA Changes in the Substantia Nigra of 3 Month Old Methamphetamine-Treated GDNF Heterozygous Versus Wildtype Mice, B Go, H A Boger, J F McGinty; Neurosciences, MUSC.

069 Effects of the Abused Inhalant Toluene on Neurons in the Medial Prefrontal Cortex, Jacob T Beckley, John J Woodward; College of Graduate Studies, Neurosciences, MUSC.
070 Magnetic Resonance Spectroscopy Reveals That NAA Levels May Be an Early Indicator of Neurodevelopmental Outcome in Neonates with Chorioamnionitis. C Bryce Johnson¹, Denise M Mulvihill², Karen C Lee³, Lakshmi D Katikaneni³, Dorothea D Jenkins³, Laura G Rollins³, Paul Morgan⁴;¹Neurosciences’s CAIR, Medicine, MUSC, ²Radiology, Medicine, MUSC, Pediatrics, Medicine, MUSC, ³Pediatrics, Medicine, MUSC, ⁴Neurosciences’s CAIR, Medicine, MUSC, Radiology, Medicine, MUSC.

Session 7: PhD II

071 Postpartum Depression and Vitamin D: An Exploratory Study. Pamela K Murphy¹, Thomas Hulsey², Myla Ebeling², Martina Mueller³, Carol Wagner⁴;¹Graduate Studies, Nursing, MUSC, ²Medicine, Pediatric Epidemiology, MUSC, ³Nursing, MUSC, ⁴Medicine, Neonatology, MUSC.

072 Organ Doses and Projection Angle in Cone Beam CT. Wenjun He¹, Dennise Magill², Emily Tavrides³, Walter Huda³, Hai Yao⁴;¹MUSC-Clemson Joint Bioengineering Program, ²Radiology and Radiological Science, MUSC, ³Radiology and Radiological Science, ⁴Bioengineering, Clemson.

073 Mechanisms of Celastrol Mediated Protection Against Aminoglycoside-Induced Hair Cell Death in the Inner Ear. Shimon P Francis¹, Tiffany G Baker¹, Carlene S Brandon¹, Inga I Kramarenko¹, Fu-Shing Lee², Lisa L Cunningham¹;¹Graduate Studies, Pathology and Laboratory Medicine, MUSC, ²Graduate Studies, Otolaryngology, MUSC.

074 Classifying Multi-Channel Neural Recordings: The Detection of Complex Dynamics. Joshua E Swearingen, Marcelo Reyes, Catalin V Buhusi; Neuroscience, MUSC.

075 Long-term Exposure to a High Saturated Fat and Cholesterol Diet Leads to Altered Morphology in the Hippocampus. Linnea R Freeman, Alfred B Moore, Claudia M Umphlet, Nicholas C Gregory, Ann-Charlotte Granholm; Graduate Studies, Neurosciences, MUSC.

076 Pro-NGF Interaction with P75 May Be Responsible for the Cholinergic Degeneration Observed in Alzheimer’s Disease. Ashley M Fortress¹, Kris L Helke², Ann-Charlotte Granholm³;¹Neurosciences, MUSC, ²Comparative Medicine, MUSC, ³Neurosciences & Center on Aging, MUSC.

077 Chronic RGD Peptide Administration in the Nucleus Accumbens Attenuates Cocaine-Primed Reinstatement. Armina T Wiggins, Peter W Kalivas; MUSC.

078 Isozymes of Sphingosine Kinase Play Partially Overlapped Roles in Tumor Cells. Peng Gao¹, Charles D Smith²;¹Pharmaceutical Sciences, MUSC, ²MUSC.

079 Transdermal Dl-Methylphenidate Potentiates the PK Interactions with Ethanol in a Mouse Model. Guinevere H Bell¹, Andrew J Novak², William C Griffin III², Kennerly S Patrick¹;¹Pharmacy, Pharmaceutical Sciences, MUSC, ²Institute of Psychiatry, Psychiatry and Behavioral Sciences, MUSC.

080 Hypertension, Diabetes and Hypercholesterolemia Associated with Stroke Among Caucasians and African Americans. Andrea D Boan¹, David L Bachman², Robert J Adams², Daniel T Lackland¹;¹Biostatistics and Epidemiology, MUSC, ²Neurology, MUSC.
Identification of Functional Promoter Regions of Two Human DihydroCeramide Synthase (CerS/LASS) Genes: Mechanisms of Regulation in Head and Neck Cancer Cells (HNSCC), Marisa A Meyers, Besim Ogretmen; Graduate Studies, MUSC.

A Bayesian Hierarchical Model to Derive Novel Gene Networks From Gene Ontology Fingerprints, Tingting Qin¹, Lam C Tsoi¹, Andrew B Lawson², Jim W Zheng¹; Biochemistry and Molecular Biology, MUSC, Medicine, DBE, MUSC.

Using Consistent Differential Expression Pattern (CDEP) to Identify Genes Involved in Metastasis From Multiple Microarray Data Sets, Lam C Tsoi¹, Tingting Qin¹, Elizabeth Slate², Jim W Zheng¹; Biochemistry and Molecular Biology, MUSC, Medicine, DBE, MUSC.

Session 8: PhD III

Alternative Pathway Is Responsible for Complement Activation in Dextran Sulfate Sodium-Induced Colitis, Jennifer Schepp-Berglind¹, Carl Atkinson¹, Fei Qiao¹, Gary Gilkeson², Stephen Tomlinson¹; Microbiology and Immunology, MUSC, Rheumatology, MUSC, Ralph H. Johnson VA Medical Center.

Pathogenic Natural IgM Antibodies Recognizing Different Antigens Mediate Injury Following Ischemic Stroke in Rag1-/- Mice, Andrew F Elvington¹, Carl Atkinson¹, Liudmila Kulik², Hong Zhu³, Jin Yu³, Mark S Kindy³, V Holers³, Stephen Tomlinson¹; CGS, Microbiology and Immunology, MUSC, Medicine and Immunology, UCHSC, Neuroscience Institute, Neuroscience, MUSC.

Characterizing the Function, Expression, and Regulation of Antiphagocytic Protein 1, a Virulence Factor of Cryptococcus Neoformans, Virginia E Williams¹, Maurizio Del Poeta²; Microbiology & Immunology, MUSC, Biochemistry & Molecular Biology, MUSC.

Targeting Membrane Associated HSP90 Inhibits Activation of Nuclear Factor Kappa B By Kaposi's Sarcoma Associated Herpesvirus, Michael DeFee¹, Zhiqiang Qin², Lu Dai³, Bryan Toole³, Jennifer Isaacs⁴, Chris Parsons⁵; Microbiology and Immunology, Dental Medicine, MUSC, Medicine, MUSC, Regenerative Medicine and Cell Biology, MUSC, Pharmacology, MUSC, Medicine, Microbiology and Immunology, Dental Medicine, MUSC.

Identification of Small Molecule Compounds That Promote HSC Self-renewal and Expansion Ex Vivo, Joshua N Kellner, Daohong Zhou; Pathology, MUSC.

Quantitation and Spatial Localization of Phosphorylated and Acylated Aquaporin 0 in Human Lenses, Danielle B Gutierrez¹, Zhen Wang², Donita Garland³, Kevin L Schey²; Medical University of South Carolina, Vanderbilt University, University of Pennsylvania.

Perfluorinated Compounds in Northern Fur Seals (Callorhinus Ursinus), Jocelyn R Flanary¹, Paul R Becker²; Graduate Studies, MCBP, MUSC, National Institute of Standards and Technology.

Identification and Characterization of Ionizing Radiation Responsive MicroRNAs, Melissa N Scheiber, Yong Wang, Daohong Zhou; Pathology and Laboratory Medicine, MUSC.
092 Regulation of Ultraviolet Light-Induced Ceramide and Programmed Cell Death By Ceramide Synthase, Thomas D Mullen¹, Lina M Obeid²; ¹Medicine, MUSC, ²Medicine, Biochemistry Molecular Biology, General Internal Medicine (Ralph Johnson VAMC).

093 Targeting Glucosylceramide As a Potential New Treatment for Cryptococcosis, Ryan M Rhome¹, Maurizio Del Poeta²; ¹Graduate Studies, Biochemistry and Molecular Biology, MUSC, ²Graduate Studies, Biochemistry and Molecular Biology, Microbiology and Immunology, MUSC.

094 Role of Acid β-Glucosidase 1 in the Regulation of IL-6 Secretion and P38δ Signaling, David Perry¹, Vindodh Rajagopalan¹, Kazuyuki Kitatani², Russell Jenkins¹, Yusuf Hannun¹; ¹Graduate Studies, Biochemistry, MUSC, ²Tottori University.

095 Functional Relevance of Hox-Specified Positional Identities in Adult Vasculature, Nathanael D Pruett¹, Richard Visconti², Tim McQuinn³, Alexander Awgulewitsch¹; ¹Medicine, MUSC, ²Regenerative Medicine and Cell Biology, MUSC, ³Pediatric Cardiology, Regenerative Medicine and Cell Biology, MUSC.

096 Evaluation of Cultured Rat Aneurysmal SMCs As a Surrogate Model System to Investigate Elastogenic Therapies in Human Aortic Aneurysms, Carmen E Gacchina¹, Anand Ramamurthi²; ¹College of Graduate Studies, Bioengineering, Clemson University-MUSC, ²Bioengineering, Clemson University-MUSC.

96.1 Assays of Porcine Retina Metabolism: A Translational Tool For Drug Discovery in Retinal Degenerative Diseases, Joy Obidike¹, Craig Beeson², Barb Rohrer³; ¹Pharmaceutical Sciences, MUSC, ²MUSC.

Session 9: Postdocs/Residents/Fellows I

097 Differentiation Potential of Embryonic Heart Chicken Cushion Tissue, Agnes Nagy Mehesz, Sergei Znoyko, Zoltan Hajdu, Richard P Visconti, Yukiko Sugi, Russell A Norris, Vladimir R Mironov, Roger R Markwald; Regenerative Medicine and Cell Biology, MUSC.

098 Chronic Administration of KB-R7943 Induces Upregulation of Cardiac NCX1, Olga Chernysh¹, Lin Xu¹, Christiana S Kappler¹, Santhosh K Mani², Donald R Menick¹; ¹Cardiology, MUSC, ²Cardiology, MUSC.

099 Role of Histone Deacetylases in Regulating Sodium/Calcium Exchanger Expression in Adult Cardiomyocytes, Mona S Li, Santhosh K Mani, Benjamin K Addy, Thirumagal Thiagarajan, Christine B Kern, Donald R Menick; Medicine, Cardiology, MUSC.

100 Beta-Adrenergic Receptor Stimulated Ncx1 Upregulation is Mediated Via CaMKII/AP-1 Signaling Pathway in Adult Cardiomyocytes, Santhosh K Mani, Erin A Egan, Benjamin K Addy, Thirumagal Thiagarajan, Christine B Kern, Donald R Menick; Medicine, Cardiology, MUSC.

101 Prdx1 Regulates PTEN Activity in the Nucleus, Juxiang Cao, Jennifer Schulte, Carola Neumann; Medicine, Cell and Molecular Pharmacology and Experimental Therapeutics, MUSC.

102 Expression of the Transcription Factor SOX2 in the Injured Cochlear Nerve, Manna Li, Vinu Jyothi, Ashley M Smith, Juhong Zhu, Lauren A Kilpatrick, Liya Liu, Hainan Lang; Pathology and Laboratory Medicine, MUSC.
Hsp70 Inhibits Aminoglycoside-Induced JNK Activation, Inga I Kramarenko, Carlene S Brandon, Shimon P Francis, Lisa L Cunningham; MUSC.

Peroxiredoxin 1 Regulates P38 MAPK Activity, Brittany P Turner, Hui Zheng, Scott T Eblen, Carola A Neumann; Pharmacology, MUSC.

The Non Homologous End-Joining (NHEJ) Pathway is Dispensable for the Functional Recovery of Hematopoietic Stem Cells and Progenitor Cells After Ionizing Radiation Injury, Ningfei An, Senthil Kumar Pazhanisamy, Daohong Zhou; Pathology and Laboratory Medicine, MUSC.

Session 10: Postdocs/Residents/Fellows II

Magnetic Resonance T2* Measurement of Myocardial Iron Deposition in Sickle Cell Disease: Risk Factors and Relationship with Cardiac Function, Alexander I Ngwube¹, Andrew Hardie², Sherron Jackson¹, Luis Ramos-Duran², Joseph Schaefer², Ibrahim Shatat¹, Miguel Abboud³, Ram Kalpathi¹; ¹Pediatric Hematology and Oncology, MUSC, ²Radiology, MUSC, ³Children's Cancer Center of Lebanon, Beirut, Lebanon.

Prevalence and Risk Factors of Microalbuminuria in Children with Sickle Cell Disease, Lauren J Becton¹, Elizabeth Rackoff², Debra Disco², John K Orak³, Sherron Jackson², Ram Kalpathi², Ibrahim Shatat³; ¹Pediatrics, MUSC, ²Pediatrics, Hematology/Oncology, MUSC, ³Pediatrics, Nephrology, MUSC.

Level-Dependent Changes in Perception of Speech Envelope Cues in Younger Adults with Normal Hearing, Xin Wang, Jayne B Ahlstrom, Amy R Horwitz, Judy R Dubno; College of Medicine, Otolaryngology, MUSC.

Role of SDF-1 Expression and Hematopoietic Stem Cells in Spiral Ganglion Preservation, Lauren A Kilpatrick¹, Manna Li², Vinu Jyothi², Hainan Lang²; ¹Medicine, Otolaryngology, MUSC, ²Medicine, Pathology and Laboratory Medicine, MUSC.

Subcellular Localization of Dihydroceramide Desaturase (DEGS-1) as a Mechanism for Fenretinide Sensitivity, Leslie Wooten-Blanks, Jacqueline M Kraveka; Pediatric Hematology/Oncology, MUSC.

Role of CD147 in the Malignant Phenotype of Therapy-Resistant Tumor Subpopulations, Lu Dai, Mark Slomiany, Lauren Tolliver, Bryan Toole; Regenerative Medicine and Cell Biology, MUSC.

New Drug Leads As Potential Treatments for Calcium-Induced Retinal Degeneration, Nathan R Perron¹, Mausumi Bandyopadhyay², Craig C Beeson¹, Baerbel Rohrer²; ¹College of Pharmacy, Pharmaceutical Sciences, MUSC, ²College of Medicine, Ophthalmology, MUSC.

CXCL13 Secretion By Human Oral Squamous Cell Carcinoma Tumor Cells Stimulates RANK Ligand Expression in Bone Marrow Stromal/Preosteoblast Cells, Yuvaraj Sambandam¹, William L Ries², James S Norris³, Sakamuri V Reddy¹; ¹Darby Children's Research Institute, MUSC, ²College of Dental Medicine, MUSC, ³Microbiology and Immunology, MUSC.

Cue Induced Alcohol Seeking Behavior But Not Food Seeking Behavior is Associated With Increases in Amygdala and Nucleus Accumbens Glutamate Transmission, Justin T Gass, Foster Olive; College of Medicine, Psychiatry, Center for Drug & Alcohol Programs, MUSC.
ORAL PRESENTATIONS:
College of Health Professions (CHP) Building A – 12:00 – 3:15 pm

Session 11: Undergraduate III: 12:15 – 3:00 pm – Room CHP 204

12:15 - 12:30
115 Regulation of Mitochondria Dynamics By Ran-Binding Protein 2, James K Lee¹, Cho Kyoung-In², Yeh Andrew³, Ferreira Paulo²; ¹Biology, Duke University, ²Ophthalmology, Duke University Medical Center.

12:30 - 12:45
116 Activation of Smad2 and P38 Pathways is Differentially Regulated By TGFbeta2 and is Further Regulated By Retinoic Acid in NIH3T3 Fibroblasts, Kimberly M Sauls¹, Loretta L Hoover², Steven W Kubalak²; ¹Winthrop University, ²Regenerative Medicine and Cell Biology, MUSC.

12:45 - 1:00
117 GILT Regulates Cytokine Gene Expression in Prostate Cancer Cells, Ramiz N Hamid¹, Azizul Haque²; ¹SC Governor's School for Science and Math, ²Medicine, Microbiology and Immunology, MUSC.

1:00 - 1:15
118 Increased Beta-arrestin 1 Expression Inhibits Apoptotic Signaling Pathways Induced By Tumor Necrosis Factor-alpha (TNF-alpha), Melissa N Youssef¹, Alessandra Bitto², Hongkuan Fan², Keith T Borg², Perry V Halushka³, James A Cook⁴; ¹Furman University, ²Neuroscience, MUSC, ³Graduate Studies, MUSC.

1:15 - 1:30
119 Role of a 5' Enhancer of Mouse Nkx2.5 for Second Heart Field Specific Expression, Ellen P Knoll¹, Chris D Clark², Kyu-Ho Lee²; ¹College of Charleston, ²Pediatric Cardiology, MUSC.

1:30 - 1:45 Break

1:45 - 2:00
120 Modeled Microgravity Induces S100A8 Mediated Calcium Signaling in Preosteoclast Cells, Giffin Daughtridge, Yuvaraj Sambandam, Sakamuri V Reddy; Charles P. Darby Children’s Research Institute, MUSC.

2:00 - 2:15
121 A Possible Lipofuscin Precursor in Mouse Photoreceptors, Nicholas P Boyer¹, Ioannis Koutalos²; ¹Clemson University, ²Ophthalmology.

2:15 - 2:30
122 Cytoprotection Exhibited By Melatonin Depends on Receptor-Mediated Pathways Associated with MTR1 and MTR2, Casey M O'Dell¹, Arabinda Das², Joshua A Smith³, Russel J Reiter⁴, Abhay K Varma², Naren L Banik²; ¹Erskine College, ²Neurosciences, MUSC, ³Cellular and Structural Biology, U of Texas.

2:30 - 2:45
123 Measuring Changes in Protein Expression in the Nucleus Accumbens Following Cocaine Self-Administration, Geetanjali Pathak, Kathryn J Reissner, Peter Kalivas; Neurosciences, MUSC.

2:45 - 3:00
124 The Prevalence of Pressure Ulcers After Spinal Cord Injury and the Relationship to Socioeconomic Conditions, Bridget Peters¹, James S Krause², Lee Saunders³; ¹Spelman College, ²Health Sciences and Research, MUSC.
### Session 12: Clinical Prof/Masters V: 12:00 – 3:00 pm – Room CHP 201

#### 12:00 - 12:15
125 Racial/Ethnic Differences in Stroke Symptom Awareness and Stroke Knowledge Among Stroke Survivors, Brandon Marion¹, Charles Ellis²; ¹College of Medicine, MUSC, ²College of Health Professions, MUSC.

#### 12:15 - 12:30
126 REACH Risk Factor Survey: A Comparison of Preventive Practices of African Americans With and Without Diabetes, Dennis Orwat¹, Jacketta Cobbs², Lisa Vandemark², Carolyn Jenkins²; ¹College of Medicine, MUSC, ²College of Nursing, MUSC.

#### 12:30 - 12:45
127 Bronchopulmonary Carcinoids: Prevalence and Factors of Survival, Marc McLawhorn¹, Rebecca Johnson², Steven Trocha², Mitchell Worley³, Grace Wheeler⁴, Christine Schammel⁴, James Stephenson², William Bolton²; ¹Medicine, MUSC, ²Surgery, Greenville Hospital System, ³Wofford College, ⁴ Furman University.

#### 12:45 - 1:00
128 Analysis of HPV Infection in Head and Neck Squamous Cell Carcinoma, Kevin P Gibbs¹, Semyon Rubinchik⁴, Geoffrey Pitzer⁵, M. Boyd Gillespie⁶, Natalie Sutkowski⁷; ¹College of Medicine, MUSC, ²Microbiology & Immunology, MUSC, ³Otolaryngology-Head and Neck Surgery, MUSC.

#### 1:00 - 1:15
129 The Utility of Carrier Screening Mutation Panels for Diagnosis of Cystic Fibrosis in South Carolina, Emile R Dalton¹, Daynna J Wolff²; ¹College of Medicine, MUSC, ²Pathology and Laboratory Medicine, MUSC.

#### 1:15 - 1:30
130 Reducing Procedural Pain and Discomfort Associated with Transcranial Direct Current Stimulation, James L McFadden¹, William Beam², Jeff J Borckardt³; ¹College of Medicine, MUSC, ²MUSC, ³Psychiatry, MUSC.

#### 1:30 - 1:45 Break

#### 1:45 - 2:00
131 Normothermia After Gastrointestinal Surgery: Holy Grail or False Idol?, Simon J Lehtinen¹, Georgiana Onicescu², Kathy Kuhn³, Nestor F Esnaola⁴; ¹Medicine, COM, MUSC, ²Biostatistics, Bioinformatics, and Epidemiology, MUSC, ³Quality and Outcomes Management, MUSC, ⁴Medicine, Surgery, MUSC.

#### 2:00 - 2:15
132 Cardiac Magnetic Resonance Image Quality is Surprisingly Good in the Obese: A Study of 2677 Subjects, John R Spratt¹, Marcus Y Chen², W Patricia Bandettini³, Christine Mancine⁴, Peter Kellman⁵, Andrew E Aral²; ¹College of Medicine, MUSC, ²Laboratory of Cardiac Energetics, National Heart, Lung, and Blood Institute.

#### 2:15 - 2:30
133 Effect of Chronic Transfusion Therapy on Progression of Neurovascular Pathology in Pediatric Patients with Sickle Cell Anemia, Sarah K Bishop¹, Gisele Matheus², Robert J Adams³, Sherron Jackson¹, Miguel R Abboud⁴, Ram Kalpathi¹; ¹Pediatric Hematology Oncology, MUSC, ²Neuroradiology, MUSC, ³Neurology, MUSC, ⁴Children's Cancer Center of Lebanon, American University of Beirut Medical Center.

#### 2:30 - 2:45
134 Calcified and Non-Calcified Atherosclerotic Plaque Burden in Black and White Women Undergoing Coronary CT Angiography, John W Nance Jr¹, Luis Ramos-Duran², Pamela B Morris³, Joseph A Abro², Philip Costello⁴, U Joseph Schoepf⁵; ¹College of Medicine, MUSC, ²Radiology, MUSC, ³Medicine, MUSC, ⁴Radiology, Medicine, MUSC.

#### 2:45 - 3:00
135 Unique Unbalanced Translocation Involving Partial Trisomy 9p and Partial Monosomy Yq: A Case Report, Joshua D Fuller¹, Maria del Carmen Montoya², Barbara R Dupont³, Kenton R Holden⁴, Michael J Lyons³; ¹MUSC College of Medicine, ²Catholic University of Honduras, ³Greenwood Genetic Center, ⁴Greenwood Genetic Center, MUSC Neurosciences and Pediatrics.
Session 13: Clinical Prof/Masters VI: 12:15 – 3:15 pm – Room CHP 202

12:15 - 12:30
136 Cisplatin-induced Ototoxicity and Nephrotoxicity, Dylan J Sheridan¹, Lisa L Cunningham²; ¹College of Medicine, Pathology and Laboratory Medicine, MUSC, ²Pathology and Laboratory Medicine, MUSC.

12:30 - 12:45
138 GILT Accelerates Reductive Processing of PSMA and CD4+ T Cell Recognition of Prostate Cancer Cells, Bently P Doonan, Azizul Haque; Microbiology and Immunology, MUSC.

12:45 - 1:00
139 Pleiotrophin, A Tumor Promoter in Bladder Cancer, Tanisha R Hutchinson, Omar Moussa; MUSC.

1:00 - 1:15
140 Investigation of the Relative Invasiveness of EMMPRIN-Hi and -Lo U87 Luc+ Glioma Cells in the Pontine Region Using a Live Rat Model: The Molecular Perspective, Doug K Christie¹, Courtney E Abrams¹, Lauren B Tolliver², Bryan P Toole², Bernard L Maria³; ¹College of Medicine, MUSC, ²Regenerative Medicine and Cell Biology, MUSC, ³Pediatrics, Medical College of Georgia.

1:15 - 1:30
141 Investigation of the Relative Invasiveness of EMMPRIN-Hi and -Lo U87 Luc+ Glioma Cells in the Pontine Region Using a Live Rat Model: The Surgical and Radiological Perspective, Courtney E Abrams¹, Doug K Christie¹, Lauren B Tolliver², Bryan P Toole², Bernard L Maria³; ¹College of Medicine, MUSC, ²Regenerative Medicine and Cell Biology, MUSC, ³Pediatrics, Medical College of Georgia.

1:30 - 1:45 Break

1:45 - 2:00
142 Antimicrobial Activity of Natural Products From Medicinal Plants, Juliana M Head¹, Dayan Ranwala², Caroline Westwater¹; ¹College of Dental Medicine, Craniofacial Biology, MUSC, ²Institute for Nutraceutical Research, Clemson University Coastal Research and Education Center.

2:00 - 2:15
143 The Role of Prx Transcription Factors in Salivary Gland Development, Daniel R West¹, Mary Ann Baybo², Christine B Kern³, Michael J Kern⁴; ¹College of Dental Medicine, MUSC, ²Regenerative Medicine and Cell Biology, MUSC.

2:15 - 2:30
144 The Effects of Oxidized LDL Immune Complexes on Collagen IV Production By Human Mesangial Cells, Alex H Winters¹, Souzan Abdel-Razek², Maria Lopes-Virella²; ¹College of Medicine, MUSC, ²Endocrinology, MUSC.

2:30 - 2:45
145 Bradykinin and Angiotensin-II Induce Distinct Permeability Changes and Differentially Recruit Signaling Molecules in Podocytes, Dezmond B Sumter¹, Mamon Dey¹, Thomas A Morinelli⁵, David P Turner³, John R Raymond⁶, Monika Gooz⁷; ¹Nephrology, MUSC, ²Nephrology, MUSC; RH Johnson VAMC, ³Pathology and Lab Medicine, Hollings Cancer Center, MUSC.

2:45 - 3:00
146 Sepsis-Induced Neuroinflammation, Rachel D Maree¹, Joshua Hirschhorn², S Mohanty², Hongkuan Fan², James Cook², Narayan R Bhat³; ¹Medicine, MUSC, ²Neurosciences, MUSC.

3:00 - 3:15
147 Presence of Mature Immunostimulatory Dendritic Cells is Increased in Patients with Allergic Fungal Rhinosinusitis, Brendan P O'Connell¹, Jennifer K Mulligian², Carl Atkinson³, Ryan M Mulligian², Benjamin S Bleier², Sarah E Casey³, Rodney Schlosser²; ¹College of Medicine, MUSC, ²Otolaryngology-Head and Neck Surgery, MUSC, ³Microbiology and Immunology, MUSC.
Session 14: PhD VI: 12:30 – 2:30 pm – Room CHP 205

12:30 - 12:45
148 Epigenetic Modification of RXRa in Human Colon Carcinomas By the Green Tea Polyphenol, EGCG, Vondina R Brown¹, Jay Morris², Kathleen V Coleman³, Michael J Wargovich²; ¹Graduate Studies, MCBP, MUSC, ²Graduate Studies, Cell and Molecular Pharmacology, MUSC, ³Cell and Molecular Pharmacology, MUSC.

12:45 - 1:00
149 CD44 Membrane Dynamics in Metastatic Breast Cancer Cells, George D Grass¹, Mark G Slomiany², Bryan P Toole³; ¹Graduate Studies, Regenerative Medicine and Cell Biology, MUSC, ²Regenerative Medicine and Cell Biology, MUSC.

1:00 - 1:15
150 Racial Disparity in Surgery Recommendation for Oral and Oropharyngeal Cancer in the US, Yanqiu Weng, Jeffrey Korte, Anbesaw Selassie; Biostatistics and Epidemiology, MUSC.

1:15 - 1:30
151 Ratios of C16ceramide and C16dihydroceramide Rather Than C16ceramide Alone Appear to Dictate Apoptotic Outcome Following TRAIL Stimulation, Tejas S Tirodkar, Christina Voelkel-Johnson; College of Graduate Studies, MCBP, MUSC.

1:30 - 1:45 Break

1:45 - 2:00
152 4'-Phosphopantetheinytransferase Activates 10-Formyltetrahydrofolate Dehydrogenase, Kyle Strickland¹, Alexis Hoeferlin², Sergey Krupenko²; ¹Biochemistry, MUSC, ²MUSC.

2:00 - 2:15
153 Pathogenesis of Cone Photoreceptor Loss in Mice with Disrupted Rod Visual Cycle, Peter H Tang, Patrice Goletz, Rosalie K Crouch; Medicine, Ophthalmology, MUSC.

2:15 - 2:30
154 Extending the REDCap Data Model to Accept External Datasets, Adrian M Nida, Jihad S Obeid; Graduate Studies, Biochemistry, MUSC.

Session 15: PhD VII: 12:00 – 3:15 pm – Room CHP 206

12:00 - 12:15
155 ROC Analyses of Correlated DES Data Suggest Redefinition of Diagnostic Criteria, Jody D Ciolino¹, Daniel Pohl², Donald Castell², Paul J Nietert³; ¹Biostatistics and Epidemiology, Medicine, COGS, MUSC, ²Digestive Disease Center, Gastroenterology and Hepatology, MUSC, ³Biostatistics and Epidemiology, Medicine, MUSC.

12:15 - 12:30
156 Seeing the Forest for the Trees: Graphical Methods for Logic Forest, Bethany J Wolf, Elizabeth G Hill, Elizabeth H Slate; Biostatistics and Epidemiology, MUSC.

12:30 - 12:45
157 Alternative Stopping Rules for Proportional Odds Model Dose Finding Clinical Trial Design with Ordinal Toxicity Grading, Emily M Van Meter¹, Dipankar Bandyopadhyay², Elizabeth Garrett-Mayer²; ¹Division of Biostatistics and Epidemiology, MUSC, ²Division of Biostatistics and Epidemiology, Department of Medicine, MUSC.
12:45 - 1:00
158 A Proteomic Analysis of Temperature-dependent Virulence Factors in Vibrio Coralliilyticus, Nikole E Kimes¹, Wesley R Johnson², Lisa E Kilpatrick³, Pamela J Morris²; ¹Graduate Studies, Molecular and Cellular Biology and Pathobiology, MUSC, ²Biology, College of Charleston, ³National Institute of Standards and Technology.

1:00 - 1:15
159 Downregulation of the Complement Inhibitory Protein, Crry, is Protective in an Orthotopic Bladder Cancer Model Through Modulation of the Adaptive Immune Response, Michelle L Rapisardo¹, Carl Atkinson², Stephen Tomlinson³; ¹College of Graduate Studies, Microbiology and Immunology, MUSC, ²College of Medicine, ³Cell and Molecular Pharmacology, MUSC.

1:15 - 1:30
160 MAPK Phosphorylation of SPF45 on Ser222 Enhances SPF45 Alternative Splicing Activity: A Novel Mechanism of Pre-mRNA Regulation By MAP Kinases, Adnan M Al-Ayoubi¹, Hui Zheng², Tao Bai², Scott T Eblen²; ¹Graduate Studies, Cell and Molecular Pharmacology, MUSC, ²Cell and Molecular Pharmacology, MUSC.

1:30 - 1:45 Break

1:45 - 2:00
161 Heat Shock Inhibits Cisplatin-induced Activation of P53 and STAT-1 in Adult Mouse Utricle, Tiffany Baker¹, Inga I Kramarenko², Mona Taleb³, Shimon P Francis¹, Carlene S Brandon², Keely Morris³, Fu-Shing L Lee², Lisa L Cunningham³; ¹College of Graduate Studies, Pathology and Laboratory Medicine, MUSC, ²Pathology and Laboratory Medicine, MUSC, ³College of Medicine, MUSC.

2:00 - 2:15
162 Non-Melanoma Skin Cancer and the Risk of Second Primary Cancers: A Systematic Review, Lee Wheless¹, Joshua Black², Anthony J Alberg¹; ¹Biostatistics and Epidemiology, MUSC, ²MUSC, Yale.

2:15 - 2:30
163 Inhibition of Cx43/ZO-1 Interaction Improves Gap Junction Intercellular Communication, Reduces Connexon Hemichannel Activity, and Increases Myocyte/Fibroblast Differential Adhesion, J Matthew Rhett, Jane Jourdan, Michael P O'Quinn, Robert G Gourdie; Regenerative Medicine and Cell Biology, MUSC.

2:30 - 2:45
164 ZO-1 Regulates the Phosphorylation of Connexin 43 At Its Carboxyl Terminus, Joseph Palatinus, Robert Gourdie; Regenerative Medicine and Cell Biology, MUSC.

2:45 - 3:00
165 Regulation of VCAM-1 By Retinoid and TGFb Signaling During Formation of the Epicardium, M Elizabeth Burton¹, Laura E Brichler², Loretta L Hoover¹, Steven W Kubalak¹; ¹Regenerative Medicine and Cell Biology, MUSC, ²College of Charleston.

3:00 - 3:15
166 Evidence of a Novel Cove Visual Cycle in the Mammalian Retina, Ryan O Parker¹, Rosalie K Crouch²; ¹Graduate Studies, Neurosciences, MUSC, ²Medicine, Ophthalmology, MUSC.

Session 16: PhD VIII: 12:00 – 3:15 pm – Room CHP 207

12:00 - 12:15
167 Absence of Sphingosine Kinase 1 Inhibits Joint Erosions and Local Inflammation in TNF-alpha Induced Arthritis, DeAnna A Baker¹, Lina M Obeid², Gary S Gilkeson³; ¹MUSC, ²Medicine, Rheumatology, VA, ³Medicine, VA.
12:15 - 12:30
168 A Proposed Role for Sphingosine Kinase 1 in the P53 Pathway: Implications in Carcinogenesis and Thymic Development, Linda A Heffernan-Stroud, Lina M Obeid; MUSC MSTP, MCBP, DOM, VA.

12:30 - 12:45
169 Regulation of CC Ligand 5/RANTES By Secretory Acid Sphingomyelinase – Implications for Compartmentalization of Ceramide Formation, Russell W Jenkins, Christopher J Clarke, Daniel N Canals, Jolanta Idkowiak-Baldys, Kazuyuki Kitatani, Yusuf A Hannun; Biochemistry and Molecular Biology, MUSC.

12:45 - 1:00
170 Host Sphingosine Kinase 1 and Its Product Sphingosine-1-Phosphate Modulate the Phagocytosis of Cryptococcus Neoformans By Alveolar Macrophages, Travis J McQuiston, Maurizio Del Poeta; MUSC.

1:00 - 1:15
171 Bcr-abl Dependent Regulation of Sphingomyelin Synthase 1, Tara Burns, Paola Signorelli, Subathra Marimuthu, Young Choi, Maristella Villani, X Yang, Daohong Zhou, Chiara Luberto; Biochemistry and Molecular Biology, MUSC.

1:15 - 1:30
172 Sphingosine-1-Phosphate Receptor Signaling in Embryonic Blood Vessel Formation, Brent A Wilkerson, Amber N Stratman, Paul A Fleming, Patrick J Gazzolo, George E Davis, Christopher J Drake, W M Argraves, Kelley M Argraves; Regenerative Medicine and Cell Biology, MUSC.

1:30 - 1:45 Break

1:45 - 2:00
173 Uncovering the Antibiotic Potential of the Marine Bacterium Pseudovibrio Denitrificans, Maria I Vizzaino, Peter Moeller, Pamela J Morris; Graduate Studies, MCBP-MBES, MUSC; Hollings Marine Laboratory, MBES, MUSC; Hollings Marine Laboratory; Toxin Chemistry, NOAA National Ocean Service; College of Charleston, Hollings Marine Laboratory.

2:00 - 2:15
174 Salinity Effects on DMSP Concentrations in Fragilariopsis Cylindrus, Barbara R Lyon, Peter A Lee, Michael G Janich, Giacomo R DiTullio; College of Graduate Studies, Marine Biomedicine Environmental Science, MUSC; Hollings Marine Lab, College of Charleston, Department of Medicine, MUSC, Ralph. H. Johnson VA Medical Center.

2:15 - 2:30
175 The Red Tide Dinoflagellate, Karenia Brevis, Exhibits Chloroplast-Associated Metacaspase Activation And Caspase-Like Activities During Senescence, Jillian G Lynch, Frances M Van Dolah; CGS, MBES, Marine Biotoxins Program, NOAA, CCEHBR.

2:30 - 2:45
176 Post-transcriptional Regulation of the DNA Replication Fork Protein, PCNA, in the Florida Red Tide Dinoflagellate, Karenia Brevis, Stephanie A Brunelle, Frances M Van Dolah; MBES, MUSC, CCEHBR, NOS, NOAA.

2:45 - 3:00
177 The Bottlenose Dolphin (Tursiops Truncatus) As a Model Species to Study Infectious Disease: Lacaziosis (Lacazia Loboi), Leslie G Burdett, Randall S Wells, Jeffrey D Adams, David S Rotstein, Teri K Rowles, William A McLeLLan, D H Pabst, Lori H Schwacke; Graduate Studies, Biostatistics and Epidemiology, MUSC; Chicago Zoological Society, Mote Marine Laboratory, Sarasota, FL; NOAA, Center for Coastal Environmental Health and Biomolecular Research, University Corporation for Atmospheric Research, NOAA/NMFS, Office of Protected Resources, Biology and Marine Biology, University of North Carolina at Wilmington, NOAA, Center for Human Health Risk; Graduate Studies, Biostatistics and Epidemiology, MUSC.
3:00 - 3:15
178 Transcriptional Control and Targeting of Acid Ceramidase in Prostate Cancer Radiotherapy, Joseph C Cheng¹, Lorianne S Turner¹, Ayman EM Mahdy¹, Thomas H Beckham¹, Jun Li², S Tucker Marrison¹, Xiang S Liu¹, James S Norris¹; ¹Microbiology and Immunology, MUSC, ²Radiation Oncology, MUSC.

Session 17: Postdoc/Resident/Fellow III: 12:00 – 3:15 pm – Room CHP 203

12:00 - 12:15
179 Effects of Second Hand Smoke on Dendritic Cell Regulation and Function in Chronic Rhinosinusitis, Jennifer K Mulligan¹, Carl Atkinson², Rodney J Schlosser¹; ¹Otolaryngology, MUSC, ²Microbiology & Immunology, MUSC.

12:15 - 12:30
180 Mechanism of Long Range Looping-Mediated Termination of DNA Replication in Schizosaccharomyces Pombe, Samarendra K Singh, Deepak Bastia; Biochemistry and Molecular Biology, MUSC.

12:30 - 12:45
181 Hematopoietic Stem Cells Repair Ionizing Radiation-Induced DNA Double Strand Breaks in a Cell Cycle-Dependent Manner, Senthil Kumar Pazhanisamy, Ningfei An, Yong Wang, Daohong Zhou; Pathology & Laboratory Medicine, MUSC.

12:45 - 1:00
182 Identification and Characterization of C9 Methyl Transferase Gene in Cryptococcus Neoformans, Arpita Singh¹, Liana Casquinha da Silva², Maurizio Del Poeta³; ¹Biochemistry and Molecular Biology, MUSC, ²Instituto Superior Tecnico, Portugal, ³Biochemistry and Molecular Biology, Microbiology and Immunology, MUSC.

1:00 - 1:15
183 Key Role for Neutrophil Sphingolipids in the Killing of Cryptococcus Neoformans, Asfia Qureshi¹, Angus Grey², Kevin Schey³, Chiara Luberto¹, Maurizio Del Poeta³; ¹Medicine, Biochemistry and Molecular Biology, MUSC, ²Medicine, Cell and Molecular Pharmacology and Experimental Therapeutics, MUSC, ³Medicine, Biochemistry and Molecular Biology, Microbiology and Immunology, MUSC.

1:15 - 1:30
184 Role of Sphingomyelin Synthases in Protein Secretion, Subathra Marimuthu, Del Poeta Maurizio, Chiara Luberto; Biochemistry and Molecular Biology, MUSC.

1:30 - 1:45 Break

1:45 - 2:00
185 N-cadherin-ZO-1 Complexes Coupled to Actin Polymerization Drive Membrane Remodeling of Cx43 Gap Junctions, Andrew W Hunter, Robert G Gourdie; Regenerative Medicine and Cell Biology, MUSC.

2:00 - 2:15
186 Bone Marrow Contribution to Heart Valve Remodeling in Response to Myocardial Infarction, Zoltan Hajdu, Roger R Markwald, Richard P Visconti; Regenerative Medicine and Cell Biology, MUSC.

2:15 - 2:30
187 Glucose Consumption Rates of Temporomandibular Joint Disc Cells, Lixia Zhang¹, Jonathan Kuo², Michael Kern³, Hai Yao¹; ¹MUSC, Clemson University, ²Clemson University, ³MUSC.

2:30 - 2:45
188 Estimates of Cochlear Nonlinearities in Adults with Normal and Impaired Hearing, Gayla L Poling, Jayne B Ahlstrom, Amy R Horwitz, Judy R Dubno; College of Medicine, Otolaryngology - Head & Neck Surgery, MUSC.
2:45 - 3:00
189 Congenic Ly5.1 Mice – An Animal Model of Human Auditory Nerve, Vinu Jyothi¹, Manna Li¹, Daohong Zhou¹, Bradley A Schulte², Hainan Lang¹; ¹Pathology and Laboratory Medicine, MUSC, ²Pathology and Laboratory Medicine, Otolaryngology, MUSC.

3:00 - 3:15
190 Fa2h Knockout Mice Exhibit Central Nervous System Disruption, Providing a Model of Human FA2H Deficiency, Kathleen A Potter¹, Michael J Kem², Jagadish K Venkata¹, George Fullbright¹, Akbar A.K. Pathan¹, Bärbel Rohrer³, Xianlin Han⁴, Hiroko Hama¹; ¹Biochemistry and Molecular Biology, MUSC, ²Regenerative Medicine and Cell Biology, MUSC, ³Ophthalmology and Neurosciences, MUSC, ⁴Internal Medicine, Washington University School of Medicine.
ABSTRACTS

001 2-Hydroxypropyl-Beta-Cyclodextrin Removes All-Trans Retinol From Frog Rod Photoreceptors in a Concentration-Dependent Manner, Daniel Johnson1, Chunhe Chen2, Yiannis Koutalos2; 1Physics, College of Charleston, 2Ophthalmology, Neurosciences, MUSC.

All-trans retinol (vitamin A) is highly insoluble and its efficient transport across extra- and intracellular aqueous space requires specialized carriers. A model system for the study of the mechanism of transfer from cell to carrier is provided by vertebrate rod photoreceptors, in which large quantities of all-trans retinol are generated after light exposure. Imaging of the fluorescence of all-trans retinol in single rod photoreceptors was used to measure its removal by different concentrations of the non-specific carrier 2-hydroxypropyl-beta-cyclodextrin. The rate of all-trans retinol removal increased linearly with carrier concentration, indicating that the transfer occurs through a collision-based mechanism.

002 X-ray Tube Current Modulation and E/DLP Conversion Factors in CT, Dennise M Magill1, Wenjun He3, Emily Tavrides3, Hai Yao4, Walter Huda3; 1Radiation Health Physics, Oregon State University, 2Bioengineering, Clemson, 3Radiology and Radiological Science, MUSC, 4Bioengineering, Clemson.

The purpose of this study was to quantify how axial and longitudinal x-ray tube current modulation influence effective dose per unit dose-length product (E/DLP) conversion factors in chest CT. Simulations were conducted of a chest CT examination using a 4 cm beam width with projections obtained at every 15° x-ray tube position at a constant tube output (120 kV). A radiographic patient dosimetry software package (PCXMC) was used to quantify relative patient effective dose as a function of the angular position and longitudinal location (z) of the x-ray tube. Typical angular and longitudinal mA modulation schemes were obtained from the scientific literature. E/DLP conversion factors were generated for: (a) longitudinal modulation alone; (b) angular modulation alone; and (c) combined 2D modulation. An angular mA modulation scheme with an AP/PA tube current one third of the lateral tube current reduces the E/DLP conversion factor in chest CT by 5%. For x-ray tube movement along the z-axis, the maximum to minimum ratio of patient effective dose was 5:1. In chest CT imaging, the longitudinal mA modulation changes the tube current approximately six fold between the central lung area and the upper thorax region above the patient’s lungs. Application of this longitudinal mA modulation scheme reduces the E/DLP conversion factor in chest CT by 22%. The combined use of longitudinal and angular mA modulation schemes in chest CT examinations could reduce E/DLP conversion factors by ~26%. We concluded that the effect of the longitudinal modulation yields a higher dose reduction than the angular modulation, but without accounting for mA modulation a calculated E/DLP overestimates the dose by ~26%.

003 Differences in Cortico-Limbic Activation in Patients Receiving Three Weeks of Real or Sham RTMS, Dakota Hadley1, Samet Kose2, Li Xingbao2, Paul Morgan3, Berry A Anderson2, Kevin Johnson2, Ziad A Nahas2, Mark A George2; 1College of Charleston, Brain Stimulation Lab, MUSC, 2Brain Stimulation Lab, MUSC, 3Brain Stimulation Lab, MUSC, Ralph H. Johnson VA Medical Center.

Background: Daily prefrontal rTMS was initially developed as a potential antidepressant with the working hypothesis that stimulation of prefrontal cortex would also affect connected limbic regions and reset a prefrontal cortex-limbic circuit involved in mood regulation. Many studies have shown that cortical stimulation of the left prefrontal cortex also results in activation of limbic and other emotion centers. Methods: We scanned 23 depressed patients with the interleaved technique who were exiting phase I of a larger study, which consisted of 3 weeks of either sham or real rTMS. Separate within-group and then between-group analyses were done to compare remitters versus nonresponders and to compare those who had received real rTMS versus those who had not. We also looked at changes due to intensity of stimulation. Results: For the entire group, left prefrontal rTMS resulted in activations in cortical as well as connected limbic regions. There was an interaction effect between real and sham and the intensity of stimulation. At 100% motor threshold (MT), those who received sham showed more activation. However, at 120%MT the real group showed more. There was no significant difference between remitters and nonresponders. Discussion: Left prefrontal TMS applied within the MRI scanner to the left prefrontal cortex in depressed patients causes changes in cortical as well as limbic connected regions visible with the interleaved TMS/fMRI technique. The interaction effect seen with the dosage and real versus sham could be due to two things. At 120%MT, the real group showed more activation which could be due to neuroplastic changes as a result of three weeks of TMS. The real group had been receiving a 120%MT dosage for three weeks which could be the reason the sham group showed more activation at 100% MT; 100% MT for the real group was not a high enough dose. Funding from: NIH R01 MH069887 (opt-TMS trial), SURP.

004 Seizure Detection System for Scalp EEG Monitoring, Rebecca L Wilson1, Jonathan Halford2; 1College of Charleston, 2Neurosciences, MUSC.

Abstract not available.
005 CRF Reduces GABA Release Onto VTA Dopamine Cells: Neuroadaptations After Chronic Cocaine Self-Administration, Courtney L Williams¹, Arthur C Riegel²; ¹Biology, College of Charleston, ²Neuroscience, MUSC.

Abstract not available.

006 Altered Versican Processing in Mouse Models of ADAMTS5 Deficiency Leads to Severely Hypertrophic Semi-lunar Valves, Alexandria C Bahan¹, Suneel S Apte², Christine B Kern³; ¹Cardiovascular Developmental Biology Center, MUSC, Honors College, College of Charleston, ²Lerner Research Institute, Biomedical Engineering, Cleveland Clinic, ³Cardiovascular Developmental Biology Center, MUSC.

Abstract not available.

007 Immunohistochemical Analysis of Mechanisms Mediating Accelerated Vascular Disease in a Lupus Mouse Model Lacking the Inducible Nitric Oxide Synthase Gene, Jashalynn C German¹, K J Smith², Ann Hofbauer³, James C Oates³, Samar Hammad⁴; ¹Spelman College, ²Medicine, Regenerative Medicine and Cell Biology, MUSC, ³Rheumatology and Immunology, MUSC.

Systemic inflammation is increasingly being considered central to the pathogenesis of atherosclerosis and a key risk factor for cardiovascular disease (CVD). A murine lupus nephritis model, MRL/lpr, was used in the study. Our group has previously shown that atherosclerotic plaque scores were higher in the MRL/lpr mice deficient in the inducible nitric oxide synthase (NOS2) gene than in the matched control mice. Furthermore, levels of plasma spingosine-1-phosphate (S1P), a blood borne lipid mediator, were shown to be higher in the NOS2 knockout (KO) mice compared to controls. Using an immunohistochemistry approach, we examined whether the genetic deletion of NOS2 affects fat accumulation and inflammation in the vessel wall. Endothelial cells were probed using CD34, and activated endothelial cells probed using antibodies against platelet/endothelial cell adhesion molecules (PECAM). Oxidized low-density protein (oxLDL) and macrophages in the aorta were determined using anti-oxLDL and the macrophage marker F4/80, respectively. Aortas were also immunostained for sphingosine kinase 1 (SK1), the enzyme that generates S1P. Aortas were probed for reactive nitrogen species (RNS) using anti-nitrotyrosine antibodies. The endothelium of the NOS2 KO mice appeared damaged and lacked integrity. Higher levels of PECAM were present in endothelial cells from NOS2 KO mice than control mice. F4/80 confirmed the presence of macrophages in both NOS2 KO and control mice; however, more macrophages were distinguished deeper in the arterial wall of the NOS2 KO mice. Higher level of RNS found in control mice. SK1 was detected mostly in the NOS2 KO mice, predominately around the fat-containing cells. The anti oxLDL antibodies detected a presence of oxLDL in the extracellular matrix in the NOS2 KO mouse.

This study provides evidence that accelerated CVD in KO mice might be mediated by higher levels of modified lipoprotein, involvement of the endothelial/ macrophage system, and alteration in the shingolipid pathway. Farzan Soodavar, Mohammed Al Gadban, Demarcus Heller (summer student 2008), Dr. Gabe Virella's lab., Joan Colglazier, Pathology & Laboratory Medicine, Margaret Romano, Dr. Toshihiko Kawamori, College of Graduate Studies, NIH Training Grant: R25HL92611, NIH/NHLBI: HL079274 (S.H.)

008 Aphasia in the United States: A Ten Year Review (1997-2006), Amanda Kinnamon¹, Meredith Crum¹, Kathryn Edwards¹, Laura B Branan¹, Meryl Hughes¹, Launa Fuhrman¹, Clara Dismuke², Charles Ellis¹; ¹Health Professions, Communication Sciences and Disorders, MUSC, ²Pharmacy, Clinical Pharmacy and Outcomes Sciences, MUSC.

Recent estimates indicated that approximately 800,000 Americans will experience a stroke in 2009. It is believed that 21-38% of individuals who experience an acute stroke will be left with aphasia. Few reports have examined national data to determine general trends over an extended period of time. The purpose of this project was to use national data to determine the number, regional distribution and characteristics of patients with aphasia over a ten-year period (1997-2006) and to use available cost data to highlight the differences in cost between 1997 and 2006. Methods. This study was descriptive secondary data analyses. Data for this project was obtained from the AHRQ Healthcare Cost and Utilization Project (HCUP) database. We examined data from the National Inpatient Sample (NIS) (1997-2006) using ICD-9 codes for aphasia to identify the incidence, demographic trends, and US regional distribution of patients discharged with a diagnosis of aphasia. Results: Between 1997 and 2006 the incidence of aphasia was approximately 100,000 per year. During the 10-year period, the majority of patients were 65 years of age and older, female, had Medicare as a primary payer source and resided in the South. Length of stay (LOS) and hospital charges related to stroke specifically was generally consistent in the US form 1997-2006 and mirrors regional patterns of stroke when considering only those patients with aphasia. Few reports have examined those factors that determine the true magnitude of aphasia and other neurologically based disorders of communication.
Effect sizes allow us to compare the magnitude of the results from one treatment to another. In the area of communication disorders, clinicians are now more than ever required to draw upon current research findings to guide their clinical practice. Consequently, reporting “statistical significance” alone does not give information about the size of magnitude of the statistically significant difference. Therefore, the purpose of this project was to examine reports of “effect size” in previously published studies in the area of adult neurogenic disorders of communication. Methods: This study was a retrospective review of literature published in the Journal of Speech, Language, and Hearing Research (JSLHR) between 2003 and 2007 in the area of adult neurogenic disorders. We examined the proportion of articles published in the area of adult neurogenic communication disorders that reported effect size when the results were statistically significant. We reviewed full texts of all articles published in volumes 46-50 of the JSLHR (30 issues) to identify reports of effect size. Effect size measures considered included: Cohen’s d, Hedge’s g, Glass’s Δ, f, w (Chi-square), f2 (regression), Eta squared (h2), partial Eta squared (hp2), Omega squared (ω2), and the Intraclass correlation (rI). Results: 37 articles were published in 24 of the 30 issues of JSLHR in the area of adult neurogenic disorders. Twelve of the 37 articles (32%) were treatment articles primarily in the area of aphasia. Five of the 37 articles (14%) reported qualitative findings or did not include a quantitative analysis. Of the remaining 32 articles, only six (19%) that reported statistically significant results also reported an effect size. Conclusions: Consistent reporting of the “effect size” can assist clinicians in determining the statistical, practical and clinical significance of clinical research of adult neurogenic disorders.

010 Aphasia in the Stroke Belt. Elizabeth McCutchen1, Nicole Simpson1, Carly Georgiades1, Ann Weber1, Sunshine Evans1, Clara Dismuke2, Charles Ellis; 1Health Professions, Communication Sciences and Disorders, MUSC, 2Pharmacy, Clinical Pharmacy and Outcomes Sciences, MUSC.

Background: It is expected that approximately 800,000 Americans will suffer a new or recurrent stroke in 2009. Of these stroke victims, roughly 100,000 patients acquire aphasia. Few reports have considered the regional distribution of persons with aphasia in the U.S particularly in the “Stroke Belt”. The purpose of this project was to use national and state level data to examine the distribution of new cases of aphasia in the U.S. Methods: We examined data from the AHRQ Healthcare Cost and Utilization Project (HCUP) to determine the incidence of aphasia by geographical region. National and state HCUP databases were searched to obtain the following information: (1) incidence of stroke by U.S regions (Northeast, Midwest, West, and South), (2) incidence of aphasia by U.S. regions, and (3) incidence of stroke among “stroke belt” states. Results: We found that the largest number of patient discharged from U.S. hospitals in 2006 with stroke was in the South followed by the Midwest, Northeast and the West. A higher number of patients discharged from U.S. hospitals with a primary or secondary diagnosis of aphasia existed in the South (32.9%), followed by the Midwest (27.1%), West (22.4%) and Northeast (17.6%). A review of data from five of the 11 traditional “stroke belt” states indicated that the highest number of patients discharged with a diagnosis of stroke was in the state of North Carolina followed by Tennessee, Kentucky, South Carolina and Arkansas. Conclusions: A review of 2006 HCUP data revealed that aphasia as a primary or secondary diagnosis mirrored traditional patterns of higher stroke incidence in the southeast or “stroke belt” region of the U.S. Future studies should be conducted to examine regional patterns related to stroke and aphasia related outcomes and in particular costs and associated functional outcomes.

011 The Effects of an Oral Motor Protocol on the Feeding Skills of Infants Born With Congenital Heart Defects. Laura R French, Jennifer L Biro, Jamie D Lee, Debra M Martin, Kerry E Mitchum, Chau M Nguyen, Kathryn Williams, Patricia Coker; Health Professions, Occupational Therapy, MUSC.

Introduction/Rationale: Infants with Complex Congenital Heart Defects (CCHD) often experience difficulty with bottle/breast feeding. This poster presents the results of a pilot study on the effectiveness of an oral motor program for infants born with CCHD. The specific aim of this study is to examine if an oral motor stimulation protocol can improve feeding behaviors of infants born with CCHD. Methods: A non-randomized clinical trial was used with full term infants born with CCHD, specifically single ventricle anatomy. The experimental group (n=10) received the oral motor protocol once daily, six days per week until bottle/breast feeds were initiated. The data collected from the experimental group was compared to archived data collected from infants born between 2005 to 2006. The infants in the comparison group (n=10) met the same inclusion criteria as the experimental group, but did not receive the oral motor protocol. Data collected included: date of birth, Ear Nose and Throat (ENT) and modified barium swallow studies (MBS) evaluations, number of days to initiation of first feed, number of days to full oral feeds, gastronomy tube (g-tube) placement, and length of stay in the hospital. Results: Preliminary analysis of data reveal that infants receiving the oral motor treatment reached full bottle/breast feeding 2 days sooner and discharged from the hospital on average 10 days earlier than infants in the comparison group. Three of the infants in the experimental group received g-tube placements versus 4 infants in the comparison group. Both groups had
3 infants with abnormal ENT and MBS evaluations, and 3 infants with atypical MBSS. Conclusions: Infants with CCHD who receive an oral motor protocol demonstrate improved feeding behaviors which may contribute to earlier discharge from the hospital and reduced need for g-tube placement. These results are preliminary and require further data collection, analysis, and study. We would like to acknowledge Paige Merrill, Courtney Jarrard, and Francis Kline-Woodard, the co-investigators of the study.

012 Sociodemographic Predictors of Diabetes Fatalism in Primary Care Adults with Type 2 Diabetes, Julius E Hamilton, Leah A Bonaparte, Emma G Carter, Joni Strom, Leonard E Egede; College of Medicine, MUSC; Ralph H. Johnson VAMC.

Background: Diabetes fatalism is defined as “a complex psychological cycle characterized by perceptions of despair, hopelessness, and powerlessness”. Prior work has shown that diabetes fatalism is associated with poor self-care, poor glycemic control and decreased quality of life. This study examined sociodemographic predictors of diabetes fatalism in a primary care sample. Methods: Data on 213 subjects with type 2 diabetes recruited from the MUSC University Internal Medicine Clinic was examined. Race was defined as non-Hispanic White and non-Hispanic Black. Diabetes fatalism was assessed by a previously validated 12-item Diabetes Fatalism Scale (DFS-12). The 12-items on the DFS-12 are scored on a 5-point Likert scale with scores ranging from 1 (strongly disagree) to 5 (strongly agree) with higher scores reflecting higher levels of diabetes fatalism. Minimum and maximum scores for the DFS-12 are 12 and 60 respectively. Subjects were administered the DFS-12 scale. Mean scores on the DFS scale were compared by sociodemographic characteristics including age, gender, race/ethnicity, marital status, education, employment, insurance status, income, and health status using t-test and ANOVA. Multiple linear regression was used to assess the independent correlates of diabetes fatalism. STATA V10 was used for statistical analysis. Results: 54% of the sample were African Americans, 43% were 65 years and older, 62% were women, 48% were married, 26% had less than high school education, 29% were employed, 9% were uninsured, 28% had income <$10,000, and 24% had worse health status compared to the previous year. In this sample, the DFS-12 had a Cronbach’s α of 0.75 with mean score of (28.2 ± 7.4) and range of 12-49. In unadjusted analysis, mean DFS-12 score was significantly different by ethnicity (Whites 30.4 ± 6.1, Blacks 26.3 ± 7.9; p<0.0001) and health status (worse 32.3 ± 6.9, better/same 26.9 ± 7.2, p<0.0001). In the adjusted model controlling for covariates, independent correlates of diabetes fatalism were white race/ethnicity, younger age (18-49 years), and poor perceived health status. Other covariates were not significantly associated with diabetes fatalism. Conclusion: In this sample of primary care patients with type 2 diabetes, predictors of diabetes fatalism included white race/ethnicity, younger age, and poor health status. Further studies are needed to identify strategies to decrease diabetes fatalism and associated poor diabetes outcomes. Funding provided by grant#5T35DK007431 and the MUSC Center for Health Disparities Research.

013 Effect of Ethnicity and Health Literacy on Medication Adherence, Blood Pressure and Glycemic Control in Adults with Type 2 Diabetes, Leah A Bonaparte, Julius E Hamilton, Emma G Carter, Joni Strom, Leonard E Egede; College of Medicine, MUSC; Ralph H. Johnson VAMC.

Background: Health literacy is defined as “the degree to which individuals have the capacity to obtain, process, and understand basic health information and services needed to make appropriate health decisions. There is conflicting data on the effect of health literacy on medication adherence, blood pressure (BP), and glycemic control in type 2 diabetes. This study examined the impact of ethnicity and health literacy on medication adherence, blood pressure (control, and glycemic control in adults with type 2 diabetes. Methods: Data on 213 subjects with type 2 diabetes recruited from the MUSC University Internal Medicine Clinic was examined. Race was defined as non-Hispanic White and non-Hispanic Black. Health literacy was assessed with the S-TOFHLA and categorized as adequate and inadequate functional health literacy. Good BP control was defined as BP <130/80 mmHg and good glycemic control was defined as hemoglobin A1c (HbA1c) <=7%. Medication adherence was assessed with the 4-item Morisky adherence scale and categorized as adherent vs. non-adherent. Covariates included age, gender, marital status, education, employment, insurance status, income, and health status. Medication adherence, BP and glycemic control were compared across ethnic and health literacy categories using chi square. Multiple logistic regression was used to assess the independent effects of ethnicity and health literacy on medication adherence, BP control, and glycemic control controlling for covariates. STATA V10 was used for statistical analysis. Results: 54% of the sample were African Americans, 43% were 65 years and older, 62% were women, 48% were married, 26% had less than high school education, 29% were employed, 9% were uninsured, 28% had income <$10,000, and 24% had worse health status compared to the previous year. In this sample, 21% had inadequate health literacy, 52% were non-adherent to medications, 43% had good blood pressure control and 46% had good glycemic control. In unadjusted analyses, whites were more likely to be non-adherent to medications compared to black (62% vs. 43%, p=0.0006), but there were no ethnic differences in BP and glycemic control. There were also no significant differences in medication adherence, BP, or glycemic control by health literacy levels. In adjusted analyses, whites were less likely to be non-adherent to medications compared to black, but the difference was only marginally
significant (OR 0.53, 95% CI 0.25-1.12, p=0.09). No other comparisons were significant. Conclusion: In this sample of primary care patients with type 2 diabetes, levels of medication adherence, BP control, and glycemic control were less than optimal. Functional health literacy was not significantly associated with the diabetes outcomes measured in this study, while ethnicity was only marginally associated with outcomes. Efforts to improve diabetes outcomes should target all patients regardless of ethnicity and functional health literacy. Funding provided by grant#ST35DK007431 and the MUSC Center for Health Disparities Research.

014 The Effect of Unemployment and Low Cost Prescription Generic Plans on Healthcare, Andre S Dyer1, Andrea D Boan2, Samuel Conyers2, Daniel T Lackland5; 1College of Medicine, MUSC, 2Biostatistics and Epidemiology, MUSC.

Unemployment rates in the United States currently stand at 9.5% which represents a 3.7% increase in unemployment from last year’s 5.8% unemployment rates. It is evident that increasing unemployment rates have placed a significant burden on our health care system as evidenced in the drastic increases in emergency room discharges over the period from 2000 through 2007 with unemployment being a possible contributory factor. It is our postulation that when people become unemployed, they generally lose their health care insurance as well because this is usually provided by their employer. Therefore, if a person becomes unemployed, there is a significant chance that they may also lose their access to a regular means of health care and the ER essentially becomes one of the most immediate means of primary care. South Carolina’s current unemployment rate is 12.1%, a 2.6% difference above the national average. It therefore supports logical thought that compared to the impact that unemployment has had on health care from a national perspective, South Carolina may have to contend with an even greater burden due to our increased unemployment rates. Methods. It is the intent of the researcher to observe the possible impact of the recently increased availability of medication at a reduced cost to see if this increased accessibility has a significant impact on the control of diabetes as well as other chronic illnesses. It is our intention to obtain information regarding the possible impact of companies like Wal-Mart and Bi-lo who offer low cost prescription medication on the prevalence of chronic illness. A map of the state illustrating the spread of these companies will be examined along with a comparative view of the prevalence of a number of chronic illnesses. Our intent is to determine what associations exist if any, based on a comparison of these patterns. Results. We noticed that certain areas with higher levels of unemployment also had a higher prevalence of diabetes and hypertension and also that certain areas of lower unemployment had a lower prevalence of diabetes and hypertension. Based on information gathered regarding the density of Wal-Mart stores with pharmacies, it is not possible to state whether these stores are able to make any significant impact on the control of chronic illness. What we can conclude is that they have provided increased availability of low cost prescription medication to the public at large and hopefully this will aid in the attempt to curb the prevalence of many chronic illness which plague the state. Conclusions. Due to increased availability of affordable medication, made possible by the advent of low cost generic programs, many conditions and chronic illnesses including hypertension and diabetes may be better controlled in patients living with these illnesses. Also, as a result of this increased availability, the negative effects of unemployment on health care may not be as devastating in cases where cost is considerably decreased. MUSC College of Graduate Studies Summer Health Professionals Research Program

015 Knowledge and Education of MUSC Health Professions Students Pertaining to the Prevention, Diagnosis and Treatment of Oral, Head and Neck Cancer, Jillian L Rinehart1; Terry A Day2; Susan G Reed2; Katherine R Sterba4; 1College of Medicine, MUSC, 2Otolaryngology - Head and Neck Surgery, MUSC, 3CDM, 4Stomatology, MUSC, 5Biostatistics & Epidemiology, MUSC.

Background. South Carolina has one of the highest mortality rates for oral, head and neck cancers in the country. Therefore it is essential for health professions students in the state to be knowledgeable about the prevention, detection and treatment of this disease. Methods. In 2009, the authors surveyed 614 students using a written questionnaire (response rate, 83.95 percent) and an online version of the same questionnaire to reach students not attending classes (response rate, 22.4 percent). The questionnaire included questions about oral cancer risk factors, diagnostic signs, symptoms and examination procedures, as well as questions about student smoking habits and student views on future curriculum changes. Results. Oral, head and neck cancer knowledge and education questions were evaluated in three categories: knowledge of risk factors; knowledge of signs, symptoms and exam procedures; and attitudes about oral cancer knowledge and education. Averages for the total percentage of correctly answered questions for each category were identified. Students in the College of Dental Medicine proved students proved most knowledgeable (69.6%, 66.39%, 69.3%), followed by students in the College of Medicine (61.8%, 57.12%, 64.6%) and students in the Physician Assistant program (52.8%, 50.86%, 60.2%). Students in every group surveyed showed a lack of knowledge of two oral cancer non-risk factors, family history of cancer and poor oral hygiene. Responses for these two criteria ranged from 0.0% to 44.2%. Additionally, the percentage of correct answers for the most common age of diagnosis question was exceedingly low. Responses ranged from 9.40% to 27.40% in this category. Overall, medical students...
felt most comfortable palpating lymph nodes in necks of patients (80%), while occupational therapy students reported a 0.0% response when asked if their knowledge about oral cancer was current. Conclusion. Although students’ level of knowledge has improved in the past six years, it is crucial to the health of South Carolina citizens that educators and the legislature work together to better integrate oral, head and neck cancer prevention, diagnosis and treatment skills into the state’s health professional training curricula. A worthy step toward this goal will be the demonstration of these skills on future South Carolina board examinations. MUSC College of Graduate Studies Summer Health Professionals Fellowship

016 A Survey of the Driving Curricula of Accredited Occupational Therapy Programs in the United States, Stacie Barber1, Megan Crawford2, Nikki Oder2, Amanda Urowsky2, Hon Yuen2; 1Health Professions, MUSC, 2MUSC.

The increase in the aging population in the United States has created a new demand for driving evaluation and rehabilitation. Driving is a fundamental skill necessary to maintain community involvement, quality of life and independence, and, therefore, Occupational Therapy has sought to meet this need by including driving under their scope of practice. Driving Evaluation and Rehabilitation has been adopted by AOTA as an emerging area of practice and has implemented an initiative to integrate training curricula on older-driver assessments and rehabilitation into Occupational Therapy schools. The purpose of this study is to determine the extent to which driving evaluation and rehabilitation is included in the curricula of Occupational Therapy programs in the United States. A 10-item questionnaire will be sent through email to program directors of each institution to gather this data. The questionnaire will be sent through Survey Monkey up to a maximum three times to ensure optimal response. The aim of this email survey is to compile data concerning the inclusion of education and training provided in the area of driving rehabilitation and evaluation in Occupational Therapy programs throughout the nation.

017 A Survey of Important Criteria in Driving Rehabilitation, Cristopher M DeLuna, Jessica R Emerson, Katherine J Falkiewicz, Amanda M Holman, Allison J DuBois, Hon K Yuen; Health Professions, Occupational Therapy, MUSC.

Driving simulators are becoming an increasingly realistic tool to evaluate fitness to drive. Currently there is no literature outlining important criteria necessary to include in a driving simulator scenario. Purpose: To compile a list of criteria deemed important in the scenarios used in driving simulators. Compiling this data would benefit those who are setting up a driving simulator to use in driver rehabilitation. Methods: All certified driving rehabilitation specialists within the United States listed on the Association for Driver Rehabilitation Specialists directory were contacted via email and given a link to the Survey Monkey website containing a survey. This survey contains items compiled from past studies of items used in on-road driving examinations. Participants were asked to rate the importance of factors for inclusion in a driving scenario.

018 What Are the Potential Benefits of a Laptop Computer Ergonomics Educational Session?, Allison K Strock1, Emily K Chaka1, Rebecca A Harley1, Alyssa V Harris1, Rachel C Miron1, Brianna L Bailey1, Peter Bowman2; 1CHP, Occupational Therapy, MUSC, 2OTD, OTR/L, CHP, Occupational Therapy, MUSC.

There is limited research regarding ergonomic laptop/notebook computer use. Due to the rising popularity of laptop/notebook computers, there is a need to further explore this area of research. 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. Over 150 graduate students from the College of Health Professions at the Medical University of South Carolina participated in this study. Participants were randomly assigned to either an experimental or a 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. Two weeks 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. 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.

019 Differences in Tooth Morphogenesis of Orpk Mutant Mice, Vatsal Suthar1, Courtney Haycraft2; 1College of Dental Medicine, MUSC, 2College of Medicine, MUSC.

The orpk mutant mouse, which has defects in formation of cilia, develops an ectopic molar but no work has been done to investigate the morphology of the teeth in this mouse model. The tooth defects in patients with defective cilia suggests that the orpk mutant teeth will reveal altered dentin and enamel secretion, abnormal growth of roots and pulp chambers, and atypical periodontal ligament (PDL) structure. The organization and arrangement of cells within the tooth were evident via H&E staining in all three stages of development. In addition to the H&E stain, Picro-red (PR) staining was used to observe collagen type I arrangement of PDL in P7, P30, and P90 samples. Contrasting mutant dentition to wild type showed a decrease in dimensions of tooth structures of the mutant samples in all three
stages. Based on the results from observing mice at three different stages of development (P7, P30, and P90) there is evidence demonstrating a quantifiable difference in the amount of cementum and dentin in mutant dentition. Determinations were made based on H&E staining on slides obtained from each sampled stage. Picro red staining, however, showed no quantifiable measure of atypical PDL growth. The antibodies used in this study (AMELX, DSP, OSTEO, SOST, Ac.a,g) were excluded from any presented data due to the lack of observable staining. Summer Health Professions Research Program, AADR Fellowship Program

**020 The Effects of Hydrogel Construction on Pancreatic Beta Cell Phenotype**

Type 1 diabetes is caused by autoimmune-mediated destruction of pancreatic beta cells, leading to unregulated glycemia and secondary disease. A potential treatment strategy for this disease is development of a beta cell implant derived from differentiated stem cells. Our goal was to bioengineer a hydrogel matrix to potentially serve as the synthetic ECM of such an implant. We evaluated several hydrogels containing various concentrations of thiol-modified gelatin, thiol-modified hyaluronan, and a PEGDA crosslinker. The collagen:hyaluronan ratios used were 0:100, 25:75, 50:50, 75:25. Crosslinker concentration was varied to achieve gel stiffness of 10Pa and 100Pa. Each gel was seeded with MIN6 pancreatic beta cells at a concentration of 8x10^4 cells/150microL hydrogel. Cell viability and morphology was assessed by staining under confocal microscopy. Cellular morphology was compared to MIN6 cells grown in Matrigel, a basement membrane preparation closely resembling native ECM. Our study showed cellular viability was hampered by low cellular density. MIN6 clusters were hypoplastic if seeded at concentrations below 8x10^4 cells/150microL, suggesting the importance of cell-cell interactions. Additionally, cells grown in 0% collagen had markedly lower viability while cells grown in 25%, 50%, and 75% collagen all had similar viability. This suggests that extracellular collagen concentrations of at least 25% are required for proper beta cell viability. Cellular morphology was not recreared using our hydrogels as compared to Matrigel, possibly due to the lack of integrin binding sites found on collagen and hyaluronan. I would like to acknowledge Leonard E. Egede, M.D., MS for funding of this project and the Summer Health Professions Program in the College of Graduate Studies for providing this research opportunity.

**021 Tendon Graft Ossification in a Bone Tunnel: Growth Factor-Loaded Hydrogel and Release Assay**

Anterior Cruciate Ligament (or ACL) injuries are relatively common among the young active population, with as many as 200,000 occurring each year in the US alone. Current graft technologies allow for stable fixation of the graft, although donor site complications are prevalent. In order to replace this bone-patellar tendon-bone graft with an alternative graft type, a mechanism for recreation of the natural bone tendon interface must be elucidated. Currently, growth factors including HGF, IGF-1, and BMP-2 loaded within hydrogels for sustained release are being explored. These growth factors were loaded in hydrogels of various concentrations, using both Hyaluronan (HA) and Gelatin, which simulate the natural ECM, or poly(ethylene glycol) (also known as PEG) a synthetic but biocompatible polymer. Two different concentrations (1% and 2.5%) of poly (ethylene glycol) diacrylate (PEGDA) which crosslinks the molecules was used in each in addition to the presence of heparin in some samples. The results show a large disparity in the release profile between the types of GF used in each case. PEG consistently released a large volume of GF in a sustained manner over time. In the HA-Gelatin hydrogels, the results were more disparate. HGF exhibited a strong release profile with 2.5% PEGDA as well as when heparin was present, likely due to the rapid degradation of HGF in solution. In contrast, IGF was more rapidly released by those hydrogels prepared without heparin, as well as those with 1% PEGDA. A cell migration assay was performed using BMP-2 to test the migration of osteoblast though 8um pores within a transwell, onto various types of hydrogel. BMP-2 clearly had a strong chemotactic effect, and those hydrogels prepared without heparin had significantly more cells, likely meaning that over the first 36 hours these hydrogels released significantly more growth factor than those prepared with heparin. MUSC College of Graduate Studies - Summer Health Professions Research Program

**022 Prenatal Vitamin D Supplementation and the Innate Immune System: Vitamin D As an Inducer of MCP-4/CCL13 During Pregnancy**

Introduction: Vitamin D is an important immunomodulatory hormone. Hypovitaminosis D has been associated with numerous autoimmune and inflammatory conditions, as has the cytokine monocyte chemoattractant protein-4 (MCP-4/CCL13). Our research examined the link between MCP-4/CCL13 and vitamin D status during pregnancy in an attempt to further understand the mechanistic relation between these factors. Methods: We utilized serum
Heart disease is the number one killer of both men and women in the US and is projected to cost more than three hundred billion dollars in direct health care costs and lost productivity in 2009. Those most at risk are over those over the age of twenty with high cholesterol, hypertension, diabetes, and/or obesity; and those over the age of eighteen who smoke and/or are inactive. Chronic hypertension can lead to cardiac hypertrophy which most commonly occurs in one of the ventricles of the heart; over time this hypertrophy can lead to heart failure, arrhythmias, and heart attacks. Cardiac hypertrophy is the enlargement or thickening of the myocardium of the heart. This enlargement includes increased size of the myocytes and remodeling of the extracellular matrix, ECM. Most notably to the research conducted is the remodeling of collagen with cardiac hypertrophy, and the role of several ECM proteins in this remodeling. Both cat and mouse animal models were used to show that with hypertrophy the amount of collagen in the myocardium increases. Knock-out mice were used to characterize the involvement of several ECM proteins including sparcc, lumican, pcpe2. It was observed that collagen increase with hypertrophy was less in mice not expressing lumican or pcpe2; no significant decrease was observed in mice not expressing sparcc. An increase in the collagen producing myofibroblasts was observed in hypertrophied hearts of all mouse lines studied. It is the goal that further understanding the role of specific proteins in cardiac hypertrophy could lead to better prevention and treatments of heart disease. Dr. Egede’s NIH Training Grant; SHP research program

**024 Characterizing the Role of Distinct ECM Proteins in Remodeling of the ECM with Cardiac Hypertrophy.**

Kelly E Pace\(^1\), Amy Bradshaw\(^2\); \(^1\)Medicine, MUSC, \(^2\)Medicine, Cardiology, MUSC.

Inflammatory Bowel Disease (IBD) can be defined as a series of inflammatory conditions that affect the gastrointestinal tract. IBD is most commonly represented by Crohn’s Disease (which may affect any area in the entire GI tract, but is typically localized to the terminal ileum portion of the small intestine and the large intestine) and Ulcerative Colitis (which is localized to the large intestine and rectum). A major complication of IBD is intestinal epithelial injury that primarily results from the release of proteases by polymorphonuclear leukocytes (PMN). Previous studies have shown that periostin (90 kDa...
matricellular protein) is mostly produced by fibroblasts, up-regulated during cellular injury, and stimulates fibroblasts to produce collagen. Thus, we investigated the role of periostin in epithelial repair following culturing of both epithelial (T84 intestinal) cells and intestinal fibroblasts on filters. In particular, intestinal fibroblasts were cultured on one side of the 5 micron filters and epithelial cells were cultured on the underside to resemble an in vivo configuration. The fibroblast/epithelial cell complex was allowed to become confluent. It has been revealed that periostin is present in close proximity to the sub-epithelial fibroblasts and recently we have shown that periostin is expressed by T84 intestinal epithelial cells. “Scratch” injuries were made after the fibroblast/epithelial complex was confluent. Results show that periostin is expressed at the site of the scratch injury. Prior to epithelial injury cultured T84 cells monolayers were exposed to the inflammatory cytokine II-6 and exposed to the non-inflammatory cytokine II-10. Results indicate that II-6 treatment of epithelial/ fibroblast cell monolayers increase expression periostin and II-10 reduces expression of periostin. Because of this expression of periostin, we conclude that periostin plays a role in the inflammatory responses of T84 epithelial cells and hypothesize that periostin attracts PMN to areas of inflammation, which contributes to the dysregulated cycle of intestinal inflammation observed in IBD.

**027** Prdx Inhibits Akt Activity Via Regulating Akt Phosphatases, Rebecca Weber¹, Brittany Turner², Juxiang Cao², Jennifer Schulze², Carola Neumann²; ¹College of Medicine, MUSC, ²Pharmacology, MUSC.

Abstract not available.

**028** Immunotherapy of Oral and Pharyngeal Cancer. Isaac F Dingle¹, Brian D Hoe³, Semyon Rubinchik², Wei Sun², M Boyd Gillespie³, Natalie A Sutkowski³; ¹College of Medicine, Otolaryngology - Head and Neck Surgery, MUSC, ²Microbiology and Immunology, MUSC, ³Otolaryngology - Head and Neck Surgery, Hollings Cancer Center, MUSC, ⁴Microbiology and Immunology, Hollings Cancer Center, MUSC.

Placental Growth Factor (PIGF) was recently identified as a novel therapeutic target for inhibiting tumor angiogenesis. PIGF is a member of the vascular endothelial growth factor (VEGF) family, which binds to and signals through the VEGF-R1 receptor. Tumor cells produce PIGF and VEGF in response to hypoxic conditions caused by chemotherapy, radiation or VEGF inhibition therapy. In tumors, hypoxia inducing factor HIF1-alpha often upregulates PIGF and VEGF, which then enter the periphery, binding to and recruiting endothelial cells, and initiating neovascularization. While VEGF has an essential role in normal vascularization and development, PIGF does not. Normally, PIGF has a limited pattern of expression, but it is unexpectedly produced in many types of tumors. Recently, gene expression microarray studies have identified PIGF transcripts in a variety of head and neck squamous cell carcinomas (HNSCC). Consistent with these studies, we have found that PIGF is expressed in different human HNSCC cell lines, indicating that PIGF inhibition might have therapeutic benefit in HNSCC. The primary aims of my project were to 1) isolate and develop immortalized B-cells expressing IgG antibodies specific for PIGF, 2) verify the existence of PIGF in common HNSCC lines, and 3) assist in the development of functional assays to evaluate the biological activity of the newly developed anti-PIGF antibodies. Building upon previous work, we continued development of six immortalized B-cell populations that produce IgG with affinity to recombinant human PIGF. We also began preliminary testing of the human antibodies on intracellular PIGF binding in common HNSCC cell lines, using immunohistochemistry and Western blotting. In addition, we worked to develop functional assays in which we could test the antibodies for inhibition of chemotactic and angiogenic activity. This preliminary research sets the stage for ex vivo immunohistochemical testing of primary HNSCC tumor specimens for PIGF involvement.

**029** Determining the Role of the E3 Ubiquitin Ligase EDD in Cisplatin Resistant Ovarian Cancer: Regulation By ERK2 Phosphorylation, Danielle W Clark, Hui Zheng, Jennifer R Bethard, Scott T Eblen; Cell and Molecular Pharmacology and Experimental Therapeutics, MUSC.

Abstract not available.

**030** Pure Intraductal Papillomas (IDP) of the Breast: Differential Effect of Histologic Variants on Core Needle Biopsy As Demonstrated in Final Surgical Excised Pathology, Kristen N Arnold¹, Steven D Trocha², Garrett Rowe³, Stephen Mitchell³, David P Schammel⁴, Brian P McKinley²; ¹College of Medicine, MUSC, ²Surgery, Greenville Hospital System, ³Clemson University, ⁴Pathology Associates.

Introduction: The clinical management of breast intraductal papillomas (IDP) diagnosed on core biopsy (CNB) is confusing due to the presence of associated breast pathology. Our study focused on CNB that demonstrated pure IDP without associated breast pathology and identification of subgroups that might be associated with subsequent atypical ductal/lobular hyperplasia (ADH/ ALH), lobular/ductal carcinoma in situ (L/DCIS) or invasive cancer (IDC) in surgical excisions. Methods: We performed a single-institution, retrospective review of women diagnosed with one of four histological variants of pure IPD (typical (T), atypical (AT), sclerosing (S), or florid hyperplasia (FH)) by CNB from 11/00 -9/08. Standard clinicopathologic data was collected. All CNB with additional breast pathology outside the IPD such as ADH, ALH, DCIS, LCIS, or IDC were excluded. Results: Seventy-three patients were identified for inclusion in the study. L/DCIS or IDC was noted in 12/73 (22%) on final pathology. Upgrading was demonstrated in 12% (4/34) T, 53% (9/17) AT, 25% (3/12) S, and 0% (0/10) FH. Identification of atypia in the subsequent excision
was noted in 6% (2/34) typical, 3% (4/12) sclerosing, and 10% (1/10) florid hyperplasia. Surgical management after CNB was 70 excisional biopsies, 2 lumpectomies, and 1 simple mastectomy. Conclusion: When focusing on pure IDP without confounding breast pathology on CNB, we demonstrate a significant upgrade to L/DCIS or IDC in CNBs that have AT (53%) features, followed by S (25%) and T(12%). CNBs with FH may warrant no further therapy. We currently manage these four subtypes with excisional biopsy. Supported by the Department of Surgery at Greenville Memorial Hospital and the CUR2E Program (Clinical Undergraduate and Resident Research Experience)

**031 Combination of Low Dose Estrogen and VEGF Protects C6 Astroglia From Glutamate and TNF-α Induced Apoptosis.** Rebecca G Lopez, Arabinda Das, Joshua A Smith, Abhay K Varma, Narendra L Banik; College of Medicine, Neuroscience, MUSC.

Numerous studies have shown the protective benefits of either estrogen treatment or VEGF administration following spinal cord injury. Estrogen’s protective effects have been attributed to its ability to modulate Ca2+ mediated events such as calpain activation and caspase activation, which result in apoptosis. VEGF plays a critical role in angiogenesis. VEGF has also been found to promote survival following serum-starvation in multiple neuronal cell types. Spinal cord injury involves numerous secondary injury pathways including oxidative stress, increased ic[Ca2+], glutamate excitotoxicity, and ischemic injury. Given the variety of pathways involved in SCI, combination treatment with both estrogen and VEGF may prove more beneficial than either treatment alone. To our knowledge, the use of combination estrogen and VEGF for treatment of SCI has not been studied. In particular, we focused on the injury and treatment of C6 astroglia, as these are the most numerous non-neuronal cells in the CNS, and are involved in numerous CNS regulation and signaling functions. We hypothesized that treatment with estrogen and VEGF in combination following exposure to either L-glutamic acid (LGA) or TNF-α (Tumor Necrosis Factor) would confer greater cell protection than either treatment alone. To test our hypothesis, C6 astroglia were exposed to either L-glutamic acid (LGA) or TNF-α. A 15-minute post-insult treatment consisted of administration of estrogen, VEGF, or a combination of both. Cell viability was evaluated using trypan blue dye exclusion test. Apoptotic activity was evaluated using Western blot analysis for cell death markers, Wright staining, Apoptag, and caspase activity assays. While cytoprotection was noted for cells undergoing post-treatment with either estrogen or VEGF, a significant increase in protection was found in cells receiving combination treatment. Our findings suggest that combination therapy significantly increases cell viability in both glutamate and TNF-α exposed C6 astroglia, and thus shows potential for the treatment SCI.

**032 Methamphetamine Preconditioning: Protective Effects on the Monoaminergic Systems in the Brain.** Onica L Washington, Marcelo Llanos, Amber Hodges, Bruce Ladenheim, Michael T McCoy, S Lud Jayanthi, Jean Cadet, Irina Krasnova; 1College of Medicine, MUSC, 2National Institute on Drug Abuse, Molecular Neuropsychiatry Branch.

Abuse of the drug methamphetamine (METH) has been on the rise in recent years. It is known that METH causes neurotoxic effects in the human brain such as loss of gray matter, neuronal apoptosis, and depletion of dopamine (DA) and serotonin (5-HT) axons. In the present study, we used an escalating dose regimen of METH injections on rats in order to mimic progressively larger doses of the drug taken by chronic abusers. This METH preconditioning caused protection against depletion of DA, 5-HT, and their metabolites in the nucleus accumbens and attenuation of decreases in 5-HT levels in the hippocampus and hypothalamus caused by METH challenge. Together, our data suggest that METH preconditioning can cause development of a tolerance to the drug and protection against the neurotoxic effects of high METH doses in the brain. Molecular Neuropsychiatry Branch and Intramural Research Program of National Institutes of Health

**033 The Effects of PEPA, an AMPAkine, on Activity and BDNF Expression in Rats Following an Acute Administration of Amphetamine.** Laura E Briggs, Sarah E Eisenstein, Timothy W Whitfield, Adrian M Gomez, Jacqueline F McGinty; Neurosciences, MUSC.

Psychostimulant-mediated plasticity in projections from the prefrontal cortex (PFC) to the nucleus accumbens (NAC) underlies addictive drug seeking and relapse. Brain-derived neurotrophic factor (BDNF) promotes synaptic plasticity in the cortico-accumbens pathway through its activation of intracellular signaling, regulation of gene expression and glutamatergic neurotransmission. BDNF infusions within the mPFC attenuate the reinstatement of cocaine-seeking in rats with a cocaine history. BDNF expression is upregulated by administration of AMPAkines, a class of compounds that potentiates glutamatergic AMPA receptors. The purpose of this study was to determine whether systemic administration of PEPA (4-[2-(phenylsulphonylamino) ethylthio]-2,6-di uorophenoxacyetamide), an AMPAkine, increases BDNF expression in the PFC, NACs and dorsal striatum (dStr) when coupled with amphetamine. If systemic administration of PEPA is able to induce BDNF expression, these compounds could potentially be utilized for therapeutic purposes. Rats were first injected with either PEPA [1 mg/kg, intraperitoneal (i.p.)] or saline, after which they were immediately injected with an acute dose of amphetamine (1 mg/kg, i.p.). Behavioral activity was then recorded in photocell chambers for three hours, after which rats were anesthetized and euthanized. Overall, the two treatment groups exhibited similar locomotor patterns in regard to both vertical activity and distance
traveled. Similarly, no significant difference in BDNF immunoreactivity between the two groups was observed. These data suggest that a 1mg/kg dose of PEPA has no effect on AMPH-induced activity or BDNF expression. Supported by P50 DA015369 and the MUSC Medical Scientist Training Program

034 Benefits of a Tracheostomy Team: Four-Year Pre and Post Statistics, Elaina L Simpson, Danielle A Gill, Amy H Dickson, Laurel H Hays; CHP, Communication Sciences & Disorders, MUSC.

Implementing a tracheostomy team can be a valuable tool in improving patient care. Care for tracheostomized patients is expensive and optimal care requires the skill of knowledgeable healthcare providers. This project compares data on tracheostomized patients receiving care at the Medical University of South Carolina prior to and then four years following the initiation of a multidisciplinary tracheostomy team. The purpose of this project was to quantify the benefits of creating a specialized multidisciplinary tracheostomy team and to implement a standardized plan of care by knowledgeable and qualified healthcare providers. Baseline data on mortality rates, length of stay, decannulation rates, and costs were collected during a chart review using a standardized template on all patients from age 18 – 90 years who had received a tracheotomy and had been discharged from our hospital between September 1, 2001 through August 30, 2002. To assess progress, medical charts were then reviewed 4-years later on patients discharged from our hospital between September 1, 2006 through August 30, 2007. A comparison was then made between the two data sets. Based on 123 chart reviews for discharges between 2001-2002, the following data was collected: in-hospital deaths at 26%, mean length of stay at 42 days, median length of stay at 38 days, decannulation rate at 35%, and total charges at $10,595,521. Based on 176 chart reviews for discharges between 2006 – 2007, the following data was collected: in-hospital deaths at 13%, mean length of stay at 36 days, median length of stay at 32 days, decannulation rate at 27%, and total charges at $44,659,049. Discussion points after the review of this data include: does instituting a standardized plan of care, daily rounds, and staff inservices 1) increase survival rates, 2) decrease the length of stay, 3) accelerate decannulation rates, and 4) decrease costs.

035 Videofluoroscopic Swallow Study Practices in Pediatric Dysphagia, Shannon A Torres, Katherine C Viars, Laura E Draize, Amy M Hartenburg, Kate W Humphries, Kelly C MacDonald, Bonnie Martin-Harris; Health Professions, Communication Sciences and Disorders, MUSC.

Introduction: Survival of pre-term infants results in increased incidence of feeding/swallowing disorders and videofluoroscopic swallow studies (VFSS Clinical observation and informal discussions with colleagues point to varied practice patterns in the implementation, interpretation, and reporting of VFSS results. Method: A web-based survey was conducted to obtain current practice patterns for VFSS. Participants included 80 members of Special Interest Division 13 (ASHA) – Swallowing and Swallowing Disorders. Results: Commercially Prepared Very Thin Liquid – Yes (32.4%), No (67.6%), Commercially Prepared Thin Liquid – Yes (67.6%), No (32.4%), Nectar Thick Liquid - Yes (62.7%), No (37.3%), Honey Thick Liquid- Yes (52.9%), No (47.1%); Modification of Commercially Prepared Barium – Yes (20.6%), Sometimes (38.2%), No (20.6%); Consistency of Modified Commercially Prepared Barium – Very Thin (32.7%), Thin Liquid (42.3%), Nectar Thick Liquid (32.7), Honey Thick Liquid (32.7%); Rationale for Modification – Flavor Enhancement (48.4%), Encourage Cooperation (30.6%), Simulate Current Diet (59.7%), Standardized Order of Presentation – Yes (58.2%) No (3%) Patient Dependent (38.8%); First Bolus Presentation – Thin Liquid (55.6%), Very Thin Liquid (20%), Other (17.8%), Nectar Thick (6.7%), Honey Thick (0%); Mode of Administration – Nipple (slow or fast) (93.8%), Nipple (cross cut or enlarged opening) (41.5%), Syringe (9.2%); Temperature of Liquid – Room (76.1%), Warmed (17.9%), Chilled (6%); Barium – Room (76.1%), Warmed (17.9%), Chilled (6%); Fluoroscopy Exposure Time: > 60seconds < 90seconds (31.3%), >90 <120seconds (25.4%), >30 <60seconds (20.9%), >120 <180 seconds (13.4%), >180seconds (4.5%), <30 (4.5%); VFSS conducted with Upper GI Exam – Yes (5.9%), Most of the Time (5.9%), Half of the Time (25%), Rarely (30.9%), No (32.4%); Presentation of Barium – SLP (48.5%), Care Giver (39.7%), Nurse (3%); Need for Standardization of – Consistencies (74.6%), Interpretation and Measurement (63%), Protocol (58.2%), Terminology (56.7%), Reporting (56.7%). Conclusion: The results of this study provide support for the necessity to develop test standardized protocols, interpretation, and reporting of VFSS results in bottle-fed infants.

036 Does Reporting Race Matter in Occupational Therapy Research?, Yolonda J Stuckey, Molly L Chapell, Christina L Eulau, Hazel L Breland; College of Health Professions, Occupational Therapy, MUSC.

Limited evidence exists in occupational therapy that suggests race/ethnicity is a significant variable of therapeutic outcomes. Yet, a review of occupational therapy studies published in the American Journal of Occupational Therapy (AJOT) indicates that the reporting of the race/ethnicity of participants in OT studies remains unpredictable. The purpose of this study was to examine the proportion of research articles that report the race/ethnicity of the participants. A retrospective review of literature in the AJOT from 2000 -2008 was completed to determine what proportion of articles in occupational therapy research reported the race/ethnicity of the participants. Only articles that included participants were reviewed. Data collection included number of participants, race/ethnicity, and differences in outcomes based on race/
In human walking, deviations from the preferred gait pattern typically increase energetic cost. Therefore, it is often assumed that minimizing energetic cost is a primary goal of walking. We investigated whether subjects preferred gaits with minimal energetic cost when walking downhill, a context in which a simple model predicts that propulsion is assisted by gravity. We hypothesized that subjects would be able to voluntarily reduce their muscle activity from the preferred gait pattern, thus decreasing energetic cost. Twelve healthy subjects walked downhill at 1.25 m/s (0, 0.05, 0.10, and 0.15 gradients). For each slope, subjects performed a normal trial and a relaxed trial, in which they were instructed to allow gravity to assist them and use as little muscle activity as possible. We quantified stride period, stride period variability, muscle activity (rectus femoris; vastus medialis; biceps femoris; medial gastrocnemius; soleus), and energetic cost. During the normal trials, increasing slope caused a decrease in stride period, an increase in stride period variability, changes in muscle activity, and a decrease in energetic cost (by 32-39%). Compared to normal walking, using a relaxed strategy caused an increase in stride period and stride period variability, a decrease in biceps femoris swing phase activity, and a decrease in energetic cost at the steeper slopes (by 16%). Our results indicate that subjects normally take advantage of the propulsion provided by a downhill slope to decrease energetic cost. However, they do not do so optimally, as energetic cost was decreased further by voluntarily reducing muscle activity, thus walking more like a simple model. Subjects may normally avoid the energetically cheaper relaxed strategy due to increased stride period variability, a metric correlated with instability. These results may have clinical implications for gait rehabilitation, as patients may only achieve the most energetically optimal gait if their stability is ensured.

The Effect of Occupational Therapy Research: Does It Really Matter?, Katherine L Lancaster, Harriet P Gallivan, Jessica L Prescott; College of Health Professions, Occupational Therapy, MUSC.

In human walking, deviations from the preferred gait pattern may be essential to the external validity of occupational therapy research findings and when available can enhance evidence-based practice.

The Level of Evidence of Stroke Research in Occupational Therapy, Samantha Maslyn, Claudia Cassell, Elise Gardner; Occupational Therapy, MUSC.

Stroke is the third leading cause of death in the United States, killing over 143,579 people each year, and has been found to affect the largest percentage of people in the Southeastern United States. Stroke is also a leading cause of serious long-term disability. Occupational therapy (OT) services are a part of stroke rehabilitation. To enhance clinical practice, OTs are supposed to engage in evidence-based practice. Thus, the purpose of this study was to examine the level of evidence of stroke research in three occupational therapy journals between 1998 and 2006. In this retrospective review of literature, we appraised the level of evidence for stroke rehabilitation and OT in the American Journal of Occupational Therapy (AJOT), British Journal of Occupational Therapy (BJOT), and Canadian Journal of Occupational Therapy (CJOT).

To determine the level of evidence of the reviewed studies and included for analysis, the Hierarchy of Strength of Evidence (adapted from Moore, McQuay, & Gray, 1995) was used. Twenty-six stroke studies published in AJOT during the 8 years reviewed included level of evidence ranging from I to V, the majority of evidence found in levels IV and V. We appraised 19 stroke studies in BJOT with the level of evidence ranging from I to IV, the majority of evidence found in levels III and V. CJOT published three articles from 1998-2006 with levels of evidence ranging from IV-V. In conclusion, this topic is indeed an important professional topic and the data indicates that there is a need to move forward with increasing the rigor of stroke research in occupational therapy on an international level to ensure best practices as a profession driven by research in occupational therapy on an international level.

Can We Decrease Energetic Cost During Walking By Consciously Reducing Muscle Activity?, Emily C Hendrix, Lindsay C Hunter, Jesse C Dean; College of Health Professions, Health Professions, Physical Therapy, MUSC.

In human walking, deviations from the preferred gait pattern typically increase energetic cost. Therefore, it is often assumed that minimizing energetic cost is a primary goal of walking. We investigated whether subjects preferred gaits with minimal energetic cost when walking downhill, a context in which a simple model predicts that propulsion is assisted by gravity. We hypothesized that subjects would be able to voluntarily reduce their muscle activity from the preferred gait pattern, thus decreasing energetic cost. Twelve healthy subjects walked downhill at 1.25 m/s (0, 0.05, 0.10, and 0.15 gradients). For each slope, subjects performed a normal trial and a relaxed trial, in which they were instructed to allow gravity to assist them and use as little muscle activity as possible. We quantified stride period, stride period variability, muscle activity (rectus femoris; vastus medialis; biceps femoris; medial gastrocnemius; soleus), and energetic cost. During the normal trials, increasing slope caused a decrease in stride period, an increase in stride period variability, changes in muscle activity, and a decrease in energetic cost (by 32-39%). Compared to normal walking, using a relaxed strategy caused an increase in stride period and stride period variability, a decrease in biceps femoris swing phase activity, and a decrease in energetic cost at the steeper slopes (by 16%). Our results indicate that subjects normally take advantage of the propulsion provided by a downhill slope to decrease energetic cost. However, they do not do so optimally, as energetic cost was decreased further by voluntarily reducing muscle activity, thus walking more like a simple model. Subjects may normally avoid the energetically cheaper relaxed strategy due to increased stride period variability, a metric correlated with instability. These results may have clinical implications for gait rehabilitation, as patients may only achieve the most energetically optimal gait if their stability is ensured.

Muscle Plasticity of the Quadriceps in Response to Velocity-Enhanced Resistance Training in a Teenager with Cerebral Palsy Improves Muscle Performance and Quality of Life: a Case Report, Catherine J VanDerwerker, Katy D Holthaus, Noelle G Moreau; College of Health Professions, Physical Therapy, MUSC.

Neurological insult in cerebral palsy (CP) causes muscle weakness. Quadriceps weakness can lead to crouch gait, characterized by increased knee flexion in stance. Over time, crouch gait severity can increase leading to insufficient knee extensor mechanism. Distal femoral extension osteotomy with patellar tendon advancement (DFEO-PTA) is sometimes performed to address altered mechanics in progressive crouch gait, but does not directly address muscle weakness. The purpose of this case report was to examine effects of velocity-enhanced resistance training (VRT) on quadriceps’ strength, muscle architecture, and functional mobility in a teenager with CP. Case Description and Methods: A 17 year old female with spastic diplegic CP underwent bilateral DFEO-PTA four years ago secondary to progressive crouch gait.
She participated in VRT on an isokinetic dynamometer 3x/week for 8 weeks. Each session included 6 sets of 5 concentric knee extension repetitions at progressively increasing velocities in 15 to 30 degree/sec increments. Outcome measures included muscle torque, power, velocity, muscle architecture using ultrasound imaging, and self-report questionnaires. Results: Left side results are presented. Peak torque increased 4%, 44%, and 29% at 30, 60, and 90 degrees/sec, respectively. Rate of force development and peak velocity increased 28% and 13%, respectively. Peak power did not change. Vastus lateralis muscle thickness increased 41.4% while rectus femoris increased 7.6%. However, rectus femoris fascicle length increased 97.4% with a fascicle angle decrease of 46.5%. There were self-reported increases in Sports/Physical Function (31%), Physical Activity (86%), and Self Esteem (18%). Conclusion: Differential adaptations were observed in the rectus femoris and vastus lateralis in response to VRT in this case report and led to self-reported changes in quality of life as well as muscle performance. These results suggest that quadriceps' architectural and performance deficits post-DFEO-PTA can be selectively improved via VRT; however, further investigation is warranted. *Funded primarily by the Thrasher Research Fund and supplemented by the Pedal-with-Pete Foundation.*

**041 Ethnic Differences in Diabetes Knowledge, Self-Care, and Glycemic Control in Adults with Type 2 Diabetes**, Emma G Carter¹, Julius E Hamilton², Leah A Bonaparte², Joni Strom², Leonard E Egede²; ¹College of Medicine, MUSC; ²College of Medicine, MUSC; Ralph H. Johnson VAMC; ³College of Medicine, MUSC; Ralph H. Johnson VAMC.

Background: Diabetes is highly prevalent in ethnic minorities and associated with increased morbidity and mortality. Knowledge and self-care are cornerstone tools of good diabetes care. This study examined ethnic differences in diabetes knowledge, self-care, and glycemic control in a primary care sample with type 2 diabetes. Methods: Data on 213 subjects with type 2 diabetes recruited from the MUSC University Internal Medicine Clinic was examined. Race was defined as non-Hispanic White and non-Hispanic Black. Valid and reliable instruments were used to assess diabetes knowledge and self-care activities including healthy diet, exercise, blood sugar testing, and foot care in the past 7 days. Glycemic control was measured by hemoglobin A1c (HbA1c) abstracted from the electronic medical records. Mean scores on diabetes knowledge (range 0-24), healthy diet (0-7), exercise (0-7), blood sugar testing (0-7), and foot care (0-7) measures as well as mean HbA1c levels were compared by ethnicity using t-test. Ordinary least squares regression was used to estimated the adjusted mean difference by ethnicity controlling for age, gender, marital status, education, employment, insurance status, income, and health status. STATA V10 was used for statistical analysis. Results: 54% of the sample were African Americans, 43% were 65 years and older, 62% were women, 48% were married, 26% had less than high school education, 29% were employed, 9% were uninsured, 28% had income <$10,000, and 24% had worse health status compared to the previous year. In this sample, mean scores were 16.2±4.3 for knowledge, 4.4±2.1 for healthy eating, 2.6±2.1 for exercise, 4.5±2.7 for blood sugar testing, 4.5±2.3 for foot care, and 7.6±1.9 for HbA1c. After adjusting for covariates, there were significant mean differences in diabetes knowledge (whites 17.8 vs. blacks 14.7, p=0.013), healthy eating (whites 4.1 vs. blacks 4.9, p=0.001), and foot care (whites 4.2 vs. blacks 4.9, p=0.023). Adjusted differences in exercise, blood sugar testing, and HbA1c were not statistically significant. Conclusion: In this sample of primary care patients with type 2 diabetes, whites scored higher on the diabetes knowledge test, while blacks reported better dietary and foot care behaviors. Exercise behavior was poor in both groups. Improving diabetes knowledge and self-care behaviors should be targets of future interventions in primary care patients with type 2 diabetes. *Funding provided by grant#5T35DK007431 and the MUSC Center for Health Disparities Research*

**042 Left Prefrontal Transcranial Magnetic Stimulation Effects on Pain Perception: A Functional Magnetic Resonance Imaging Study**, Laura Y Martin¹, Jeffrey J Borckardt², Mark S George²; ¹College of Medicine, MUSC, ²Psychiatry and Behavioral Sciences, College of Medicine, MUSC.

Abstract not available.

**043 Predicted Versus Actual: Participant Accrual in a Feasibility Study**, Christopher T Carter¹, Paul Goforth¹, Joan E Cummings², Michael J Wargovich³, Jeffrey E Korte², Jay Morris³, Dayan G Ranwala⁴, Susan G Reed¹; ¹College of Dental Medicine, Craniofacial Biology, MUSC, ²College of Medicine, Biostatistics and Epidemiology, MUSC, ³College of Medicine, Cell and Molecular Pharmacology and Experimental Therapeutics, MUSC, ⁴Costal Research and Education Center, Clemson University.

A feasibility study is an analysis of the viability of an idea. Feasibility study results provide evidence to support decisions critical to the conduct of a clinical trial. A problem is the ability to predict participant enrollment to a study from the existing hospital registry data. Using cancer incident data 2000-2002, approximately 1.7% of incident cancer cases enrolled in clinical trials. Therefore an objective of this study was to compare the predicted to the actual numbers of patients enrolling in our feasibility study. Study design included retrospective and prospective review of hospital patient schedules and charts. Major variables were: patient age, anatomic site of tumor, tumor histology, tumor morphology, treatment plan, and prior treatment for cancer. The major outcome was study eligibility and enrollment. Data management and analysis were done with Excel. Study eligibility criteria were applied to the 2005-2007 hospital registry database for the predicted
enrollment of approximately 5 new patients per week. Of the 188 patients seen at the hospital from July 13 – August 14 (5 weeks), 7 were eligible for the study. Of these 7, 2 went for radiation treatment elsewhere, 1 to another clinical trial, and 1 passed away. Of the remaining 3 potential participants, 1 consented to the study and 2 may decide to enroll. Results indicated a difference between predicted and actual number of patients. Results also directed specific changes to eligibility criteria for adequate enrollment. Changes were: 1) anatomic site to include larynx, 2) morphology to include non-squamous cell carcinoma, and to 3) include recurrent cases without previous radiotherapy. With these changes, another 16 patients would have been eligible for a total of 23. Results of this study provided evidence for directed change for sufficient participant accrual. Protocols developed may be useful to better predict and identify potential participants for clinical trials. Hollings Cancer Center Clinical Trials Office: Robin Bostic, HCC CTO Coordinator; HCC Nurse Staff: Sandra Zambetti, RN; Kim Gadsden, RN; Physician Staff; Funding in part: Hollings Cancer Center, Cancer Prevention and Control Pilot Grant Program; MUSC Summer Health; Professions Program. MUSC IRB HR

044 The Immediate Effect of Xylitol Gum and Mouthrinse on Salivary Levels of Mutans Streptococcus Bacteria, Justin M DeGarmo1, Caroline Westwater2, Hon K Yuen1; 1College of Dental Medicine, MUSC, 2College of Health Professionals, MUSC.
Xylitol is a naturally occurring sugar alcohol sweetener, which cannot be metabolized by mutans streptococcus (MS) bacteria. Several studies have revealed strong evidence linking xylitol exposure to reduced MS counts in both dental plaque and saliva. It is believed that the mastication action induced by chewing gum adds stimulation of saliva secretion. Therefore, xylitol’s effect on oral health has been studied most frequently in chewing gum. With a limited amount of studies regarding its effect by means of a mouth rinse. Unfortunately, bone resorption and erosions of the mandible observed in people with scleroderma; may associate with temporomandibular disorders which results in limited mouth opening and pain during and after repetitive movement as in gum chewing. This would be a major barrier to regular, long term usage of xylitol gum. OBJECTIVE: To compare the immediate effects of xylitol gum and xylitol mouthrinse on salivary MS levels. METHODS: This study is a randomized controlled clinical trial of 16 subjects who reflect the general US population of Scleroderma patients. The xylitol chewing gum subjects chewed 2.16 grams of xylitol gum for 10 minutes. We measured salivary MS levels before the gum chewing, immediately after, and again after waiting for 25 minutes. The xylitol mouthrinse subjects rinsed with a 10% xylitol mouthrinse solution for 2 minutes. We measured salivary MS levels before the xylitol mouthrinse, immediately after, and again after waiting for 25 minutes. RESULTS: Preliminary data analysis shows higher levels of salivary MS levels immediately after chewing xylitol gum, which then decreases to initial levels after waiting 25 minutes. Xylitol mouthrinse subjects tended to have increased salivary MS levels immediately after xylitol mouthrinse, which then stayed at that high level after the 25 minute waiting period. CONCLUSION: Xylitol chewing gum seems to be more effective at reducing salivary MS levels than the xylitol mouthrinse during the 25 minute waiting period. This may be attributed to the chewing gums’ increased salivary stimulation during the 25 minute waiting period. Further studies are needed to validate our findings. We thank Dr. James Sterrett for his help with making our xylitol mouthrinse, Karen Richardson and Missy Atwater for their tremendous help with our administrative needs, and Samantha Mahoney for her help in patient recruitment.

045 Mandible Growth in Late Teen Caucasian Males, Nathan D Head1, Paul Nietert2, Jing Zhou1; 1Dental Medicine, MUSC, 2Biostatistics & Epidemiology, Medicine, MUSC, 3Dental Medicine, Orthodontics, MUSC.
Objectives: Late mandible growth after the pubertal growth peak is observed in some orthodontic patients. There is currently no reference for the prediction of mandible growth in late teens or earlier twenties. The objective of this pilot study is to evaluate the percentage and growth rate of the mandible during late teen and early twenties. Methods: Thirty-four Caucasian males (15 to 18 years old) were enrolled in this study. The craniofacial growth parameters of the subjects, including the sagittal growth of the mandible, were analyzed with Dolphin software on the scanned 300 dpi digital images of the existing pre- and post-treatment lateral cephalometric radiographs. Annualized average changes of maxillary and mandibular sagittal lengths were compared among different cervical vertebral maturation stages (CVMS) and craniofacial skeletal patterns. Results: The subjects initially in CVMS4 had an average annualized mandible growth of 1.471 mm/year (n=17). The subjects initially in CVMS5 had an average annualized mandible growth of 0.901 mm/year (n=13). The subjects initially in CVMS6 had an average annualized mandible growth of 0.647 mm/year (n=4). An inverse relationship was determined between patient initial CVMS and average mandible growth (P=0.040) and average maxilla growth (P=0.037). Mandible growth had a high correlation (r=0.819) with maxilla growth. A linear regression model showed a negative correlation between anterior facial height (N-Me) and mandible growth (r=-0.488). This study showed mandible growth in late teen is related to the patient’s cervical vertebral stage. This result will improve our clinical knowledge for patients with a mandibular prognathism potential and help with the planning of orthodontic and orthopedic treatment. College of Dental Medicine T32 Grant; Summer Health Professionals Research Program.
Purpose: To compare the prognostic value of CT signs of right ventricular (RV) dysfunction for predicting adverse outcome in acute pulmonary embolism (PE). Methods and Materials: We evaluated 260 patients with acute PE for the following CT signs of RV dysfunction: Abnormal position of the inter-ventricular septum, inferior vena cava (IVC) contrast reflux, RV diameter (RVD)/left ventricular diameter (LVD) ratio on axial sections and four chamber (4CH) views, RV volume (RVV)/left ventricular volume (LVV) ratio. We recorded comorbid conditions and adverse events defined as 30-day mortality or need for cardiopulmonary resuscitation, mechanical ventilation, pressors, rescue thrombolysis, or surgical embolectomy. Results: Twenty patients (7.7%) died within 30 days and 57 patients (21.9%) had non-fatal adverse events. On ROC analysis, position of the interventricular septum and IVC reflux where predictive of non-fatal adverse events but not of 30-day mortality. RVDaxial/LVDaxial ratio >1.1, RVD4CH/LVD4CH ratio >1.2, and RVV/LVV ratio >1.2 had the highest discriminative power for predicting 30-day mortality and non-fatal adverse events. The area under the curve for these parameter for predicting adverse events were not significantly different (0.565-0.674, p=0.51-0.84). On multivariate analysis, after adjusting for comorbid conditions, hazard ratios of RVV/LVV for 30-day mortality and non-fatal adverse events were 7.15 (p<0.01) and 4.32 (p<0.01), respectively, compared with 3.01 (p=0.02) and 2.68 (p<0.01) for RVDaxial/LVDaxial, and 3.37 (p=0.01) and 2.19 (p=0.01) for RVD4CH/LVD4CH. Conclusion: RVV/LVV ratio is an independent predictor of adverse outcomes in acute PE and is superior to measurements on axial sections and 4CH views for identifying high risk patients.

047 Detection of Coronary Artery Anomalies Using Non-Contrast Coronary Artery Calcium Scoring Studies, P Tim Maddux, Doo Kyoung Kang, Joseph Abro, Christian Thilo, U Joseph Schoepf; Radiology and Radiological Sciences, MUSC.

Purpose: To determine, whether coronary artery anomalies can be detected on non-contrast coronary artery calcium scoring (CCS) studies. Materials and Methods: This study was approved by the institutional review board. One hundred twenty-six patients (mean age 62 years; 35 women) who underwent non-contrast CCS and contrast enhanced coronary CT angiography (CCTA) were included. Thirty-three patients were diagnosed with having a coronary anomaly on CCTA, while coronary anomalies had been excluded in 93 control patients. Two blinded experienced observers (R1 and R2) independently evaluated the CCS study of each patient for: 1) visibility of coronary artery origins, 2) detection of coronary anomalies, and 3) benign or malignant (i.e. inter-arterial) course. Agreement between physicians was assessed. Using CCTA as the reference standard, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of CCS studies for detecting coronary anomalies was calculated. Results: CCTA identified 33 coronary anomalies. Of these, 16 had a benign course and 17 had a malignant course. Based on non-contrast CCS studies, R1 correctly identified the left main (LM) coronary artery origin in 123 out of 126 patients; the left anterior descending (LAD) coronary artery origin in 125 out of 126 patients; the circumflex (Cx) coronary artery origin in 120 out of 126 patients; and the right coronary artery (RCA) origin in 117 out of 126 patients. R2 correctly identified the LM coronary artery origin in 121 out of 126 patients; the LAD coronary artery origin in 122 out of 126 patients; the Cx coronary artery origin in 105 out of 126 patients; and the RCA origin in 103 out of 126 patients. R1 identified 34 coronary anomalies and classified 19 as malignant; R2 identified 27 coronary anomalies and classified 15 as malignant. Inter-observer reproducibility for detection of coronary anomalies was good (k=0.76). Inter-observer agreement for detection of malignant coronary anomalies was even stronger (k=0.80). On average between the two readers, coronary artery anomalies were diagnosed with 85.2% sensitivity, 96.4% specificity, 90.5% PPV, and 94.1% NPV based on non-contrast CCS studies. Conclusion: Benign and malignant coronary artery anomalies can be detected with fairly high accuracy on non-contrast enhanced CCS studies. CCS studies should be reviewed for signs of coronary artery anomalies in order to identify malignant variants with possible impact on patient management.

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048 Short-Term Effects of Repetitive Transcranial Magnetic Stimulation on Cerebral Blood Flow to Limbic System Structures, Daniel Pasko1, Tal Herbsman2, Kevin Johnson3, Paul Morgan4, Ziad Nahas5, Mark George6; 1Medicine, Psychiatry & Behavioral Sciences, MUSC, 2Psychiatry, University of Wisconsin-Madison, 3Neurosciences, MUSC, 4Radiology, MUSC, 5Psychiatry & Behavioral Sciences, MUSC.

Abstract not available.

049 Reliability of Stroke Diagnosis and Outcomes of TPA Treatment Using the REACH MUSC Stroke Program, Karon N Hammonds, Robert J Adams; Neurosciences, MUSC.

Despite FDA approval of tissue plasminogen activator (tPA) in 1996, less than half of ischemic stroke patients without relative contraindications receive tPA in part due to limited stroke expertise . The REACH MUSC program utilizes telemedicine to provide stroke consultations at 6 rural hospital emergency departments across South Carolina. This project uses retrospective chart analysis to determine treatment outcomes and the reliability of diagnoses via
infections. After controlling for CD4 count, rural residence (1.3%). Infection with multiple species occurred in 9.4% of Schistosoma mansoni (7.1%), and Strongyloides stercoralis. Ascaris lumbricoides (17.1%), Trichuris trichiura (8.7%), species were the most prevalent (56.3%), followed by

Results: Of 1,541 HIV-1 seropositive individuals screened, re-evaluated twelve weeks following albendazole therapy. of individuals with soil-transmitted helminth infection was correlated with helminth infection at ten sites in Kenya. Prevalence and correlates of helminth co-infection in helminth endemic areas. Methods: HIV-1 infected individuals (CD4>200 cells/ul) were screened for helminth infection, including rural residence and lack of education, predicted co-infection, while lower CD4 counts did not. Thanks to all of the participants and the clinics and organizations caring for persons living with HIV/AIDS who participated in this study; the staff of the University of Washington/KEMRI/FHCRC; Frederick Kirui, Jonathan Chebotibin, Beryl Obura, Andele Nyambura

052 Hemophagocytosis Lymphohistiocytosis: Description of Clinical and Associated Genetic Findings in 16 Patients, John T Lucas1, Munira Shabbir2, Adnan Alayoubi3, Kei Suzuki Shirai2, Charles Greenberg2, John Lazarchick1; 1Pathology, MUSC, 2Hematology/Oncology, MUSC, 3Cellular and Molecular Pharmacology and Experimental Therapeutics, MUSC.

Hemophagocytic Lymphohistiocytosis (HLH) is a rare, fatal disorder characterized by hemophagocytosis within the marrow, fever, hepatosplenomegaly, lymphadenopathy, severe cytopenias, hepatic dysfunction, coagulopathy, and sometimes neurological involvement. This syndrome is associated with diverse processes including: late presenting genetic mutations with masked phenotypes, infection, rheumatologic, and hematologic malignancies. Presently, the underlying cause of HLH is unknown. We present a consecutive series of 16 adults with HLH diagnosed at our institution between 2004-2009 and corresponding sequence analysis of several genes associated with the hemophagocytosis phenotype. All diagnoses were confirmed by pathology. The median age was 54 years (range: 18-71 years), and a male: female ratio of 2:1. All patients uniformly presented with fever. Half of the patients presented with evidence of hepatomegaly or splenomegaly. The most predominant laboratory abnormalities included: anemia, leukopenia and thrombocytopenia. CMV and EBV were implicated in several cases. The underline illnesses associated with HLH are diverse. The underlying causes were as follows; acute leukemia (n=2), infection (n=3), rheumatologic (n=1), post transplant (n=3) sickle cell disease (n=2), Adult Onset Still’s Disease (n=1), unknown (n=3) and T-Cell Lymphoma (n=1). Mortality rate was 77% with a median survival time since diagnosis of 58 days. Sequence analysis of associated genes is ongoing. In conclusion, due to the high mortality rate associated with HLH, early treatment with immunosuppressant is warranted, and a thorough diagnostic evaluation to identify the underlying cause should be undertaken.
Importance of Long-term Video Electroencephalography to Differentiate Epilepsy From Non-Epileptic Events in Children: MUSC Four-Year Experience, Annie W Chen¹, Robert P Turner²; ¹College of Medicine, MUSC, ²Pediatric Neurology, MUSC.

Long-term video encephalographic (VEEG) monitoring has been increasingly used to differentiate between epilepsy and non-epileptic events. The purpose of this retrospective review was to determine the percentage of pediatric patients receiving inpatient VEEG monitoring who experienced non-epileptic events (NEE) without electrographically-confirmed seizures, as well as the subset of these children concurrently taking one or more anti-epileptic drugs (AEDs). This retrospective review included all inpatient pediatric (0-17 years of age) long-term VEEG admissions from January 2005 through December 2008. A total of 280 patients (158 females and 122 males) were monitored for these four years. VEEG analysis was carried out by board-certified electroencephalographers (American Board of Clinical Neurophysiology). The mean age was 8.6 years, and monitoring duration averaged 3.2 days. Primary referral sources were pediatric neurologists and pediatric epileptologists. The majority of VEEG referrals were for “intractable seizures.” Overall, 22% of patients had normal EEGs, 28% had recorded NEE, 23% had abnormal inter-ictal EEGs, and 27% had recorded electrographic seizures. In the population of patients with normal EEGs, 62% had been taking one or more AEDs, and in the group with NEE, 51% were taking one or more AEDs. NEE consisted of either physiologic (e.g. sleep myoclonus or stereotypic actions misinterpreted as seizures) or non-physiologic (e.g. conversion) events. This study suggests that long-term VEEG monitoring in the pediatric group may detect a significant number of children possibly misdiagnosed as having epilepsy and therefore taking unnecessary medications.

How Does Patient Size Affect Radiation Doses in Cardiac NM Imaging?, Eugene Mah, Samir Tipnis, Leonie Gordon, David Davison, Walter Huda; MUSC.

Cardiac imaging patients are typically injected with a fixed amount of radioactive tracer irrespective of their weight. The nominal effective dose to the patient is readily available in published data, which are based on a standard reference weight of 70 kg, and for children aged 1 to 15 years. However, the true patient weight, and hence the true effective dose, can be substantially different from these published values.

The Role of Cubilin in HDL Homeostasis, Obaidullah Aseem, Jeremy L Barth, Marion A Cooley, Sandra C Klatt, W Scott Argraves; Medicine, Regenerative Medicine and Cell Biology, MUSC.

Cubilin is a multiiligand receptor capable of mediating the endocytosis of HDL apolipoprotein A-I (apoA-I). The significance of cubilin-mediated apoA-I endocytosis to HDL homeostasis has not been established. Through study of mice heterozygous for targeted cubilin gene deletion, we have found that cubilin haploinsufficiency results in >20% decrease in blood levels of HDL. The underlying mechanism for this effect is not yet known. Given that the liver is the major site of HDL biosynthesis, we studied the expression of cubilin in the liver. We found that although there was no detectable expression of cubilin mRNA, cubilin protein was immunohistologically detected in the liver. The analysis showed cubilin immunoreactive protein in a punctate distribution on hepatocytes. To determine the source of liver-associated cubilin, we assayed blood and detected fragments of cubilin in fractions of whole plasma. To determine the possible influence of liver-associated cubilin on apoA-I, we evaluated the impact of cubilin haploinsufficiency on hepatic expression of apoA-I mRNA and protein. While apoA-I mRNA levels were not significantly altered, an immunohistological analysis showed alteration in the pattern of distribution of apoA-I in liver hepatocytes from cubilin-deficient mutants. These findings highlight a potential role for cubilin in regulating hepatic HDL biosynthesis.

Poly-N-Acetyl Glucosamine Nanofibers From a Marine Diatom Promote Wound Healing and Defensin Expression Via an AKT1/ETS1-Dependent Pathway, Haley Buff¹, Elizabeth Perkins¹, Aiguo Zhang², Juanita Eldridge¹, Marina Demcheva³, Arun Seth², John Vournakis³, Robin Muise-Helmericks¹; ¹Regenerative Medicine and Cell Biology, Hollings Cancer Center, MUSC, ²Sunnybrook Research Institute, ³Marine Polymer Technologies, Inc.

Recent findings show that treatment of cutaneous wounds with poly-N-acetyl-glucosamine nanofibers (pGlcNAC/Taliderm), a novel polysaccharide material derived from a marine diatom, results in an increased kinetics of wound healing that can be attributed, in part, by a marked increase in angiogenesis. Our published data suggests that treatment of primary endothelial cells (EC) with this nanofiber results in a marked increase in cell migration, which is due to an integrin-dependent up-regulation of the Ets1 transcription factor. We show that pGlcNAC stimulation of Ets1 results from the activation of Akt1 by these nanofibers. Nanofiber treatment results in marked increases in the expression of genes involved in cellular recruitment, such as IL-1 (a known Ets1 target), VEGF and several defensins (β3, α1, α4, and α5), small anti-microbial peptides recently shown to act as chemo attractants. Both pharmacological inhibition of the PI3K/Akt1 pathway and pharmacological inhibition of the PI3K/Akt1 pathway and Akt1 knockdown using shRNAs results in decreased expression of these chemotactic factors. Akt1 null mice exhibit a delayed wound healing phenotype that is partially rescued by Taliderm nanofibers. Taliderm treated wounds show an increase in defensin expression that is Akt1 dependent. Taken together our findings suggest a central role of the Akt1→Ets1 pathway in the regulation of cutaneous wound healing by pGlcNAC nanofibers and support the use of these fibers as a novel and effective treatment for wound healing.

Electroencephalography to Differentiate Epilepsy From Non-Epileptic Events in Children: MUSC Four-Year Experience, Annie W Chen¹, Robert P Turner²; ¹College of Medicine, MUSC, ²Pediatric Neurology, MUSC.

Long-term video encephalographic (VEEG) monitoring has been increasingly used to differentiate between epilepsy and non-epileptic events. The purpose of this retrospective review was to determine the percentage of pediatric patients receiving inpatient VEEG monitoring who experienced non-epileptic events (NEE) without electrographically-confirmed seizures, as well as the subset of these children concurrently taking one or more anti-epileptic drugs (AEDs). This retrospective review included all inpatient pediatric (0-17 years of age) long-term VEEG admissions from January 2005 through December 2008. A total of 280 patients (158 females and 122 males) were monitored for these four years. VEEG analysis was carried out by board-certified electroencephalographers (American Board of Clinical Neurophysiology). The mean age was 8.6 years, and monitoring duration averaged 3.2 days. Primary referral sources were pediatric neurologists and pediatric epileptologists. The majority of VEEG referrals were for “intractable seizures.” Overall, 22% of patients had normal EEGs, 28% had recorded NEE, 23% had abnormal inter-ictal EEGs, and 27% had recorded electrographic seizures. In the population of patients with normal EEGs, 62% had been taking one or more AEDs, and in the group with NEE, 51% were taking one or more AEDs. NEE consisted of either physiologic (e.g. sleep myoclonus or stereotypic actions misinterpreted as seizures) or non-physiologic (e.g. conversion) events. This study suggests that long-term VEEG monitoring in the pediatric group may detect a significant number of children possibly misdiagnosed as having epilepsy and therefore taking unnecessary medications.

How Does Patient Size Affect Radiation Doses in Cardiac NM Imaging?, Eugene Mah, Samir Tipnis, Leonie Gordon, David Davison, Walter Huda; MUSC.

Cardiac imaging patients are typically injected with a fixed amount of radioactive tracer irrespective of their weight. The nominal effective dose to the patient is readily available in published data, which are based on a standard reference weight of 70 kg, and for children aged 1 to 15 years. However, the true patient weight, and hence the true effective dose, can be substantially different from these published values.

The Role of Cubilin in HDL Homeostasis, Obaidullah Aseem, Jeremy L Barth, Marion A Cooley, Sandra C Klatt, W Scott Argraves; Medicine, Regenerative Medicine and Cell Biology, MUSC.

Cubilin is a multiiligand receptor capable of mediating the endocytosis of HDL apolipoprotein A-I (apoA-I). The significance of cubilin-mediated apoA-I endocytosis to HDL homeostasis has not been established. Through study of mice heterozygous for targeted cubilin gene deletion, we have found that cubilin haploinsufficiency results in >20% decrease in blood levels of HDL. The underlying mechanism for this effect is not yet known. Given that the liver is the major site of HDL biosynthesis, we studied the expression of cubilin in the liver. We found that although there was no detectable expression of cubilin mRNA, cubilin protein was immunohistologically detected in the liver. The analysis showed cubilin immunoreactive protein in a punctate distribution on hepatocytes. To determine the source of liver-associated cubilin, we assayed blood and detected fragments of cubilin in fractions of whole plasma. To determine the possible influence of liver-associated cubilin on apoA-I, we evaluated the impact of cubilin haploinsufficiency on hepatic expression of apoA-I mRNA and protein. While apoA-I mRNA levels were not significantly altered, an immunohistological analysis showed alteration in the pattern of distribution of apoA-I in liver hepatocytes from cubilin-deficient mutants. These findings highlight a potential role for cubilin in regulating hepatic HDL biosynthesis.

Poly-N-Acetyl Glucosamine Nanofibers From a Marine Diatom Promote Wound Healing and Defensin Expression Via an AKT1/ETS1-Dependent Pathway, Haley Buff¹, Elizabeth Perkins¹, Aiguo Zhang², Juanita Eldridge¹, Marina Demcheva³, Arun Seth², John Vournakis³, Robin Muise-Helmericks¹; ¹Regenerative Medicine and Cell Biology, Hollings Cancer Center, MUSC, ²Sunnybrook Research Institute, ³Marine Polymer Technologies, Inc.

Recent findings show that treatment of cutaneous wounds with poly-N-acetyl-glucosamine nanofibers (pGlcNAC/Taliderm), a novel polysaccharide material derived from a marine diatom, results in an increased kinetics of wound healing that can be attributed, in part, by a marked increase in angiogenesis. Our published data suggests that treatment of primary endothelial cells (EC) with this nanofiber results in a marked increase in cell migration, which is due to an integrin-dependent up-regulation of the Ets1 transcription factor. We show that pGlcNAC stimulation of Ets1 results from the activation of Akt1 by these nanofibers. Nanofiber treatment results in marked increases in the expression of genes involved in cellular recruitment, such as IL-1 (a known Ets1 target), VEGF and several defensins (β3, α1, α4, and α5), small anti-microbial peptides recently shown to act as chemo attractants. Both pharmacological inhibition of the PI3K/Akt1 pathway and Akt1 knockdown using shRNAs results in decreased expression of these chemotactic factors. Akt1 null mice exhibit a delayed wound healing phenotype that is partially rescued by Taliderm nanofibers. Taliderm treated wounds also show an increase in defensin expression that is Akt1 dependent. Taken together our findings suggest a central role of the Akt1→Ets1 pathway in the regulation of cutaneous wound healing by pGlcNAC nanofibers and support the use of these fibers as a novel and effective treatment for wound healing.
method for enhancing wound healing. Marine Polymer Technologies, Inc.

**057** Effect of Mechanical Conditioning and Elastogenic Factors on Elastin Regeneration in 3-D Tissue Constructs, L Venkataraman, A Ramamurthi; Clemson-MUSC Bioengineering.

Elastin, a structural protein, provides these arteries mechanical resilience and regulate healthy smooth muscle cell (SMC) phenotype. In vascular pathologies e.g., vascular aneurysms, rapid elastic matrix breakdown occurs due to release of matrix-metalloproteases (MMPs) by inflammatory cells recruited to the site of injury or calcific/lipid deposition. The generated elastin peptides in turn induce hyper-proliferation of SMCs, ossification and MMP release, leading to loss of elasticity, and ultimately vessel wall rupture. To date, efforts to tissue-engineer elastic vessel replacements using autologous, healthy vascular SMCs have been impeded by their poor elastogenicity and lack of knowledge of materials/methods to stimulate elastic matrix production and assembly. Previously, we determined the elastogenic benefits of hyaluronan oligomers (HA-o) and TGF-beta1 in 2-D-cultures of healthy rat aortic SMCs (RASMCs). However, to better mimic the spatio-temporal characteristics of the ECM environment in vivo, we presently study the dose-dependant effect of these factors delivered together, to RASMCs cultured within 3-D compacted collagen gels, over 4 weeks. Other studies have suggested benefits of cyclic stretch to modulating cell orientation and matrix synthesis. Presently, we sought to determine the optimal dose of HA-TGF-beta1 under static loading on elastin synthesis, matrix deposition, crosslinking, orientation and distribution. These doses would then be delivered to cellularized scaffolds subjected to cyclic stretch in order to enhance elastic matrix deposition, orientation. At physiologic pH and temperature, collagen-I polymerizes and compacts, the rate and direction of which can be controlled by the cell-seeding density and providing lateral restrainers/anchors. Within formed constructs, a more fibrous elastic matrix was preferentially deposited along its edges, while amorphous clumps were distributed throughout its volume. Ongoing quantitative studies seek to determine matrix deposition in these constructs and correlate these to their mechanical properties. We expect that this study will establish feasibility of stimulating and maximizing matrix production within tissue engineered vascular constructs.

**058** Modulating Effects of PMNs on Induced Elastin Regeneration in Proteolytically-injured Vascular Smooth Muscle Cell Cultures, Emily L Ongstad, Anand Ramamurthi; Clemson-MUSC Bioengineering.

Aortic aneurysm is the 15th leading cause of death in the United States among individuals age 65 and older. Known pathophysiological mechanisms of abdominal aortic aneurysms (AAA) include degradation of elastic and collagen matrices by proteolytic enzymes, phenotypic switch and apoptosis of smooth muscle cells (SMCs) in the vascular media, and a subsequent infiltration of inflammatory cells. At this time, aneurysm regression by repair of elastic matrices is not possible because adult vascular SMCs poorly synthesize elastin. Our lab previously identified a combination of exogenous factors that increased elastin synthesis, elastic matrix yield, elastic fiber formation, and maturation by healthy adult rat aortic SMCs (RASMCs). Toward therapeutic application of these factors, we sought to demonstrate elastogenic utility to injured/activated SMCs. The ECM within mature RASMC cultures was selectively depleted of elastin by treatment with porcine pancreatic elastase Type I (0.75 U/mL, 45 min), while causing <10% cell loss. When cultured for 21 days after injury, elastic matrix repair and new matrix deposition were rather limited. When TGF-beta1 and HA oligomers (HA-o) were supplemented during this period, elastic matrix amounts were restored to pre-injury levels through new elastic fiber deposition. Since AAAs are typically associated with inflammation, it is necessary to incorporate this facet into our experiments so as to study the effect of matrix debridement by inflammatory cells on elastogenic induction of SMCs. Toward this, autologous polymorphonuclear leukocytes (PMNs) were isolated from rat whole blood, characterized, and supplemented to SMC cultures during 21 days of post-injury culture in the presence or absence of TGF-beta1 and HA-o. Broadly, our results showed that TGF-beta1 and HA-o suppressed PMN-induced injured SMC proliferation, and induced a fibrotic response characterized by accumulation of collagen. This data suggests that injured vascular SMCs can be elastogenically stimulated for regenerative matrix repair despite the presence of PMNs.

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

Emphysema is a chronic obstructive disease that is characterized by airflow limitation and chronic inflammation. The single greatest risk factor in its pathogenesis is cigarette smoke inhalation. One of the most potent pro-inflammatory systems present in the lung is the complement system. In-vitro experiments by others have shown that cigarette smoke can activate complement through direct pathways. Therefore, activation of lung complement by cigarette smoke may be an important pathogenetic factor contributing to chronic inflammation. While in-vitro studies demonstrate cigarette smoke ability to activate complement few studies have addressed its role in-vivo. Here we have utilized an acute cigarette smoke induced lung injury model to investigate whether cigarette smoke exposure activates the complement system in-vivo and whether complement deficiency ameliorates lung damage. To gain insight into the role of complement three groups of mice (C3 deficient, factor B deficient and wild type) were exposed to cigarette smoke for three days,
with mice receiving two exposures of four cigarettes/day. Twelve hours after the final exposure, lung tissues and lavage samples were collected. Immunohistochemistry and western blotting analysis demonstrated that complement was activated and deposited in wt mice exposed to cigarette when compared to wt non-smoke controls. Furthermore, qRT-PCR demonstrated a significant increase in gene transcription for C3, C5, and fB. Given these data we compared mice deficient in either C3 (central component of complement) and fB (alternative pathway component) with wt exposed animals. C3 and fB deficient mice had significantly reduced lung injury profiles as assessed by histology, LDH and lung cytokine profiles. Additionally, analysis of lavage sample shows a significant reduction in neutrophil and macrophage recruitment to the lung. Taken together these studies demonstrate that the complement system is activated in the lung in response to cigarette smoke exposure, and that complement deficiency ameliorates acute lung injury.

**060 Fli-1 Transcription Factor is Involved in Cytokine Production and the Inflammatory Response Through TLR4 Stimulation**, Emmanuel O Reyes-Cortes1, Sarah K Williams2, Gary S Gilkeson2, Dennis K Watson2, Xian K Zhang2; 1Graduate Studies, Medicine, MUSC, 2Rheumatology & Immunology, Medicine, MUSC, VA, 3Pathology & Laboratory Medicine, MUSC.

Toll-like receptors (TLRs) play an important role in the innate immune response. Lipopolysaccharide (LPS) activates NF-kappa B by triggering TLR4, which results expression of proinflammatory cytokines and chemokines including TNF-alpha and IL6. Overexpression of inflammatory cytokines also plays a crucial role in septic shock. Fli-1 is a transcription factor from the Ets family, primarily expressed in hematopoietic cells, whose overexpression has been correlated with the development of systemic lupus erythematosus. The Fli-1 protein has two transcriptional regulatory domains, designated ATA and CTA, for amino-terminal transcriptional and carboxy-terminal transcriptional activation domains, respectively. We generated mice that expressed a truncated Fli-1 protein lacking CTA (Fli-1&DeltaCTA). To study the role of Fli-1 transcription factor in innate immunity, we measured cytokine production and clinical responses in Fli-1&DeltaCTA/ Fli-1&DeltaCTA and wild-type B6 mice after LPS injection. LPS was injected in 5-7 Fli-1&DeltaCTA/ Fli-1&DeltaCTA and wild-type B6 mice at the dose of 10 mg/kg and serum was collected 1 hour and 6 hours after injection. Concentrations of TNF-alpha, IL6 and MCP-1 were determined by ELISA. Another 10 mice in each group were observed for clinical septic shock after LPS injection. Significantly higher levels of MCP-1, IL6, and TNF-alpha were detected in Fli-1&DeltaCTA/ Fli-1&DeltaCTA B6 mice compared to wild-type controls 1 hour after LPS injection (IL-6: 29,243 pg/mL in Fli-1&DeltaCTA/ Fli-1&DeltaCTA mice vs. 17,088 pg/mL in wild-type controls; TNF-alpha: 13,135 pg/mL in Fli-1&DeltaCTA/ Fli-1&DeltaCTA mice vs. 6,758 pg/mL in wild-type controls; MCP-1: 64,026 pg/mL in Fli-1&DeltaCTA/ Fli-1&DeltaCTA mice vs. 45,890 pg/mL in wild-type controls). Fli-1&DeltaCTA/ Fli-1&DeltaCTA mice also had significant higher IL-6 than wild-type control 6 hours after LPS injection (64,906 pg/mL in Fli-1&DeltaCTA/ Fli-1&DeltaCTA mice vs. 31,367 pg/mL in wild-type controls). Fli-1&DeltaCTA/ Fli-1&DeltaCTA B6 mice also showed severe septic shock symptoms whereas wild-type mice looked relatively normal 24 hours after LPS injection. Our data demonstrate that Fli-1 transcription factor is involved in cytokine production and inflammatory response mediated by NF-kappa B.

**061 Administration of a Vaccine Composed of a Immortalized Dendritic Cells Pulsed with Premalignant Oral Lesion Lysate Results in an Increase in CD4+ and CD8+ T Cells in the Tongue**, Anna-Maria A Clark1, Rita I Young2; 1Graduate Studies, Microbiology and Immunology, MUSC, 2Otolaryngology, MUSC.

Most studies with dendritic cell vaccines have focused on eliminating or preventing the progression of already established malignancies. This is complicated by the immune suppression that is often exhibited in the presence of solid carcinomas. The goal of this study is to determine if an immune response can be elicited by administering a dendritic cell vaccine during the premalignant stages of oral squamous cell carcinoma (OSCC), prior to the development of systemic immune suppression. Mice treated with the carcinogen 4-nitroquinoline-1-oxide (4NQO) in drinking water develop premalignant oral lesions which subsequently progress to OSCC. As previous studies in our lab demonstrated that premalignant lesions and OSCC share overexpression of common tumor antigens, dendritic cells of the immortalized cell line JAWS II were pulsed with premalignant lesion lysate and administered to 4NQO-treated C57BL6 mice exhibiting premalignant lesions. Immunohistochemical analysis demonstrated a similar increase in the number of CD8+ and CD4+ cells in the tongues of both the 4NQO-treated mice immunized with premalignant lesion-pulsed dendritic cells and the 4NQO-treated mice immunized with keratinocyte-pulsed dendritic cells compared to 4NQO-treated mice injected with saline. These studies indicated that stimulated immortalized dendritic cells, regardless of pulsing with premalignant lesions or keratinocytes, may be able to elicit an upregulation of T cells in premalignant lesions of the tongue. Therefore, future experiments will be carried out using primary dendritic cells derived from GFP bone marrow.

**062 Acid Ceramidase Upregulation Following Radiation Therapy Desensitizes Cancer Cells to Taxol**, Thomas H Beckham1, Joseph C Cheng1, Ayman E Mahdy2, Xiang Liu2, James S Norris2; 1Graduate Studies, Microbiology and Immunology, MUSC, 2Microbiology and Immunology, MUSC.

Combination therapies in cancer treatment provide a
promising means of increasing the effectiveness of the same treatments in isolation, but enhanced efficacy should not be assumed. Therapies that modify cellular mechanics have the potential to provide protection against additional modes of treatment. We have shown that radiation therapy increases levels of the pro-proliferative enzyme Acid Ceramidase (AC) in PPC1 prostate cancer cells, desensitizing them to radiation as well as other therapies including Taxol. Taxol is a mitotic inhibitor that attacks rapidly growing cancer cells. Taxol treatment significantly increased levels of pro-apoptotic long chain ceramides while decreasing levels of anti-apoptotic sphingosine-1-phosphate (S1P) and its precursor, sphingosine, suggesting that the ceramide pathway plays an important role in Taxol mediated cell killing. Although the combination of Taxol and radiation is commonly used for the treatment of advanced prostate cancer, the benefit of combination therapy hasn’t been widely explored. It has been shown that radiation therapy desensitizes cells to Taxol in other cancer cell lines. Here we demonstrated that the increased levels of AC induced by radiation contributes to desensitization of cells to Taxol in vitro. Various treatment schedules of PPC1 cells with radiation and Taxol enhance cell survival versus cells treated with Taxol alone, with the greatest protection being conferred by irradiating cells prior to treatment with Taxol. Lower levels of caspase 3/7 activity were detected in cells pretreated with radiation, also indicating increased resistance. The resistance phenotype appears to be at least partially through AC up-regulation since down regulation of AC by siRNA abolished radio-protection and re-sensitized the cells to radiation-chemotherapy. This study provides further evidence that AC plays an important role in cancer therapies and should be considered as a co-target when radiation therapy is used. Supported by PPG NIH/NCI PO1 CA97132-01A1

**063 The Isolation and Structural Characterization of Novel Toxins From the Harmful Algae, Prymnesium Parvum,** Matthew J Bertin1, Paul V Zimba2, Kevin R Beauchesne3, Peter Moeller4; 1Marine Biomedicine and Environmental Sciences Center, MUSC, Hollings Marine Laboratory, 2Center for Coastal Studies, Texas A&M University, Corpus Christi, TX, 3JHT in support of the Hollings Marine Laboratory, NOAA, Charleston, SC, 4Marine Biomedicine and Environmental Sciences Center, MUSC, Hollings Marine Laboratory, Charleston.

The golden alga, Prymnesium parvum, has been implicated in fish and aquatic animal kills in the United States since 1985. This algae is most often associated with blooms in estuarine and marine waters, but has been observed to affect inland waters and aquaculture facilities. Prymnesium parvum is globally distributed and widely observed in the United States. Texas has been particularly affected with P. parvum documented in ≥ 29 reservoirs and causing the deaths of over 27 million fishes. In addition to widespread ecological impacts, an economic burden is also felt by state and local economies due to year class losses of fish for stocking lakes as well as loss of fishing and recreational use of the affected body of water. Two ichthyotoxic and hemolytic compounds have been described and structurally characterized from P. parvum, prymnesin -1 and -2. Based on preliminary data from both the Moeller lab and others we propose that undescribed and more ecologically relevant toxins are present in P. parvum. First P. parvum cell mass was cultured and collected from wild blooms and extracted with ethyl acetate followed by methanol. These crude extracts were tested for cytotoxicity against mammalian cell lines (N2A and GH4) with activity observed in the methanol fraction. Bioassay-guided fractionation using high pressure liquid chromatography (HPLC) has identified multiple cytotoxic fractions. These fractions will be further isolated using HPLC and structurally characterized using mass spectrometry (MS) and nuclear magnetic resonance spectroscopy (NMR). Subsequent assays will characterize the ichthyotoxic, algicidal, and cytotoxic activity of these novel compounds. Isolating and characterizing novel toxin(s) from P. parvum will lead to improved detection methods and further research avenues including toxin neutralization, characterization of toxin bioactivity, and possible anticancer properties. Supported by NOAA/NOS

**064 Virtual Screening for Novel Inhibitors of Pbp2 From Neisseria Gonorrhoea, a Critical Enzyme in Penicillin Resistance,** Richard E Trager, Alena Fedarovich, Christopher Davies; Graduate Studies, Biochemistry and Molecular Biology, MUSC.

New cases of antibiotic resistance are increasing worldwide, creating a need for novel antibiotic treatments. Current beta-lactam antibiotics target penicillin-binding proteins (PBPs). PBPs are critical enzymes that maintain the peptidoglycan layer in bacteria, but also harbor mutations associated with resistance to beta-lactams. To discover new inhibitors of PBPs, virtual screening methods, such as the program DOCK, can be employed to search large numbers of compounds at a fraction of the cost and time needed to screen in vitro or in vivo. DOCK screens for new inhibitors by searching for the lowest energy conformation of the ligand and substrate. The structures of PBP2 have been solved, derived from both penicillin-susceptible and -resistant strains of N. gonorrhoeae. Using these structures, virtual screens are performed to generate a list of possible new inhibitors of PBP2. The top candidates can then be tested for inhibition of PBP2 in vitro using enzymatic assays. National Institute of General Medical Sciences, grant number 5R01GM066861-07

**065 Role of C18-Pyridinium Ceramide in Autophagy Induced Cell Death in Human Head and Neck Squamous Cell Carcinomas (HNSSC),** David Sentelle, Besim Ogretmen, Yusuf Hannun; CGS, BMB, MUSC.

Abstract not available.
066 MKP-1 is Required for Maximal 1,25(OH)2D3-Induced RANKL Expression and Osteoclastogenesis, Alfred C Griffin, Carlos Rossa, Keith L Kirkwood; Craniofacial Biology, MUSC.

Widely accepted as a catabolic bone hormone, Vitamin D3 (VitD3) and its most active form 1,25(OH)2D3, are well known to stimulate osteoclastogenesis by induction of receptor activator of nuclear factor kappaB (NF-kappaB) ligand (RANKL). The MAP Kinase Phosphatase (MKP) family of proteins have been classically known for their ability to negatively regulate MAP Kinase activity by dephosphorylating MAPK proteins. MKP-1 is a founding member of this family of phosphatases that has been well documented to negatively regulate the innate immune response through dephosphorylation of p38, ERK, and JNK activity. Objectives: To determine the role of MKP-1 in VitD3–induced RANKL gene expression in murine bone marrow stromal cells (BMSC) and the role of MKP-1 in VitD3-supported osteoclastogenesis. Methods: Bone marrow cells from tibias and femurs of 6-10 week old MKP-1-/- and MKP-1+/+ mice (n=4) were collected and allowed to adhere 5-10 days in a-MEM containing 10% serum. BMSC (5 x105) were co-cultured with RAW264.7 cells (5 x105) for 6 days in the presence of VitD3. Co-cultures were stained for Tartrate Resistant Acid Phosphatase (TRAP). Results: Real-time qPCR results reveal that untreated BMSCs from MKP-1-/- mice have a 36-fold increase in steady-state mRANKL gene expression in comparison to untreated MKP-1+/+ cells following normalization to GAPDH. Surprisingly, in VitD3 treated cultures mRANKL expression was 34-fold higher in MKP-1+/+ bone marrow cells than the MKP-1-/- cells when normalized to untreated controls. Co-culture data revealed that RAW cells incubated with VitD3 treated MKP-1-/- BMSCs differentiated with 31% fewer osteoclasts (TRAP+, >=3 nuclei) than MKP-1+/+ co-cultures. Conclusion: These results suggest a permissive role for MKP-1 in the 1,25(OH)2D3 induction of RANKL expression in bone marrow stromal cell populations and subsequent osteoclastogenesis. Supported by NIH T32DE017551, 1R01DE018290, and 2P20 RR017696-06.

067 SPARC Has a Critical Role in Collagen Fiber Morphology of the Periodontal Ligament, Jessica Trombetta, Amy Bradshaw; MUSC.

The periodontal ligament (PDL) attaches the cementum layer of the tooth to the alveolar bone. The PDL is important to allow the teeth to bear masticatory loads. In addition, the PDL is involved in orthodontic movement, proprioception and possibly tooth eruption. Periodontal disease causes the degradation of the PDL and is a major contributing factor to tooth loss and bone resorption in patients. Understanding the composition of the PDL is an important part to identifying methods of regeneration and repair. The PDL consists primarily of fibroblasts, but nerves and blood vessels can also be found within the tissue. Fibroblasts secrete and mediate turnover of the extracellular matrix (ECM) that consists primarily of collagens I and III with a number of other resident ECM and matricellular proteins. The PDL has a high turnover rate of collagen throughout adulthood. However, with aging, the PDL becomes a less dynamic tissue. SPARC, a matricellular protein, has been shown to bind to collagens I and III and is also implicated as a mediator of collagen turnover and phagocytosis. In addition, expression of SPARC increases with aging of PDL fibroblasts. In the SPARC knockout (KO) mouse we see an altered PDL phenotype that progresses with the age of the mouse. The PDL of SPARC KO mice have altered fibroblast orientation and quantity, decreased collagen fiber density, disorganization of collagen fibers, and changes in collagen morphology when compared to wild type littermates. Using LPS injections to model periodontal disease, we find increased bone loss in the SPARK KO mice versus wild type littermates. These results demonstrate that SPARC is essential for the maintenance of the PDL and implicate future roles of SPARC in PDL regeneration. We would also like to acknowledge Keith Kirkwood and Carlos Rossa for discussions, information, and technical assistance pertaining to the PDL, Lauren Land and Yuhua Zhang for technical support. Funding provided by NIH/NIDCR P20 RR017696-06.

068 Oxidative Stress MRNA Changes in the Substantia Nigra of 3 Month Old Methamphetamine-Treated GDNF Heterozygous Versus Wildtype Mice, B Go, H A Boger, J F McGinty; Neurosciences, MUSC.

Dopaminergic neurons are believed to be particularly prone to oxidative stress due to their high rate of oxygen metabolism, low levels of antioxidants, and high iron content. An increase in the formation of toxic hydroxyl radicals and a decrease in the ability to detoxify them are major risk factors in PD that may underlie the vulnerability of mitochondrial complex I to damage in SN DA neurons. For example, glutathione depletion in the SN of PD patients is accompanied by a decrease in catalase and glutathione peroxidase activity that weakens a cell’s ability to counteract oxidative stress. Furthermore, oxidative stress has been implicated in the neurotoxic damage associated with methamphetamine-induced toxicity. Therefore, in this study, methamphetamine (METH HCl, 10 mg/kg, i.p.) or saline was injected into 2.5-month-old WT and GDNF-/- mice every 2 hrs for 8 hrs. Two weeks post-injection (3 months of age), the substantia nigra was dissected out, homogenized and RNA extracted for analysis using the SuperArray RT2 Profiler PCR Array System Pathway-Focused Gene Expression Profiling technique for detection of markers associated with “Oxidative Stress and Antioxidant Defense”. Initial analysis indicates that 3 month old GDNF-/- mice have lower mRNA expression of certain endogenous anti-oxidants, such as extracellularly localized superoxide dismutase 3 (SOD-3), glutathione peroxidase 3, and neuronal localized peroxiredoxin 3 compared to saline-treated WT mice. Two weeks after undergoing a toxic METH binge, GDNF-/- mice demonstrated an increase in endogenous anti-
oxidant support by exhibiting a greater increase of mRNA expression of SOD-3, glutathione peroxidase 3, and glial localized peroxiredoxin 6 compared to METH-treated WT mice. In addition, METH-treated GDNF+/- mice had increased mRNA expression of inducible nitric oxide synthase (iNOS) compared to METH-treated WT mice. These data suggest an important role of oxidative stress in the exacerbated DAergic damage observed in METH-treated GDNF+/- mice at 3 months of age. Supported by NIA PO1 AG023630.

069 Effects of the Abused Inhalant Toluene on Neurons in the Medial Prefrontal Cortex, Jacob T Beckley, John J Woodward; College of Graduate Studies, Neurosciences, MUSC.

Abused inhalants remain an understudied, yet significant health problem, particularly among adolescents. Toluene (methylbenzene) is a prototypical abused inhalant and is commonly found in household products including lacquers, paints and glues. Previous work from this laboratory has established that toluene, at behaviorally relevant concentrations, has selective effects on various ligand-gated and voltage-activated ion channels. Evidence from human and animal studies also suggest that toluene, like other drugs of abuse, may especially target neurons within brain areas, such as the prefrontal cortex (PFC), that are associated with addiction. The PFC is critical for executive function, working memory and decision-making, processes that are significantly impacted in drug abusers. Dysregulation of glutamatergic transmission in PFC neurons that innervate the nucleus accumbens (NAc) is also thought to mediate the heightened motivation to seek drugs even after prolonged periods of abstinence. Despite important findings linking drug abuse to PFC dysfunction and actions of toluene on ion channels, there is virtually nothing known about the cellular effects of inhalants on the PFC. Here, we used whole-cell electrophysiology and acute brain slices to determine the effect of toluene on deep-layer pyramidal neurons in the medial PFC. In neurons from adolescent rats (P22-26), toluene (1, 3 mM) had little effect on measures of intrinsic excitability. Toluene also had no effect on stimulus-evoked AMPA-mediated currents but dose-dependently inhibited NMDA-mediated excitatory post-synaptic responses (1 mM: 74+/−9% of baseline, F=3.8653, P<0.05; 3 mM: 61+/−9% of baseline, F=10.60, P<0.01). In contrast, toluene dose-dependently potentiated GABA-mediated inhibitory post-synaptic currents (1 mM: 142+/−12% of baseline, F=4.301, P<0.05; 3 mM: 170+/−29%, F=6.625, p<0.05). The results from these studies are the first to show selective effects of toluene on synaptic transmission in PFC neurons and are critical for establishing a better understanding of the effects of toluene on the addiction neurocircuitry. Supported by AA007474 and DA013951.

070 Magnetic Resonance Spectroscopy Reveals That NAA Levels May Be an Early Indicator of Neurodevelopmental Outcome in Neonates with Chorioamnionitis, C Bryce Johnson1, Denise M Mulvihill2, Karen C Lee3, Lakshmi D Katikaneni3, Dorothea D Jenkins3, Laura G Rollins3, Paul Morgan4; 1Neuroscience’s CAIR, Medicine, MUSC, 2Radiology, Medicine, MUSC, Pediatrics, Medicine, MUSC, Pediatrics, Medicine, MUSC, 4Neuroscience’s CAIR, Medicine, MUSC, Radiology, Medicine, MUSC.

Abstract not available.

071 Postpartum Depression and Vitamin D: An Exploratory Study, Pamela K Murphy1, Thomas Hulsey2, Myla Ebeling3, Martina Mueller4, Carol Wagner5; 1Graduate Studies, Nursing, MUSC, 2Medicine, Pediatric Epidemiology, MUSC, 3Nursing, MUSC, 4Medicine, Neonatology, MUSC.

Abstract not available.

072 Organ Doses and Projection Angle in Cone Beam CT, Wenjun He1, Dennise Magill2, Emily Tavrides3, Walter Huda3, Hai Yao4; 1MUSC-Clemson Joint Bioengineering Program, 2Radiology and Radiological Science, MUSC, 3Radiology and Radiological Science, 4Bioengineering, Clemson.

Purpose: To investigate how x-ray tube projection angle influences patient doses in cone beam CT. Method: We used the PCXMC software package to compute organ doses to patients. We modeled a typical x-ray spectrum using 120 kV x-ray tube voltage and 6 mm Al filtration. Two cone beam irradiation geometries were modeled: (a) a standard CT gantry; and (b) a C-arm. Both systems made use of a detector with dimensions of 30 cm x 40 cm. For the CT gantry system, the source to isocenter distance was 57 cm, and the SID was 93 cm. For the C-arm system, the source to isocenter distance was 78.5 cm, and the SID was 120 cm. Organ dose to the five most radiosensitive organs (breast, colon, lung, red bone marrow, and stomach) were obtained for each cone beam arrangement at 15 degree intervals as the x-ray tube rotates through 360 degrees around the patient. Results: On average, patient doses using the C-arm were ~60% of those obtained using the CT gantry. Ratios of maximum to minimum doses as a function of x-ray tube angle ranged from ~2.3:1 for the lung to ~31:1 for the stomach. For the breast, colon, and stomach the highest doses were obtained for AP projections, whereas for the lung and red bone marrow, PA projections resulted in the highest organ doses. In all cases, dose minima were obtained when the x-ray beam entered the patient in a lateral orientation. Conclusions: The high maximum to minimum dose ratios for radiosensitive organs such as the stomach and breast indicate that modulation of the x-ray tube current with projection angle could result in substantial dose reductions in cone beam CT.
073 Mechanisms of Celastrol Mediated Protection Against Aminoglycoside-Induced Hair Cell Death in the Inner Ear, Shimon P Francis¹, Tiffany G Baker¹, Carlene S Brandon¹, Inga I Kramarenko¹, Fu-Shing Lee², Lisa L Cunningham¹; ¹Graduate Studies, Pathology and Laboratory Medicine, MUSC, ²Graduate Studies, Otolaryngology, MUSC.

The sensory hair cells of the inner ear transduce mechanical stimulation caused by sound and head movement into neural signals of hearing and balance. These cells are susceptible to death caused by noise, aminoglycoside antibiotics, cisplatin and ageing. Aminoglycoside antibiotics are used in the treatment of bacterial infections, but have serious side effects that include irreversible hearing loss.

The goal of this research project is to further investigate the molecular mechanisms underlying ototoxic drug-induced hair cell death in order to develop a practical co-therapy to prevent it. Our laboratory has previously demonstrated that upregulation of heat shock proteins (Hsps) inhibits aminoglycoside-induced hair cell death and hearing loss. However, clinical heat shock therapy is poorly tolerated by patients. Pharmacological induction of Hsps may be a more feasible clinical approach to the protection of aminoglycoside-exposed hair cells. Celastrol is a small molecule that has been identified as a pharmacological Hsp inducer. Our data indicate that celastrol is protective against aminoglycoside-induced hair cell death in the adult mouse utricle in vitro. Here we have examined the mechanisms underlying celastrol’s protective effect.

Treatment with celastrol results in robust upregulation of Hsp70 and Hsp32 expression. JNK phosphorylation is an early apoptotic signaling event in aminoglycoside ototoxicity, and Hsps have been shown to inhibit JNK phosphorylation in other systems. Therefore, we analyzed JNK phosphorylation by western blot. Exposure to neomycin (an aminoglycoside antibiotic) resulted in JNK phosphorylation, and celastrol inhibited neomycin-induced JNK phosphorylation. We next analyzed whether the protective effect of celastrol requires the major heat shock transcription factor Hsf1. Utricles from Hsf1 /− mice and their wild-type littermates were cultured in celastrol and then exposed to the aminoglycoside antibiotic gentamicin. Celastrol was protective against gentamicin-induced hair cell death in wild-type mice, and this protective effect was retained in utricles from Hsf1 /− mice (Three-way ANOVA, F1,59 = 10.48, p < 0.001, n=67). These data indicate that Hsf1 is not required for celastrol’s protective effect.

mRNA analysis revealed that celastrol induces Hsp32 expression (but not Hsp70 expression) in utricles from Hsf1 /− mice. These data suggest that Hsp32 may be an important mediator of celastrol’s protective effect against aminoglycoside-induced hair cell death. The National Institutes of Health R01 DC07613; DC07613-SI

074 Classifying Multi-Channel Neural Recordings: The Detection of Complex Dynamics, Joshua E Swearingen, Marcelo Reyes, Catalin V Buhusi; Neuroscience, MUSC.

Neurons emit spikes of action potentials in series that contain information in both the firing rate as well as the temporal pattern. Many conventional analysis techniques average over relatively large windows, which may lose fine spiking patterns in the millisecond range. Neurons may also switch between a number of more general spiking patterns, reflecting the nature of the larger neural network they exist within. Additionally, advances in multi-channel recording make it possible to record simultaneously from many neurons, bringing even more need for statistical methods of pattern analysis in electrophysiological data. In this study we use a method of unsupervised classification to segregate neural recordings from awake, behaving animals, both by trial within a neuron, as well as across neurons recorded within a single session. This method creates a similarity score between trials, and uses a matrix of these scores as a dimension-reduced input to a k-means clustering algorithm. Preliminary results suggest that these new methods of spike train analysis can be used to successfully stratify neurons according to complex functional dynamics that may otherwise go unnoticed. Xinghua Lu, Department of Biochemistry; NLM training grant Training of Toolmakers for Bio-Medical Informatics

075 Long-term Exposure to a High Saturated Fat and Cholesterol Diet Leads to Altered Morphology in the Hippocampus, Linnea R Freeman, Alfred B Moore, Claudia M Umphlet, Nicholas C Gregory, Ann-Charlotte Granholm; Graduate Studies, Neurosciences, MUSC.

The damaging effects of a “Western Diet” to overall health is currently of great interest as it has been found to be a main culprit for obesity, type II diabetes, cancer and cardiovascular issues. However, its effects on the brain and cognition are not currently well understood. Previous work from our laboratory has shown that a 10% hydrogenated coconut oil and 2% cholesterol diet resulted in worse performance on the 12-day water radial arm maze, increased cholesterol and triglyceride levels, and decreased dendritic microtubule associated protein 2 (MAP2) staining in the hippocampus. We have also recently shown that each component of the “Western Diet” alone (saturated fat, trans fat, or cholesterol) resulted in alterations in hippocampal morphology and serum triglyceride/cholesterol levels. A reduction in dendritic integrity and fatty acid metabolism combined with an increase in microgliosis as measured by antibodies against MAP2, 5-LOX, and OX-6, respectively, revealed damaging effects after just 8 weeks on the various diets. Our current study has further evaluated the damaging effects of the “Western Diet” to cognition and hippocampal morphology using the 10% hydrogenated coconut oil and 2% cholesterol diet for 6 months starting at the age of 7 months in Fischer 344 rats. Serum was collected in order
to analyze triglyceride and cholesterol levels. Finally, we are analyzing the hippocampal morphology with the antibodies used and hypothesize an even greater reduction in MAP2 and 5-LOX immunoreactivity and an even greater increase in OX-6 immunoreactivity due to long-term treatment with the diet. Our previous studies have shown that this type of diet alters behavior and hippocampal morphology in just 8 weeks. We have designed the current study to more closely resemble the time period of exposure for humans (long-term treatment) and how this may impact the aging brain. Supported by NIH T32 DA 07288-12 and F31-DA025458-01

076 Pro-NGF Interaction with P75 May Be Responsible for the Cholinergic Degeneration Observed in Alzheimer’s Disease. Ashley M Fortress, Kris L Helke, Ann-Charlotte Granholm; 1Neurosciences, MUSC, 2Comparative Medicine, MUSC, 3Neurosciences & Center on Aging, MUSC.

Learning and memory impairments occurring with normal aging and Alzheimer’s disease are associated with degeneration of the basal forebrain cholinergic neurons (BFCNs). BFCNs extend their axons to the hippocampus and are dependent on nerve growth factor (NGF) for survival and maintenance. Cholinergic terminals in the hippocampus bind NGF at its high-affinity receptor, trkA, and the trkA-NGF complex is transported to the BFCN cell bodies via classical retrograde transport mechanisms to promote BFCN survival. Loss of NGF transport to the BF is correlated with both cognitive deficits and BFCN degeneration, posing an important role for this system in memory processing. The precursor to NGF, pro-NGF, binds with high affinity to the low-affinity NGF receptor, p75, and its co-receptor sortilin; and this complex has been demonstrated to induce cell death in vitro. Previous work in our laboratory has shown that systemic administration of NGF increases the expression of trkA in the BF and enhances memory performance. Currently, the working hypothesis is that disrupted retrograde signaling of NGF with aging results in reduced trkA activation and elevated p75 response, resulting in a propelling degeneration of the cholinergic neurons. However, we suggest that there is a secondary or concurrent increase in pro-NGF in aging, resulting in recruitment of p75 and sortilin to form a trimeric complex that signals to the BFCNs to induce cell death. To test this hypothesis, aged rats were given bilateral stereotaxic intrahippocampal injections of pro-NGF or saline; young saline animals were also used to test the effects of aging alone. Twenty-four hours after injection, western blotting revealed: 1) p75 was elevated in a step wise fashion with aging and pro-NGF treatment, 2) Pro-NGF treatment decreased the expression of the precursor form of the TrkA receptor, and 3) that pro-NGF is colocalized with sortilin in the BFCNs. To our knowledge, this is the first in vivo study to show that pro-NGF accumulation may serve to upregulate the p75 receptor and consequently result in BFCN degeneration. NIH/NIA AG10755

077 Chronic RGD Peptide Administration in the Nucleus Accumbens Attenuates Cocaine-Primed Reinstatement. Armina T Wiggins, Peter W Kalivas; MUSC.

Cocaine addiction often causes an intense craving that persists after long periods of abstinence and can contribute to relapse. This craving may be stabilized by enduring drug-induced synaptic plasticity that reinforces future drug use. Some of the most noted adaptations involve changes in the protein content of the PSD and morphological changes in dendritic spines in the nucleus accumbens (NAc). We have previously described (Toda, J. Neurosci, 2006) an increase in actin cycling in the nucleus accumbens after chronic cocaine administration that may contribute to the drug-induced plasticity in protein expression and dendritic spine morphology. In recent studies, actin polymerization and spine morphology have been shown to be regulated by beta integrins. We have explored the role of integrins in a non-contingent and contingent models and have found transient changes in integrin expression in the postsynaptic density during the expression of cocaine-primed behavioral sensitization and reinstatement. We are currently exploring the role of beta integrins in the contingent model. Animals underwent cocaine self administration training or received yoked saline, extinction training for 21 days and on the last day animals received 15mg/kg ip cocaine injection for a cocaine primed reinstatement test. We modulated integrin function with microinfusions of RGD peptides into the NAc during cocaine self-administration, extinction or prior to a cocaine primed reinstatement test. Only modulation of integrin signaling during self-administration attenuates cocaine-primed reinstatement but not cue-induced reinstatement. Ongoing studies are investigating the role and mechanism of integrin signaling on altered cocaine-induced neuroplasticity on the extracellular matrix. Supported by NIH T32 DA 07288-12 and F31-DA025458-01

078 Isozymes of Sphingosine Kinase Play Partially Overlapped Roles in Tumor Cells. Peng Gao, Charles D Smith; 1Pharmaceutical Sciences, MUSC, 2MUSC.

Sphingosine kinases (SphKs) play key roles in tumor cell proliferation, angiogenesis and inflammation by catalyzing the formation of sphingosine-1-phosphate (S1P). However, the functions of the two isozymes, SphK1 and SphK2, in tumor epithelial cells are not fully understood. Therefore, we are using genetic and pharmacologic approaches to assess their roles in sphingolipid metabolism, signaling, proliferation and migration. In the first approach, isozyme-selective siRNAs are being used to targetly reduce the expression of SphK1/2 in tumor cells. Ablation of SphK2 or both SphK1 and SphK2 suppressed A-498 kidney adenocarcinoma cell proliferation more intensely and drove more cells into apoptosis than did selective depletion of SphK1. Interestingly, SphK2 depletion elevated the expression of SphK1 and increased the production of
S1P, but this did not rescue cells from the suppression of proliferation. In contrast, SphK1-selective depletion did not affect SphK2 expression, but decreased S1P levels and elevated the levels of most pro-apoptotic ceramide species. Depletions of SphK1 and/or SphK2 have similar effects on AKT phosphorylation (decrease), total ERK (decrease) and ERK1 phosphorylation (increase) except that SphK2 depletion decreased the phosphorylation of ERK2 while SphK1-selective depletion didn’t affect it. SphK2 depletion seemed to inhibit the glycosylation of vascular cell adhesion molecule 1, whereas SphK1-selective depletion resulted in slight decreases in its expression. In agreement with these results, SphK2 depletion reduced cell migration, while the SphK1-selective depletion had minimal effect on this process. In the second approach, the roles of the SphK isozymes are being dissected pharmacologically using a SphK2-selective (ABC294640) and a SphK1/2 dual inhibitor (ABC294735). A possibly SphK1-selective inhibitor has also been identified by high-throughput screening and is being characterized. Overall, these data indicate that SphK1 and SphK2 have partially overlapping functions in tumor cell signaling and proliferation. However, selective targeting of SphK2 appears to have the greatest potential for anticancer therapy without toxicity to the patient.

**079 Transdermal Dl-Methylphenidate Potentiates the PK Interactions with Ethanol in a Mouse Model.**

Guinevere H Bell, Andrew J Novak, William C Griffin III, Kennerly S Patrick; 1Pharmacy, Pharmaceutical Sciences, MUSC, 2Institute of Psychiatry, Psychiatry and Behavioral Sciences, MUSC.

**Objective:** Test the hypothesis that transdermal dl-methylphenidate (MPH) will potentiate the metabolic interaction with ethanol relative to oral dosing; and accordingly increase abuse potential and toxicity. Methods: The first murine model of transdermal MPH was developed using a ¼ MPH patch (Daytrana® 10mg) with/without ethanol (3g/kg gavage). The average MPH dose was established by analyzing residual MPH in used patches. This dose (7.5mg) was subsequently used for oral MPH-ethanol comparisons. MPH and ethylphenidate (EPH) in blood, brain, and urine were enantioselectively analyzed by GC-MS using prolyl chiral derivatization and EI-SIM of piperdyl fragments with a deuterated internal standard. Behavioral studies were conducted in parallel. Results: Ethanol significantly elevated concentrations of d-MPH and l-MPH in blood, brain, and urine relative to water (p<0.05). The "ethanol effect" was potentiated by transdermal MPH delivery compared to oral dosing (p<0.01). Ten times more l-MPH reached the circulation using the transdermal route. In the ethanol-transdermal MPH group, the concentrations of l-EPH were greater than d-EPH in all 3 biological matrices (p<0.01). Locomotor activity was maximal at 3h following patch application. Conclusions: Ethanol induced a pronounced elevation of the active d-MPH isomer, especially when using transdermal delivery. The high circulating level of l-MPH following transdermal dosing appears to competitively inhibit carboxylesterase 1 to yield l-EPH, thus “sparring” metabolic clearance of d-MPH. These findings indicate transdermal MPH potentiates the liability for both abuse and cardiovascular toxicity with concomitant ethanol, should this animal model hold for ADHD patients treated with Daytrana®. NIAAA RO1AA016707

**080 Hypertension, Diabetes and Hypercholesterolemia Associated with Stroke Among Caucasians and African Americans.**

Andrea D Boan, David L Bachman, Robert J Adams, Daniel T Lackland; 1Biostatistics and Epidemiology, MUSC, 2Neurology, MUSC.

Secondary stroke prevention remains a key component of all stroke programs. In addition to stroke specific strategies, the treatment of co-morbid conditions such as hypertension, diabetes, and hypercholesterolemia is an important consideration. The racial disparities recognized in the incidence of stroke are also evident with hypertension and diabetes with African Americans having a higher prevalence and earlier onset of disease. The purpose of the study was to assess racial differences among stroke rates associated with hypertension, diabetes, and hypercholesterolemia in South Carolina. Stroke hospitalizations in South Carolina were assessed for the discharge period 1996-2009. All strokes (ICD 430-438) were included in the patient-based analytical database. Patients were categorized as first vs. multiple strokes based on the number of stroke hospitalizations during the study period. Hypertension, diabetes, and hypercholesterolemia were based on diagnosis at discharge. The percent of stroke patients with hypertension and diabetes was considerably greater than the general population. In 1996, 47.3% of stroke discharges also were diagnosed with hypertension, 24.7% with diabetes, and 7.7% with hypercholesterolemia. These percentages significantly increased to 60.7%, 28.1%, and 36.7% in 2008 (p<0.01, p<0.01, p<0.01 respectively). Racial differences were evident with African Americans than Caucasians more likely to have hypertension (61% vs. 56%; OR(95%CI) = 1.24 (1.23, 1.27); p<0.01), diabetes (35.7% vs. 23.8%; OR(95%CI) = 1.77 (1.74, 1.81; p<0.01), however Caucasians were more likely to have hypercholesterolemia (23.8% vs. 17.9%; OR(95%CI) = 0.69 (0.68, 0.71); p<0.01). Both stroke age groups (< 65/65+ yrs) had significant rates of hypertension, diabetes, and hypercholesterolemia that increased during the time period (all p<0.01; except diabetes <65 p=0.42). The hospital discharge system provides a valuable resource to monitor stroke patterns and risk factors. Hypertension, diabetes and hypercholesterolemia are major co-morbid conditions associated with stroke hospitalizations for both case and stroke histories. These results identify need for hypertension, diabetes, and hypercholesterolemia treatment and control as part of secondary stroke prevention. In addition, stroke hospitalizations represent an opportunity for aggressive treatment of this at-
risk population. Project Support: Stroke Education & Prevention in SC STEP-SC funded by the Health Sciences SC; and Stipend Support: SPTCR Grant Number 1TL1RR029881-01 from the National Center For Research Resources

081 Identification of Functional Promoter Regions of Two Human DihydroCeramide Synthase (CerS/LASS) Genes: Mechanisms of Regulation in Head and Neck Cancer Cells (HNSCC), Marisa A Meyers, Besim Ogretmen; Graduate Studies, MUSC.

The human longevity assurance gene 1 (LASS1) encodes for dihydroceramide synthase 1 (dhCerS1), and generates C18-ceramide in the de novo ceramide synthesis pathway; while dihydroceramide synthase 6 (dhCerS6) generates C16-ceramide via the de novo pathway. Our preliminary data showed that dhCerS1 and thus endogenous C18-ceramide is down-regulated in HNSCC, and upon treatment with chemotherapeutic agents, such as gemcitabine/doxorubicin or Imatinib (Gleevec), dhCerS1/LASS1 mRNA is up-regulated, leading to apoptosis. Conversely, dhCerS6/C16-ceramide is up-regulated in HNSCC, correlating with an increase in cellular proliferation in HNSCC cells. Thus, the mechanisms, which activate and repress dhCerS1/LASS1 and dhCerS6/LASS6, respectively, need to be elucidated to understand their roles in cancer apoptosis and proliferation. Here we have cloned the functional dhCerS1 (~1550bp) and dhCerS6 promoters (~1600bp) that regulate their expression. We also characterized the minimal core promoter regions of each gene in various HNSCC cell lines. These regions correspond to -300 to -80 bp upstream of the +1 start site for dhCerS1, and -800 to -1bp upstream of the +1 start site for dhCerS6. Mapping potential binding proteins of the dhCerS1 core promoter region revealed many SP1 and SP3 transcription factor binding sites. RNAi knock-down and over-expression studies revealed SP1 as the direct transcriptional activator of the dhCerS1 promoter and were confirmed with CHIP and gel-shift assays. Mutation of a triplet in the full-length dhCerS1 promoter located 100 base pairs up-stream of the core promoter region restored promoter activity comparable to that of the core promoter. This suggests a repressor protein binding region immediately up-stream of the core promoter, possibly regulating its activation. In summary, preliminary data shows promising future directions to elucidate the molecular mechanisms which mediate the up-regulation of dhCerS1 transcription, specifically inducing apoptosis, in HNSCC cells. Supported in part by the Graduate Assistance in Areas of National Need (GAANN) Training Grant in Lipidomics and New Technologies from the United States Department of Education

082 A Bayesian Hierarchical Model to Derive Novel Gene Networks From Gene Ontology Fingerprints, Tingting Qin1, Lam C Tsoi1, Andrew B Lawson2, Jim W Zheng1; 1Biochemistry and Molecular Biology, MUSC, 2Medicine, DBE, MUSC.

We used ontology fingerprints to study candidate genes associated with lipid concentration in plasma. The ontology fingerprint of a gene is a set of ontology terms overrepresented in the PubMed abstracts linked to the gene along with the terms’ corresponding enrichment p-value. By comparing ontology fingerprints between gene pairs, we inferred gene-gene relationship to construct a gene network. In the network, genes are nodes and the similarity scores between genes are weighted edges. In order to eliminate biologically irrelevant gene connections from the gene network, we developed a Bayesian hierarchical model to use existing pathway information to infer biologically relevant threshold for the weighted edges in the network. The results show that there is a trend of consistent score threshold across different biological pathways, indicating that there exists a standard threshold to separate biologically coherent gene connections from noises. Applying the identified threshold and algorithms based on graph theory, we were able to identify network modules that are biologically relevant to lipid concentrations from the candidate genes identified from a Genome wide association study. Supported by grants IRG 97-219-08 from the American Cancer Society; RR017696-05 and PhRMA Foundation Research Starter Grant (WJZ, TTQ). LCT is supported by NLM training grant 5-T15-LM007438-02.

083 Using Consistent Differential Expression Pattern (CDEP) to Identify Genes Involved in Metastasis From Multiple Microarray Data Sets, Lam C Tsoi1, Tingting Qin1, Elizabeth Slate2, Jim W Zheng1; 1Biochemistry and Molecular Biology, MUSC, 2Medicine, DBE, MUSC.

Abstract not available.

084 Alternative Pathway Is Responsible for Complement Activation in Dextran Sulfate Sodium-Induced Colitis, Jennifer Schepp-Berglind1, Carl Atkinson1, Fei Qiao1, Gary Gilkeson2, Stephen Tomlinson1; 1Microbiology and Immunology, MUSC, 2Rheumatology, MUSC, Ralph H. Johnson VA Medical Center.

Crohn's disease (CD) and ulcerative colitis (UC) are chronic inflammatory disorders of the intestine and generally referred to as inflammatory bowel disease (IBD). Although complement is implicated in causing tissue injury that is associated with inflammatory bowel disease (IBD), there is surprisingly little data available on the role of complement in the pathogenesis of the disease. We hypothesize that complement plays a key role in the pathogenesis of IBD via the direct effect of complement activation products on tissue injury and via effects on inflammation. In order to begin evaluating how the
complement system may contribute to gut inflammation and its potential role in IBD pathogenesis, we compared the severity of dextran sulfate sodium-induced colitis in C3, Factor B (FB), and MBL (Mannose Binding Lectin)/C1Q-deficient and control mice (C57BL6). Five days after consuming 5% dextran sulfate sodium in their drinking water, the control mice and the MBL/C1Q-deficient mice suffered greater weight loss, uniformly bloody diarrhea as compared with the minor changes in the C3 and FB-deficient mice. The control and MBL/C1Q-deficient also developed shortened colons and had larger spleens than either of the complement deficient mice. Histological examination of the distal colons showed a massive increase in neutrophils and mononuclear cell infiltration as well as greater epithelial cell destruction in the control mice and MBL/C1Q-deficient compared to minimal damage to the C3 and FB-deficient mice. To further investigate the inflammatory response, we evaluated cytokine profiles and showed a significant decrease in levels of the pro-inflammatory cytokines, TNF-α and IFN-γ, in the C3 and FB-deficient mice compared to controls and MBL/C1Q-deficient mice. We have shown that the injury induced by DSS absorption is minimized in the distal colon of C3 and FB-deficient mice, but not the MBL/C1Q-deficient mice, which concludes that the alternative pathway of activation is responsible for complement activation. Also, it raises the possibility that regulating complement activation may help protect against IBD inflammation and pathogenesis. Future studies are underway to determine the therapeutic potential of different complement inhibitory proteins. T32 AR050958-04

085 Pathogenic Natural IgM Antibodies Recognizing Different Antigens Mediate Injury Following Ischemic Stroke in Rag1-/- Mice. Andrew F Elvington1, Carl Atkinson1, Liudmila Kulik2, Hong Zhu2, Jin Yu3, Mark S Kindy3, V Holers2, Stephen Tomlinson1; 1CGS, Microbiology and Immunology, MUSC, 2Medicine and Immunology, UCHSC, 3Neuroscience Institute, Neuroscience, MUSC.

Natural IgM antibodies play an important role in injury following ischemia and reperfusion (I/R). Specificity against nonmuscle myosin heavy chain type II A and C has previously been shown to be important for causing injury in mouse models of intestine and hindlimb I/R. Collaborators identified additional IgM specificities that are involved in causing intestinal I/R injury in a murine model, namely annexin IV and certain phospholipids. Here, we demonstrate a role for naturally occurring anti-annexin IV and anti-phospholipid IgM antibodies in causing cerebral injury following murine ischemic stroke. Of clinical relevance, we further show that these antibodies bind hypoxic, but not normoxic, human endothelial cells in vitro, and that anti-annexin IV and anti-phospholipid IgM is present in normal human sera. Mice were subjected to 60 min middle cerebral artery occlusion followed by 24 h reperfusion. Compared to C57BL/6 wt type controls, Rag1-/- mice had significantly smaller cerebral infarct volumes (8.5% +/- 5.4% vs. 26% +/- 12.8%) and improved survival 24 h post reperfusion. Treatment of Rag1-/- mice individually with anti-phospholipid mAb C2 or anti-annexin IV mAb B4 (100 µg prior to reperfusion) restored injury following ischemic stroke (22 +/- 7% and 28 +/- 13% infarct vol respectively). Reconstitution with anti-citritillinated fibrinogen mAb D5 (control mAb) did not reconstitute injury. Immunofluorescence microscopy demonstrated IgM and C3 deposition on endothelial surfaces in the penumbria region and within parenchymal areas of the infarcted brain of wt and Rag1-/- mice treated with mAb. There was no detectable IgM or C3 in sections from untreated Rag1-/- mice. To investigate binding of these mAbs in human endothelial cells, HUVEC were subjected to 3 hours hypoxia followed by 3 hours reoxygenation. Both B4 and C2 bind to hypoxic HUVEC more so than to normal HUVEC. These data demonstrate that there are a several pathophysiologically important epitopes that are recognized across multiple tissues by a subset of natural antibodies, and that these epitopes are likely to contribute to human I/R injury.

086 Characterizing the Function, Expression, and Regulation of Antiphagocytic Protein 1, a Virulence Factor of Cryptococcus Neoformans, Virginia E Williams1, Maurizio Del Poeta2; 1Microbiology & Immunology, MUSC, 2Biochemistry & Molecular Biology, MUSC.

Cryptococcus neoformans (Cn) is an environmental pathogen responsible for the most common cause of fungal meningitis, primarily infecting immunocompromised individuals. The fungus produces many virulence factors to aid in its ability to evade the host immune response. One such virulence factor is antiphagocytic protein 1 (App1). App1 is a protein produced by Cn that inhibits phagocytosis by alveolar macrophages. App1 has been found to inhibit complement-mediated phagocytosis and its function is dependent on complement receptor 3 (CR3). Here we further characterized App1’s function and how its expression is regulated. We found that App1 binds to CR3, providing a mechanism for the inhibition of phagocytosis of Cn by macrophages. Interestingly, we also found App1 binds to CR2 and, therefore, it may have additional effect(s) on the host immune response, as CR2 is mainly found on the surface of lymphocytes and not AMs. In addition, we found that App1 is localized in the fungal cell wall or capsule of Cn, giving it access to the extracellular environment. Finally, we show that the level of App1 protein dramatically increases in low glucose environment, and its up-regulation is directly correlated to the decrease of glucose concentration. Since the environment in which AMs reside is characterized by a low glucose concentration, this study reveals that, following inhalation, App1 may have an important role in the adaptation of Cn cells to the host alveolar environment. Graduate assistance in areas of national need in lipid biology and new technologies (GAANN grant)
Targeting Membrane Associated HSP90 Inhibits Activation of Nuclear Factor Kappa B By Kaposi’s Sarcoma Associated Herpesvirus, Michael DeFee, Zhiquiang Qin, Lu Dai, Bryan Toole, Jennifer Isaacs, Chris Parsons, 1Microbiology and Immunology, Dental Medicine, MUSC, 2Medicine, MUSC, 3Regenerative Medicine and Cell Biology, MUSC, 4Pharmacology, MUSC, 5Medicine, Microbiology and Immunology, Dental Medicine, MUSC.

Abstract not available.

Identification of Small Molecule Compounds That Promote HSC Self-renewal and Expansion Ex Vivo, Joshua N Kellner, Daohong Zhou; Pathology, MUSC.

Induced pluripotent stem cells (iPSCs) are pluripotent stem cells derived from a mature or differentiated cell after activation by retroviral transfection of embryonic stem cell genes Oct4, Nanog, Sox and KLF4. This process can be enhanced by small molecule compounds identified by their ability to facilitate reprogramming of the cell through epigenetic modifications. We tested these compounds in a hematopoietic stem cell (HSC) culture to determine if these small molecule compounds could expand the number of HSCs in ex vivo cultures. We isolated murine Lin-cflt+(LK+) cells and cultured them in serum-free medium supplemented with hematopoietic growth factors, stem cell factor (SCF, 50ng/ml), thrombopoietin (TPO, 50ng/ml) and fetal liver tyrosine kinase 3 ligand (FLT-3L, 50 ng/ml) for 7 days. From 30 small molecules screened, we identified four compounds, SD3, SD12, SD19 and SD25, that significantly expanded the Lin-c-kit+Sca1+CD48- long-term HSC (LT-HSC) population greater than 3 fold compared to control, as determined by flow cytometry. The HSC expansion was then confirmed by the cobblestone-area forming colony (CAFC) assay, which showed that all four compounds increased HSC expansion compared to control. We then isolated LKS+ and LKS- cells to determine whether these compounds promote HSC self-renewal or induced hematopoietic progenitor cell dedifferentiation. No production of HSCs was seen in the LKS- cultures but significant expansion of the LT-HSC population was seen in the LKS+ cultures. These findings suggest that small molecule compounds can be added to HSC ex vivo cultures to promote HSC self-renewal and expansion. These compounds could be used clinically for ex vivo expansion of HSC umbilical cord blood (UCB) to increase total HSC numbers for HSC transplantation, which would enable more therapeutic options for treatment of hematopoietic malignancies.

Identification of Small Molecule Compounds That Targeting Membrane Associated HSP90 Inhibits Activation of Nuclear Factor Kappa B By Kaposi’s Sarcoma Associated Herpesvirus, Michael DeFee, Zhiquiang Qin, Lu Dai, Bryan Toole, Jennifer Isaacs, Chris Parsons, 1Microbiology and Immunology, Dental Medicine, MUSC, 2Medicine, MUSC, 3Regenerative Medicine and Cell Biology, MUSC, 4Pharmacology, MUSC, 5Medicine, Microbiology and Immunology, Dental Medicine, MUSC.

Quantitation and Spatial Localization of Phosphorylated and Acylated Aquaporin 0 in Human Lenses, Danielle B Gutierrez, Zhen Wang, Donita Garland, Kevin L Schey; 1Medical University of South Carolina, 2Vanderbilt University, 3University of Pennsylvania.

Ocular lens aquaporin 0 (AQP0) functions as a water channel and adhesion protein and is critical to lens transparency. AQP0 phosphorylation regulates water permeability and affects AQP0 trafficking and protein-protein interactions. Recently, a C18:1 lipid modification and acetylation were discovered on AQP0. We hypothesize that these modifications are variably distributed with fiber cell age to alter AQP0 function and maintain lens transparency. Our objective is to map the distribution and abundance of these modifications in spatially-resolved regions from young and aged lenses. Human lenses were dissected into 5 to 7 regions, enriched for membrane protein, digested with trypsin, spiked with peptide internal standards, and analyzed by nano-liquid chromatography tandem mass spectrometry. The C18:1 lipid modification was characterized via on-tissue Lys-C digestion and profiling. Lens sections were water washed, incubated with or without Lys-C, spotted with matrix, and analyzed by matrix-assisted laser desorption/ionization. Phosphorylation at S235 peaks at a normalized lens distance (r/a) of ~0.76 from the lens center (r/a = 0) in younger lenses and at an r/a of ~0.85 in aged lenses; it does not appear to change with age. N-terminal acetylation increases from 37% to 77% in the center of young and aged lenses. The C18:1 lipid modification manifests in the inner cortex; the majority resides at the N-terminus of the protein. Phosphorylation of AQP0 decreases its interaction with calmodulin, affecting AQP0 water permeability. In older lenses, the region of maximum phosphorylation coincides with nuclei degradation. Increase in percent acetylation with age is likely due to the truncation of the unmodified N-terminus, suggesting that acetylation protects the N-terminus. The C18:1 lipid modification on the N-terminus may result from longevity in the membrane. This modification may alter AQP0 protein-protein or protein-membrane interactions and affect AQP0 water permeability and/or its role as a junctional protein. NIH EY-13462

Perfluorinated Compounds in Northern Fur Seals (Callorhinus Ursinus), Jocelyn R Flanary, Paul R Becker; 1Graduate Studies, MCBP, MUSC, 2National Institute of Standards and Technology.

Perfluorinated compounds (PFCs) are contaminants of emerging concern with worldwide distribution. PFCs exhibit toxicological effects in laboratory animals and may pose a risk of adverse effects in marine mammals. There have been several studies examining PFCs in marine mammals; however, to date perfluorooctane sulfonate (PFOS) is the only compound that has been analyzed in northern fur seals (Callorhinus ursinus). In this...
study we report concentrations of thirteen perfluorinated compounds measured in northern fur seals. Samples were collected from animals harvested on St. Paul Island, Alaska in 2006 and 2007. Liquid chromatography/tandem mass spectroscopy (LC/MS/MS) was used to perform the analyses. In plasma, perfluoroundecanoic acid (PFUnA) was the most abundant compound with a median concentration of 5.4 ng/g ranging from < LOD to 18.0 ng/g, followed by perfluorononanoic acid (PFNA) at 3.4 ng/g (1.2 to 9.7 ng/g) and PFOS at 2.8 ng/g (< LOD to 18.6 ng/g). Interestingly, PFOS is not the most abundant compound as it is in most environmental studies, suggesting a different source or preferential metabolism of the C11 and C9 carboxylic acid compounds. The results reported here demonstrate that several perfluorinated compounds are at measurable quantities in the northern fur seal, with some PFCs being measured for the first time in this species. Currently, analyses are being performed on liver and kidney samples from the same animals as the plasma to help understand the body distribution of PFCs in northern fur seals.

091 Identification and Characterization of Ionizing Radiation Responsive MicroRNAs, Melissa N Scheiber, Yong Wang, Daohong Zhou; Pathology and Laboratory Medicine, MUSC.

MiRNAs are small ~22 nucleotide non-coding RNA molecules that play an important role in regulation of many cell processes. However, the roles of miRNAs in regulation of cellular responses to ionizing radiation (IR) have not been well characterized. Using a microarray assay, our laboratory has identified a set of 43 miRNAs that were differentially expressed in irradiated normal human WI38 fibroblasts. Among these miRNAs, 17 miRNAs were up-regulated and 26 were down-regulated by IR. The differential expression for five of these miRNAs was confirmed by real-time RT-PCR and determined to be statistically significant. A time course study revealed significant changes in the expression of these IR-responsive microRNAs (IR-miRNAs) at 3 days post IR and continued at this level until day 14 when the cells were deemed senescent. In addition to being time dependent, an IR dose responsive curve demonstrated significant dose dependent changes in the expression of these IR-microRNAs. The dose- and time-dependent changes in IR-miRNA expression after IR exposure suggest that IR-miRNAs may be used for radiation dosimetry. Interestingly, the induction of three of the five IR-miRNAs (miR-17, miR-106a and miR-155) were shown to be influenced by p53 and/or p38 MAPK. Intensive investigation is underway to identify targets of these three IR-miRNAs, in efforts to further elucidate the role of miRNAs in the regulation of cellular responses to IR.

092 Regulation of Ultraviolet Light-Induced Ceramide and Programmed Cell Death By Ceramide Synthase, Thomas D Mullen1, Lina M Obeid2; 1Medicine, MUSC, 2Medicine, Biochemistry Molecular Biology, General Internal Medicine (Ralph Johnson VAMC).

Germicidal ultraviolet light (UV-C) induces programmed cell death in mammalian cells through DNA damage and activation of the intrinsic pathway of apoptosis. The sphingolipid ceramide is often generated in programmed cell death and has been shown to mediate this process in a variety of systems including UV-C-induced death. Several studies have implicated acid sphingomyelinase (aSMase)-derived ceramide in mediating UV-C induced cell death, but few have examined the role of de novo ceramide synthesis and/or ceramide synthases (CerS), which are known to be involved in several cell death models. In this study, we found that UV-C irradiation of MCF-7 breast adenocarcinoma cells caused large increases in ceramide after 24 hours. Concomitantly, UV-C decreased sphingosine and slightly increased total sphingomyelin at 24 hours. The de novo sphingolipid synthesis inhibitors myriocin—an inhibitor of serine palmitoyltransferase—and fumonsin B1 (FB1)—an inhibitor of CerS—both reduced basal ceramide levels, but only FB1 was able to partially inhibit the late ceramide induction. Interestingly, by depleting basal ceramide levels, myriocin seemed to unmask the UV-C induced ceramide generation. FB1, on the other hand, unmasked some species (e.g. C16-ceramide, C22-C26-ceramides) while inhibiting others (C18-C20-ceramides). Interestingly, in vitro CerS activity was unaffected by UV-C treatment. Unexpectedly, FB1—but not myriocin—inhibited cell death as determined by trypan blue staining. However, the reduction of cell death was not associated with an inhibition in other components of the cell death machinery including Bax activation, cytochrome c release, and caspase activation. Inhibition of the intrinsic pathway of apoptosis by Bcl-XL over-expression, Bak small interfering RNA, or a caspase inhibitor resulted in partial prevention of late (24 hours) but not early (0-12 hours) ceramide increases. These data suggest that there are multiple stages of ceramide generation: early ceramide generation through an unidentified mechanism and late generation and that involves an FB1-sensitive CerS that does not depend on de novo synthesis. Furthermore, this CerS mediates the late production of a specific subset of ceramide species (C18-through C20-ceramide). The late ceramide production is likely controlled by components of the intrinsic pathway and, in turn, might regulate late events of programmed cell death in response to UV-C. NIH/NIEHS 5T32ES012878, NIH/NIEHS 1F30 ES016975-01, NIH R01AG016583, and NIH C06 RR018823.
093 Targeting Glucosylceramide As a Potential New Treatment for Cryptococcosis. Ryan M Rhome1, Maurizio Del Poeta2; 1Graduate Studies, Biochemistry and Molecular Biology, MUSC, 2Graduate Studies, Biochemistry and Molecular Biology, Microbiology and Immunology, MUSC.

Abstract not available.

094 Role of Acid β-Glucosidase 1 in the Regulation of IL-6 Secretion and P38δ Signaling. David Perry1, Vindodh Rajagopalan1, Kazuyuki Kitatani2, Russell Jenkins1, Yusuf Hannun1; 1Graduate Studies, Biochemistry, MUSC, 2Tottori University.

Gaucher disease is a lysosomal storage disease caused by genetic defects in acid β-glucosidase 1 (gba1) and is characterized by increased inflammation, neurodegeneration, and increased rates of multiple myeloma. IL-6 has been proposed to be a main factor in the pathogenesis in this disease owing to its involvement in many of the pathologies associated with Gaucher disease. Previous studies in our lab have shown that loss of gba1 results in hyperphosphorylation of p38 and increased IL-6 secretion in response to PMA treatment in MCF-7 cells. Interestingly, loss of p38δ largely attenuated the increase in IL-6 due to loss of gba1, even though p38δ is not required for IL-6 secretion with PMA alone. On the other hand, overexpression of p38δ led to increased IL-6 secretion in MCF-7 cells. These findings demonstrate that loss of gba1 results in increased signaling through p38δ to increase IL-6, which is consistent with clinical findings in Gaucher disease. A remaining question is how gba1 regulates p38δ. Future work aims to elucidate this mechanism and to explore p38δ as a novel therapeutic target in Gaucher disease and other inflammatory conditions. MSTP; Abney Scholarship; SCE&G

095 Functional Relevance of Hox-Specified Positional Identities in Adult Vasculature. Nathanael D Pruett1, Richard Visconti2, Tim McQuinn2, Alexander Awgulewitsch1; 1Medicine, MUSC, 2Regenerative Medicine and Cell Biology, MUSC, 3Pediatric Cardiology, Regenerative Medicine and Cell Biology, MUSC.

Abstract not available.

096 Evaluation of Cultured Rat Aneurysmal SMCs As a Surrogate Model System to Investigate Elastogenic Therapies in Human Aortic Aneurysms. Carmen E Gacchina1, Anand Ramamurthi2; 1College of Graduate Studies, Bioengineering, Clemson University-MUSC, 2Bioengineering, Clemson University-MUSC.

Abdominal aortic aneurysms (AAAs) are direct outcomes of vascular inflammation, wherein the elastic matrix is disrupted by MMPs released by inflammatory cells, leading to vessel wall weakening, expansion, and rupture. Since surgical grafting at AAA sites can cause significant long-term complications, there is a need for non-invasive therapies to regenerate elastic matrix to stabilize elastic matrix and regress AAAs. However, such regeneration is impeded by poor elastogenicity of adult SMCs, and lack of tools to up regulate elastin precursor synthesis, matrix deposition, and fiber formation. We previously demonstrated elastogenic benefits of hyaluronan oligomers (HA-o) and TGF-beta1 to adult rat aortal SMC cultures (aSMCs). In this study, we seek to investigate the elastogenic benefit of these factors to induced rat AAA-derived SMCs (aRASMCs), and compare their phenotype and responses to human AAA-derived SMCs (aHASMCs), justifying their study as surrogates. Rat AAAs were induced by peri-adventitial treatment of the infrarenal abdominal aortae with CaCl2, and demonstrated matrix calcification, inflammatory cell recruitment, elastic matrix degradation, and vessel expansion (~45%) similar to early human AAAs. Cells isolated from induced rat AAAs, from human AAAs, and from respective healthy aortae, were cultured for 3 weeks in the absence of any supplements (control), or with HA-o (0.2-20ug/ml) and TGF-beta1 (1-10ng/ml). Relative to healthy control cells, both aRASMCs and aHASMCs appeared smaller and spread. The aRASMCs and aHASMCs produced less tropoelastin and matrix elastin, relative to their respective healthy controls. Synthesis of matrix elastin was enhanced by both aRASMCs (2.51 ± 0.32-fold) and aHASMCs (3.01 ± 0.52-fold) with the addition of supplements, as well as a reduction in calcific deposits and protease activity, as compared to their respective aneurysmal controls. These results indicate aRASMCs mimic aHASMCs phenotype and elastogenic potential and serve as a satisfactory model system to investigate elastogenic therapies for treatment of human AAAs. NIH C06RR018823 (PI: Dooley L); NIH R21EB006078-01A1 and RO1HL092051-01A1, AHA SDG 0335085N (PI: Ramamurthi A); NIH Institutional Training Grant HL 007260 (Gacchina C)

96.1 Assays of Porcine Retina Metabolism: A Translational Tool For Drug Discovery in Retinal Degenerative Diseases. Joy Obidike1, Craig Beeson2, Barb Rohrer2; 1Pharmaceutical Sciences, MUSC, 2MUSC.

Oxidative and calcium stress contribute to the pathology of retinal degenerative diseases. We hypothesize that these stressors cause mitochondrial damage, resulting in both decreased ATP production and decreased maximal respiratory capacity, which contributes to retinal degeneration. We have used the 661W photoreceptor cell line to develop a model for retinal degeneration using extracellular flux measurements in response to calcium and oxidative stress. Cells treated with 1 mM A23187 (calcium ionophore) and 50 mM tBuOOH showed a 50% decrease in mitochondrial capacity as measured by oxygen consumption rates (OCR), within 30 minutes post-treatment. However, cell death was not apparent until 48 hours after treatment. From a separate cellular assay, we have identified twelve lead compounds that protected against calcium stress from A23187. The focus of our
current study is to provide a translational bridge between the cell-line and whole animal models to test these lead compounds. Thus, we have used porcine retinal punches in the Seahorse XF24 instrument, which allows for direct tissue analysis. This is the first successful use of tissue in the XF24. Our methods allow recapitulation of basic retinal pharmacology by blocking both ligand and voltage-gated calcium channels using ryanodine and nifedipine, respectively. For these compounds, OCR decreased by approximately 49% and 38%, respectively, OCR increased in response to 0.4 µM FCCP (uncouples mitochondria) and decreased via inhibition of the mitochondrial F1F0 ATPase using 5 µM oligomycin. In the future, we will assess metabolism in porcine retina under calcium/oxygen stress, and evaluate protection using the lead compounds. Foundation for Fighting Blindness; Environmental Stress and Signaling Training Grant 5T32ES012878; IMSD

097 Differentiation Potential of Embryonic Heart Chicken Cushion Tissue, Agnes Nagy Mehesz, Sergei Znoyko, Zoltan Hajdu, Richard P Visconti, Yukiko Sugi, Russell A Norris, Vladimir R Mironov, Roger R Markwald; Regenerative Medicine and Cell Biology, MUSC.

Embryonic endocardial cushions (EC) are the precursors of the mature cardiac heart valves and septum. Physiologically EC differentiates into a fibrous connective tissue. Growing evidence that EC cells can switch to osteogenic, myogenic, chondrogenic differentiation under certain experimental and pathological conditions strongly suggests that cushion tissue is multipotential. To investigate the differentiation potential of EC, we used two experimental approaches. In the first set of experiments, chicken EC (HH25 and HH29) were dissected, dissociated and cultured in osteogenic, chondrogenic and adipogenic differentiation media for 21 days. In the second set of experiments, embryonic quail EC (HH17 and HH24) were dissected and transplanted into the forelimb of HH17 chicken embryos. After three weeks of culturing in differentiation media, EC cells exhibited osteogenic, chondrogenic, adipogenic differentiation, which were demonstrated by Alizarin Red S, Alcian Blue, and Red Oil O stainings, respectively. Immunostaining with collagen type II antibody (chondrogenic) and alkaline phosphatase staining (osteogenic) were used as additional markers. After implantation into chicken limb buds, quail EC cells underwent osteogenic, chondrogenic, and myogenic differentiation, which was confirmed by colocalization of quail specific and osteogenic, chondrogenic, and myogenic differentiation markers. Our data strongly suggest that EC has multilineage differentiation potential. Current efforts are focused on (1) elucidation of the specific factors that control commitment of EC cells to the fibrogenic cell lineage and prevent differentiation to other cell lineages, (2) on identification of the developmental window during which cushion cells exhibit this multipotentiality, and (3) whether this multilineage potential reflects intrinsic properties of individual EC cells or instead manifests the different developmental origins of EC cells. The multilineage plasticity of EC mesenchymal cells at early stages of EC morphogenesis must be considered in our ongoing efforts to understand the cellular and molecular mechanisms of abnormal valvulogenesis and the pathogenesis of congenital heart defects. NSF/EPSCOR EPS-0447660 & NSF – FIBR 0526854 to VM.

098 Chronic Administration of KB-R7943 Induces Upregulation of Cardiac NCX1, Olga Chernysh1, Lin Xu1, Christiana S Kappler1, Santhosh K Mani2, Donald R Menick1; 1Cardiology, MUSC, 2Cardiology, MUSC.

Abstract not available.

099 Role of Histone Deacetylases in Regulating Sodium/Calcium Exchanger Expression in Adult Cardiomyocytes, Mona S Li, Santhosh K Mani, Benjamin K Addy, Thirumagal Thiagarajan, Christine B Kern, Donald R Menick; Medicine, Cardiology, MUSC.

Abstract not available.

100 Beta-Adrenergic Receptor Stimulated Ncx1 Upregulation is Mediated Via CaMKII/AP-1 Signaling Pathway in Adult Cardiomyocytes, Santhosh K Mani, Erin A Egan, Benjamin K Addy, Thirumagal Thiagarajan, Christine B Kern, Donald R Menick; Medicine, Cardiology, MUSC.

The sodium calcium exchanger gene (Ncx1) is upregulated in cardiac hypertrophy and is often found elevated in end-stage heart failure. Studies have shown that the change in its expression contributes to contractile dysfunction. Beta-adrenergic receptor (beta-AR) signaling plays an important role in the regulation of calcium homeostasis in the cardiomyocyte, but chronic activation in periods of cardiac stress contributes to heart failure by mechanisms which include Ncx1 upregulation. Here we show that beta-AR stimulated Ncx1 upregulation is dependent on Ca2+/Calmodulin-Dependent Protein Kinase II (CaMKII). Beta-AR-stimulated Ncx1 expression is mediated by activator protein 1 (AP-1) factors and is independent of cAMP-response element-binding protein (CREB) activation. The MAP kinases (ERK1/2, JNK and p38) are not required for AP-1 factor activation. CaMKII activity is required for AP-1 mediated Ncx1 upregulation. Chromatin immunoprecipitation demonstrated that beta-AR stimulation activates the ordered recruitment of JunB homodimers which then are replaced by c-Jun homodimers binding to the proximal AP-1 elements of the endogenous Ncx1 promoter. In conclusion, this work has provided insight into the intracellular signaling pathways and transcription factors, which regulate Ncx1 gene expression in a chronically beta-AR-stimulated heart.
101 Prdx1 Regulates PTEN Activity in the Nucleus, Juxiang Cao, Jennifer Schulte, Carola Neumann; Medicine, Cell and Molecular Pharmacology and Experimental Therapeutics, MUSC.

We have recently shown that the peroxidase Prdx1 interacts with the tumor suppressor PTEN. This interaction is essential to protect PTEN from oxidation-induced inactivation of its lipid phosphatase activity, which is essential for its tumor suppressive function. PTEN has recently been linked to regulate genomic stability. Since Prdx1-/-murine embryonic fibroblasts (MEFs) show higher levels of oxidized DNA adducts than Prdx1 containing MEFs, we were examining if Prdx1 regulates PTEN nuclear function as a guardian of the genome. Examining nuclear PTEN protein levels in Prdx1-lacking cells revealed levels of nuclear PTEN to be lower in Prdx1-/-MEFs compared to Prdx1 containing MEFs. Treatment of MEFs with H2O2 lowered PTEN protein levels in the nucleus more in Prdx1-/-MEFs compared to Prdx1 containing MEFs. Localizing Prdx1 to the nucleus in Prdx1-/-MEFs enhanced nuclear PTEN levels, whereas cytosolic Prdx1 did not. These data suggest that Prdx1 regulates nuclear PTEN levels in the nucleus either by importing PTEN into the nucleus or by preventing its nuclear degradation, probably in an oxidation dependent manner. Investigating expression of Rad51, whose expression has been shown to depend on PTEN lipid phosphatase activity, we found that in Prdx1-/-MEFs Rad51 levels to be lower compared to Prdx1+/+MEFs. These data suggest that Prdx1 protects the genome in part by regulating nuclear PTEN protein levels. Supported by grants from the NIEHS-K22 ES012985, ACS-IRG-97-219-05, and Abney research Foundation

102 Expression of the Transcription Factor SOX2 in the Injured Cochlear Nerve, Manna Li, Vinu Jyothi, Ashley M Smith, Juhong Zhu, Lauren A Kilpatrick, Liya Liu, Hainan Lang; Pathology and Laboratory Medicine, MUSC. Abstract not available.

103 Hsp70 Inhibits Aminoglycoside-Induced JNK Activation, Inga I Kramarenko, Carlene S Brandon, Shimon P Francis, Lisa L Cunningham; MUSC.

Induction of heat shock proteins inhibits aminoglycoside-induced hair cell death in the adult mouse utricle in vitro. In addition, we have recently shown that overexpression of heat shock protein 70 (Hsp70) inhibits aminoglycoside-induced cochlear hair cell death and hearing loss in vivo. Aminoglycoside-induced hair cell death is mediated by c-Jun N-terminal kinases (JNKs). We have examined the effects of heat shock protein induction on activation of JNKs in the mouse utricle preparation. Utricles from adult CBA mice were heat shocked in vitro and were exposed to neomycin for 12 hours. Western blot analysis indicates that neomycin exposure results in robust activation of JNK. In addition, heat shock inhibits this neomycin-induced JNK phosphorylation. In order to determine if Hsp70 inhibits JNK phosphorylation, utricles from mice that constitutively overexpress Hsp70 (and their wild-type littermates) were treated with neomycin for 12 hours. Western blot data indicate that Hsp70 overexpression inhibits neomycin-induced JNK phosphorylation. We have begun to examine downstream targets of JNK, and our data indicate that at least three known specific targets of JNK are phosphorylated in utricles treated with neomycin. Taken together, these data suggest that the protective effect of Hsp70 against aminoglycoside-induced hair cell death is mediated in part by inhibition of JNK activity. Our recent data indicate that the protective effect of Hsp70 induction is mediated at least in part by supporting cells. In response to heat shock, Hsp70 upregulation occurs primarily in supporting cells with relatively little upregulation in hair cells. We have recently developed a method of efficient and exclusive transfection of supporting cells of the adult mouse utricle using adenovirus. We have used this technique to express Hsp70 in supporting cells only. Upregulation of Hsp70 in supporting cells promotes hair cell survival. These data indicate that supporting cells directly mediate hair cell survival. Supported by National Institutes of Health (NIDCD 5R01 DC007613 and DC07613-51). Additional support by NIH/NCRR extramural research facilities construction (C06) grants C06 RR015455 and C06 RR14516

104 Peroxiredoxin 1 Regulates P38 MAPK Activity, Brittany P Turner, Hui Zheng, Scott T Eblen, Carola A Neumann; Pharmacology, MUSC. Abstract not available.

105 The Non Homologous End-Joining (NHEJ) Pathway is Dispensable for the Functional Recovery of Hematopoietic Stem Cells and Progenitor Cells After Ionizing Radiation Injury, Ningfei An, Senthil Kumar Pazhanisamy, Daohong Zhou; Pathology and Laboratory Medicine, MUSC.

Bone marrow hematopoietic stem cells (HSCs) and hematopoietic progenitor cells (HPCs) are crucial to maintain lifelong homeostasis. Cancer treatment by chemotherapy or radiotherapy suppresses hematopoietic function via induction of DNA double-strand breaks (DSBs) in HSCs and HPCs, which is one of the major side effects to cancer patients. DSBs can be repaired by the error-free homologous recombination (HR) and error-prone non homologous end joining (NHEJ) pathways. However, how HSCs and HPCs repairing DSBs has not been studied and therefore, was investigated in the present study using ionizing radiation (IR) and a mouse model. The repair of DSBs was analyzed by gamma-H2AX immunofluorescent microscopy and confirmed by comet assay. The results showed that HPCs were highly proficient in repair of IR-induced DSBs. In addition, HPCs repairing IR-induced DSBs appears mainly via NHEJ because the repair can be inhibited by NU7026 (a specific DNA-PK inhibitor). In contrast, HSCs, particularly these in quiescence (G0
Mean T2* values in the myocardium were significantly lower than T2* values measured in the paravertebral muscles in the same patients (31.2 ± 6.6 versus 48.2 ± 5.1, p<0.05). Two patients (10%) had low cardiac T2* (17 and 22) indicating significant myocardial iron deposition. In addition, borderline low T2* values (26 each) were noted in two additional patients (10%) suggesting high myocardial iron deposition. There was a weak but not significant correlation between cardiac T2* and left ventricular end-diastolic volume (r=0.17), left ventricular ejection fraction (r=0.21) and right ventricular end-diastolic volume (r=0.37). Also, there was no statistically significant correlation between myocardial T2* and transfusional burden (r = -0.26), duration of transfusion (r = -0.35), serum ferritin (r = -0.4) and liver iron concentration by biopsy (r = -0.33) and liver T2* (r=0.04). CONCLUSION: Our study shows that patients with SCD develop significant cardiac iron overload (low cardiac T2*) than previously reported. However, there was no significant correlation between cardiac T2* and parameters of ventricular function even in patients with high myocardial iron content. The lack of correlation between cardiac T2* and serum ferritin, liver iron content and transfusion burden in our cohort concurs with previous studies. Thus the risk factors for cardiac iron accumulation and its correlation with cardiac function in this patient population remain unclear. Further prospective studies are needed to understand the pathogenesis and the consequences of cardiac iron overload in patients with SCD.

106 Magnetic Resonance T2* Measurement of Myocardial Iron Deposition in Sickle Cell Disease: Risk Factors and Relationship with Cardiac Function, Alexander I Ngwube, Andrew Hardie, Sherron Jackson, Luis Ramos-Duran, Joseph Schoepf, Ibrahim Shatat, Miguel Abboud, Ram Kalpathi; 1Pediatric Hematology and Oncology, MUSC, 2Radiology, MUSC, 3Children’s Cancer Center of Lebanon, Beirut, Lebanon.

BACKGROUND: Children with thalassemia major (TM) and sickle cell disease (SCD) receiving chronic blood transfusion are at risk of developing cardiac iron overload. Magnetic resonance imaging (MRI) has emerged as a non-invasive tool for the direct measurement of myocardial iron deposition in these patients. Previous studies have shown that patients with TM develop significant myocardial iron deposition that correlates with transfusion burden and cardiac function. However, the prevalence of myocardial iron overload, the risk factors and its relationship with cardiac function in patients with SCD are not well known.

OBJECTIVE: To review the patterns of cardiac iron overload using cardiac MRI in our cohort of children with SCD.

METHODS: Cardiac MRI studies performed in children with SCD at a steady state from January 2009 to June 2009 at our institution were reviewed. We abstracted demographic and laboratory data and reviewed their transfusion history. These patients were receiving chronic blood transfusion every 3–4 weeks. All patients had been on chelation therapy desferrioxamine and/or deferasirox. In each patient, MR (1.5T Avanto™, Siemens) T2* measurements were performed in the interventricular septum, as well as in the paravertebral muscles as an internal control. Cardiac T2* value of 25-46 was considered normal as previously published.

RESULTS: A total of 20 patients with Hb SS (50% male), with a mean age of 14 years were studied. The mean duration of blood transfusion was 9.5 ± 5.3 years. Seventeen patients (85%) were on chronic transfusion for stroke or abnormal TCD and three (15%) for other reasons such as recurrent pain crises and priapism. Overall, the mean cardiac T2* was 31.2 ± 6.6 ms in our patients. Mean T2* values in the myocardium were significantly higher than T2* values measured in the paravertebral muscles in the same patients (31.2 ± 6.6 versus 48.2 ± 5.1, p<0.05). Two patients (10%) had low cardiac T2* (17 and 22) indicating significant myocardial iron deposition. In addition, borderline low T2* values (26 each) were noted in two additional patients (10%) suggesting high myocardial iron deposition. There was a weak but not significant correlation between cardiac T2* and left ventricular end-diastolic volume (r=0.17), left ventricular ejection fraction (r=0.21) and right ventricular end-diastolic volume (r=0.37). Also, there was no statistically significant correlation between myocardial T2* and transfusional burden (r = -0.26), duration of transfusion (r = -0.35), serum ferritin (r = -0.4) and liver iron concentration by biopsy (r = -0.33) and liver T2* (r=0.04). CONCLUSION: Our study shows that patients with SCD develop significant cardiac iron overload (low cardiac T2*) than previously reported. However, there was no significant correlation between cardiac T2* and parameters of ventricular function even in patients with high myocardial iron content. The lack of correlation between cardiac T2* and serum ferritin, liver iron content and transfusion burden in our cohort concurs with previous studies. Thus the risk factors for cardiac iron accumulation and its correlation with cardiac function in this patient population remain unclear. Further prospective studies are needed to understand the pathogenesis and the consequences of cardiac iron overload in patients with SCD.

107 Prevalence and Risk Factors of Microalbuminuria in Children with Sickle Cell Disease, Lauren J Becton, Elizabeth Rackoff, Debra Disco, John K Orak, Sherron Jackson, Ram Kalpathi, Ibrahim Shatat; 1Pediatrics, Hematology/Oncology, MUSC, 1Pediatrics, MUSC, 2Pediatrics, Nephrology, MUSC.

Objective: Sickle cell disease (SCD) is associated with a large spectrum of renal abnormalities, one of which, microalbuminuria/proteinuria (MA/P), is a known predictor of end-stage renal disease. We studied ninety children with SCD (57% male; mean age 11.4 ±5.2 years) to determine the prevalence and examine risk factors associated with MA/P. Patients and Methods: Spot urine microalbumin-to-creatinine ratio was measured. Medical records were reviewed for demographic and biochemical data. Medication use, resting office blood pressures (BP), vaso-occlusive pain crises (VOC), and monthly transfusions were recorded. Results: Fourteen children (15.5%) had MA/P. Hemoglobin (Hb) levels were significantly lower in the group with MA (8.8 1.1 g/dL vs. 9.8 1.4 in those without MA/P), and were significantly correlated with MA (rho =-0.24, p=0.03). Hypertension classification was also associated with MA (p=0.058), with 11.1% being hypertensive, 6.2% prehypertensive and 82.2% normotensive. In a multivariate logistic regression model, both Hb and BP classification remained significantly associated with MA. Conclusions: MA is a simple screening biomarker of early kidney injury in children with SCD. Larger studies to evaluate predictive...
factors of MA and the relationship to BP are needed.

108 Level-Dependent Changes in Perception of Speech Envelope Cues in Younger Adults with Normal Hearing. Xin Wang, Jayne B Ahlstrom, Amy R Horwitz, Judy R Dubno; College of Medicine, Otolaryngology, MUSC.

Speech levels are constantly changing and this temporal envelope is an important cue for understanding speech. Results of physiological and behavioral studies suggest that the cochlea responds nonlinearly to incoming signals that change in level. Specifically, the normal growth of response of the cochlea’s basilar membrane is more linear at the lowest and highest stimulus levels, and more compressed at medium to higher stimulus levels. It is hypothesized that cochlear nonlinearities affect changes in speech envelope fluctuations with overall increases in speech level as follows. The speech envelope will flatten as the level of speech increases from lower, more linear, to higher, more compressive, regions. With further increases to the highest, more linear, levels, speech envelope fluctuations will increase. As a result, level-dependent changes in perception of speech envelope cues may reveal effects of nonlinearities. We hypothesize that speech recognition will improve as speech level increases from low to medium-high and then will decline with further increases in level. In the current study, speech recognition scores are measured as a function of speech level for younger adults with normal hearing. Speech sounds are consonants, vowels, and sentences that were processed to reduce frequency cues so that effects of modifications of the speech temporal envelope can be revealed. Specifically, “noise vocoder” processing extracts the temporal envelope from the speech signal in a relatively small number of processing bands and uses noise as the carrier signal. As voiced speech level increases, background noise level also increases, maintaining a fixed difference between speech and background levels to minimize sensation-level effects on speech recognition scores. Discussion of results will include the role of nonlinearities on perception of speech envelope cues.

[Work supported by NIH/NIDCD] Supported by grants R01 DC00184 and P50 DC00422 from NIH/NIDCD.

109 Role of SDF-1 Expression and Hematopoietic Stem Cells in Spiral Ganglion Preservation. Lauren A Kilpatrick1, Manna Li2, Vinu Jyothi2, Hainan Lang2; 1Medicine, Otolaryngology, MUSC, 2Medicine, Pathology and Laboratory Medicine, MUSC.

BACKGROUND: The degeneration of hair cells and spiral ganglion neurons (SGNs) is an important pathologic process in the development of sensorineural hearing loss. In a murine model, predictable and reproducible damage to SGNs occurs through the application of ouabain to the round window. Recent evidence has shown that the chemokine stromal cell-derived factor-1 (SDF-1) is a potent chemoattractant of hematopoietic stem cells (HSCs) and helps to provide trophic support to injured tissues during development and maturation. Based on preliminary findings, our hypothesis for the current study is that engrafted HSCs and expression of SDF-1 play an important role in protecting SGNs and preventing their further degeneration in the setting of cochlear injury.

METHODS: Following approved IACUC protocols, mice underwent preoperative auditory functional measurements, including auditory brainstem response (ABR) testing. Under anesthesia, a 60-minute application of ouabain to the round window niche of the right ear was performed; mice were allowed to recover at designated intervals of one, three, seven, fourteen, and thirty days. Auditory functional measurements were repeated prior to cochlear dissection. Total RNAs isolated from the spiral ganglia and cochlear sections were assessed by quantitative real-time RT-PCR and immunostaining for SDF-1. RESULTS: Real-time RT-PCR for SDF demonstrates increased expression following ouabain injury; SDF-1 expression peaks at approximately days seven to fourteen post-injury. Immunostaining for SDF-1 supports this data.

CONCLUSIONS: SDF-1 has been described as a chemoattractant of HSCs in neural tissue. Previous studies have indicated that HSC engraftment in the cochlea is increased following injury. We hypothesized that SDF-1 expression is increased following ouabain exposure and cochlear injury as demonstrated in this study using real-time RT-PCR and immunolabeling for SDF-1 in mice. Further knowledge about the cochlear microenvironment, including SDF-1, is critical to maximizing HSC engraftment in the injured cochlea and providing a therapeutic option for sensorineural hearing loss. AAO-HNS CORE Grant 136165

110 Subcellular Localization of Dihydroceramide Desaturase (DEGS-1) as a Mechanism for Fenretinide Sensitivity. Leslie Wooten-Blanks, Jacqueline M Kraveka; Pediatric Hematology/Oncology, MUSC.

Abstract not available.

111 Role of CD147 in the Malignant Phenotype of Therapy-Resistant Tumor Subpopulations. Lu Dai, Mark Slomiany, Lauren Tolliver, Bryan Toole; Regenerative Medicine and Cell Biology, MUSC.

Abstract not available.

112 New Drug Leads As Potential Treatments for Calcium-Induced Retinal Degeneration. Nathan R Perron1, Mausumi Bandopadhyay2, Craig C Beeson1, Baerbel Rohrer2; 1College of Pharmacy, Pharmaceutical Sciences, MUSC, 2College of Medicine, Ophthalmology, MUSC.

Calcium stress contributes to the pathology of retinal degeneration. We have used a mouse photoreceptor cell line (661W) to develop an in vitro assay for retinal degeneration resulting from calcium-induced stress.
Following assay development, a progressively stringent screening method was employed to identify possible pharmaceutically active compounds that prevent calcium-induced retinal degeneration. These screening efforts have identified two drug lead compounds that display protective activity against calcium stress. At 1 micromolar, these compounds were able to prevent damage from both 10 micromolar A23187, as well as 600 micromolar IBMX in 661W cells. In addition, these compounds also effectively prevented calcium-induced damage to whole mouse retinas. We believe that through further testing in whole animals as well as through lead optimization methods, a new drug to treat the diseases associated with retinal degeneration, such as age-related macular degeneration (AMD) and retinitis pigmentosa (RP), could be developed in the future. Funded by the Foundation Fighting Blindness Translational Research Acceleration Program.

113 CXCL13 Secretion By Human Oral Squamous Cell Carcinoma Tumor Cells Stimulates RANK Ligand Expression in Bone Marrow Stromal/preosteoblast Cells, Yuvaraj Sambandam1, William L Ries2, James S Norris3, Sakamuri V Reddy1; 1Darby Children’s Research Institute, MUSC, 2College of Dental Medicine, MUSC, 3Microbiology and Immunology, MUSC.

Oral squamous cell carcinomas (OSCC) are malignant with a potent activity of local bone invasion; however the molecular mechanisms of tumor osteolysis are unclear. Chemokine ligand-13 (CXCL13) has been implicated in OSCC tumor development/progression. RANK ligand (RANKL) expressed in bone marrow stromal/preosteoblast cells is critical for osteoclastogenesis. We showed subcutaneous injection of OSCC cells onto the surface of calvaria in NCr-nu/nu athymic mice develop tumors in 4-5 weeks and tumor cell invasion of bone/osteoelastic tissue. We identified CXCL13 stimulation of RANKL expression in OSCC cells. Therefore, we hypothesized that CXCL13 production by OSCC cells induce RANKL expression in stromal/preosteoblast cells in the bone microenvironment. Interestingly, treatment of human bone marrow stromal cells (SAKA-T) and MC3T3 murine preosteoblast cells with conditioned media (20%) obtained from SCC14a cells significantly increased RANKL expression while incubation with anti-CXCR5 specific antibody markedly decreased RANKL expression. Western blot analysis demonstrated that recombinant hCXCL13 treatment (0-15 ng/ml) of SAKA-T and MC3T3 cells for a 6 h period significantly increased (5-fold) RANKL expression. Real-time PCR analysis identified a dose-dependent stimulation of CXCR5 mRNA expression in these cells. CXCL13 stimulation significantly increased p-ERK1/2 levels in SAKA-T cells in a time (0-30 min) dependent manner. Furthermore, CXCL13 stimulation of SAKA-T and MC3T3 cells transiently transfected with hRANKL gene promoter-Luc reporter plasmid demonstrated a significant increase (3.5 and 3.0-fold respectively) in RANKL gene promoter activity. Transcription factor array (SuperArray) screening by real-time PCR identified high levels of MEF2B, MYC, MYOD1 and NFATc3 mRNA expression in CXCL13 stimulated SAKA-T cells. We show that CXCL13 (0-20 ng/ml) dose-dependently increased the NFATc3 protein expression in SAKA-T cells. We further demonstrate that over-expression of NFATc3 stimulates RANKL expression in these cells. Chromatin-immune precipitation (ChiP) assay confirmed NFATc3 binding to the hRANKL promoter region. In summary, CXCL13 production by OSCC cells stimulates RANKL expression in bone marrow stromal/preosteoblast cells and that NFATc3 is a downstream target of the CXCL13/CXCR5 axis to stimulate RANKL expression. Thus, our results implicate CXCL13 as a potential therapeutic target to prevent OSCC bone invasion/osteolysis. Supported by the C06 RR015455 from the Extramural Research Facilities Program of the National Center for Research Resources.

114 Cue Induced Alcohol Seeking Behavior But Not Food Seeking Behavior is Associated With Increases in Amygdala and Nucleus Accumbens Glutamate Transmission, Justin T Gass, Foster Olive; College of Medicine, Psychiatry, Center for Drug & Alcohol Programs, MUSC.

Alcoholism is a chronically relapsing disorder characterized by periods of heavy alcohol consumption followed by unsuccessful attempts at abstinence. Relapse is one of the most problematic aspects in the treatment of alcoholism and is often triggered by alcohol-associated environmental cues. Evidence indicates that glutamate neurotransmission plays a critical role in cue-induced relapse-like behavior. Previous studies have shown that blockade of glutamatergic transmission can prevent reinstatement of drug-seeking behavior, but few studies have examined specific changes in glutamate levels in discrete brain regions resulting from alcohol cues. The purpose of this study was to use enzyme-based microsensor technology to monitor changes in extracellular glutamate in specific brain regions during cue-induced reinstatement of alcohol-seeking behavior. Male Wistar rats were implanted with indwelling jugular vein catheters and intracerebral guide cannula aimed at the basolateral amygdala (BLA) or nucleus accumbens (NAc) core and then trained to self-administer alcohol intravenously (Gass & Olive, 2007) or food reward in combination with a light/tone stimulus. Animals then underwent extinction training and were implanted with precalibrated glutamate biosensors inserted in the BLA or NAc core. Changes in glutamate neurotransmission were then monitored in a 1 hr cue-induced reinstatement testing period whereby each press on the active lever resulted in the presentation of the alcohol- or food-associated cues (but no alcohol or food). As determined by GluOx-coated biosensors, extracellular levels of glutamate were significantly increased in the BLA and NAc core during cue-induced reinstatement of alcohol-seeking behavior. The cumulative change in extracellular glutamate was greater for cue-induced reinstatement of...
alcohol-seeking behavior versus that of food-seeking behavior. These results indicate that increases in BLA and NAc core glutamate transmission may be a neurochemical substrate of alcohol-seeking behavior. These results will hopefully lead to improved therapies for the prevention of relapse to alcohol consumption elicited by alcohol-associated environmental cues. Supported by NIAAA grants AA013852 (MFO) and AA007474 (JTG).

115 Regulation of Mitochondria Dynamics By Ran-Binding Protein 2, James K Lee1, Cho Kyoung-In2, Yeh Andrew1, Ferreira Paulo2; 1Biology, Duke University, 2Ophthalmology, Duke University Medical Center.

The microtubule-based motor proteins, kinesins and dyneins, mediate the intracellular trafficking of mitochondria. Kinesins generally move cargoes toward the periphery of the cell, but the regulation of the assembly/disassembly of cargoes onto/from kinesins and regulation of kinesins' motor activity by their cargoes is not understood. The Ferreira laboratory found that a tripartite domain of Ran-binding protein 2 (RanBP2) is sufficient to activate directly the conventional kinesin, KIF5B, to levels close to those seen in vivo. In addition, uncoupling of the interaction of RanBP2 with KIF5B in cell culture lines promotes the perinuclear clustering of mitochondria. Yet, the precise and primary effects of RanBP2 in mitochondria trafficking and dynamics are not understood. To address this issue in real time, I am employing real-time lapse microscopy and imaging analyses to measure and discern several biophysical parameters of mitochondria dynamics in real-time upon uncoupling RanBP2 from KIF5B in culture cell lines. I expect the outcome of this study to provide new insights into the immediate effects of RanBP2 in the regulation of intracellular transport steps of mitochondria and a subset of kinesin members. Duke University; Medical University of South Carolina; SC Governor’s School for Science and Math.

116 Activation of Smad2 and P38 Pathways is Differentially Regulated By TGFbeta2 and is Further Regulated By Retinoic Acid in NIH3T3 Fibroblasts, Kimberly M Sauls1, Loretta L Hoover2, Steven W Kubalak2; 1Winthrop University, 2Regenerative Medicine and Cell Biology, MUSC.

The Kubalak lab has previously shown in both NIH3T3 and isolated dispersed heart cells that retinoids can enhance Smad2 phosphorylation (pSmad2) in response to a 1-hour exposure to TGFbeta2. However, the effect of retinoids on TGFbeta2-mediated p38 phosphorylation (p-p38) is not known. This study was designed to compare TGFbeta2 activation of pSmad2 (canonical) versus p-p38 (non-canonical) and compare the effect of retinoic acid on these two pathways. In NIH3T3 cells there is a dose response effect observed for phosphorylation of Smad2 by TGFbeta2 with a half maximal response at 0.2 ng/ml TGFbeta2. In contrast, phosphorylation of p38 MAPK by TGFbeta2 occurred at a half maximal concentration of 0.02 ng/ml TGFbeta2. This suggests a differential sensitivity of these two pathways to TGFbeta2 activation by an order of magnitude. The data also suggests there is a concentration of TGFbeta2 that activates p38 MAPK but has no effect on accumulation of pSmad2. At higher concentrations, p38 and Smad2 pathways are simultaneously activated; however, p38 phosphorylation decreases at higher TGFbeta2 levels. Consistent with previous data published by the lab for pSmad2, retinoic acid had no effect on p-p38. However, retinoic acid blunts TGFbeta2-mediated signaling thorough the p38 pathway and also shifts its half-maximum dose response. Collectively these data show the differential sensitivity of canonical signaling through Smad2 and non-canonical signaling through p38 to TGFbeta2, and the differential effect of retinoic acid, which blunts p38 MAPK phosphorylation while enhances Smad2 phosphorylation. MUSC SURP Program

117 GILT Regulates Cytokine Gene Expression in Prostate Cancer Cells, Ramiz N Hamid1, Azizul Haque2; 1SC Governor’s School for Science and Math, 2Medicine, Microbiology and Immunology, MUSC.

Human prostate cancer cells lack an important enzyme, gamma-interferon-inducible lysosomal thiol-reductase (GILT), altering the profile of peptides displayed to lymphocytes, thereby preventing functional mobilization of CD4+ T cells which orchestrate the immune response. The absence of GILT facilitates escape of the tumor cells from the immune system. The immune system is regulated by intercellular signaling molecules called cytokines. Interleukin 8 and Prostaglandin E synthase are cytokines that promote angiogenesis, or the proliferation of blood vessel networks into cancerous growths, supplying nutrients and oxygen while removing waste, inducing tumors to grow and metastasize. Indoleamine 2,3 dioxygenase is a T-cell inhibitor that degrades amino acid tryptophan, starving T cells and causing tumor tolerance. Here, we show how induced GILT expression in prostate cancer cells affects cytokine gene expression. We also show that that GILT expression enhances immune recognition of prostate cancer cells by downregulating several angiogenic factors and inhibitory molecules. These data suggest that induction of GILT expression in prostate cancer cells may attenuate their immune escape mechanisms and allow them to be destroyed by T cells.

118 Increased Beta-arrestin 1 Expression Inhibits Apoptotic Signaling Pathways Induced By Tumor Necrosis Factor-alpha (TNF-alpha), Melissa N Youssef1, Alessandra Bitto2, Hongkuan Fan2, Keith T Borg2, Perry V Halushka3, James A Cook1; 1Duke University, 2Neuroscience, MUSC, 3Graduate Studies, MUSC.

Beta-arrestins 1 and 2 are ubiquitously expressed proteins that alter signaling by G-protein-coupled receptors. Recently, our laboratory has demonstrated that Beta-arrestins 1 and 2 also play multifaceted roles
as signaling adapter proteins that inhibit inflammatory cytokine expression. Additionally, it has been suggested that the Beta-arrestin 1 isoform inhibits signaling pathways inducing cellular apoptosis. However, the effect of Beta-arrestin 1 on apoptosis resulting from the inflammatory cytokine Tumor Necrosis Factor-alpha (TNF-alpha) has not been determined. Tumor Necrosis Factor-alpha induces cellular apoptosis, which contributes to multiple organ system failure in sepsis, the major cause of death in Critical Care Units. Therefore, we proposed the hypothesis that the signal protein Beta arrestin-1 inhibits cellular apoptosis induced by TNF-alpha in Human Embryonic Kidney (HEK) cells. Apoptotic signaling was induced in the HEK cells by TNF-alpha stimulation and was quantified by assessing Caspase-3/7 activity. To determine if Beta arrestin-1 prevents apoptosis in HEK cells following human recombinant TNF-alpha activation, the cells were transfected with Beta-arrestin 1 or the empty vector pcDNA. Western blot analysis demonstrated significant (p<0.05, n = 3) overexpression of Beta-arrestin 1 relative to the empty vector in the transfected cells. Caspase-3/7 was significantly activated (p<0.05, n = 3) in TNF-alpha stimulated cells compared to the non-stimulated control group. Tumor Necrosis Factor-alpha stimulated Caspase-3/7 activity was suppressed 41.4% (p<0.05, n = 3) in Beta-arrestin 1 transfected cells compared to the empty vector control groups. These results demonstrate that HEK cells with increased expression of Beta-arrestin 1 reduce apoptotic signaling pathways when stimulated with TNF-alpha. Understanding the role of Beta-arrestin 1 in preventing cellular apoptosis in response to inflammation may lead to novel approaches in the treatment of sepsis. 

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119 Role of a 5' Enhancer of Mouse Nkx2.5 for Second Heart Field Specific Expression. Ellen P Knoll1, Chris D Clark2, Kyu-Ho Lee3; 1College of Charleston, 2Pediatric Cardiology, MUSC.

Congenital heart disease (CHD) spans a wide range of structural and functional abnormalities in early heart development, and approximately 35,000 children are born each year with some form of CHD. One-third of these cases are due to malformations of the outflow tract (OFT), which gives rise to both the pulmonary artery and the aorta. The OFT and right ventricular (RV) myocardium (muscular heart tissue) is derived from the second heart field (SHF), a spatiotemporally distinct source of cardiac progenitor cells originating outside the primary heart tube. The cardiac transcription factor gene Nkx2.5 is an important regulator of the SHF program: loss of Nkx2.5 function results in severe OFT and RV hypoplasia, while hypomorphic Nkx2.5 alleles are linked to OFT malformations such as double outlet right ventricle or Tetralogy of Fallot in mouse models and in humans. The Nkx2.5 gene operates within a complex network of upstream regulators and downstream target genes, many of which are also implicated in OFT CHD. As part of our effort to characterize upstream modifiers of Nkx2.5-related OFT CHD, we are characterizing species-specific SHF enhancers from the chick and mouse Nkx2.5 genes. These enhancers appear to represent two major classes of archetypal regulatory regions conserved through various vertebrate species. Comparative analysis of common versus divergent TF binding motifs and high throughput knockout experiments will provide insight into the critical transcriptional events governing SHF specific expression of Nkx2.5 and their effect on OFT morphogenesis. SC Center of Biomedical Research Excellence P20 RR016434

120 Modeled Microgravity Induces S100A8 Mediated Calcium Signaling in Preosteoclast Cells, Giffin Daughtridge, Yuvaraj Sambandam, Sakamuri V Reddy; Charles P. Darby Children's Research Institute, MUSC.

NASA's primary problem with long-term space flight is accelerated bone loss. This is due to an increase in osteoclast bone resorption over osteoblast bone formation, however the mechanism is unclear. We used the NASA developed Rotary Cell Culture System (RCCS) to simulate microgravity to RAW 264.7 osteoclast progenitor cells for 24 hr and cultured them to form osteoclasts in parallel with ground based control cells. We found that microgravity increases osteoclastogenesis. A microarray analysis revealed an approximately 71 fold increase in the S100A8 gene encoding calcium binding protein indicating that calcium signaling pathway is involved in microgravity increased osteoclast activity. S100A8 mRNA and protein expression showed upregulation in preosteoclast cells following 24 hr in microgravity. Microgravity also induced cytosolic calcium increases while an S100A8 knock-down abolished cytosolic calcium release in preosteoclast cells. In summary, microgravity induces S100A8 calcium binding protein expression which modulates calcium uptake in preosteoclast cells and thus represents a potential therapeutic target for preventing bone loss in astronauts during space flight.

121 A Possible Lipofuscin Precursor in Mouse Photoreceptors, Nicholas P Boyer1, Ioannis Koutalos2; 1Clemson University, 2Ophthalmology.

Abstract not available.

122 Cytoprotection Exhibited By Melatonin Depends on Receptor-Mediated Pathways Associated with MTR1 and MTR2, Casey M O'Dell1, Arabinda Das2, Joshua A Smith2, Russel J Reiter3, Abhay K Varma5, Naren L Banik2; 1Erskine College, 2Neurosciences, MUSC, 3Cellular and Structural Biology, U of Texas.

Cell death in central nervous system (CNS) injuries and diseases is attributed to many factors including glutamate toxicity and oxidative stress. Melatonin has been implicated in neuroprotection of motoneurons and astroglia in models of spinal cord injury, traumatic brain injury, and cerebral ischemia. These effects appear to be
mediated, at least in part, by melatonin receptors 1 and 2. In order to elucidate the role of individual melatonin receptors in cytoprotection, over expression of melatonin receptor 1 (MTR1), melatonin receptor 2 (MTR2), and orphan g-protein receptor 50 (GPR50) in motoneurons and astroglia were analyzed. Cultures were assessed for cytoprotection following exposure to toxic glutamate levels (500μM) by examining viability, biochemical and structural markers of apoptosis, presence of cell death markers, and intracellular Ca2+ levels. MTR1 and MTR2 alone exhibited cytoprotective effects when over expressed in cell culture. However, tandem over expression of MTR1 and MTR2 showed greater protection. GPR50 did not exhibit cytoprotective effects, consistent with previous studies indicating GPR50 dimerizes with MTR1 and MTR2 resulting in antagonistic effects, particularly with MTR1.

RT-PCR and Western blot analysis demonstrated that upregulation of MTR1 and MTR2 attenuated expression of caspase-3, caspase-8, caspase-9, and other cell death markers. In order to confirm involvement of MTR-mediated pathways in neuroprotection following melanatonin treatment, the melatonin receptor antagonist luzindole was employed. Our data demonstrated that luzindole significantly ameliorated the neuroprotective effects of melanatonin treatment following glutamate toxicity. These results indicate that both MTR1 and MTR2 play an important role in melatonin-mediated cell protection. RNA interference silencing both MTR1 and MTR2 was also utilized to confirm receptor-mediated effects of melatonin and demonstrated that knock down of both receptors resulted in increased glutamate-induced cell death. These findings suggest that the cytoprotection exhibited by melatonin may depend on receptor-mediated pathways associated with MTR1 and MTR2.

Results indicate that both MTR1 and MTR2 play an important role in melatonin-mediated cell protection. RNA interference silencing both MTR1 and MTR2 was also utilized to confirm receptor-mediated effects of melatonin and demonstrated that knock down of both receptors resulted in increased glutamate-induced cell death. These findings suggest that the cytoprotection exhibited by melatonin may depend on receptor-mediated pathways associated with MTR1 and MTR2.

Discussion/Conclusion: Additional factors could be tested in order to determine any significance between PU and SES. However, there is reason to conclude that in order to reduce susceptibility to secondary conditions the patient must have a certain income which in turn will increase level of healthcare they receive reducing the chances of PUs becoming problematic.

125 Racial/Ethnic Differences in Stroke Symptom Awareness and Stroke Knowledge Among Stroke Survivors, Brandon Marion1, Charles Ellis2; 1Spelman College, 2College of Medicine, MUSC, 3College of Health Professions, MUSC.

In 2009, it is expected that approximately 800,000 Americans will experience a stroke. Despite the high incidence of stroke and the associated mortality and morbidity, knowledge of stroke risk factors and early warning signs of stroke remains generally poor among Americans. Studies also suggest that stroke-related knowledge differs by race/ethnicity with racial/ethnic minorities exhibiting less stroke-related knowledge although at higher risk for stroke. Similar observations have also been noted among stroke survivors who are at high risk for recurrent stroke. However, the literature remains unclear whether racial/ethnic differences exists in stroke-related knowledge in stroke survivors. The purpose of this study was to examine the influence of race/ethnicity on stroke-related knowledge among stroke survivors. Methods. Black and White stroke survivors completed structured surveys of stroke awareness, stroke knowledge, and health literacy using previously validated survey instruments. Surveys were designed to quantify: (1) demographic information (age, sex, educational level, marital status, employment, and insurance), (2) awareness of common early warning signs/symptoms of stroke, (3) general stroke knowledge, (3) and
health literacy by race/ethnicity. Results. Sixty-eight stroke survivors participated in this study. On average, Blacks were younger at age of stroke onset than Whites (52.3 vs 61.2; p<.01). Blacks also achieved lower scores on the REALM-R literacy test than Blacks (4.0 vs 7.0; p<.01). There were no significant differences on the 20 item Stroke Knowledge Test. Similarly, there were no differences were observed in recognition of the five early warning signs of stroke or first action to call 9-1-1 in the event of a stroke. Conclusions. In this pilot study, stroke-related knowledge among stroke survivors did not differ by race/ethnicity even though significant differences were observed in age of stroke onset and health literacy. Funded by the MUSC Center for Health Disparities Pilot Grant Program

126 REACH Risk Factor Survey: A Comparison of Preventive Practices of African Americans With and Without Diabetes, Dennis Orwat1, Jacketta Cobbs2, Lisa Vandemark2, Carolyn Jenkins3; 1College of Medicine, MUSC, 2College of Nursing, MUSC.

Introduction: Diabetes is a leading cause of morbidity in, and is a heavy financial burden for SC, which has a higher prevalence of diabetes than the national average. Objective: To examine the differences between African Americans who report a diagnosis of diabetes and those who do not report a diagnosis of diabetes in terms of overall health, health problems, treatment, and preventive practices.

Methods: An telephone survey of approximately 850-900 African Americans living in Charleston and Georgetown Counties was conducted from 2002-2007. Respondents were selected by random digit dialing annually. Results: Respondents reporting a diagnosis of diabetes accounted for 18.5%, or 826 of those surveyed. Those reporting a diagnosis of diabetes were less likely to have a positive perception of their health, had more days of poor health, and had more comorbidities than those without diabetes. Respondents reporting a diagnosis of diabetes were more likely to be treated for their comorbidities and were more likely to change their dietary habits positively, while at the same time doing less physical activity. The ability to recognize signs and symptoms of stroke or heart attack were not significantly different between those with and without diabetes, but were very low for both groups (5.3%-10.6%).

Conclusions: Significant differences exist between the populations of those with and without diabetes in certain health promotion and disease prevention activities. There is much room for improvement among those with diabetes in terms of improving rates of pneumococcal and influenza vaccination, weight control, exercise, access to care, and education about stroke and heart attack.

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127 Bronchopulmonary Carcinoids: Prevalence and Factors of Survival, Marc McLawhorn1, Rebecca Johnson2, Steven Trocha2, Mitchell Worley2, Grace Wheeler2, Christine Schammel3, James Stephenson2, William Bolton4; 1Medicine, MUSC, 2Surgery, Greenville Hospital System, 3Wofford College, 4Furman University.

Background: Over the last 30 years, the incidence of bronchopulmonary carcinoma has increased substantially, ~6% per year. Over the same interval, survival associated with both typical and atypical subtypes has declined. While bronchopulmonary carcinoma remains an extremely rare tumor (1.6 cases per 100,000), recent trends in incidence and survival rates challenge conventional belief in the benign nature of these tumors. In response to the growing significance of this condition over the past several decades, this study serves to describe a 25-year experience with pulmonary carcinoma at a single institution as well as to identify prognostic indicators within this growing patient population.

Methods: A retrospective review was conducted of all patients diagnosed with pulmonary carcinoma from January 1985 to May 2009. Results: From 1985-2009, 52 patients were diagnosed with pulmonary carcinoma at this institution. The majority of patients (82%) presented with typical histology; these patients tended to be younger and more often female than patients with atypical histology (p=0.013, 0.002 respectively). Lobectomy was the most common surgical intervention (52%) followed by wedge resection (19%). Video-assisted thoracoscopic (VATS) accommodated shorter hospital stays than open thoracotomy. Two-thirds of patients were symptomatic at presentation, with cough as the most common symptom (29%). Multivariate analysis revealed atypical histology to be the lone predictor of poorer prognosis (HR=11.3, 95% CI: 2.7, 47.6). Conclusion: The increased incidence of pulmonary carcinoma over the previous 2-3 decades is reflected in our institution. Tumor histology remains the best predictor of survival.

128 Analysis of HPV Infection in Head and Neck Squamous Cell Carcinoma, Kevin P Gibbs1, Semyon Rubinchik2, Geoffrey Pitzer2, M. Boyd Gillespie3, Natalie Sutkowski2; 1College of Medicine, MUSC, 2Microbiology & Immunology, MUSC, 3Otolaryngology-Head and Neck Surgery, MUSC.

Head and neck squamous cell carcinoma (HNSCC) ranks fifth worldwide in annual incidence with approximately 50,000 new cases annually in the United States. Traditional risk factors for HNSCC are smoking, alcohol use, and poor oral hygiene; however, recently, clinicians have identified an etiologically distinct form of HNSCC related to Human Papillomavirus (HPV) infection. HPV-related tumors tend to present in oropharyngeal sites of younger patients without histories of alcohol or tobacco use. Interestingly, these HPV-related HNSCC respond better to chemoradiation and have better overall prognosis. In South Carolina, African American males have a higher incidence...
of HNSCC than any other ethnic group, and present at a younger age with more advanced stage disease and generally have poorer outcomes. The objective of this study was to determine if this cancer disparity might be related to differences in incidence of HPV+ disease, which has better survival rates. We therefore set up a system for studying parameters of HPV infection in the different racial groups. 28 HNSCC specimens were analyzed for HPV viral load and oncogene expression, and viral integration status. Viral load was measured by testing tumor genomic DNA for HPV-16 E6 and E7 genes using qPCR, while viral oncogene expression was measured in tumor RNA by qRT-PCR. HPV-positive specimens were tested for integration status by measuring E2/E6 viral gene ratios in genomic DNA. 15 of 28 patients tested positive for HPV, having viral loads of >0.01 copies/cell with significant expression of E6 and E7 oncogenes. Viral integration was observed in 4 patients, while episomal forms were observed in 6 patients, and 5 patients had mixed integrated and episomal forms. This system is currently being used to test HPV status in a larger cohort of patients in order to assess whether HPV infection has a role in this cancer disparity. Summer Health Professionals Research Program

129 The Utility of Carrier Screening Mutation Panels for Diagnosis of Cystic Fibrosis in South Carolina, Emile R Dalton¹, Daynna J Wolff²; ¹College of Medicine, MUSC, ²Pathology and Laboratory Medicine, MUSC.

Cystic Fibrosis (CF) is one of the most commonly inherited recessive genetic diseases in the United States, with approximately 1,000 new cases diagnosed each year, 10 – 15 of which are born in South Carolina (SC). The highest rates of CF are found in Caucasians (1/2,500-3,500), with much smaller rates for Hispanics, non-Hispanic blacks and others. Over 1,200 mutations have been identified in the gene causing CF (CFTR) and panels including the most common mutations have been developed specifically for carrier screening in Caucasians. Since MUSC is one of only three accredited CF centers in SC that aids with diagnosis of the disorder, it is imperative that the MUSC Molecular Genetic laboratory have an effective screening test for detection of both carriers and patients with CF. For this study, we assessed our current CF mutation screening test’s (Innogenetics) sensitivity for detecting mutations in patients diagnosed with CF and compared the sensitivity of our test with other FDA-approved CF panel tests to determine the best mutation screen to offer SC’s patient population with mixed ethnicities. We collected data on mutation status from 76 patients who were diagnosed with CF at MUSC. We compared the sensitivity of the in-house analyte specific reagent (ASR) Innogenetics assay that tests for 36 mutations with five different FDA-approved CF mutation panel assays, three of which included the core ACMG-recommended panel of 23 mutations, (Hologic, Nanosphere, Osmotech), two panels that included the core 23 and additional mutations (Celera and Luminex), and one other ASR from Roche. The diagnostic sensitivity for the in-house Innogenetics CF ASR assay was 77.6% (59/76). The diagnostic sensitivities of the other panels were: panels that tested Core 23 mutations (73.7%), CF Genotyper V. 3.0 from Abbott/Celera (76.3%), Luminex Tag It CFTR40 Panel (76.3%) and Roche CF Linear Array Panel (75%). Our studies reveal that the Innogenetics CF ASR assay is a diagnostically-sensitive and cost-effective initial screen to identify and diagnose the majority of our CF patients (77.6%) prior to sending out for further gene testing.

130 Reducing Procedural Pain and Discomfort Associated with Transcranial Direct Current Stimulation, James L McFadden¹, William Beam²; Jeff J Borckardt³; ¹College of Medicine, MUSC, ²MUSC, ³Psychiatry, MUSC.

Abstract not available.

131 Normothermia After Gastrointestinal Surgery: Holy Grail or False Idol?, Simon J Lehtinen¹, Georgiana Onicescu², Kathy Kuhn³, Nestor F Esnaola⁴; ¹Medicine, COM, MUSC, ²Biostatistics, Bioinformatics, and Epidemiology, MUSC, ³Quality and Outcomes Management, MUSC, ⁴Medicine, Surgery, MUSC.

Introduction: Surgical site infections (SSIs) are a leading cause of postoperative morbidity and costs. The Centers for Medicare and Medicaid Services request that hospitals report the percentage of pts with a first postoperative temperature ≥ 36°C after colorectal (CR) surgery. There is no evidence that immediate postoperative hypothermia (IPH, T< 36°C) is associated with a higher incidence of incisional SSIs (ISSIs) after CR or non-CR gastrointestinal (GI) surgery. Methods: We conducted a case-control study to explore the association between IPH and ISSIs after GI surgery. All pts who underwent GI surgery and were entered into our American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) database between 3/2006-3/2009 were identified. Cases consisted of all pts who developed ISSIs within 30 days after surgery. Characteristics between cases and controls were compared using univariate random effects regression models. The independent risk factors for ISSIs were identified using multivariate random effects logistic regression models. Results: 146 cases and 323 controls were identified; 82% of patients underwent non-CR GI surgery. Cases and controls were similar with respect to percentage of pts with IPH (29.4% v. 34.7%, respectively, P=0.27). Patients who underwent emergent surgery or had contaminated wounds had higher rates of perioperative normothermia. There was no association between IPH and ISSIs, even when controlling for pt/surgery-characteristics, emergency/elective status, and wound class (adjusted OR, 1.14; 95% CI, 0.65-2.00; P=0.66). The independent risk factors for ISSIs were diabetes, surgical complexity, small bowel surgery, and non-laparoscopic surgery. Conclusions: Immediate postoperative hypothermia is not independently associated with ISSIs after GI surgery. Process measures
focusing on postoperative normothermia after CR surgery and efforts to optimize normothermia rates after non-CR GI surgery may be of limited clinical value. Clinical trials are needed to determine the benefit for active intraoperative warming in patients undergoing non-CR GI surgery. MUSC SUCCESS Center, College of Graduate Studies Summer Health Professionals (SHP) Program, Grant: Short Term Research Training for Health Professional Students; Grant Number: NIH/NIDDK 5T35DK007431-25

132 Cardiac Magnetic Resonance Image Quality is Surprisingly Good in the Obese: A Study of 2677 Subjects, John R Spratt1, Marcus Y Chen2, W Patricia Bandettini2, Christine Mancine2, Peter Kellman2, Andrew E Arai2; 1College of Medicine, MUSC, 2Laboratory of Cardiac Energetics, National Heart, Lung, and Blood Institute.

Introduction: The effect of patient obesity on cardiac magnetic resonance imaging (CMR) image quality has not been characterized. Wide-bore MRI systems facilitate the imaging of large patients. We hypothesized that CMR image quality would be good in obese patients imaged on a wide-bore MRI scanner. Methods: The quality of cine and delayed enhancement (DE) MRI images was reviewed for patients imaged on a wide-bore Siemens Magnetom Espree 1.5T MRI scanner at the NIH-Suburban Hospital MRI Center. The primary study endpoint was the number of studies considered excellent or good vs. fair, poor, or non-diagnostic quality as a function of BMI. Secondary endpoints were similar analyses in males vs. females and subjects with normal vs. decreased LVEF. The data were analyzed using Pearson chi-square testing. Results: 2759 CMR exams were performed during the study period (1017 female, 1742 male), including cine images in 2677 subjects and DE images in 2607 subjects. Only the 708 (27.1%) studies with a visible infarction were included in analysis of DE image quality. 963 (34.9%) subjects were overweight (BMI 25-30) and 865 (31.4%) were obese (BMI >30). 92.6% of cine images and 89.1% of DE images were of good or excellent quality and there was no significant relationship between BMI and image quality in cine (P=0.885) or DE (P=0.169). Decreased LVEF predicted lower image quality for both techniques (P<0.001). Sex had no effect on image quality in either technique (P=0.955 for cine, P=0.108 for DE). Conclusions: CMR image quality is not compromised in large subjects imaged with a wide-bore cardiac-capable MRI scanner. Reduced image quality in patients with lower LVEF likely relates to the compromised breath-holding abilities of patients in heart failure and higher frequency of arrhythmias. Thus, obesity should not be a reason not to consider CMR if appropriate equipment and expertise are available.

133 Effect of Chronic Transfusion Therapy on Progression of Neurovascular Pathology in Pediatric Patients with Sickle Cell Anemia, Sarah K Bishop1, Gisiele Matheus2, Robert J Adams3, Sherron Jackson1, Miguel R Abboud1, Ram Kalpathi1; 1Pediatric Hematology Oncology, MUSC, 2Neuroradiology, MUSC, 3Neurology, MUSC, 4Children’s Cancer Center of Lebanon, American University of Beirut Medical Center.

Background: Chronic blood transfusion (CBT) is currently the standard of care for primary and secondary stroke prevention in children with sickle cell anemia (SCA) who have had an abnormal Transcranial Doppler (TCD) or cerebral vascular accident (CVA). However, the effect of CBT on cerebral vasculopathy observed radiographically is not well known. Methods: We reviewed pediatric SCA patients on CBT for abnormal TCD (n=12) or CVA (n=22). Baseline cerebral MRI/MRA scans were compared with the most recent scans available for each patient and independently scored by a neuroradiologist. Results: Thirty-four patients with a mean age of 6.47 years at the time of baseline MRI/MRA were studied. The average elapsed time from baseline to current scans was 7.26 years. Overall, patients had a mean change from baseline MRI and MRA scores of +0.76 and +1.03 respectively, indicating worsening vasculopathy. There was a significant difference in mean change of MRI/MRA scores between patients who had CVA and abnormal TCD (MRI; +1.23 vs. -0.08, p = 0.001 and MRA; +1.54 vs. +0.08, p = 0.02). Patients with abnormal baseline MRA had worsening scores compared to those with normal baseline MRA (54% vs. 9.5%, p = 0.01). Also, patients who had CVA were more likely to have an abnormal baseline MRA and worsening scores compared to abnormal TCD patients. Conclusion: Our study demonstrates that a subset of patients with SCA experience progression of cerebral vasculopathy despite CBT. This is especially true for patients with baseline CVA and/or abnormal baseline MRA. CBT for abnormal TCD not only prevents primary stroke, but also confers protection against the development and/or progression of cerebral vasculopathy. This effect appears to be real given our large cohort of patients with longer follow up as compared to previous studies. Further studies are needed to determine the clinical significance of these radiographic findings.

134 Calcified and Non-Calcified Atherosclerotic Plaque Burden in Black and White Women Undergoing Coronary CT Angiography, John W Nance Jr1, Luis Ramos-Duran2, Pamela B Morris1, Joseph A Abro2, Philip Costello2, U Joseph Schoepf3; 1College of Medicine, MUSC, 2Radiology, MUSC, 3Medicine, MUSC, 4Radiology, Medicine, MUSC.

Purpose: Computed tomographic (CT) coronary artery calcium scoring has shown differences in the calcified coronary plaque burden according to race and gender but no data exists on the influence of race on the entire atherosclerotic plaque burden in women. Our aim was
Additional chromosomal material from 9p, a deletion of gene, indicating the presence of a male sexual constitution. Identified one X chromosome and one copy of the SRY of 46,X,+mar.ish der(9). The karyotype was revised after

**Results:** Cytogenetic analysis initially revealed a karyotype Y chromosome and chromosome 9 were performed. Methods: Cytogenetic analysis and FISH studies of the Y chromosome and the short arm of chromosome 9. Unbalanced translocation involving the long arm of the analysis he was found to have a previously unreported chromosome could be identified. However, upon further analysis it was found to have a previously unreported unbalanced translocation involving the long arm of the Y chromosome and the short arm of chromosome 9. Methods: Cytogenetic analysis and FISH studies of the Y chromosome and chromosome 9 were performed. Results: Cytogenetic analysis initially revealed a karyotype of 46,X,+mar.ish der(9). The karyotype was revised after further analysis to 46,X,der(Y)(Y;9)(q11.21;p13.3). FISH identified one X chromosome and one copy of the SRY gene, indicating the presence of a male sexual constitution. Additional chromosomal material from 9p, a deletion of Yq12, and Y centromere material were confirmed by FISH.

Conclusion: Unbalanced translocations involving Yq and 9p are rare with only two other cases previously reported. Although our patient has small genitalia, he does not exhibit the degree of impaired sexual differentiation seen with the other two cases. Partial monosomy 9p resulting in deletion of the DMRT1 gene that has been associated with sex reversal was identified in the other cases but not in our case. Our patient has partial trisomy 9p which has been reported in over 150 cases. The typical manifestations include intellectual disability, short stature, and dysmorphic facial features, but presentations vary depending on the size of the trisomic segments involved. Our patient’s clinical features are most likely related to partial trisomy 9p. Genetic counseling will be important as the patient’s father could be carrying a balanced translocation which would confer a significant recurrence risk for unbalanced offspring or miscarriages.

**135 Unique Unbalanced Translocation Involving Partial Trisomy 9p and Partial Monosomy Yq: A Case Report,** Joshua D Fuller1, Maria del Carmen Montoya2, Barbara R Dupont3, Kenton R Holden4, Michael J Lyons2, 1MUSC College of Medicine, 2Catholic University of Honduras, 3Greenwood Genetic Center, 4Greenwood Genetic Center, MUSC Neurosciences and Pediatrics.

Introduction: We present a 4 year old Honduran male with neurodevelopmental delays, dysmorphic facial features, micropenis, and small habitus. Chromosome analysis initially revealed a single X chromosome and a marker chromosome derived from the short arm of chromosome 9 which was consistent with Turner syndrome as only one sex chromosome derived from the short arm of chromosome 9. Our patient has small genitalia, he does not exhibit the degree of impaired sexual differentiation seen with the other two cases. Partial monosomy 9p resulting in deletion of the DMRT1 gene that has been associated with sex reversal was identified in the other cases but not in our case. Our patient has partial trisomy 9p which has been reported in over 150 cases. The typical manifestations include intellectual disability, short stature, and dysmorphic facial features, but presentations vary depending on the size of the trisomic segments involved. Our patient’s clinical features are most likely related to partial trisomy 9p. Genetic counseling will be important as the patient’s father could be carrying a balanced translocation which would confer a significant recurrence risk for unbalanced offspring or miscarriages.

**136 Cisplatin-induced Ototoxicity and Nephrotoxicity,** Dylan J Sheridan1, Lisa L Cunningham2, 1College of Medicine, Pathology and Laboratory Medicine, MUSC, 2Pathology and Laboratory Medicine, MUSC.

Cisplatin is one of the most potent and widely used chemotherapeutic agents. Two major drawbacks of using cisplatin clinically are its ototoxic and nephrotoxic effects. Although cisplatin has been used for over 30 years to treat many types of cancer, the mechanisms of its ototoxicity and nephrotoxicity are poorly understood. The goal of this study was to develop a protocol that would produce cisplatin-induced hearing loss in mice. Auditory Brainstem Response (ABR) measurements were used to record hearing thresholds in mice before and after cisplatin treatment. Preliminary data indicate that a single dose of cisplatin (16 mg/kg) results in a small hearing loss without significant mortality. Histopathological analyses show little evidence of severe morphological changes in the kidneys of cisplatin-treated mice. However, preliminary evidence suggests that both p53 and STAT-1 are activated in kidney tubule cells after cisplatin treatment. Further investigation will help elucidate the mechanisms of cisplatin-induced toxicity with the long-term goal of developing a protective pharmacological co-therapy. Dr. Leonard Egede; NIH Short-term training in metabolic diseases; Carlene Brandon; Tiffany Baker; Shimon P. Francis; Dr. Debra Hazen-Martin; Nancy Smythe; Carol Moskos; Margaret Romano; Jim Nicholson; Dr. Hainan Lang.

**137 WITHDRAWN**

**138 GILT Accelerates Reductive Processing of PSMA and CD4+ T Cell Recognition of Prostate Cancer Cells,** Bently P Doonan, Azizul Haque; Microbiology and Immunology, MUSC.

Prostate cancer is the second most common cancer among men in the United States. No effective treatment currently exists for metastatic or late stage prostate
cancer. Immunotherapy has emerged as a promising option for treating this malignancy, but more research is needed before it will become clinically applicable. Our laboratory has shown that prostate cancer cells either express, or can be induced to express, HLA class II molecules that could be exploited for targeting prostate tumors by CD4+ T cells. While studies have identified several prostate cancer antigens, such as prostate specific antigen (PSA), prostatic acid phosphatase (PAP), and prostate specific membrane antigen (PSMA), PSMA is a particularly attractive target because its expression is upregulated tenfold in advanced prostate cancer. Also, the immunodominant PSMA epitope, PSMA459, contains a central cysteine residue that may be susceptible to an oxidation reaction in biological fluid. Our ongoing study suggests that prostate cancer cells lack an important enzyme, Gamma-Interferon-inducible Lysosomal Thiol reductase (GILT), that may hinder antigen processing and immune activation. Here, we generated GILT-expressing prostate cancer cell lines and investigated the role of GILT in PSMA processing and CD4+ T cell recognition of malignant prostate cells. Mass spectral analysis showed that PSMA459 becomes cysteinylated in the presence of cystine, which perturbs peptide processing and immune activation by CD4+ T cells. Functional T cell assay confirmed that GILT expression in prostate cancer cells restores PSMA processing and presentation to T cells. Together, these data suggest that GILT can improve self-Ag processing and T cell recognition of prostate cancer cells, providing a novel pathway for future prostate cancer immunotherapy studies. Funding provided by National Cancer Institute.

139 Pleiotrophin, A Tumor Promoter in Bladder Cancer, Tanisha R Hutchinson, Omar Moussa; MUSC.

Pleiotrophin (PTN), is a developmentally regulated signaling molecule which usually shows peak levels of expression in the immediate postnatal period of normal development. However, PTN has also been found to be up-regulated in many tumors. PTN is being characterized here as a tumor promoter and a possible prognostic marker in bladder cancer. PTN is known to exhibit many tumorigenic properties including migration, invasion and angiogenesis. We have shown that PTN can transform immortalized, non-transformed SV-HUC cells and induce a two-fold increase in migration in these cells. As a potential prognostic marker, we have shown that PTN is highly up-regulated in bladder tumors and that higher PTN expression correlates with higher grade and stage of bladder tumor samples. We also observed a correlation between PTN expression and decreased overall survival of patients with bladder cancer. Together our findings indicate that PTN may promote tumorigenesis in bladder cancer, and since it is a secreted molecule, PTN may also serve as a diagnostic/prognostic tool for bladder cancer in the future.

140 Investigation of the Relative Invasiveness of EMMPRIN-Hi and -Lo U87 Luc+ Glioma Cells in the Pontine Region Using a Live Rat Model: The Molecular Perspective, Doug K Christie¹, Courtney E Abrams¹, Lauren B Tolliver², Bryan P Toole², Bernard L Maria³; ¹ college of Medicine, MUSC, ²Regenerative Medicine and Cell Biology, MUSC, ³Pediatrics, Medical College of Georgia.

Diffuse pontine glioma is the fourth most prevalent pediatric central nervous system tumor. Extracellular matrix metalloproteinase inducer (EMMPRIN, EM), a cell surface glycoprotein, has been shown to be highly upregulated in malignant cancer cells. It has been shown to stimulate production of hyaluronan (HA) and matrix metalloproteinase, which may confer several advantages on tumor cells, including resistance to therapy and increased invasiveness. EMMPRIN also has interactions with monocarboxylate transporters, which are used by cancer cells to efflux lactate resulting from glycolysis. Both glycolysis and the ability to secrete lactate contribute to increased drug resistance and malignant behavior in cancer cells. The present study sought to separate populations of luciferase-transfected (Luc+) U87 glioma cells into EM-hi and EM-lo fractions, engraft those cells into the pons of a live nude rat, and measure the invasiveness of the resultant tumors using bioluminescent imaging. Western blots were performed to confirm the results of the cell sorting, and invasion assays were performed to confirm increased invasiveness of the EM-hi fraction in vitro. We were unable to show that the EM-hi fraction correlated with increased invasiveness in vivo due to the fact that a viable tumor was only observed in the rat that received 100,000 cells, as opposed to the 50,000 cells that were injected into the other animals. However, this may be significant, as 50,000 cells were sufficient to initiate tumor growth in previous studies that did not utilize cell sorting. It may be that the viability of U87 Luc+ cells is decreased after the process of cell sorting using flow cytometry. Lu Dai, MUSC; Dr. Mark Slomiany, MUSC; Debbie Shoemaker, College of Graduate Studies, MUSC.

141 Investigation of the Relative Invasiveness of EMMPRIN-Hi and -Lo U87 Luc+ Glioma Cells in the Pontine Region Using a Live Rat Model: The Surgical and Radiological Perspective, Courtney E Abrams¹, Doug K Christie¹, Lauren B Tolliver², Bryan P Toole², Bernard L Maria³; ¹ College of Medicine, MUSC, ²Regenerative Medicine and Cell Biology, MUSC, ³Pediatrics, Medical College of Georgia.

Diffuse pontine glioma is the fourth most prevalent pediatric central nervous system tumor, and is considered particularly difficult to treat because of its extreme invasiveness. Extracellular matrix metalloproteinase inducer (EMMPRIN) is a cell-surface glycoprotein that has been shown to be highly upregulated in malignant cancer
cells. It is known to stimulate production of hyaluronan (HA), a glycosaminoglycan expressed at increased levels in many types of tumor cells, including gliomas, as well as Matrix Metalloproteinases (MMPs). Previous research suggests that the upregulation of HA and MMPs in glioma cells may confer several advantages, such as increased invasiveness. By sorting a population of luciferase-transfected (Luc+) U87 human glioma cells into EMMPRIN-high and -low fractions, and then engrafing them into the pontine region of a live nude rat, the present study sought to demonstrate the relative growth rates and invasiveness of each cell type using bioluminescence imaging (BLI) and magnetic resonance imaging (MRI). BLI involves visualization via the light emissions of the pigment luciferin, catalyzed by the luciferase transfected in the engrafted cells used in this experiment. Through injection of luciferin and its subsequent catalysis, bioluminescent images of the pontine region were collected over a period of five weeks to track the changes of the glioma cells. Western blots were performed to confirm the results of cell sorting, and invasion assays were performed to confirm the increased invasiveness of EMMPRIN-high U87 cells in vitro. Based primarily on the BLI tracking, the experiment indicated that the 50,000 cell count per animal utilized in previous unsorted cell studies may not be sufficient after the sorting process to generate a tumor of significant size. To maintain viability of U87 Luc+ cells, utilization of 100,000 sorted cells per animal may be required for future studies due to the flow cytometry procedure used for sorting. 

Lu Dai, MUSC; Dr. Mark Slomiany, MUSC; Debbie Shoemake, College of Graduate Studies, MUSC

142 Antimicrobial Activity of Natural Products From Medicinal Plants, Juliana M Head1, Dayan Ranwala2, Caroline Westwater1;
1 College of Dental Medicine, Craniofacial Biology, MUSC; 2 Institute for Nutraceutical Research, Clemson University Coastal Research and Education Center.

Background: Candida species are the major fungal pathogen of humans, and represent an important public health problem. Treatment of candidiasis is hampered because antifungal agents tend to have fungistatic activity, host toxicity, and are ineffective against emerging Candida pathogens. Thus, there is a great impetus to identify innovative antifungal therapies, including new antifungal agents. Historically, plants have provided a source of inspiration for novel compounds because they provide a natural blueprint for the development of new drugs, and they contain a variety of phytochemicals that can be used for the treatment of disease. Although many plants are claimed to have health benefits, few studies have evaluated anti-infective properties using standardized methods of extraction and in vitro testing. Objective: The goal of this study was to evaluate the antifungal activity of crude plant extracts derived from a variety of South Carolina plants that have reported health benefits. Methods: Crude extracts were prepared from three locally grown plant species (cilantro, muscadine and feverfew) using a variety of extraction methods. To determine in vitro antifungal activity, plant extracts were tested against three Candida species (Candida albicans, Candida glabrata, and Candida parapsilosis) using the disc diffusion assay. Results: Cilantro (leaf) and muscadine (skin and seed) extracts showed potent inhibitory activity against all species tested; however, the strength of inhibition appeared to be dependent on the extraction method used. Feverfew leaf extracts did not inhibit any Candida species examined. Conclusion: Our results demonstrate that cilantro and muscadine possess strong antifungal properties in vitro. Therefore, this “field-to-bedside” research may ultimately lead to the identification of new plant-derived bioactive compounds with therapeutic value. Supported in part by grants R21AI076721, T32DE017551, and the 2009 MUSC Summer Health Professional Program.

143 The Role of Prx Transcription Factors in Salivary Gland Development, Daniel R West1, Mary Ann Baybo2, Christine B Kern2, Michael J Kern2; 1 College of Dental Medicine, MUSC; 2 Regenerative Medicine and Cell Biology, MUSC.

Rationale: Prx transcription factors, Prx1 and Prx2, are encoded by homeobox genes which have been shown to play a major role in craniofacial development. For example, mandibular hypoplasia and cleft palate, along with tooth malformations and hair follicle alterations, have been observed when both Prx1 and Prx2 are deleted. Hypothesis: Our hypothesis was that Prx transcription factors also play an important role in salivary gland development. Understanding the development of these glands is important since the lack of saliva in humans leads to gross tooth decay and many oral health issues. Methods: Both wild type (Prx1+/+ Prx2+/+) and double knockout (Prx1-/- Prx2-/-) mouse embryos were harvested at various timepoints (E13.5-E18.5 days), then fixed, embedded in paraffin wax, sectioned with a microtome, and stained using various histological stains. Hematoxylin and Eosin staining was used to compare the morphology and position of the sublingual and submandibular salivary glands while Periodic Acid/Schiff’s (PAS) Mucin stain was used to look at their differentiation. Immunohistochemistry (IHC) was used to determine the location of Prx1 and Prx2 expression, along with a possible downstream target: Platelet Derived Growth Factor Receptor-Beta (PDGFR-Beta). Whole SMG were dissected from wild type E17.5 mouse embryos and used for RNA extraction followed by reverse transcription PCR to determine if both isoforms of Prx1 are expressed. Results: The data demonstrated that the SMG in Prx double knockout embryos are hypoplastic, undifferentiated, and malpositioned when compared to the WT embryos. Also, Prx1 increases in expression through timepoints E13.5, E14.5, and E16.5, while PDGFR-Beta decreases through the same timepoints in WT embryos. Of the two isoforms of Prx1 expressed in SMG, Prx1a is more greatly expressed. This study demonstrates that Prx
transcription factors are instrumental in proper salivary gland development, and suggests that Prx transcription factors may regulate the PDGF signaling pathway in SMG morphogenesis. Summer Health Professionals Research Program

144 The Effects of Oxidized LDL Immune Complexes on Collagen IV Production By Human Mesangial Cells, Alex H Winters1, Souzan Abdel-Razek2, Maria Lopes-Virella2; 1College of Medicine, MUSC, 2Endocrinology, MUSC.

Diabetic nephropathy is caused by expansion of the mesangial matrix, which is maintained by mesangial cells. The primary structural component of the mesangial matrix is type IV collagen. Ongoing work in Dr. Lopes-Virella's lab has shown that oxidized low density lipoprotein immune complexes (oxLDL-IC) induce increased collagen IV production by human mesangial cells. The cell signaling pathways involved in this process are not well understood, and this project investigated several common pathways to determine which are involved and to what degree. The pathways observed were p38, MAPK, PKC, JNK, JAK/STAT, and MEK; cells were exposed in vitro to one of three doses of inhibitors to these pathways before being exposed to oxLDL-IC. The results indicate that of the pathways observed, the PKC pathway is primarily involved in the over-expression of type IV collagen by human mesangial cells due to oxLDL-IC exposure. p38 pathway inhibition showed moderate inhibition of type IV collagen over-expression at the doses used. JNK pathway inhibition showed a biphasic pattern of type IV collagen expression. Inhibition of the MEK, MAPK, and JAK/STAT pathways appeared to have little effect on type IV collagen over-expression. Further trials and modified inhibitor doses are needed to confirm these findings. Work funded by the Summer Health Professionals Program

145 Bradykinin and Angiotensin-II Induce Distinct Permeability Changes and Differentially Recruit Signaling Molecules in Podocytes, Dezhond B Sumter1, Mamon Dey1, Thomas A Morinelli2, David P Turner1, John R Raymond2, Monika Gooz2; 1Nephrology, MUSC, 2Nephrology, MUSC; RH Johnson VAMC, 3Pathology and Lab Medicine, Hollings Cancer Center, MUSC.

The aim of our investigation was to study bradykinin (BK) and angiotensin II (ANGII) induced signal transduction mechanisms behind their effects on glomerular podocytes permeability. We treated confluent mouse podocytes on transwell membranes with (10-10-10-6 M) BK or (5x10-9–10-6 M) ANG II and measured permeability of the cells using fluorescent bovine serum albumin. To characterize activation of various receptor tyrosine kinases, differential phosphorylation of epidermal growth factor receptor (EGFR), and activation of intracellular kinases, we employed a Phospho-Kinase RTK Array (PKRTKA), EGF Pathway Phospho Antibody Microarray (EGFPAM), and Phospho-Kinase Antibody Array (PKAA), respectively. We studied the phosphorylation of extracellular signal regulated kinase (pERK 1/2) via Western blot. Further, we measured increase in intracellular free calcium by the calcium sensitive fluorescent dye Fluo3. BK induced concentration dependent decrease in podocyte permeability in contrast to ANGII which increased the cells permeability. Using PKRTKA we have determined that ANGII and BK increased phosphorylation of EGFR, ErbB2, and Axl. Additionally ANGII increased the activation of MSP-R; whereas BK induced the phosphorylation of PDGFRB, SCF and MuSK. Employing EGFPAM we have determined that BK induced EGFR phosphorylation at Y1110, Y1172 and Y1197 and ANGII induced phosphorylation of EGFR at Y869. Using PKAA, we found that ANGII and BK increased the phosphorylation of p38a, MEK1/2, and STAT2; however, ANGII also activated STAT3, JNK, TOR, AMPK alpha, Lyn, STAT5 alpha, Fgr, STAT3, and STAT6. BK induced concentration-dependent (10-11-10-7M) activation of ERK 1/2 through bradykinin B2 receptor. Further, BK induced concentration-dependent increase in intracellular free calcium concentration. ANGII concentration-dependently (10-7-10-6M) increased pERK1/2 however, lower concentrations had no effect. We conclude that bradykinin and angiotensin II signaling transduction involve different signaling molecules in podocytes that could explain their different effect on permeability changes. We thank Dr. Peter Mundel for providing us the mouse podocyte cell line. This work was supported by NIH 5K01DK070054, the Dialysis Clinic Inc. and the Paul Teschan Research Grant to MG, and the REAP from the VA Research Services

146 Sepsis-Induced Neuroinflammation, Rachel D Maree1, Joshua Hirschhorn2, S Mohanty2, Hongkuan Fan2, James Cook2, Narayan R Bhat2; 1Medicine, MUSC, 2Neurosciences, MUSC.

There are indications that systemic infections and resulting inflammation may contribute to neurodegeneration associated with chronic diseases such as Alzheimer’s and Parkinson’s diseases. It is likely that sepsis, an inflammatory condition that occurs in the host when infected, can adversely affect brain function. In fact, there have been studies using peripheral administration of bacterial lipopolysaccharide (LPS) in animals as a model for sepsis that indicates such a link. However, the true sepsis models such as ‘cecal ligation and puncture (CLP)’ have never been used for testing neuroinflammatory changes. Therefore, in our project, we compared the effects of LPS injection and CLP on neuroinflammation in C57BL/6 mice. Sets of mice were either injected with LPS (10mg/kg) or subjected to CLP, respective controls being injected with saline or ‘Sham’ operated. After 24h, the animals were sacrificed and hemibrains from each subject were either fixed in paraformaldehyde for immunohistochemistry (IHC) or frozen for biochemical analyses. IHC of brain sections using Iba-1 as a marker of activated microglia confirmed a strong neuroinflammatory response to LPS.
injection and a moderate response to CLP. Real time RT-PCR analysis showed induced expression of inducible nitric oxide synthase (iNOS) with a relatively stronger response to LPS injection than CLP similar to Iba-1 expression. The results obtained suggest that CLP-induced sepsis, as with LPS injection, signals a neuroinflammatory response with potential neurological consequences. American Academy of Neurology (AAN) Medical Student Summer Research Scholarship

**147 Presence of Mature Immunostimulatory Dendritic Cells is Increased in Patients with Allergic Fungal Rhinosinusitis**

Brendan P O’Connell¹, Jennifer K Mulligan², Carl Atkinson³, Ryan M Mulligan², Benjamin S Bleier², Sarah E Casey³, Rodney Schlosser²; ¹College of Medicine, MUSC, ²Otolaryngology-Head and Neck Surgery, MUSC, ³Microbiology and Immunology, MUSC.

Patients with allergic fungal rhinosinusitis (AFRS) display a Th2 immune response in the local sinonasal mucosal environment, though the mechanism by which this occurs remains unclear. Dendritic cells (DCs) are highly efficient antigen presenting cells that regulate the induction of Th1 and Th2 immune responses, however their role in AFRS is not well understood. The presence of mature DCs in the sinonasal mucosa of AFRS was investigated to determine if there was an increased number of DCs capable of stimulating Th2 immune responses. Sinus and inferior turbinate specimens were collected from patients with AFRS (n=10), chronic rhinosinusitis without nasal polyps (CRSsNP) (n=7) and nondiseased patients undergoing cerebrospinal fluid leak repair or pituitary tumor resection (n=6). Tissue samples were stained immunohistochemically for costimulatory B7 molecules, CD80 and CD86, known stimulators of Th2 immune responses expressed by mature DCs. Expression of CD1a, a molecule that is selectively expressed on specialized antigen presenting cells, was also investigated through immunohistochemical staining. Analysis of sinus tissue samples in patients with AFRS demonstrated increased numbers of cells staining positive for CD80, CD86, and CD1a compared to controls. CRSsNP patients had slightly elevated levels of these molecules, however the presence of mature DCs was much less than in AFRS. Turbinate mucosa from patients with AFRS also demonstrated elevated levels of CD80 and CD86 compared to normal controls. Average turbinate CD1a staining was higher in AFRS than controls although this data was not statistically significant. Analysis of CRSsNP turbinates revealed few CD1a positive and no CD80 or CD86 expression. In conclusion, AFRS patients displayed increased presence of mature DCs capable of stimulating Th2 immune responses in both sinus and turbinate subsites. These results suggest that DCs may play a role in the modulation of elevated Th2 immune responses observed in this patient population. Funded in part by the Flight Attendant Medical Research Institute

**148 Epigenetic Modification of RXRa in Human Colon Carcinomas By the Green Tea Polyphenol, EGCG, Vondina R Brown¹, Jay Morris², Kathleen V Coleman³, Michael J Wargovich²; ¹Graduate Studies, MCBP, MUSC, ²Graduate Studies, Cell and Molecular Pharmacology, MUSC, ³Cell and Molecular Pharmacology, MUSC.

Abstract not available.

**149 CD44 Membrane Dynamics in Metastatic Breast Cancer Cells**

George D Grass¹, Mark G Slomiany², Bryan P Toole³; ¹Graduate Studies, Regenerative Medicine and Cell Biology, MUSC, ²Regenerative Medicine and Cell Biology, MUSC.

Introduction: Accumulating evidence indicates the plasma membrane is composed of numerous heterogeneous domains termed ‘lipid rafts’. These rafts are dynamic scaffolds for signaling complexes and represent major compartments for internalization. It is believed raft stability is dependent upon membrane cholesterol and underlying attachments to the cytoskeleton. Raft stabilization may also occur on the plasma membrane via direct matrix-cell surface interactions. We have previously demonstrated that the stability of drug efflux transporters and cell survival signaling receptors are modulated by their association with CD44, which is in turn bound to hyaluronan (HA)—an extracellular sugar polymer scaffold for CD44 and its membrane protein partners. Thus, HA aids in breast cancer progression by establishing an optimal environment for tumorigenic cell signaling pathways and chemoresistance. It is postulated that HA is internalized following cleavage into smaller fragments, which avoid multimeric CD44 interactions. As such, our laboratory has demonstrated in breast cancer cells that disruption of HA-CD44 interactions with oligomers of HA (o-HA) similarly results in CD44 internalization and associated receptors and transporters, but in a less organized fashion. Methods: Employing the metastatic breast cancer cell line MDA-MB-231, HA-CD44 interactions were probed via administration of o-HA and various transport inhibitors for indicated periods of time. Internalization assays were performed using a reversible cell surface biotinylation technique followed by a non-detergent-based lipid raft isolation protocol. Results: Disruption of constitutive HA-CD44 interactions with o-HA results in accelerated CD44 internalization compared to controls. Raft isolation demonstrates that CD44 is in similar raft fractions as binding partners MCT4 and EMMPRIN. Conclusions: Perturbation of HA-CD44 interactions with o-HA results in rapid internalization of CD44 and associated complexes. CD44 associates with known binding partners in lipid rafts.

**150 Racial Disparity in Surgery Recommendation for Oral and Oropharyngeal Cancer in the US**

Yanqiu Weng, Jeffrey Korte, Anbesaw Selassie; Biostatistics and Epidemiology, MUSC.

Purpose: to investigate the impact of racial, clinical,
demographic and socioeconomic factors on the likelihood of patients being recommended for surgery after a diagnosis of oral or oropharyngeal cancer; and to investigate predictors of the impact of race on the recommendation for surgery. Method: 68445 cases of oral and oropharyngeal cancer were extracted from the Surveillance, Epidemiology, and End Results (SEER) database for 1988 to 2005. County-level rurality data were merged using the US Department of Agriculture Rural-Urban Continuum Codes dataset. Bivariate analyses and multivariable logistic regression analyses were conducted to evaluate the association between race and surgery recommendation adjusted for tumor stage, tumor site, age, gender, marital status, residence area, socioeconomic status, and year of diagnosis; interaction effects between race and covariates were investigated as well. Results: African Americans were less likely than Caucasians to be recommended for surgery at the initial diagnosis, even if they were similar in demographic, socioeconomic and clinical conditions. Stratifying by residence area and tumor site, African Americans from rural areas with cancer of lip or buccal mucosa were at the highest risk of not being recommended for surgery (OR 4.4) compared to Caucasians; African Americans from urban areas with cancer in the oropharyngeal region were at similar risk of not being recommended for surgery (OR 1.2) compared to Caucasians. These observed racial disparities were attenuated with increasing age. Age, gender, marital status, socioeconomic status, year of diagnosis and tumor stage were all significantly associated with whether surgery was recommended. Conclusion: We observed substantial racial disparities in whether surgery was recommended for patients presenting with oral and oropharyngeal cancer in the US. The degree of racial disparity was stronger for younger patients, patients living in rural counties, and was stronger for cancer of lip and buccal mucosa than for oropharyngeal cancer.

151 Ratios of C16ceramide and C16dihydroceramide Rather Than C16ceramide Alone Appear to Dictate Apoptotic Outcome Following TRAIL Stimulation. Tejas S Tirodkar, Christina Voelkel-Johnson; College of Graduate Studies, MCBP, MUSC.

Sphingolipids are bioactive mediators of cell signaling and are known to be involved in important cellular processes such as apoptosis, cell proliferation, senescence and angiogenesis. As such they are vital to cancer research. The focus of our group is the study of the sphingolipid, C16-ceramide which is synthesized by the enzyme ceramide synthase 6 (CerS6 or LASS6), in the apoptosis of colon cancer cells. Using two isogenic colon cancer cell lines that differ in their response to TRAIL mediated cell death (cell lines SW480 and SW620) we have established that increase in CerS6 expression results in sensitivity to TRAIL while a downregulation of CerS6 expression renders TRAIL resistance. Since these cells are hard to transfect, we generated an adenovirus expressing CerS6 (AdCerS6) for better modulation of gene expression. Infection of the TRAIL resistant cell line SW620 with the AdCerS6 virus resulted in high levels of CerS6 expression, however the cells remained resistant to TRAIL induced apoptosis. Analysis of the sphingolipid profile revealed comitomt high levels of C16-ceramide and dihydro-C16-ceramide. We hypothesized that the increase in dihydro-C16-ceramide inhibited the pro-apoptotic role of C16-ceramide. To test this hypothesis we used a chemical inhibitor C8-cyclopropenyl ceramide (CPPC) to inhibit the enzyme dihydroceramide desaturase (DEGS-1) that converts dihydro-C16-ceramide to C16-ceramide in TRAIL sensitive SW480 cells. This inhibition rendered the sensitive cells resistant to TRAIL mediated cell death suggesting that the ratio of C16-ceramide to dihydro-C16-ceramide is important in determining the apoptotic response. Efforts are now being directed towards studying the effects of downregulation of the DEGS-1 using siRNA. Also under scrutiny is the connection between the enzymes DEGS-1 and CerS6 to better understand the resulting sphingolipid profile and the consequent response to TRAIL mediated apoptosis.

152 4'-Phosphopantetheinyl Transferase Activates 10-Formyltetrahydrofolate Dehydrogenase, Kyle Strickland1, Alexis Hoeferlin2, Sergey Krupenko2; 1Biochemistry, MUSC, 2MUSC.

Acyl carrier proteins (ACPs) serve to tether phosphopanthethinyl-thioester intermediates in a wide variety of biochemical reactions. These domains are post-translationally modified by the addition of 4'-phosphopantetheine (4-PP) at a conserved serine residue. This modification is catalyzed by a class of enzymes called 4'-phosphopantetheinyl transferases (PPTs), which transfer the 4-PP group from coenzyme A to ACP substrates. In contrast to yeast and lower organisms which utilize multiple PPTs to modify its carrier proteins, it has been suggested that humans require only a single, broad-specificity PPT for all phosphopantetheinylation reactions. One of the most abundant folate enzymes, 10-formyltetrahydrofolate dehydrogenase (FDH), consists of two independent catalytic domains connected by an intermediate domain with sequence homology to acyl carrier proteins. This enzyme catalyzes the NADP-dependent conversion of 10-formyltetrahydrofolate (10-FTHF) to tetrahydrofolate (THF) and carbon dioxide. Recent studies have shown that FDH is modified by addition of a 4'-phosphopantetheine (4-PP) prosthetic group at Ser354 of the linker region, and this moiety is responsible for the transfer of the formyl group from the amino-terminal 10-FTHF hydrolase domain to the carboxy-terminal aldehyde dehydrogenase domain of FDH. The present studies demonstrate that the broad-specificity PPT is capable of activating FDH catalysis in vitro and modifying FDH with a fluorescent 4-PP analogue. Silencing the PPT enzyme by siRNA inhibits FDH modification by cell lysate, and PPT-silenced cells exhibit decreased proliferation and...
undergo G1-arrest. These results indicate that FDH is activated and modified by this PPT and suggest that mammals utilize a single enzyme for completing all cellular phosphopantetheinylation reactions.

153 Pathogenesis of Cone Photoreceptor Loss in Mice with Disrupted Rod Visual Cycle, Peter H Tang, Patrice Goletz, Rosalie K Crouch; Medicine, Ophthalmology, MUSC.

The vertebrate retina consists of both rod and cone photoreceptors mediating low-light and bright-light vision, respectively. Both photoreceptors are dependent upon the recycling of vitamin A to regenerate visual pigments. Metabolic processing of vitamin A for rod visual pigment regeneration, the “rod visual cycle”, is well established and involves the generation and transportation of chromophore (11-cis retinal, the aldehyde form of vitamin A) from the retinal pigment epithelial (RPE) cells to the rods. Recent evidence suggests the process for generating visual pigment in cones differs from that in rods; however, the mechanism is not understood. A disruption in the ability of the RPE cell to generate chromophore, as seen in one form of the human eye disease Leber congenital amaurosis, leads to rapid cone degeneration, yet rods survive much longer. A possible explanation is that under normal chromophore levels, rods secrete a factor to promote cone survival. When the chromophore supply is disrupted, the rod visual cycle is inactive and this “cone survival factor” is not synthesized, leading to rapid cone degeneration. A targeted disruption of the rod visual cycle was used for this investigation. We evaluated cone survival in mice with a mutation in the gene for rhodopsin (Rho-/-), the G-protein coupled receptor (GPCR) found in the rod outer segment that binds with chromophore to form visual pigment. Distribution of cones across the dorsal-ventral axis of the retina was visualized with immunofluorescence of cone opsins on flat-mounted retina at various ages. Corresponding cross sections were evaluated for cone morphology, and cone function was quantified by electroretinography for comparative purposes. Results from this study will help to elucidate the possible roles of rods in cone survival, and could indicate potential targets for therapeutic development. Supported by National Institutes of Health R01 EY04939 (RKC), and CO6 RR015455, Foundation Fighting Blindness, Inc. (RKC), and Research to Prevent Blindness unrestricted grant (Department of Ophthalmology, MUSC), Senior Scientific Investigator Award (RKC), Medical Student Research Fellowship (PHT)

154 Extending the REDCap Data Model to Accept External Datasets, Adrian M Nida, Jihad S Obeid; Graduate Studies, Biochemistry, MUSC.

Secondary use of electronic medical data for research has become one of the major priorities of the Clinical and Translational Science Awards (CTSA) consortium. Clinical investigators have long collected data for research projects using any means from spreadsheets to web-based systems. What has been lacking and demanded by researchers is the ability to tap into the breadth of existing electronic data in EMR’s and avoid repeated data entry. The focus of this discussion is the ability to link data from the EMR to corresponding research data in individual research projects. Currently, we are encouraging our researchers to standardize data collection using REDCap (Research Electronic Data Capture tool). Our focus has been to extend this utility to import data from live EMR systems such as: MUSC’s Patient Repository System, Oacis; and its Outpatient Clinical Documentation System, Practice Partner. This discussion will cover the architectural designs and technical implementation of the work done to date to connect REDCap to the external live systems mentioned above.

155 ROC Analyses of Correlated DES Data Suggest Redefinition of Diagnostic Criteria, Jody D Ciolino, Daniel Pohl, Donald Castell, Paul J Nietert; 1Biostatistics and Epidemiology, Medicine, COGS, MUSC, 2Digestive Disease Center, Gastroenterology and Hepatology, MUSC, 3Biostatistics and Epidemiology, Medicine, MUSC.

Screening tools have the potential to reduce disease related mortality by enabling physicians to diagnose diseases in asymptomatic individuals or to identify individuals at risk of developing disease may reduce disease related mortality. Diagnostic tests based on multiple biomarkers, rather than a single biomarker, have enhanced capacity to achieve the sensitivity and specificity needed to achieve this clinical gain. Statistical methods that model complex biologic interactions and that are easily interpretable allow for translation of biomarker research into diagnostic tools. Ensemble methods are an effective means of exploring data for important predictors. Many ensemble methods identify important predictors but fail to describe interactions among predictors. Also, there are only limited graphical methods for displaying ensemble models, making clinical interpretation difficult. Logic Forest, our ensemble version of a multivariable regression method called logic regression (Ruczinski et al. 2003), identifies not only important predictors but important interactions as well. We develop graphical methods for describing relationships between predictors that occur in a Logic Forest model. We demonstrate these graphical techniques using simulated data with a true underlying model. We also apply Logic Forest to periodontal disease data to determine possible associations between genetic and health factors and periodontal disease in a population of diabetic African Americans. Supported by National Institute of General Medicine Grant T32GM074934, National Cancer Institute.
157 Alternative Stopping Rules for Proportional Odds Model Dose Finding Clinical Trial Design with Ordinal Toxicity Grading, Emily M Van Meter, Dipankar Bandyopadhyay, Elizabeth Garrett-Mayer; 1Division of Biostatistics and Epidemiology, MUSC, 2Division of Biostatistics and Epidemiology, Department of Medicine, MUSC.

Currently many dose finding clinical trial designs, including the continual reassessment method (CRM) and the standard 3 + 3 design, dichotomize toxicity outcomes based on pre-specified dose-limiting toxicity criteria. This loss of information is particularly inefficient due to the small sample sizes in phase I trials. Common Toxicity Criteria (CTCAEv3.0) classify adverse events into grades 1 through 5, which range from 1 as a mild adverse event to 5 as death related to an adverse event. This dose finding trial design extends the CRM to include ordinal toxicity outcomes as specified by CTCAEv3.0 using the proportional odds model. As compared to the dichotomous CRM under various prior distributions, target dose-limiting toxicity rates, overall sample sizes, and cohort sizes, the proportional odds design performs as well as the dichotomous CRM on all criteria compared, and notably with more precision to estimate the maximum tolerated dose (MTD). Additionally, in situations where patients are exposed to highly toxic dose levels, this ordinal design adjusts to a safer dose level quicker than the dichotomous CRM. An extension of this project now considers alternative stopping rules for the proportional odds design instead of implementing a pre-determined total trial sample size. The first stopping rule stops a trial when the target dose changes by less than 10% and six patients have been treated in the dose range. Another stopping rule ends the dose finding trial based on the precision of the estimated dose. Simulation study results suggest that not only is it beneficial to incorporate ordinal toxicities into phase I trial designs, but alternative stopping rules can reduce the number of patients needed to estimate the MTD for use in future phase II/III efficacy studies. Supported by the NINDS/NIH Biostatistics Training with Application to Neuroscience (BTAN) grant T32 NS480007-01A1, P.I.: Yuko Y. Palesch, Ph.D.

158 A Proteomic Analysis of Temperature-dependent Virulence Factors in Vibrio coralliilyticus, Nikole E Kimes, Wesley R Johnson, Lisa E Kilpatrick, Pamela J Morris; 1Graduate Studies, Molecular and Cellular Biology and Pathobiology, MUSC, 2Biology, College of Charleston, 3National Institute of Standards and Technology.

Over the past 30 years, the emergence of new infectious diseases as well as the reemergence of old infectious diseases has increased in both human and animal populations. Interestingly, a number of these diseases, including those caused by Vibrio pathogens (e.g., V. cholerae) are associated with warmer temperatures, making the study of temperature-dependent pathogenicity an area of increasing interest. Susceptibility to temperature-related infectious disease is most clearly evidenced in coral reef ecosystems in which unprecedented global degradation has occurred due in large part to Vibrio-related infectious disease outbreaks. Vibrio coralliilyticus, for example, is a globally distributed bacterium known to cause disease in a variety of marine organisms. Infection experiments have been used to characterize V. coralliilyticus as a temperature-dependent coral pathogen, resulting in coral bleaching at 25°C and coral lyses at temperatures above 27°C. Increased protease activity has been correlated with the increased virulence of V. coralliilyticus as water temperatures rise from 20°C to 30°C. We hypothesize that a more generalized temperature-dependent induction of virulence factors is necessary to drive the mechanisms underlying the pathogenicity of V. coralliilyticus. Our study used two-dimensional liquid chromatography coupled with tandem mass spectrometry (2D-LC-MS/MS) to detect proteins produced by V. coralliilyticus grown at 24°C or 27°C. Concurrently, we sequenced the genome of V. coralliilyticus and used the predicted proteome to identify the 2D-LC-MS/MS generated spectra. Our results reveal that V. coralliilyticus cultivated at a higher temperature (27°C) express a greater number of virulence factors compared to cultivation at a lower temperature (24°C). In addition, possible mechanisms of virulence have been identified including, quorum sensing, flagellar-mediated motility, secretion systems, host degradation, and antibiotic resistance. This study’s significance is enhanced by recent climate change predictions calling for increases in ocean water temperatures and increased observations of infectious diseases, especially during the summer months. Supported by a National Science Foundation Biodiversity Surveys and Inventories Grant (DEB0516347) to PJM and a National Science Foundation Graduate Research Fellowship to NEK.

159 Downregulation of the Complement Inhibitory Protein, Cry, is Protective in an Orthotopic Bladder Cancer Model Through Modulation of the Adaptive Immune Response, Michelle L Rapisardo, Carl Atkinson, Stephen Tomlinson; 1College of Graduate Studies, Microbiology and Immunology, MUSC, 2College of Medicine, Microbiology and Immunology, MUSC.

In general, monoclonal antibody immunotherapy for cancer has fallen short of clinical expectations. A contributing factor to the ineffectiveness of antibody therapy for some cancers is thought to be to the over expression of complement inhibitory proteins on the tumor cell surface. We hypothesize that overcoming complement resistance of tumor cells will not only enhance antibody therapy, but will enhance the outcome of a normally ineffective humoral immune response and induce a protective cellular immune...
response to the tumor. To investigate this, the complement inhibitor, Crry, was downregulated in vitro on the bladder tumor cell line, MBT-2, by siRNA transfection. The resulting MBT-2/Crrynormal tumor cell line, together with control MBT-2/Crrylow were studied in an orthotopic bladder cancer model to determine the effects of Crry down regulation on animal survival, tumor growth and induced immune response. We found that Crry down regulation is protective in this model. Mice inoculated with MBT-2/Crrylow tumor cells had a significantly reduced bladder tumor burden at day 21 compared with those inoculated with MBT-2/Crrynormal. Further, tumors from mice inoculated with Crrylow cells had an increase in C3 deposition on the tumor surface at day 14, indicating increased complement activation. Since complement is known to play a role in modulating the adaptive immune response we investigated both humoral and cellular immune responses in mice inoculated with Crrylow and Crrynormal tumor cells. The downregulation of Crry resulted in an enhanced adaptive immune response to the tumor. In order to extend our findings to a more clinically relevant situation we attempted an in vivo siRNA transfection to downregulate Crry on an already established tumor in the bladder. The bladder provides an ideal model to investigate this, as it provides a contained vesicle for delivery of the anti-Crry siRNA through a catheter, eliminating the problems associated with systemic treatment. We have shown the feasibility of this approach, showing that Crry is downregulated 48 hours post transfection by immunohistochemical staining. Next we will examine whether this is therapeutically beneficial and how it affects the immune response to the tumor.

160 MAPK Phosphorylation of SPF45 on Ser222 Enhances SPF45 Alternative Splicing Activity: A Novel Mechanism of Pre-mRNA Regulation By MAP Kinases, Adnan M Al-Ayoubi1, Hui Zheng2, Tao Bai2, Scott T Eblen2; 1Graduate Studies, Cell and Molecular Pharmacology, MUSC, 2Cell and Molecular Pharmacology, MUSC.

Abstract not available.

161 Heat Shock Inhibits Cisplatin-induced Activation of P53 and STAT-1 in Adult Mouse Utricle, Tiffany Baker1, Inga I Kramarenko2, Mona Taleb3, Shimon P Francis1, Carlene S Brandon2, Keely Morris3, Fu-Shing L Lee2, Lisa L Cunningham2; 1College of Graduate Studies, Pathology and Laboratory Medicine, MUSC, 2Pathology and Laboratory Medicine, MUSC, 3College of Medicine, MUSC.

Cisplatin is an effective chemotherapeutic drug implemented in the treatment of a wide variety of cancers. However, a proportion of patients who receive cisplatin develop significant permanent hearing loss. The ototoxic effects of cisplatin result in part from damage to the sensory hair cells of the inner ear. We have previously shown that heat shock preconditioning inhibits cisplatin-induced hair cell death in vitro (Cunningham and Brandon, 2006). The molecular and cellular mechanisms underlying cisplatin-induced hair cell death are poorly understood. Previous studies have implicated the pro-apoptotic molecules p53 and STAT-1 as key players in cisplatin-induced hair cell death. P53 is a key mediator of the DNA damage response in cells, resulting in upregulation of specific pro-apoptotic proteins in the face of irreparable DNA damage. A previous study demonstrated that chemical inhibition of p53 inhibited cisplatin-induced hair cell death (Zhang et al. 2003). STAT-1 is a transcription factor that controls the expression of pro-apoptotic proteins in response to cellular stresses, including genotoxicity and ROS. STAT-1 is required for cisplatin-induced hair cell death in vitro (Schmitt et al. 2009). In order to examine the mechanisms underlying the protective effect of heat shock against cisplatin-induced hair cell death, we have analyzed the effect of heat shock on the activation of both p53 (p-p53 Ser15) and STAT-1 (p-STAT-1 Ser 727). Our data indicate that heat shock protein 70 (Hsp70) and Hsp32 each inhibit cisplatin-induced hair cell death. Western blot analyses reveal that cisplatin treatment results in phosphorylation (activation) of both p53 and STAT-1, and that heat shock inhibits activation of both molecules. We are currently investigating the roles of Hsp70 and Hsp32 in the inhibition of cisplatin-induced activation of p53 and STAT-1. Supported by NIH/NIDCD R01 DC007613 and 1 F30 DC010522-01 and NIH/NCRR grants C06 RR015455 and C06 RR14516 from the Extramural Research Facilities Program of the National Center for Research Resources. Thanks to the MUSC GAANN fellowship in Cell and Neurobiology.

162 Non-Melanoma Skin Cancer and the Risk of Second Primary Cancers: A Systematic Review, Lee Wheless1, Joshua Black2, Anthony J Alberg1; 1Biostatistics and Epidemiology, MUSC, 2MUSC, Yale.

Context: Based on empirical evidence, the hypothesis has been set forth that a personal history of non-melanoma skin cancer (NMSC) may be a marker of a high cancer-risk phenotype. Others hypothesize that NMSC may be a marker of high vitamin D synthesis and therefore inversely associated with risk of other malignancies. Objective: To reconcile these divergent views, we carried out a systematic review to determine the overall association between nonmelanoma skin cancer and subsequent risk of other cancers. Data Sources: PubMed and Ovid/MEDLINE databases were searched through March 2009. The formal search was supplemented by hand searches. Study selection: Articles were included if sufficient information was presented to estimate the risk of developing other cancers following NMSC. Data extraction: Articles were reviewed and data abstracted independently in duplicate with disagreements decided by consensus. Results: Of the 21 included articles, 15 presented on NMSC in relation to risk of all other cancers combined. NMSC was associated with a 17% increased future risk of another malignancy (summary random-effects RR (SRR) 1.17,
95% confidence interval (CI) 1.11-1.22). This association held true for both squamous cell carcinoma (SRR 1.21, 95% CI 1.14-1.28) and basal cell carcinoma (SRR 1.15, 95% CI 1.07-1.24), and both men (SRR 1.15, 95% CI 1.09-1.20) and women (SRR 1.10, 95% CI 1.04-1.15). Conclusions: Strong, consistent evidence indicates that a personal history of NMSC is associated with an increased risk of developing other malignancies. For reasons that are presently unknown, nonmelanoma skin cancer may be a marker of a high cancer-risk phenotype. Supported by NIH/NCI grant R01CA105069 (Alberg) and Lee Wheless was supported by grant number T32RR023258 from the National Center For Research Resources.

163 Inhibition of Cx43/ZO-1 Interaction Improves Gap Junction Intercellular Communication, Reduces Connexon Hemichannel Activity, and Increases Myocyte/Fibroblast Differential Adhesion, J Matthew Rhett, Jane Jourdan, Michael P O’Quinn, Robert G Gourdie; Regenerative Medicine and Cell Biology, MUSC.

Direct cytoplasmic communication between cells is achieved by an aggregate of membrane channels called the gap junction (GJ). Individual intercellular channels comprising GJs are formed from hexameric oligomers called connexons or hemichannels; one connexon each contributed by the plasma membranes of adjacent cells. The carboxyl(C)-terminus of the main subunit of cardiac connexons, Connexin43 (Cx43), is bound by the PDZ-2 domain of zonula occludins-1 (ZO-1). Previous work in our lab has shown that disruption of this interaction by a peptide based on the C-terminus of Cx43 – termed Alpha-Connexin-C-terminal peptide-1 (ACT-1) – results in larger GJs. We hypothesize that ZO-1/Cx43 interaction limits the rate at which connexons enter GJs. We studied the functional implications of this hypothesis: a) GJs will be larger in cells treated with ACT-1 or ZO-1 siRNA, and therefore GJ intercellular communication (GJIC) should be enhanced by disruption of Cx43/ZO-1 interaction, b) larger GJs will be recruited from membrane connexon pools, with concomitant decreases in hemichannel activity, and c) increasing junctional Cx43 will differentially increase adhesion in cells expressing more Cx43 vs those expressing less – specifically, cardiac myocytes and fibroblasts respectively. GJIC was assayed by both FRAP and scrape-loading; application of ACT-1 or ZO-1 knockdown to HeLa cells expressing Cx43 showed a robust increase in communication. Connexon function was assayed by live imaging of ethidium bromide uptake in Cx43-expressing HeLa cells. We found that coupled cells - but not uncoupled cells - treated with ACT-1 or subjected to ZO-1 knockdown displayed reduced hemichannel activity. In coculture suspension aggregates of primary cardiac fibroblasts and myocytes, we found that differential adhesion increased. Contemporaneous work in our lab indicates that treatment of cryoinfarcted hearts with ACT-1 reduces the propensity for arrhythmia. The work reported here implies potential roles for connexon transitions between hemichannels and GJs in the pathology and treatment of heart failure. South Carolina Space Grant Consortium

164 ZO-1 Regulates the Phosphorylation of Connexin 43 At Its Carboxyl Terminus, Joseph Palatinus, Robert Gourdie; Regenerative Medicine and Cell Biology, MUSC.

Abstract not available.

165 Regulation of VCAM-1 By Retinoid and TGFb Signaling During Formation of the Epicardium, M Elizabeth Burton, Laura E Brichler, Loretta L Hoover, Steven W Kubalak; Regenerative Medicine and Cell Biology, MUSC, College of Charleston.

The normal formation of the epicardium, the outer cell layer of the heart, is critical for subsequent development of the heart to proceed normally. The epicardium is derived from the proepicardium (PE), a group of mesothelial cells that forms during embryonic day (E) 9.0 in the mouse. By E10-10.5 the PE-to-epicardium transition is nearly complete and the heart is fully covered with epicardium by E11. Abnormalities in the epicardium lead to cardiac defects as shown in the retinoid X receptor a knockout mouse (RXRα-/-), a model of congenital heart disease that exhibits many cardiac malformations including epicardial defects. The RXRα-/- epicardium is slower to form and once formed, it is detached from the myocardium. The critical time point for normal epicardial attachment is between E11.5 and E12.5, with some minimal detachment being normal only at E11.5. We have also previously observed that transforming growth factor β2 (TGFβ2) is elevated in RXRα-/- hearts at midgestation. We speculate that disturbances in cell adhesion either the subepicardial extracellular matrix (ECM) or neighboring myocardial cells will result in epicardial detachment, and that this process is regulated by TGFβ2 and/or retinoid signaling. Expression of vascular cell adhesion molecule (VCAM-1), a transmembrane protein known to be involved in cell adhesion, is increased (mRNA and protein) in the RXRα-/- heart at E12.5 and E13.5 compared to the wild type (WT). Interestingly, VCAM-1 protein expression levels are similar to WT in the RXRα-/- mouse at E11.5. We also observe a misexpression of VCAM-1 in the epicardium of the RXRα-/-, which could negatively impact epicardial cell adhesion. Using a rat epicardial (REC) cell line we have observed that TGFβ2 treatments cause a downregulation of VCAM1. Chromatin immunoprecipitation (ChIP) has also revealed that both RXRα and Smad4 are able to bind to the VCAM1 promoter. Therefore, we hypothesize that misexpression of VCAM1 is the result of misregulation of TGFβ2 and/or retinoid signaling and that VCAM1 misexpression in the epicardium, as in the RXRα-/-, disrupts epicardial cell adhesion to the underlying myocardium by causing preferential binding of integrin α4 in the epicardium to VCAM1 in neighboring epicardial cells instead of myocardial cells. HL83116
Evidence of a Novel Cove Visual Cycle in the Mammalian Retina, Ryan O Parker1, Rosalie K Crouch2; 1Graduate Studies, Neurosciences, MUSC, 2Medicine, Ophthalmology, MUSC.

Absotact not available.

Absence of Sphingosine Kinase 1 Inhibits Joint Erosions and Local Inflammation in TNF-alpha Induced Arthritis, DeAnna A Baker1, Lina M Obeid2, Gary S Gilkeson3; 1MUSC, 2Medicine, Rheumatology, VA, 3Medicine, VA.

Sphingolipids, constituents of the plasma membrane, can alter cellular functions. Sphingosine 1 phosphate (S1P) in vitro is required for TNFα induced COX-2 and PGE2. Stimulation with TNFα and S1P leads to more COX-2 and PGE2 than either alone. Both sphingosine kinase (SphK) 1 and 2 are upregulated in rheumatoid synovium compared to osteoarthritis synovium. S1P1R, an S1P receptor, is upregulated in RA patients. Fibroblast-like synoviocytes (FLS) proliferate with proinflammatory cytokines and produce COX-2 and PGE2 with TNFα and S1P. We hypothesized that S1P is a critical modulator of inflammation and joint damage in rheumatoid joints. Transgenic hTNFα mice crossed with SphK1-/- mice were observed weekly for disease activity. CT images and microarray analysis evaluated disease activity and genetic profiles respectively. Mouse synoviocytes were isolated from knee joints of WT and SphK1-/- mice, cultured, and stimulated with TNFα. OA and RA synoviocytes were cultured and stimulated with hTNFα. hTNF/SphK1-/- mice had significantly decreased joint disease compared to hTNF/SphK1+/+ mice at 5 months. An erosion index was significantly decreased in hTNF/SphK1-/- mice at 4 and 5 months. Microarray analysis demonstrated significant modulation SOCS3 regulated genes in hTNF/SphK1-/- mice compared to hTNF/SphK1+/+ mice. Synoviocytes from SphK1-/- mice, stimulated with TNFα produced significantly less IL-6 and PGE2 than synoviocytes from WT mice. Similarly, human RA synoviocytes stimulated with TNFα and treated with a SphK2 inhibitor produced significantly less IL-6 and PGE2 than cells treated with TNFα alone. Genetic deletion of SphK1 significantly decreased the severity of hTNFα induced arthritis, decreased erosions and led to upregulation of SOCS3 with impact on related genes. Lack of SphK1 resulted in decreased PGE2 and IL6 production by mouse and human synoviocytes in response to TNFα. These data indicate that S1P plays a key role in TNFα induced joint inflammation and erosions and a potential target for therapeutics. R01GM062887 from the National Institute Of General Medical Sciences; ACR Research and Education Fund; 1F31AR057307-01 from National Institute of Arthritis and Musculoskeletal and Skin Diseases

A Proposed Role for Sphingosine Kinase 1 in the P53 Pathway: Implications in Carcinogenesis and Thymic Development, Linda A Hefferman-Stroud1, Lina M Obeid2; 1MUSC MSTP, MCBP, DOM, VA, 2DOM, VA.

Absotact not available.

Regulation of CC Ligand 5/RANTES By Secretory Acid Sphingomyelinase – Implications for Compartmentalization of Ceramide Formation, Russell W Jenkins, Christopher J Clarke, Daniel N Canals, Jolanta Idkowiak-Baldys, Kazuyuki Kitatani, Yusuf A Hannun; Biochemistry and Molecular Biology, MUSC.

Abstract not available.

Host Sphingosine Kinase 1 and Its Product Sphingosine-1-Phosphate Modulate the Phagocytosis of Cryptococcus Neoformans By Alveolar Macrophages, Travis J McQuiston, Maurizio Del Poeta; MUSC.

The pathogenic fungus Cryptococcus neoformans (Cn) is a major cause of morbidity and mortality in individuals with an immunocompromised state caused by human immunodeficiency virus (HIV) infection, solid organ transplantation, lymphoma and/or prolonged administration of corticosteroids. Following environmental exposure, Cn is inhaled into the lungs lodging in the alveolar spaces. As a facultative intracellular pathogen, Cn can survive in the extracellular environment of the alveolar spaces and, upon phagocytosis, within the phagolysosomes of alveolar macrophages (AMs). Under conditions not fully defined, Cn is can disseminate to cause life-threatening meningocelphalitis. Studies have shown that AM can exacerbate disease progression during immune suppression. Therefore, AMs serve an imperative role in determining the outcome of cryptococcal infection. Sphingosine kinase 1 (SK1) and its bioactive product sphingosine-1-phosphate (S1P) play a major role modulating the functions of lymphocytes, including the antimicrobial actions of AM. It is unknown if SK1 and S1P have a role affecting the outcome of invasive fungal diseases such as cryptococcosis. In this research, we investigated the effect of SK1 and S1P on the host immune response, specifically alveolar macrophages, in response to Cn. Using wild-type (SK1+/+) and SK1-deficient (SK1-/-) mice in a murine model of pulmonary cryptococcosis, we found SK1 does not affect the virulence of the facultative intracellular (wild-type) Cn strain but it is essential to the development of granulomatous inflammation required to prevent the dissemination of an obligate intracellular Cn strain. Furthermore, we found SK1 to regulate the phagocytosis of Cn by AMs while observing extracellular S1P to increase phagocytosis through a SK1-independent, S1P receptor 2-mediated mechanism. We believe this is the first research implicating the SK1-S1P pathway to directly affect the host immune response to an infectious microorganism through the regulation of phagocytosis.

Sphingosine 1 phosphate (S1P) is a major cause of morbidity and mortality in individuals with an immunocompromised state caused by human immunodeficiency virus (HIV) infection, solid organ transplantation, lymphoma and/or prolonged administration of corticosteroids. Following environmental exposure, Cn is inhaled into the lungs lodging in the alveolar spaces. As a facultative intracellular pathogen, Cn can survive in the extracellular environment of the alveolar spaces and, upon phagocytosis, within the phagolysosomes of alveolar macrophages (AMs). Under conditions not fully defined, Cn is can disseminate to cause life-threatening meningocelphalitis. Studies have shown that AM can exacerbate disease progression during immune suppression. Therefore, AMs serve an imperative role in determining the outcome of cryptococcal infection. Sphingosine kinase 1 (SK1) and its bioactive product sphingosine-1-phosphate (S1P) play a major role modulating the functions of lymphocytes, including the antimicrobial actions of AM. It is unknown if SK1 and S1P have a role affecting the outcome of invasive fungal diseases such as cryptococcosis. In this research, we investigated the effect of SK1 and S1P on the host immune response, specifically alveolar macrophages, in response to Cn. Using wild-type (SK1+/+) and SK1-deficient (SK1-/-) mice in a murine model of pulmonary cryptococcosis, we found SK1 does not affect the virulence of the facultative intracellular (wild-type) Cn strain but it is essential to the development of granulomatous inflammation required to prevent the dissemination of an obligate intracellular Cn strain. Furthermore, we found SK1 to regulate the phagocytosis of Cn by AMs while observing extracellular S1P to increase phagocytosis through a SK1-independent, S1P receptor 2-mediated mechanism. We believe this is the first research implicating the SK1-S1P pathway to directly affect the host immune response to an infectious microorganism through the regulation of phagocytosis.
171 Bcr-abl Dependent Regulation of Sphingomyelin Synthase

SMS is the class of enzymes responsible for production of sphingomyelin (SM) in mammalian cells by transferring the phosphorylcholine moiety from phosphatidylcholine (PC) onto ceramide forming SM and diacylglycerol (DAG). Since SMS can up- and down-regulate levels of ceramide, a negative regulator of cell growth and promoter of differentiation, and DAG, a well-established mitogenic factor, SMS activity may play an important role in regulating pathologies associated with aberrant cell proliferation and differentiation. Preliminary data obtained from our lab showed that K562 cells, a cellular model for chronic myelogenous leukemia (CML) because of the expression of the bcr-abl oncogene, presented elevated SMS activity and SMS1 protein compared to other leukemia and lymphoma cells lines. Importantly, increased SMS activity observed in K562 cells was recapitulated by stable expression of bcr-abl in otherwise bcr-abl negative cells whereas inhibition of the tyrosine kinase activity of bcr-abl decreased SMS activity in a time and dose-dependent manner. Expression analysis and modulation of gene expression of the two known genes responsible for SMS activity, SMS1 and SMS2, suggested that enhanced expression of SMS1, and not SMS2 was responsible for increased SMS activity in bcr-abl-positive versus negative cells, and the elevated SMS1 expression resulted from enhanced transcription. Functionally, inhibition of SMS/SMS1 activity inhibited cellular proliferation and promoted differentiation of bcr-abl-positive blasts. Pharmacological inhibition of SMS caused accumulation of ceramide and decreased DAG levels, validating the proposed enzymatic role of SMS. Furthermore, cell line obtained data were corroborated in progenitor cells isolated from patients with blast crisis CML. Future experiments will focus on examining the role of SMS1 in CML and elucidating Bcr-abl mediated transcriptional activation of SMS1.

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172 Sphingosine-1-Phosphate Receptor Signaling in Embryonic Blood Vessel Formation

S1P signaling is mediated by a family of receptors that presently includes five members, S1P1-5. Targeted deletion of S1P receptors (S1P1-3) has revealed the critical importance of S1P signaling to maturation of blood vessels formed during development. However, these studies suggest that S1P receptors are not essential for the assembly of primitive vascular structures during embryonic development. By contrast, S1P signaling has been shown to promote formation of primitive vascular networks in the allantois explant model of de novo blood vessel formation. To reconcile the disparate findings concerning the role of S1P signaling in the process of embryonic blood vessel formation, we sought to determine whether receptors other than S1P1-5 are mediating S1P signaling events critical to vasculogenesis and angiogenesis. Four other G-protein coupled receptors, Gpr3, 6, 12, and 63 are known which transduce signals following S1P stimulation. Using RT-PCR, the expression of all known S1P receptors was evaluated in angioblasts and early endothelial cell populations isolated from whole mouse embryos. In addition to S1P1-3, only Gpr63 was expressed in early endothelial cells and angioblast precursors. Furthermore, pharmacological antagonists of S1P1-3 did not disrupt salient aspects of blood vessel formation in cultured allantois explants. Together, these findings implicate a S1P receptor other than S1P1-5, possibly Gpr63, in embryonic blood vessel formation.

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173 Uncovering the Antibiotic Potential of the Marine Bacterium Pseudovibrio Denitrificans

Antibiotics, an important defense against infectious pathogens, are most often microbial natural products or their analogs. Due to the increased emergence of antibiotic-resistant bacteria, the search for novel antibiotics has prompted research in different ecosystems, including the diverse microbial community found in the coral surface mucopolysaccharide layer (SML). Coral degradation has increased the urgency to characterize the coral-associated bacteria that might produce these antibiotics due to their suggested chemical defense role against pathogens. In our studies, we are characterizing the chemical ecology of Charleston, Hollings Marine Laboratory.
of the microbial community in the gorgonian octocoral, Pseudopterogorgia americana. We hypothesize that P. americana SML-associated bacteria are a source of novel antibiotics. We first conducted an antimicrobial bioassay on 142 bacteria isolated from P. americana's SML using seven test strains known to be human or coral pathogens. One coral isolate, with 99% 16S rDNA similarity (1200 b.p.) to Pseudovibrio denitrificans demonstrated antibiotic potential against all seven test strains. To further characterize its antibiotic compound(s), the cell-free supernatant was extracted using dichloromethane, acetone, and methanol. The acetone extract inhibited Gram-positive Kocuria rhizophila, and the methanol extract inhibited Gram-positive Bacillus subtilis and Gram-negative Vibrio harveyi and V. corallilyticus. A bioassay-guided fractionation of the MeOH extract using high-performance liquid chromatography suggests the presence of at least two antibiotics in this extract, one inhibiting the Gram-negative and one inhibiting the Gram-positive bacteria. Studies are on-going to isolate, purify, and structurally characterize the three chemically distinct antibiotics using liquid chromatography, mass spectrometry, and nuclear magnetic spectroscopy. Pseudovibrios, a bacterium only found in marine environments, have not been widely studied for their production of antibiotics. These results highlight the potential of Pseudovibrio denitrificans as a viable source of bioactive natural compounds. Supported by the Sea Grant, National Ocean Service (NOS), NIH's Initiative for Maximizing Student Diversity, and the National Science Foundation Biodiversity Surveys and Inventories Program.

Salinity Effects on DMSP Concentrations in Fragilariopsis Cylindrus, Barbara R Lyon1, Peter A Lee2, Michael G Janech3, Giacomo R DiTullio2; 1College of Graduate Studies, Marine Biomedicine Environmental Science, MUSC, 2Hollings Marine Lab, College of Charleston, 3Department of Medicine, MUSC, Ralph H. Johnson VA Medical Center.

Abstract not available.

The Red Tide Dinoflagellate, Karenia Brevis, Exhibits Chloroplast-Associated Metacaspase Activation and Caspase-Like Activities During Senescence, Jillian G Lynch1, Frances M Van Dolah2; 1CGS, MBES, MUSC, 2Marine Biotoxins Program, NOAA, CCEHBR.

The dinoflagellate Karenia brevis is responsible for near annual harmful algal blooms in the Gulf of Mexico that cause extensive ecological and economic losses. Evaluation of bloom termination in other bloom forming phytoplankton has implicated a role for metacaspases, caspase orthologs, in regulating programmed cell death (PCD). We have identified five metacaspases (KbMC 1 – 5) in K. brevis all containing the well-conserved caspase catalytic diad and p20 domain previously identified in other unicellular organisms. Metacaspase expression over a growth curve, characterized by immunoblotting with a polyclonal Emiliania huxleyi metacaspase antibody, revealed an induction of both metacaspase type and quantity in stationary phase/senescent cultures. Metacaspase expression was further characterized in logarithmic and stationary phase cultures using a peptide antibody developed against the conserved histidine active site of KbMC1 and KbMC2. Preliminary results indicate an induction of full-length KbMC1 and 2 in stationary phase cultures, as well as the activated p20 domain cleavage products, suggesting both an increase in metacaspase protein abundance and activation in senescent cells. Subcellular fractionation of K. brevis followed by immunoblotting with anti-KbMC1 demonstrated that the activated form of KbMC1/2 was localized to the chloroplast, suggesting a possible role of the photosynthetic machinery in the induction of PCD. Caspase-like activities over a growth curve were characterized by quantifying the cleavage of fluorogenic canonical caspase tetrapeptides, and demonstrated that K. brevis exhibits a significant increase in caspase-like activities during the transition from early to late senescence. Together these data indicate that K. brevis may be upregulating and utilizing PCD machinery during late senescence prior to culture demise. Further characterization of PCD signaling during HAB demise is aimed at developing molecular biomarkers predictive of terminating blooms, which will contribute to improved forecasting models designed to mitigate impacts on coastal resources, local economies, and threats to public health. Funding provided by NOAA Oceans and Human Health Initiative Pre-Doctoral Fellowship and NOAA National Ocean Service’s Center for Coastal Environmental Health and Biomolecular Research.

Post-transcriptional Regulation of the DNA Replication Fork Protein, PCNA, in the Florida Red Tide Dinoflagellate, Karenia Brevis, Stephanie A Brunelle1, Frances M Van Dolah2; 1MBES, MUSC, 2CCEHBR, NOS, NOAA.

The dinoflagellate, Karenia brevis, produces harmful algal blooms that cause marine animal mortalities and human illness on a nearly annual basis. The molecular mechanisms controlling the cell cycle in this dinoflagellate are important because blooms develop through vegetative cell division. Microarray and qPCR studies demonstrate that, unlike typical eukaryotes, dinoflagellate cell cycle genes are not regulated at the transcriptional level, including replication fork proteins that are typically activated by the E2F transcription factor at the restriction point, which regulates S-phase entry. Post-transcriptional control of these genes is further suggested by the presence of a trans-spliced leader sequence on their transcripts. Here, we investigated whether the expression of the replication fork protein, PCNA, is regulated at the translational or post-translational level. Immunolocalization shows that K. brevis PCNA is constitutively present throughout the cell cycle. However, its distribution within the nucleus changes,
spread among infected Sarasota dolphins revealed lacaziosis lesions among several dolphin cases. Results were used to quantify and compare the progression of prevalence in this dolphin community where the disease and pathology reports) were used to estimate lacaziosis assessment data (i.e. photographs, veterinary records, inhabiting Sarasota Bay, Florida. Cross-sectional health resident bottlenose dolphin (Tursiops truncatus) community and health assessment data to study lacaziosis in a disease. The present study uses long-term photographic inoculation studies have provided the sumoylation post-translational modification. Thus, it appears that the expression and activity of PCNA is controlled at both the translational and post-translational levels, in the absence of transcriptional regulation. Marine Biotoxins Program, National Ocean Service, NOAA

177 The Bottlenose Dolphin (Tursiops Truncatus) As a Model Species to Study Infectious Disease: Lacaziosis (Lacazia Loboi), Leslie G Burdett1, Randall S Wells2, Jeffrey D Adams3, David S Rotstein4, Teri K Rowles5, William A McLellan6, D H Pabst6, Lori H Schwacke6; 1Graduate Studies, Biostatistics and Epidemiology, MUSC, 2Chicago Zoological Society, Mote Marine Laboratory, Sarasota, FL, 3NOAA, Center for Coastal Environmental Health and Biomolecular Research, 4University Corporation for Atmospheric Research, 5NOAA/NMFS, Office of Protected Resources, 6Biology and Marine Biology, University of North Carolina at Wilmington, 7NOAA, Center for Human Health Risk; Graduate Studies, Biostatistics and Epidemiology, MUSC.

Lacaziosis (a.k.a. lobomycosis, Lacazia loboi) is a chronic, fungal skin disease known to naturally infect only humans and dolphins. The pathogen causing lacaziosis has not been successfully cultured in vitro, and, for both humans and dolphins, the source of the disease is unknown. Furthermore, lacaziosis inoculation studies have provided limited data on the progression and pathogenicity of the disease. The present study uses long-term photographic and health assessment data to study lacaziosis in a resident bottlenose dolphin (Tursiops truncatus) community inhabiting Sarasota Bay, Florida. Cross-sectional health assessment data (i.e. photographs, veterinary records, and pathology reports) were used to estimate lacaziosis prevalence in this dolphin community where the disease has occurred since the early 1970s. Longitudinal photographic data and nonlinear growth modeling were used to quantify and compare the progression of lacaziosis lesions among several dolphin cases. Results from these epidemiological analyses indicated that the prevalence of lacaziosis among Sarasota dolphins was approximately 3% and comparable to estimates from other populations. Growth modeling of lacaziosis lesion spread among infected Sarasota dolphins revealed that disease progression varied among individuals, with growth rates ranging from 0.5% to 5% per year. Finally, bottlenose dolphin stranding data have provided evidence to suggest that the geographic distribution of lacaziosis may be changing as infected cases have emerged among previously naïve populations. We believe that bottlenose dolphins with a long-term case history of lacaziosis can serve as a model species to better understand lacaziosis progression, endemnicity, and susceptibility. Ultimately, these studies may improve our comprehension of the disease process in humans.

178 Transcriptional Control and Targeting of Acid Ceramidase in Prostate Cancer Radiotherapy, Joseph C Cheng1, Lorianne S Turner1, Ayman EM Mahdy1, Thomas H Beckham1, Jun Li2, S Tucker Morrison1, Xiang S Liu1, James S Norris1; 1Microbiology and Immunology, MUSC, 2Radiation Oncology, MUSC.

Radiation resistance in a subset of prostate cancer cells remains a challenge to prostate cancer radiotherapy. The current study on the effects of ionizing radiation on prostate cancer cells reveals that radiation programs an unpredicted resistance mechanism by activating transcription of acid ceramidase (ASAH1). Irradiated cells demonstrate limited changes of total ceramide levels while elevating levels of sphingosine and sphingosine-1-phosphate. However, luciferase-promoter-reporter assays show that radiation-induced accumulation of specific ceramide species correlates with ASAH1 transcription. What is more, transcriptional activation of ASAH1 by exogenous administration of ceramide suggests that pathways of intracellular biosynthesis of long-chain ceramides may mediate radiation-induced ASAH1 transcription. By selectively down-regulating acid ceramidase with RNA interference, we observe radio-sensitization of cells using clonogenic and cytotoxicity assays. Conversely, acid ceramidase over-expression further decreases sensitivity to radiation. Finally, utilization of the small molecule AC inhibitor, LCL385, sensitizes PPC-1 prostate cancer cells to radiation and significantly decreases tumor xenograft growth. These data suggest a new mechanism of cancer cell resistance to radiation, through up-regulation of acid ceramidase that is, in part, mediated by application of the therapy itself. An improved understanding of radiation therapy and the application of combination therapy itself. An improved understanding of radiation therapy and the application of combination therapy achieved in this study offer new opportunities for the modulation of radiation effects in the treatment of cancer. Supported by NIH P01 CA097132.

179 Effects of Second Hand Smoke on Dendritic Cell Regulation and Function in Chronic Rhinosinusitis, Jennifer K Mulligan1, Carl Atkinson2, Rodney J Schlosser1; 1Otolaryngology, MUSC, 2Microbiology & Immunology, MUSC.

In healthy adults, the immune system rests in a low level balance between T helper 1 (Th1) and T-helper 2 (Th2) responses; however in chronic rhinosinusitis (CRS) this
balance is disrupted. CRS can further be subdivided into two main categories each with differing immune phenotypes: CRS without nasal polyps (CRSwNP) which display elevated levels of both Th1 and Th2 cytokines and CRS with nasal polyps (CRSsNP) which is heavily Th2 skewed. In our preliminary studies we examined the role of antigen presenting dendritic cells (DCs), which are capable of regulating Th1/Th2 immunity, to determine their contribution to the immunopathology of CRS. Based on these results we hypothesize that cigarette smoke stimulates nasal epithelial cells to upregulate DC maturation and induces DCs to skew T-cells toward a Th2 phenotype ultimately resulting in the exacerbation of Th2 inflammation in CRS. Furthermore, it is hypothesized that patients with CRSwNP will demonstrate increased number of mature DCs. Results of earlier studies demonstrated that CRSwNP and CRSsNP patients had increased numbers of mature DCs in their peripheral blood and sinus tissue compared to controls. Additionally, there was an increased number of Th2-biased DCs in the peripheral blood of CRSsNP patients. In addition, in vitro studies demonstrated that cigarette smoke extract (CSE) exposure causes human sinonasal epithelial cells (HSNEC), from healthy controls, to induce DC maturation and increase DC production of Th2-promoting cytokines. The results of our preliminary studies demonstrate that CSE induces HSNEC to secrete products that stimulate DC maturation and skews their cytokine secretion profile to support initiation of T-cell Th2 immunity. These changes are similar to the altered immune phenotype observed in CRS, suggesting that exposure to SHS may exacerbate the already altered immune phenotype of CRS. Support by grants to RJS from the Flight Attendant Medical Research Initiative and to JKM from the American Academy of Otolaryngic Allergy.

180 Mechanism of Long Range Looping-Mediated Termination of DNA Replication in Schizosaccharomyces Pombe, Samarendra K Singh, Deepak Bastia; Biochemistry and Molecular Biology, MUSC.

Programmed replication termination in eukaryotes performs important physiological functions such as prevention of collision between a replication fork and transcription coming from opposite direction, cellular differentiation, and control of transcription and recombination. In this work we have investigated the role of Reb1 protein of S. pombe, which is a homolog of mammalian c-myb oncprotein, mediated looping-dependant termination of DNA replication. Because of close structural and functional similarities between Reb1 and c-myb, the former serves as an excellent model system to study problems of basic cancer biology such as long range, protein-mediated intra-chromosomal site-site interactions in controlling fork arrest and genome stability. We have shown that the full length Reb1p, which exist as a dimer, loops DNA over long distances both in vitro and in vivo. To investigate this phenomenon in vivo, we have designed a novel assay by positioning a mutated Reb1 site, which can no longer arrest replication forks in a self replicating S. pombe plasmid, at a distance of 1.2 kb from a functional Reb1 site in such a way that fork arrest at the mutated Ter site can be facilitated only if the protein can bring the mutated and the normal sites into productive contacts and loop out the 1.2 kb of the intervening DNA. Hence Reb1 can convert a nonfunctional replication terminus into a functional one by promoting action at a distance. For the first time we also have discovered, a fully functional Reb1 site outside the rDNA. Replication termination is enhanced at this site in presence of full length protein compared to the non looping mutant. The results have important implications for the investigations of eukaryotic myb like proteins that control replication and transcription. We have crystallized a Reb1- DNA complex that diffract to high resolution and collaborative work (at VCU, Richmond, VA) is in progress to solve its structure. Supported by grants from NIAID and NIGMS of the National Institute of Health to D.B. We thank Carlos Escalante and Rahul Jaiswal for collaborative work to solve the structure at VCU Richmond. We are also thankful to Suzan Forsburg and Sarah Sabatinos of University of Southern California.

181 Hematopoietic Stem Cells Repair Ionizing Radiation-Induced DNA Double Strand Breaks in a Cell Cycle-Dependent Manner, Senthil Kumar Pazhanisamy, Ningfei An, Yong Wang, Daohong Zhou; Pathology & Laboratory Medicine, MUSC.

Mice with mutations in various DNA repair genes exhibit accelerated aging due to hematopoietic stem cell (HSC) premature exhaustion, indicating that DNA repair is crucial for the maintenance of HSC self-renewal and hematopoietic function. However, how HSCs respond to genotoxic stress and repair DNA damage have not been well established. In this study, DNA damage and repair were analyzed to quantify IR-induced DNA double strand breaks (DSBs) in HSCs (Lin- c-kit+ Sca1+ cells) and hematopoietic progenitor cells (HPCs; Lin- c-kit- Sca1- cells) isolated from adult mouse bone marrow (BM) after the ionizing radiation (IR). Our results demonstrated that HPCs repaired the damage within 6 h after IR, whereas more than 50% DSBs were unrepaird by HSCs even at 24h after IR, indicating that HSCs are highly deficient in repair of IR-induced DSBs. The deficient DSBs repair in HSCs is attributable to their quiescence, as sorted quiescent PyroninY-low HSCs were more deficient in repairing the damage than cycling PyroninY-high HSCs. This suggestion is further supported by the observations that fetal liver HSCs and HSCs isolated from 5-FU-treated adult mouse BM repaired the damage as efficiently as HPCs. In addition, stimulation quiescent PyroninY-low HSCs into the cell cycle can promote HSCs to repair DNA damage. The difference in repair of IR-induced DSBs between quiescent and cycling HSCs is not because they express different levels of key proteins (such as Ku70, Ku80, DNA-PKcs, Lig4, XRCC4, Dclre1c, Nhej1,
Brac-1, Brac-2, MRE11a, Nbs1, Rad50, Rad51, and ATM). Instead, quiescent HSCs exhibited an insignificant activation of DNA-PKcs and minimal formation of XRCC4 and Rad51 foci after exposure to IR. These findings provide crucial insights into how HSCs respond to and repair DNA damage, which could significantly advance our understanding on how HSCs maintain their genomic stability. Supported in part by National Cancer Institute of NIH research grant R01CA86860 & CA122023.

182 Identification and Characterization of C9 Methyl Transferase Gene in Cryptococcus Neoformans, Arpita Singh1, Liana Casquinha da Silva2, Maurizio Del Poeta3; 1Biochemistry and Molecular Biology, MUSC, 2Instituto Superior Tecnico, Portugal, 3Biochemistry and Molecular Biology, Microbiology and Immunology, MUSC.

Abstract not available.

183 Key Role for Neutrophil Sphingolipids in the Killing of Cryptococcus Neoformans, Asfia Qureshi1, Angus Grey2, Kevin Schey2, Chiara Luberto1, Maurizio Del Poeta3; 1Medicine, Biochemistry and Molecular Biology, MUSC, 2Medicine, Cell and Molecular Pharmacology and Experimental Therapeutics, MUSC, 3Medicine, Biochemistry and Molecular Biology, Microbiology and Immunology, MUSC.

The key host cellular pathway(s) that are necessary to control the infection caused by inhalation of the environmental fungal pathogen Cryptococcus neoformans (Cn) are still largely unknown. In this study, we will show that the sphingolipid pathway in neutrophils is required to exert their killing activity on the fungus. Using both pharmacologic and genetic approaches, we found that inhibition of sphingomyelin synthase (SMS) activity profoundly impairs the killing ability of neutrophils by preventing the extracellular release of an antifungal factor(s). Inhibition of protein kinase D 1 (Pkd1), which controls vesicular sorting and secretion and is regulated by diacylglycerol (DAG) produced by SMS, totally blocks the extracellular killing activity of neutrophils against Cn. The expression of SMS genes, SMS activity and the levels of the lipids regulated by SMS (namely sphingomyelin, SM and DAG) are up-regulated during neutrophil differentiation. Finally, tissue imaging of lungs infected with Cn using matrix-assisted laser desorption-ionization mass spectrometry (MALDI-MS), revealed that certain SM species are associated with neutrophil infiltration at the site of the infection. This study establishes a key role for SMS in the regulation of the killing activity of neutrophils against Cn through a DAG-Pkd1 dependent mechanism, and provides new insights not only for a better understanding of fungal pathogenesis but also for the development of new therapeutic strategies against fungal microbes.

184 Role of Sphingomyelin Synthases in Protein Secretion, Subathra Marimuthu, Del Poeta Maurizio, Chiara Luberto; Biochemistry and Molecular Biology, MUSC.

Sphingomyelin synthases (SMS1 and 2) represent a class of enzymes that transfer a phosphocholine moiety from phosphatidylcholine onto ceramide thus producing sphingomyelin and diacylglycerol (DAG). SMS1 localizes in the golgi, and SMS2 localizes at the golgi and plasma membrane. Previous studies from our laboratory showed that modulation of SMS1 and, to a lesser extent, of SMS2 affected the formation of DAG at the Golgi apparatus. Similarly, down-regulation of SMS1 and SMS2 reduced the localization of the DAG-binding protein, protein kinase D (PKD) to the Golgi. Since PKD recruitment to the Golgi has been implicated in cellular secretion through the trans golgi network (TGN), the effect of down-regulation of SMSs on TGN to plasma membrane trafficking was studied. Down regulation of either SMS1 or SMS2 significantly retarded trafficking of the reporter protein vesicular stomatitis virus tagged with green fluorescence protein (VSVG3-GFP) from the TGN to the cell surface. Since a recent study demonstrated the requirement of PKD activity for insulin secretion in beta cells, we tested the function of SMS1 and/or SMS2 also in this model. Inhibition of SMS activity significantly reduced insulin secretion by rat INS-1 cells. All together these results provide the first direct evidence that both enzymes (SMS1 and 2) are capable of regulating TGN-mediated protein secretion.

185 N-cadherin-ZO-1 Complexes Coupled to Actin Polymerization Drive Membrane Remodeling of Cx43 Gap Junctions, Andrew W Hunter, Robert G Gourdie; Regenerative Medicine and Cell Biology, MUSC.

Cadherin adhesion is critical for the maintenance of gap junctions (GJs) in excitable membranes. In Hela cells, N-cadherin colocalizes with ZO-1 and F-actin at the periphery of Cx43 GJs. Mutant analysis revealed juxtaposition of N-cadherin-ZO-1 complexes with GJs was independent of PDZ-mediated ZO-1 binding to Cx43. However, blocking Cx43-ZO-1 interaction suppressed protrusive activity at GJ edges. Interestingly, positioning of N-cadherin puncta at GJ edges and coalescence of ZO-1 into discrete foci preceded the formation of finger-like protrusions of Cx43 channels. Maximum extension of channels coincided with acceleration of ZO-1 and N-cadherin puncta localized at the tips of protrusions, suggestive of an active pulling force. Inhibition of actin polymerization caused N-cadherin to segregate from GJs and limited the mobility of Cx43 channels. We propose N-cadherin-ZO-1 complexes engage and redistribute Cx43 channels at cell contacts by harnessing the force produced by actin polymerization. NIH grants HL56728, K12GM081265.
Bone Marrow Contribution to Heart Valve Remodeling in Response to Myocardial Infarction, Zoltan Hajdu, Roger R Markwald, Richard P Visconti; Regenerative Medicine and Cell Biology, MUSC.

Stem cell-based therapy for repair of damaged cardiac tissues is an area of avid research focus due to its potential to reduce human mortality associated with cardiovascular disease. While the infarcted myocardium has received considerable focus, the cardiac valves, which are known to undergo pathological remodeling in response to post-infarction myocardial remodeling, have received very little attention. We have previously shown, using a mouse model of EGFP+ hematopoietic stem cell transplantation, that cells of donor origin participate in physiological turnover of the valvular interstitial cell population. Using this model, combined with permanent LAD ligation, we investigated the changes occurring in the heart valves in response to infarction. We have previously reported that EGFP+ cells migrate into the infarcted myocardium. In addition to leukocytes that clear the cell debris, myofibroblasts and fibroblasts (SMAA+, SMemb+, Hsp47+) of donor origin were present. We detected rare bone marrow-derived myocytes in normal and infarcted hearts, but never in the infarct region. We also observed that the anterior leaflet of the mitral valve (which is anchored to the infarcted myocardium) exhibited significant post-infarction thickening. Enumeration of the valvular cells revealed that the total GFP+ cell number in the anterior mitral leaflet increased from 10.67% to 24.16%, and the GFP+/Hsp47+ cell number increased from 1.65% to 4.44%, compared with sham operated hearts. In addition to increased Hsp47 (a molecular chaperon of collagen synthesis) expression, most of the GFP+ valvular cells were also SMemb (non-muscle myosin) positive and alpha smooth muscle actin negative, suggesting a fibroblastic phenotype. Additionally, most of the GFP+ valvular cells were also CD45+ (common leukocyte antigen), which supports our previous report of their hematopoietic rather than mesenchymal origin. These findings suggest that, as with the myocardial wall, the heart valves undergo post-infarction remodeling with significant contribution from the hematopoietic compartment of the bone marrow. Supported by NIH-NCRR RR16434-08, AHA 0865325E to R.P.V. and NSF/EPSCOR EPS-0447660 & NSF – FIBR 0526854 and Foundation Leducq: Mitral 07CVD04 to R.R.M. and NIH-NCRR C06 RR018823, NIH-NCRR C06 RR015455 and NIH-NCRR 2 P20 RR16461-05A1.

Glucose Consumption Rates of Temporomandibular Joint Disc Cells, Lixia Zhang1, Jonathan Kuo2, Michael Kern3, Hai Yao1; 1MUSC, Clemson University, 2Clemson University, 3MUSC.

Introduction: The TMJ disc is a large avascular structure. Oxygen and glucose play critical roles in the metabolism of TMJ disc cells. Glucose is a general precursor for cellular glycosaminoglycan biosynthesis. The aim of this study was to investigate the effects of oxygen tension on the glucose consumption rates of TMJ disc cells. Methods: The TMJ disc isolated from 8-10 months old porcine TMJ discs. The confluenced first passage cells were cultured under 2.5, 5, 10 and 25 mM glucose concentration overnight, then further cultured under various oxygen tensions (21%, 5% and 1% O2) for 4 hours. The glucose consumption rates were measured with Sigma glucose (HK) assay kit. Results: The glucose consumption rate of TMJ disc cells was dependent on the glucose concentration of the medium and not on the oxygen tension applied during the 4 hours conditioning culture. The glucose consumption rate of the disc cells was significantly higher at 25 mM/L glucose, and fell with a decrease in glucose concentration for all values of oxygen tensions. Conclusion: The glucose consumption rate of TMJ disc cells was regulated by glucose concentration, was not dependent on oxygen tension. At 21% O2, the energy metabolism of TMJ disc cells is aerobic, but both aerobic and anaerobic metabolic pathway are present in lower O2. The results of this study support the idea that a fall in nutrient supply might be one pathway to disc degeneration. This study will provide a better understanding of the metabolisms of glucose in the TMJ discs. Supported by NIH P20RR-016461 and P20RR-017696.

Estimates of Cochlear Nonlinearities in Adults with Normal and Impaired Hearing, Gayla L Poling, Jayne B Ahlstrom, Amy R Horwitz, Judy R Dubno; College of Medicine, Otolaryngology - Head & Neck Surgery, MUSC.

The normally functioning auditory system exhibits cochlear nonlinearities, which are associated with high sensitivity, sharp tuning, and a compressive basilar-membrane response. A reduction of cochlear nonlinearities that accompanies damage to the cochlea’s outer hair cells due to age, excessive noise, or other ototoxic factors may result in reduced gain and a more linear basilar-membrane response, which may underlie perceptual difficulties experienced by individuals with cochlear hearing loss. The purpose of this study was to estimate cochlear nonlinearities in adults with normal hearing and mild-to-moderate cochlear hearing loss. A behavioral masking task was used to characterize the basilar-membrane input-output function. Typically, functions correspond to linear-compressed-linear segments, which are described in terms of breakpoints (input level corresponding to transition from the linear to compressive region), slope of the mid-level compressed region, and gain. Levels of tonal maskers required to just mask a low-level 1.0-kHz signal were measured with masker frequencies equal to (1.0 kHz) or below (0.5 kHz) the signal frequency as a function of the time delay (0-70 ms) between the masker and signal. Basilar-membrane response functions were estimated by comparing thresholds for masker frequencies equal to and below the signal frequency at each delay. Breakpoints, slopes, and gain were quantified for each
subject by applying a three-segment linear regression. Preliminary results revealed that mean gain was reduced and mean breakpoints were elevated for individuals with hearing loss, but mean compression slopes measured above the breakpoint were similar across subject groups. For individuals, a significant positive correlation was found between quiet thresholds at the signal frequency and breakpoints and a significant negative correlation between quiet thresholds and gain. Elevated breakpoints and reduced gain for individuals with cochlear hearing loss are consistent with a reduction in cochlear nonlinearities. [Work supported by NIH/NIDCD]. Supported by grants R01 DC00184 and P50 DC00422 from NIH/NIDCD.

189 Congenic Ly5.1 Mice – An Animal Model of Human Auditory Nerve, Vinu Jyothi¹, Manna Li², Daohong Zhou¹, Bradley A Schulte², Hainan Lang¹; ¹Pathology and Laboratory Medicine, MUSC, ²Pathology and Laboratory Medicine, Otolaryngology, MUSC.

Spiral Ganglion neurons (SGNs) are the primary carrier of auditory signals from the sensory hair cells to the brain. The SGNs are of two types, about 90-95% are type I which innervate the inner hair cells and the remaining are type II which carry signals to the outer hair cells. With the exception of humans, the soma of type I neurons of most mammalian species including rodents are heavily myelinated. In a previous study, we used a strain of Ly5.1 mice to investigate the role of hematopoietic stem cells in the adult mouse inner ear (Lang et al. 2006). Surprisingly, the regular morphological assessment revealed that the majority of the SGNs in the Ly5.1 mice were unmyelinated. In this study, we further examined the auditory phenotype of young adult Ly5.1 mice using light and electron microscopy, immunohistochemistry and electrophysiological measurements. Three different mouse strains (CBA/CaJ, C57/B6 and SJL/J) were used as controls. The data revealed several unusual characteristics in the Ly5.1 cochlea. Morphological analysis showed large aggregates of unmyelinated type I SGNs. Abnormal expression of myelin and gap junction proteins including CNPase, connexin 29 and connexin 43 were observed in the aggregated neurons. Corresponding to the above findings, delayed ABR wave latencies at low and middle frequencies were present. The ABR data also showed elevated thresholds and decline in the wave I amplitude I/O functions. Interestingly, this rodent model displays many features including unmyelinated SGNs similar to the human cochlea. Given this strong correlation with human cochlea, the Ly5.1 mouse model could be further exploited to understand the complexity of the human inner ear.

190 Fa2h Knockout Mice Exhibit Central Nervous System Disruption, Providing a Model of Human FA2H Deficiency, Kathleen A Potter¹, Michael J Kern², Jagadish K Venkatalar³, George Fullbright¹, Akbar A.K. Pathan¹, Bärbel Rohrer³, Xianlin Han³, Hiroko Hama¹; ¹Biochemistry and Molecular Biology, MUSC, ²Regenerative Medicine and Cell Biology, MUSC, ³Ophthalmology and Neurosciences, MUSC, ⁴Internal Medicine, Washington University School of Medicine.

Proper communication within the central nervous system (CNS) is dependent upon intact cell to cell neurotransmission. It is well established that neuronal communication is facilitated by and dependent upon axonal myelination. Fa2h (Fatty Acid 2-Hydroxylase) is present in many tissues, including nervous tissue. Within the CNS, Fa2h is responsible for the synthesis of galactosyl ceramide and sulfatide with hydroxyl fatty acid (hFA-galactolipids), a key component of myelin. Recently, it was discovered that a subset of human patients diagnosed with leukodystrophy with spastic paraparesis and dystonia had mutations in the FA2H gene. These patients exhibited a number of symptoms indicative of CNS disruption, including thinning of the corpus callosum and cerebellar atrophy. Recently we established a mouse model (Fa2h-/-) to evaluate the effects of a mutation in the Fa2h gene. Coincidentally, the mutation we created (deletion of exons 5 and 6) was the same as one of the mutations found in the human patients. HPTLC analysis confirmed that Fa2h-/- mice lacked hFA-galactolipids in the brain and sciatic nerve. Further, LC/MS/MS analysis was performed with spinal cord tissue, and, as expected, hFA-galactolipids were not detected. Similar to the human patients, we hypothesized that Fa2h-/- mice would exhibit CNS symptoms indicative of cerebellum disruption. As predicted, Fa2h-/- mice had had significantly reduced ambulation (especially vertical movements) relative to their littermate controls (p<0.01). Additionally, Fa2h-/- mice showed impaired motor coordination and motor learning when assessed using an accelerating rotarod device (p<0.01). Following behavioral testing, histological analysis of Fa2h-/- mice revealed significantly less cerebellar myelination and disrupted cellular organization, and reduced numbers of Purkinje neurons. All together, our Fa2h-/- mice provide a method not only for modeling human patients with this mutation, but also for understanding the role of Fa2h and hydroxy fatty acids in the development and maintenance of the central nervous system. Supported by NIH grants R03 NS056075 and R01 NS060807.
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