The Perry V. Halushka  
MUSC Student 2010  
Research Day  

Program and Abstracts  

Friday, November 5th 2010  

http://www.musc.edu/grad/srd/
Please stop by our Vendor Show in the Harper Center Gym next to the Poster Session and see what’s new!!
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 SRD2010 Chairman, Steven 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 SRD2010 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 5th. 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 12th in the Graduate Studies office on the 1st floor of the Basic Sciences Building. Any evaluation sheets not collected by November 19th 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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SRD2010 – SCHEDULE

FRIDAY, NOVEMBER 5th – Research Presentations

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

ORALS – CHP building A, 151-A Rutledge Ave, 2nd floor: rooms 201 – 207: 11:45 am – 3:15 pm

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Schedule of Oral Sessions:

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

"MicroRNA Control of Cardiovascular Development and Disease"

By:

Dr. Eric Olson
Robert A. Welch Distinguished Chair in Science
Annie and Willie Nelson Professorship in Stem Cell Research
Pogue Distinguished Chair in Research on Cardiac Birth Defects
Professor and Chair Department of Molecular Biology
University of Texas Southwestern Medial Center
Dallas, TX

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SATURDAY, NOVEMBER 6th – Careers Workshop XX
‘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: Stephen Bellum ('98), Patent Attorney; Cynthia Bristow ('79), Assistant Professor, Weill Cornell Medical College; Eric Buck ('07), Pentagon Force Protection Agency, PFPA Science and Technology Office; Martha Murtiashaw ('77, 81), Academia, Connecticut College; Britt Steed ('03), Account Manager, eBioscience
LOCATION OF ORAL PRESENTATIONS – SESSIONS 11-17

College of Health Professions, Building-A, 151-A Rutledge Avenue, 2nd floor

Access either:
a). from the Children's Hospital-Rutledge Tower crosswalk over Ashley Avenue at the 2nd floor level, or
b). through the Ashley Avenue Parking Garage to Rutledge Avenue to the main entrance on Rutledge.
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Student Research Day 2010 - Program

POSTER PRESENTATIONS

Harper Wellness Center Gym

8:30 am - 12:00 noon

Session 1: Undergraduate – I  #001-016
Session 2: Clinical Prof/Masters – I  #017-032
Session 3: Clinical Prof/Masters – II  #033-047
Session 4: Clinical Prof/Masters – III  #048-060
Session 5: PhD – I  #061-073
Session 6: PhD – II  #074-086
Session 7: PhD – III  #087-098
Session 8: PhD – IV  #099-109
Session 9: Postdocs/Residents/Fellows – I  #110-120
Session 10: Postdocs/Residents/Fellows – II  #121-132

ORAL PRESENTATIONS

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

Session 11: Undergraduates – II  CHP 204  11:45-3:15  #115-124
Session 12: Clinical Prof/Masters – IV  CHP 201  11:45-3:15  #125-135
Session 13: PhD – V  CHP 202  12:30-2:30  #136-147
Session 14: PhD – VI  CHP 203  12:15-2:45  #148-154
Session 15: PhD – VII  CHP 205  12:15-2:45  #155-166
Session 16: PhD – VIII  CHP 206  12:15-2:45  #167-178
Session 17: Postdocs/Residents/Fellows – III  CHP 207  11:45-3:15  #179-190
Session 1: Undergraduate I

001 Developmental Progression of Cortical GABA Transmission is Disrupted in a Rat Model of Schizophrenia, Michael T Weingarten¹, Heather Trantham-Davidson²; ¹Biology, College of Charleston, ²Neurosciences, MUSC.

002 Active Protease Involvement in Ethanol-Induced Apoptosis in Ventral Spinal Cord Motor Neurons, Kaushal S Patel, Stacy Roudabush, Nakul P Thakore, Jenna L Heissenbuttle, Varduhi H Knaryan, Ray K Swapan, Suprithi Samantaray, Naren L Banik; CofC.

003 Calpain Inhibition Protects Against Ethanol-induced Degeneration in Astroglial Cells, Nakul P Thakore¹, Jenna H Heissenbuttle², Stacy Roudabush³, Kaushal S Patel⁴, Varduhi H Knaryan⁵, Swapan K Ray⁶, Suprithi S Samantaray⁷, Naren L Banik⁸; ¹CofC, ²Trident Tech, ³New College of Florida, Sarasota, Florida, ⁴CofC, Charleston, SC, ⁵Neurosciences, MUSC, ⁶USC.

004 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, Sarah Ashton³, Perry V Halushka³, James Cook⁴; ¹Biology, Furman University, ²Neuroscience, MUSC, ³Graduate Studies, MUSC.

005 Assessing Vascular Comorbidities Among Hospitalized Parkinson's Disease Patients, Adam H Pearlman¹, Kenneth J Bergmann², Andrea A Boan¹, Daniel T Lackland¹; ¹Neurosciences, MUSC, ²FDA.

006 Modafinil Reverses Methamphetamine-Induced Memory Deficits on an Object-In-Place Task in Rats, Lauren A Ramsey¹, Carmela M Reichel², M Schwendt², J F McGinty², Ronald E See²; ¹College of Charleston, ²Neuroscience, MUSC.

007 Effects of Vasopressin and Corticotropin Releasing Factor on Corticosterone Levels in Rats, Melza R van Roijen, R Parrish Waters, Ronald E See; Neuroscience, MUSC.

008 Mechanisms of Epithelial-to-Mesenchymal Transition Mediated Radiation Resistance in Colorectal Cancer, Eric Moretz¹, Victoria J Findlay², Silvia G Vaena¹, Michael S Ashenafi³, David T Marshall³, Dennis K Watson³, Ernest R Camp³, ¹Surgery, MUSC, ²Pathology and Laboratory Medicine, MUSC, ³Radiation Oncology, MUSC, ⁴Surgery, MUSC, Charleston VAMC.

009 Using CBPR to Asses Oral Health Disparities Among the Gullah Population of Hollywood, SC - Hollywood Smiles, Christine M Hudson¹, Lynn West¹, Elizabeth Carpenter¹, Renata S Leite²; ¹CDM, Center for Oral Health Research, MUSC, ²Hollywood, SC, Mayor's Office, ³CDM, Periodontics/Center for Oral Health Research, MUSC.

010 Could Versican, a Proteoglycan, Play a Role in Early Myocardial Differentiation?, LaShardai N Conaway¹, L. Reyes², R. A. Moreno-Rodriguez², C. F. Wright³, E. L. Krug³; ¹CSU, ²Regenerative Medicine and Cell Biology, MUSC.


012 The Subcellular Localization of Activated P38 and Smad2 in Isolated Dispersed Embryonic Heart Cell Lineages in Response to TGFb2 and 9-cis RA, Kimberly M Sauls, Steven W Kubalak; Regenerative Medicine and Cell Biology, MUSC.
Session 2: Clinical-Professional-Masters I Social/Behavioral Science

017 Spasticity and Fatigue After Spinal Cord Injury: A Relationship with Socioeconomic and Demographic Factors, William H Bingham, James S Krause, Lee L Saunders; MUSC.

018 The Relationship Between Prescription Medication Use and Ability to Ambulate Distances After Spinal Cord Injury, Ryan K Kohout1, James S Krause2, Lee L Saunders2; 1College of Medicine, MUSC, 2Health Sciences and Research, College of Health Professions, MUSC.

019 Racial Disparities in Depression and Subjective Well-Being After Spinal Cord Injury: A Mediational Model, Simon A Brown1, Lee L Saunders2, James S Krause2; 1College of Medicine, MUSC, 2College of Health Professions, MUSC.

020 Does Abnormal Muscle Coactivity Decrease with Recovery Following Stroke?, Kathryn L Zettl1, Regan H Root1, Michelle L Woodbury2; 1College of Health Professions, Occupational Therapy, MUSC, 2College of Health Professions, Occupational Therapy, MUSC, Ralph H. Johnson VA Medical Center.

021 Does Active Range of Motion of Shoulder Flexion Recover Before Wrist Extension During Forward Reach in Individuals Post-Stroke?, Schayla D Ardis1, Ashley N Farina2, Jessica L Newton2, Michelle L Woodbury3; 1Health Professions, Occupational Therapy, MUSC, 2Health Professions, Occupational Therapy, MUSC, 3Health Professions, Occupational Therapy, MUSC, Ralph H Johnson VA Medical Center.

022 Does Restraining the Trunk Help Improve Coordinated Arm Movements Post-Stroke?, Caitlin Scurry1, Lindsay Rogers1, Michelle Woodbury2; 1Health Professions, Occupational Therapy, MUSC, 2Ralph H Johnson VA Medical Center, Health Professions, Occupational Therapy, MUSC.

023 Does Stroke Severity Influence Sensory-Feedback Needed for Reaching?, Kelly R Anderson1, Greg M Loftis1, Melissa K Turpin1, Michelle L Woodbury2; 1College of Health Professions, Occupational Therapy, MUSC, 2College of Health Professions, Occupational Therapy, MUSC, Ralph H. Johnson VA Medical Center.

024 Bedtime and Napping Behaviors in Preschool Children From a Low-Income Cohort, Saujanya Vadooorker1, Julie C Lumeng2; 1College of Medicine, MUSC, 2Center for Growth and Development, University of Michigan.

025 Dietary Habits of Community Dwelling Individuals with Severe and Persistent Mental Illness, Emily B Modlin, Dana M Blomquist, Shannon N Collie, Stephanie A Davidson, Shannon K Pouliot, Tara A Warner, Sarah C Wilkes, Nancy E Carson; Health Professions, Occupational Therapy, MUSC.
026 Neurocognitive Functioning Among Bariatric Surgery Candidates, Andrea N Shipp¹, Alok Madan², Laura K Campbell³; ¹College of Medicine, MUSC, ²Psychiatry and Behavioral Sciences, MUSC.

027 Health Behaviors Practiced By First-Year Health Professional Graduate Students At the Medical University of South Carolina, Lauren N Kohn, Hazel L Breland, Bailey H Mary, Hughes A Lauren, Rowell M Courtney, Tara L Scott; CHP, Division of Occupational Therapy.


029 Support Experiences in Individuals Coping with Advanced Colorectal Cancer, Elena I Gore¹, Scott Cole², Melanie B Thomas², Katherine R Sterba¹, Kristin Wallace¹; ¹Medicine, Biostatistics and Epidemiology, MUSC, ²Medicine, Hematology/Oncology, MUSC.

030 Barriers to HIV Testing: A Community Perspective, Brent A Boyer¹, Dag Shapshak², Bobby Navarro²; ¹MUSC, ²MUSC, Emergency Department.


032 Baseline Prevalence of Waterborne Parasites in Ugandan Communities As Part of a Cohort Study, Kevin M McElligott¹, James T McElligott¹, Christiana Naaktgeboren², Kristen Wolf², Andrea Summer¹, Jeffery L Deal³; ¹Medicine, Pediatrics, MUSC, ²Water Missions International.

Session 3: Clinical-Professional-Masters II Basic/Clinical Science

033 Effect of Reduced Marijuana Use on Cognitive Battery Performance Among Cannabis Dependent Adolescents, Candice S Whitaker¹, Kevin M Gray²; ¹College of Medicine, MUSC, ²Psychiatry, MUSC.

034 Treatment of Glioblastoma Multiforme Pre- and Post-Multidisciplinary Management At a Regional Teaching Hospital, Nicholas Gallagher¹, Laurel Pate², Arsalaan Salehani³, Charles Kanos⁴; ¹College of Medicine, MUSC, ²Furman University, ³Wofford College, ⁴Greenville Hospital System University Medical Center.

035 Neurosurgery in a Rural Sub-Saharan African Hospital: A Survey of Procedures and Outcomes, Joseph J Kavolus¹, Jordan Magarik¹, Joyce Nicholas², Dilan Ellegala³, Emmanuel Nuwas⁴; ¹College of Medicine, MUSC, ²Biostatistics & Epidemiology, MUSC, ³Neurosciences, MUSC.

036 Purkinje Fiber Response to Pressure Overload in an Underdeveloped Cardiac Conduction System, Amanda Northup¹, Mary S Rackley², Catalin F Baicu², Brett H Harris³, Terrence X O'Brien²; ¹College of Medicine, MUSC, ²MUSC Gazes Cardiac Research Institute, Ralph H. Johnson VA Medical Center, ³Regenerative Medicine and Cell Biology, MUSC.

037 Pilot Study Evaluating the Effectiveness of Transcranial Direct Current Stimulation (tDCS) in the Management of Perioperative Pain in Total Knee Arthroscopy, Stefanie M Robinson¹, Scott Reeves², Jeffrey Borckardt³; ¹College of Medicine, MUSC, ²Anesthesia and Perioperative Medicine, MUSC, ³Psychiatry and Behavioral Sciences, Anesthesia and Perioperative Medicine, MUSC.

038 Hyperglycemia and Outcomes of Perfusion CT Guided Therapy in Patients Treated for Acute Ischemic Stroke, Jordan A Magarik¹, Robert J Adams¹, Marc Chimowitz¹, Christine A Holmstedt¹, Edward C Jauch², Aquilla S Turk ³, Daniel Lackland¹; ¹Neuroscience, MUSC, ²Emergency Medicine, MUSC, ³Interventional Neuroradiology, MUSC.
039 Early Motor Skill Patterns in Low and High Risk Infants, Beth A Bower, Katherine Bean, Kelsey Carn, Lindsey Mays, Sara Pender, Lindsay Rowland, Sarah Shell, Patricia Coker-Bolt; Occupational Therapy, MUSC.

040 Getting the Most out of a 2D Ultrasound Measure of Muscle Thickness in Children with Cerebral Palsy, Ashley P Dew, Noelle G Moreau; Health Professions, Physical Therapy, MUSC.

041 Chemotherapy Tolerance in Colorectal Cancer Patients Post Liver Resection: A 5-year Retrospective Study At a Regional Teaching Hospital, Leah D Fryml1, William J Edenfield2, Elizabeth Bleed3, James M Mills4; 1College of Medicine, MUSC, 2Cancer Center of the Carolinas, 3PAX & Neurology, MUSC, 4Wofford College.

042 ETS1 Transcriptional Regulation of Prostate Cancer Progression, Ashley M Smith1, Victoria J Findlay1, Angen Liu2, Emily Kistner-Griffin3, David P Turner1; 1Pathology, MUSC, 2Hollings Cancer Center, MUSC, 3Biostatistics & Epidemiology, MUSC.

043 Management of Lobular Carcinoma in Situ (LCIS) and Atypical Lobular Hyperplasia Diagnosed By Core Needle Biopsy (CNB), Kristen N Arnold1, Brian Boland2, Christine MG Schammel3, David P Schammel4, Brian P McKinley5; 1MUSC College of Medicine, 2Greenville Hospital System University Medical Center, 3Paxton, 4Medical University of South Carolina, 5Pathology Associates of Greenville.

044 An Exploration of Sociodemographic, Clinical, and Psychosocial Functioning Variables in Newly Diagnosed Hollings Cancer Center Breast Cancer Patients, Kristina Andrijauskaitė1, Alok Madan2, Jeff Borckhardt3, Megan Baker4, Kent Armeson5, Katherine Sterba6; 1Biochemistry, MUSC, 2Psychiatry, MUSC, 3Psychiatry, MUSC, 4Surgery, MUSC, 5Hollings Cancer Center, MUSC, 6Biostatistics and Epidemiology, MUSC.

045 Quantification of PLGF Via RT-PCR in Head and Neck Squamous Cell Carcinoma Cell Lines, Jackson M Condrey1, Brian Hoel1, Wei Sun1, Semyon Rubinchik1, Joshua Hornig2, Marion B Gillespie2, Natalie Sutkowski1; 1Microbiology and Immunology, MUSC, 2Otolaryngology, MUSC.

046 Assessment of Predictors for Survival: 3 Year Follow-up of H&N Cancer Patients, Robert J Yawn1, Joan Cunningham2, Nadia Duffy3, Elizabeth Garrett-Mayer4, Kathleen Cartmell5, Boyd Gillespie6, Terry Day1, Susan Reed7; 1COM, 2Otolaryngology- Head & Neck Surgery, MUSC, 3COM, Medicine, MUSC, 4Center for Disease Control and Prevention, 5Hollings Cancer Center, Biostatistics, MUSC, 6Hollings Cancer Center, Cancer Prevention and Control, MUSC, 7CDM, Craniofacial Biology, MUSC.

047 The Impact of Surgical Diversion Prior to Neoadjuvant Therapy for Locally Advanced Rectal Cancer, Robert E Sweeney1, Norman R Harvey2, Deanna Mansker2, Amy Wahlquist3, David T Marshall4, David J Cole2, Elizabeth Hill3, Ernest R Camp5; 1College of Medicine, MUSC, 2Department of Surgery, MUSC, 3Department of Radiation Oncology, MUSC, 4Department of Surgery, MUSC and Ralph H. Johnson VA Medical Center.

Session 4: Clinical-Professional-Masters III Basic/Clinical Science

048 Development of a Novel Hydrogel for Synthesis of Pancreatic Islets of Langerhans, Zachary J Coffman1, Xiaoyan Liu2, Xuejun Wen3; 1College of Medicine, MUSC, 2College of Graduate Studies, Clemson-MUSC Bioengineering Program, MUSC, 3College of Graduate Studies, Clemson-MUSC Bioengineering Program, MUSC.

049 GILT Inhibits PAX-3 Protein Expression in Human Melanoma Cells, Jessica D Hathaway, Bently P Doonan, Azim Hossain, Lixia Zhang, Azizul Haque; Microbiology/Immunology, Hollings Cancer Center, MUSC.

050 A Retrospective Investigation of Lymph Node Occurrence Identified in Regional Lymph Node Dissections of Melanoma At a Regional Teaching Hospital, Alex D Gleason1, Hannah Bruch5, Christine Schammel2, Steven Trocha3; 1College of Medicine, MUSC, 2Forman University, 3Surgery, Greenville Hospital System.
051 Regulation of ERRα During Hypoxia, Alex T Damron¹, Paul McDermott²; ¹College of Medicine, MUSC, ²Cardiology, MUSC.

052 The Role of Toll-like Receptor 6 in Collagen Processing “Mechanism for Intestinal Fibrosis”, Jacqueline A Savage¹, David P Lebel¹, Titus A Reaves²; ¹Medicine, MUSC, ²Regenerative Medicine and Cell Biology, MUSC.

053 Function Studies of Quinolone Response Protein PqsE of Pseudomonas Aeruginosa, Mo Wei Yang, Yong-mei Zhang; Biochemistry and Molecular Biology, MUSC.

054 Ethanol Inhibits Metabolic Clearance of Methylphenidate and Potentiates Pharmacodynamics, Owen T Reeves¹, Hilary Bernstein², Malcom Robert₈, Kennerly S Patrick³; ¹South Carolina College of Pharmacy, ²Psychiatry and Behavioral Sciences, MUSC, ³Pharmaceutical and Biomedical Sciences, MUSC.

055 Cytokine-driven Bone Resorption with Aggregatibacter Actinomycetemcomitans, Joni Dunmyer¹, Qiyan Li², Hong Yu², Robert Zinna³, Kylie Martin⁴, Keith L. Kirkwood⁴; ¹Microbiology & Immunology and Craniofacial Biology, MUSC, ²Craniofacial Biology, MUSC, ³Center for Oral Health Research, ⁴Craniofacial Biology and Center for Oral Health Research.

056 Inhibited Biofilm Formation On Albumin-Coated Biomaterial Surfaces, Thomas E Niemeier¹, Qian Kay Kang², Xiaoyan Liu², Bou Zhou³; ¹College of Medicine, MUSC, ²Orthopedics, MUSC, MUSC/Clemson Bioengineering, ³MUSC/Clemson Bioengineering.

057 Abnormal Dental Morphology in Orpk Mice, Ben T Wietecha, Courtney J Haycraft; Medicine, Nephrology, MUSC.

058 Comparison of Digital Imaging Methods for Recording Developmental Defects of Enamel, Jeanette S Wingate¹, Susan G Reed², Carol L Wagner³, Lydia A King³, Mallika Murali¹, Bruce W Hollis³, Thomas Hulsey³; ¹Dental Medicine, MUSC, ²Craniofacial Biology, MUSC, ³Pediatrics, MUSC, ⁴George Washington University.

059 Prx Homeodomain Proteins, Key Regulators of Extracellular Matrix Expression During Secondary Palate Formation, K. Bryan Wingate¹, Michael J Kern², Christi B Kern³; ¹College of Dental Medicine, MUSC, ²Regenerative Medicine and Cell Biology, MUSC, ³Cell Biology and Anatomy, MUSC.

060 Porcine TMJ Retrodiscal Tissue Under Tensile Forces, Jon Petersen¹, Hai Yao², Greg Wright³; ¹College of Dental Medicine, MUSC, ²Clemson/MUSC Bioengineering , ³Clemson/MUSC Bioengineering.

Session 5: PhD I

061 Hematopoietic Stem Cell-Derived Fibroblasts Promote Tumor Cell Migration and Invasion, Lindsay T McDonald¹, Daniel J Neitzke², Amanda C LaRue³; ¹College of Graduate Studies, Pathology and Laboratory Medicine, MUSC, Ralph H. Johnson VAMC, ²College of Graduate Studies, Pathology and Laboratory Medicine, MUSC, ³Ralph H. Johnson VAMC, Pathology and Laboratory Medicine, MUSC, Hollings Cancer Center, MUSC.

062 Gamma-Glutamyl Transpeptidase Activity in Cancer Cell Lines, Thomas J Sadowski, Anna-Liisa Nieminen; Pharmaceutical & Biomedical Sciences, MUSC.

063 Hypoxia-Induced Cleavage of Hur is a Critical Regulator of C-Myc Mrna Stability in Head and Neck Squamous Cell Carcinoma (HNSCC), Brittany Carroll¹, Sudha Talwar¹, Angen Liu¹, Boyd M. Gillespie², Imed E. Gallouzi³, Viswanathan Palanisamy¹; ¹Craniofacial Biology, MUSC, ²Otolaryngology- Head and Neck Surgery, MUSC, ³Biochemistry, McGill University, Montreal, QC, CANADA.
064 Effect of Dendrimer Nanoparticles on Pseudomonas Aeruginosa Biofilms, Jordon D Gruber, Yong Mei Zhang; Biochemistry, MUSC.

065 The Effects of Lupus Plasma on Endothelial Nitric Oxide Synthase Activity in HAECs, Joy J N Buie¹, Ann F Hofbauer², Thomas A Morinelli³, James C Oates⁴; ¹Graduate Studies, Microbiology and Immunology, MUSC, ²Medicine, Rheumatology and Immunology, MUSC, ³Medicine, Nephrology, MUSC, VA, ⁴Medicine, Rheumatology and Immunology, MUSC, Ralph H Johnson VA Medical Center.

066 Shining the Light on Relapse Neurocircuitry: Modulating the Reinstatement of Drug-Seeking Behavior Using an Optogenetic Approach, Michael T Stefanik¹, Khaled Moussawi¹, Karl Deisseroth², Peter W Kalivas³, Ryan T LaLumiere³; ¹Neuroscience, MUSC, ²Bioengineering and Psychiatry, Stanford University.

067 Behavioral Responses to Ethanol in NMDA Receptor Knock-in Mice, Carolina R den Hartog¹, Corigan T Smothers¹, Gregg E Homanics², John J Woodward¹; ¹Neuroscience, MUSC, ²Anesthesiology and Pharmacology, University of Pittsburgh.

068 Reduced Histone Deacetylase Activity Protects the Retina From Ischemic Injury, Oday Alsarraf¹, Santhosh K Mani², Donald R Menick², Craig E Crosson³; ¹Graduate Studies, Ophthalmology, MUSC, ²Medicine, MUSC, ³Ophthalmology, MUSC.

069 K63-Linked Ubiquitinated HDAC5 Remains Nuclear and Upregulates Ncx1 in Cardiac Hypertrophy, Denise M Kimbrough¹, Santhosh K Mani², Donald R Menick²; ¹College of Graduate Studies, Molecular Cellular Biology and Pathobiology, MUSC, ²Medicine, Division of Cardiology, MUSC.

070 Akt3 Promotes Nuclear Retention of PGC-1 and ER Alpha By Regulation of the Major Nuclear Export Protein, CRM-1, Daniel G Corum¹, Robin C Muise-Helmericks²; ¹Molecular and Cellular Biology and Pathology, MUSC, ²Regenerative Medicine and Cell Biology, MUSC.

071 Fibulin-1 Regulation of Neural Crest-dependent Morphogenesis, Victor M Fresco, Marion A Cooley, Waleed O Twal, Jeremy L Barth, W Scott Argraves; Regenerative Medicine and Cell Biology, MUSC.

072 Improvement in Treatment of Hypoplastic Left Heart Syndrome- Key Component to Mortality Reduction, Joseph Sistino, Heather Bonilha; College of Health Professions, MUSC.

073 The Role of Estrogen-Related Receptors in Cardiomyocyte Metabolic Adaptation to Oxidative Stress, Kathryn F Cribben¹, Paul J McDermott²; ¹Graduate Studies, MUSC, ²Cardiology, MUSC.

Session 6: PhD II

074 IL-12 Stimulation of CD8+ T Cells Alters Ceramide Metabolism But These Changes Are Not Required for Development of IL-12-Mediated Effector Function, C. Bryce Johnson¹, David H Craig¹, Colleen A Cloud¹, Mark P Rubinstein¹, Besim Ogretmen¹, David J Cole¹; ¹Surgery, MUSC, ²Biochemistry, MUSC.

075 Effects of Fli-1 on T Cell Function in Systemic Lupus Erythematosus, Fahmin Basher¹, Maria Harrell², Erin Morris², Tamara Nowling³; ¹Department of Microbiology & Immunology, Department of Medicine/Rheumatology, MUSC, ²Department of Medicine/Rheumatology, MUSC, ³Department of Medicine/Rheumatology, MUSC; Ralph H. Johnson VA Medical Center, Charleston, SC.

076 Differences in Kappa-Lambda Ratios Identified By Proteomic Analysis of Plasma Exosomes Predict Severe Acute Graft-Versus-Host Disease, Joseph L Alge¹, Michael Janech², John Schwacke³, John Arthur², Luciano Costa⁴; ¹Medicine, MUSC, ²Medicine, Nephrology, MUSC, Ralph H. Johnson VA Medical Center, ³Medicine, Biostatistics and Epidemiology, MUSC, ⁴Hematology/Oncology, MUSC, Hollings Cancer Center.
077 Glt1 Regulation in the Nucleus Accumbens of Cocaine Dependent Rats Following Cortical BDNF Administration., Benjamin J Newcomb, Timothy W Whitfield, Jacqueline F McGinty; MUSC.

078 SPARC/Osteonectin-Null Mice Have Increased Bone Loss and Decreased Periodontal Ligament Collagen Content in Response to LPS-Induced Periodontitis, Jessica M Trombetta¹, Hong Yu¹, Daniela N Arias⁵, Carlos Rossa, JR³, Keith L Kirkwood¹, Amy D Bradshaw⁵; ¹Craniofacial Biology and Center for Oral Health Research, ²Erskine College, ³Craniofacial Biology and Center for Oral Health Research, Department of Diagnosis and, ⁵Craniofacial Biology and Center for Oral Health Research., ⁶Ralph H. Johnson VA Medical Center.

079 The Terminal Pathway of Complement in Hepatic Ischemia/Reperfusion Injury and Regeneration, Keely L Morris¹, Song He¹, Carl Atkinson¹, Paul Morgan², Stephen Tomlinson³; ¹Microbiology and Immunology, MUSC, ²Radiology, MUSC, ³Ralph H. Johnson VA Medical Center.

080 Connexin 43 Heterogeneity is Increased in the Hearts of Mice Overexpressing Cardiac-Specific Angiotensin Converting Enzyme, Erik G Strungs, Jane Jourdan, Joe Palatinus, Rob Gourdie; Regenerative Medicine and Cell Biology, MUSC.

081 Potential Impact of Common Dosing References on Vancomycin Efficacy and Toxicity in Patients with Varying Degrees of Renal Function: A Monte Carlo Analysis, Heather R Hummel¹, Margarita Taburyanskaya¹, Robert V DeClue¹, Roger White²; ¹Pharmacy, SCCP, ²Pharmacy, Pharmaceutical and Biomedical Sciences, SCCP.

082 Impact of Patient Populations with Varying Degrees of Renal Function on Vancomycin Potential Efficacy and Toxicity, Margarita Taburyanskaya¹, Haether R Hummel¹, Robert V DeClue¹, Roger White²; ¹Pharmacy, SCCP, ²Pharmacy, Pharmaceutical and Biomedical Sciences, SCCP.

083 The Role of Mitogen-Activated Protein Kinase Phosphatase-1 in Tumor Progression, Xiaoyi Zhang¹, Hong Yu², Keith L Kirkwood²; ¹Craniofacial Biology, MUSC, ²Dental Medicine, Craniofacial Biology, MUSC.

084 Evaluating the Impact of Acid Ceramidase Overexpression on Activation of and Addiction to the PKB/Akt Pathway., Thomas H Beckham, Joseph C Cheng, Xiang Liu, James S Norris; Microbiology and Immunology, MUSC.

085 Evaluating the Use of LCL124 to Circumvent Gemcitabine Resistance in Pancreatic Cancer, Sarah T Marrison¹, Clayton S Lewis⁵, Xiang Liu¹, James S Norris¹; ¹Microbiology and Immunology, MUSC, ²Pharmaceutical and Biomedical Sciences, MUSC.

086 VDR and RXRα Expression in Chemically Induced Acute Colitis, Rebecca J Weber, Jay Morris, Vondina Moseley, Michael Wargovich; Pharmacology, MUSC.

Session 7: PhD III

087 Requirement for Akt1 in the Regulation of Anti-Bacterial Effects of Poly-N-Acetylglucosamine Nanofibers (sNAG) in Cutaneous Wound Healing, Haley B Lindner¹, Aiguo Zhang², Juanita Eldridge¹, Marina Demcheva³, Philip Tschilis⁴, Arun Seth⁴, John C. Vournakis³, Robin C. Muise-Helmericks¹; ¹Regenerative Medicine and Cell Biology, MUSC, ²Sunnybrook Research Institute, ³Marine Polymer Technologies, Inc., ⁴Tufts University.

088 Regulation of P38-delta By Gba: Mechanistic Insights and Implications for Disease, David Perry¹, Kazuyuki Kitatani⁵, Patrick Roddy¹, Masayuki Wada¹, Yusuf Hannun¹; ¹Biochemistry, MUSC, ²Tottori University.

089 Fibulin-1 Binds Both HB-EGF and EGF Receptor/ErbB1 and Controls HB-EGF-dependent Proliferation, Keerthy Harikrishnan, Marion A Cooley, Victor F Fresno, Waleed O Twal, W Scott Argraves; Regenerative Medicine and Cell Biology, MUSC.
090 A Novel Function of Bves Revealed By Bimolecular Interaction Studies, Claire L Hinsch, Vincent Dammai; Pathology and Laboratory Medicine, MUSC.

091 The Modeling of the Extracellular Processing of Angiotensin in Cultured Mouse Podocytes: A Proposed Mass Action Model, Christian G Spainhour, Juan Carlos Q Velez, Michael G Janech, John H Schwacke; Biopchemistry, Bioinformatics, MUSC, Medicine, Nephrology, MUSC, Ralph H Johnson VA Medical Center.

092 Transcriptomic Changes Associated with Elastogenesis Induced in Arterial Smooth Muscle Cells By the Proteoglycan Versican Variant V3, Erin L Pardue, Kathleen R Braun, Jeremy L Barth, Waleed O Twal; Biopchemistry, Bioinformatics, MUSC, Medicine, Nephrology, MUSC, The Hope Heart Program, Benaroya Research Institute, Virginia Mason.

093 A Novel Murine Pancreatic Cancer Metastatic Model Allowing Continuous Evaluation of Tumor Burden, Elizabeth C Little, Lisa Sun, Patricia Watson, Dennis Watson, David Cole, Ramsay Camp; Microbiology and Immunology, MUSC, Surgery, MUSC, Hematology/Oncology, MUSC, Pathology, MUSC.

094 Redox Modulation of Interleukin-6 Production in MRL/lpr Mesangial Cells, Ahmad K Mashmoushi, Ann F Hofbauer, James D Crapo, Gary S Gilkeson, Jim C Oates; Microbiology and Immunology, MUSC, Medicine, MUSC; Medicine, Ralph H. Johnson VA Medical Center, Medicine, National Jewish Medical and Research Center, Medicine, National Jewish Medical and Research Center, Medicine, National Jewish Medical and Research Center; Ralph H. Johnson VA Medical Center.

095 Extracellular Hsp90 Serves As a Co-Factor for KSHV-Associated Activation of NF-κB During De Novo Infection, Michael DeFee, Qin Zhiqiang, Dai Lu, Bryan Toole, Jennifer S Isaacs, Chris Parsons; Microbiology and Immunology, MUSC; Craniofacial Biology, MUSC; Medicine, MUSC, Cell Biology, MUSC, Pharmacology, MUSC.

096 Bcr-abl Regulates Activity of Sphingomyelin Synthase in Chronic Myelogenous Leukemia Cells, Tara A Burns, P Meier, A Bai, X Yang, Y Hannun, D Zhou, Chiara Luberto; Biochemistry, MUSC.

097 Regulation of Telomerase By Sphingosine Kinase 2/Sphingosine-1-Phosphate in Human Lung Adenocarcinoma Cells, Shanmugam Panneer Selvam, Besim Ogretmen; Biochemistry and Molecular Biology, MUSC.

098 Development of Selective Small Molecule Inhibitors of Heterotrimeric G-Protein Signaling for the Treatment of Ovarian Cancer, Kevin J Bigham, Yuri K Peterson, Starr E Hazard, Joe B Blumer, Ellen Maher; Pharmaceutical & Biomedical Sciences, MUSC, Pharmacology, MUSC.

099 High Throughput Virtual Drug Discovery for Novel and Future Compounds That Cause Mitochondrial Toxicity, Richard E Trager, Lauren Wills, Christopher Lindsey, Craig Beeson, Rick Schnellmann, Yuri Peterson; Pharmaceutical and Biomedical Sciences, MUSC.

100 Structural and Functional Implications of HIV-1 Rev Oligomerization, Fabio Casu, Stuart Parnham, Marco Marenchino, Mirko Hennig; Biochemistry and Molecular Biology, MUSC.

101 A Study of Determinants of Coping in Childhood Cancer Survivors, Lea H Soderstrom, Michelle Hudspeth, Michelle Vandermaas, Katherine Sterba, Elizabeth Garrett-Mayer, Anthony Alberg; Biostatistics and Epidemiology, MUSC, Pediatrics-Hematology/Oncology, MUSC, Child Life, MUSC.

Session 8: PhD IV
102 Impaired Pro-neurotrophin Processing is Associated with Cholinergic Degeneration and Cognitive Impairment Observed in Down Syndrome, Ashley M Fortres, Mona Buhusi, Ann-Charlotte Granholm; Neurosciences, MUSC.

103 MPTP Neurotoxicity in Nigrostriatal Dopamine Neurons is Exacerbated in Gdnf Heterozygous Mice, Bok Soon Go, Heather A Boger, Jacqueline F McGinty; Neuroscience, MUSC.

104 Long-Term Treatment with a High Fat/High Cholesterol Diet in Young and Aged Rats: Inflammatory Response, Blood-Brain-Barrier Breakdown, and Cognitive Impairment, Linnea R Freeman, Ann-Charlotte Granholm; Neurosciences, MUSC.

105 Relationship Between Repetitive Traumatic Brain Injury and Substance Use Disorders Among a Female State Prison Offender Population, Monica E Cornelius, Pamela F Ferguson, E E Pickelsimer; Medicine, Biostatistics and Epidemiology, MUSC.

106 Inferring Novel Genes and Pathways That Modulate the Sphingolipid Pathway From a Novel Yeast Gene Network Derived From Ontology Fingerprints, Tingting Qin1, Lam C Tsoi1, Nabil Matmati1, Bidyut K Mohanty2, Andrew B Lawson3, Yusuf A Hannun4, Jim Zheng5; 1Bioinformatics Graduate Program, Biochemistry and Molecular Biology, MUSC, 2Biochemistry and Molecular Biology, MUSC, 3Biostatistics and Epidemiology, Medicine, MUSC.


108 Proteome Changes Associated with Salinity Stress and DMSP Accumulation in Fragilariopsis Cylindrus, Barbara R Lyon1, Peter A Lee2, Giacomo R DiTullio2, Michael G Janech3; 1Marine Biomedicine and Environmental Science, MUSC, 2Hollings Marine Lab, College of Charleston, 3Nephrology, MUSC, Ralph H. Johnson VA Medical Center.

109 Post-transcriptional Regulation of the Cell Cycle in the Red Tide Dinoflagellate, Karenia Brevis and a Potential Role for Cyclin-Dependent Kinase, Stephanie A Brunelle1, Frances M Van Dolah2; 1Marine Biomedicine, MUSC, 2Marine Biotoxins Program, CCHEBR, NOS, NOAA.

Session 9: Postdocs-Residents-Fellows I

110 C-Myc is a Downstream Target of CXCL13 to Stimulate RANK Ligand Expression in Bone Marrow Stromal/Preosteoblast Cells, Yuvaraj Sambandam1, William L Ries2, James S Norris3, Sakamuri V Reddy1; 1Charles P. Darby Children's Research Institute, Pediatrics, MUSC, 2College of Dental Medicine, MUSC, 3Microbiology & Immunology, BSB, MUSC.

111 Role of P38/Akt Signaling Pathway in the Regulation of Sodium/Calcium Exchanger Expression in Adult Cardiomyocytes, Olga Chernysh1, Santhosh K Mani1, Paige Snider2, Simon J Conway2, Donald R Menick1; 1Medicine, MUSC, 2Indiana University School of Medicine, Indianapolis, IN.

112 A Novel Pathway Modulates FGFR1 Signaling By Controlling the Receptor Trafficking to the Plasma Membrane, Jagadish kummetha Venkata, Claire Hinsch, Venkatesababa Sammanna, Vincent Dammai; Pathology, MUSC.

113 HSP70 Inhibits Aminoglycoside-Induced Activation of JNK and Downstream Signaling, Inga I Kramarenko, Carlene S Brandon, Lisa L Cunningham; Pathology and Lab Med, MUSC.

113.1 Extracellular Heat Shock Protein 90 (Ehsp90): A Novel Modulator of the Tumor Microenvironment in Prostate Cancer, Jessica E Bohonowych, Michael W Hance, Jennifer S Isaacs; Medicine, Cell and Molecular Pharmacology, MUSC.
114 ZO-1 Regulates Cx43 Function Via The Connexon Switch Mechanism In A Novel Perinexal Region Of The Plasma Membrane, J Matthew Rhett, Jane Rhett Jourdan, Robert G Gourdie; College of Medicine, Cell Biology and Anatomy, MUSC.

115 Regulation of the AGS3 - G(α)i Signaling Complex By a Seven-Transmembrane Span Receptor, Sukru S Oner, Ningfei An, Ali Vural, Billy Breton, Michel Bouvier, Joe B Blumer, Stephen Lanier; ¹Pharmacology, MUSC, ²Pathology, MUSC, ³Biochemistry, Université de Montréal.

116 Activator of G-protein Signaling 3 Null Mice II: Exploring the Functional Roles of AGS3 in the Immune System, Melissa Branham-O'Connor, Xian Xhang, Stephen M Lanier, Joe B Blumer; ¹Pharmacology, MUSC, ²Pathology, MUSC.

117 HSP70 Induced By Lipoprotein Immune Complexes Sequester Lipids in The Endosomal Compartment: Impact on Oxidative Stress and Macrophage Survival, Mohammed M Al Gadban, Kent J Smith, Dezirea Jones, Virella Gabriel, Lopes-Virella F Maria, Hammad M Samar; ¹Regenerative Medicine and Cell Biology, MUSC, ²College of Graduate Studies/ SURP, ³Immunology, MUSC, ⁴Endocrinology, MUSC.

118 Maintenance of Genome Stability By Intra-S Phase Checkpoint Protein Tof1 and Other Fork-associated Proteins As Measured By Ty1 Retro-transposition and Karyotypic Changes, Narendra K Bairwa, Bidyut K Mohanty, Radostina Stemenova, Joan Curcio, Deepak Bastia; ¹Biochemistry, MUSC, ²Laboratory of Molecular Genetics, Wadsworth Center Albany, NY.

120 Placenta Growth Factor (PLGF) As a Potential Therapeutic Target in Head and Neck Squamous Cell Carcinoma, Brian D Hoel, Wei Sun, Kenneth J Byrd, Isaac Dingle, Boyd M Gillespie, Natalie A Sutkowski; ¹Microbiology and Immunology, MUSC, ²Otolaryngology, MUSC, ³Medicine, MUSC.

Session 10: Postdocs-Residents-Fellows II

121 Role of MGlur5 During Conditioned Hyperactivity in Differentially Reared Rats, Margaret J Gill, Mary E Cain; ¹Neuroscience, MUSC, Psychology, Kansas State University, ²Psychology, Kansas State University.

122 Excitotoxic Lesions of the Dorsolateral Caudate-Putamen Impair Cocaine-primed Reinstatement in an Animal Model of Relapse, Amanda Gabriele, Ronald See; Neurosciences, MUSC.

123 The Beta-Carboline, FG7142, Produces Anxiogenic Behavior, But Fails to Induce Reinstatement to Cocaine-Seeking in Rats, R Parrish Waters, Melza R van Roijen, Ronald E See; Neuroscience, MUSC.

124 Sex Differences in Orexin 1 Receptor Mediation of Cocaine-induced Locomotion and Cocaine-seeking in Rats, Luyi Zhou, Ronald E See; Neurosciences, MUSC.

125 Loss of Object Recognition Memory Produced By Extended Access to Methamphetamine Self-Administration is Reversed By Positive Allosteric Modulation of Metabotropic Glutamate Receptor 5, Carmela Reichel, Marek Schwendt, Jacqueline F McGinty, Ronald E See; Neuroscience, MUSC.

126 Ethanol Effects on the Discriminative Stimulus Properties of Methylphenidate, Robin L. McGovern, Kennerly S Patrick, William C Griffin, III; ¹Pharmaceutical Sciences and Psychiatry and Behavioral Sciences, MUSC, ²Pharmaceutical Sciences, MUSC, ³Psychiatry and Behavioral Sciences, MUSC.

127 Spurious Elevation of Hemoglobin A1c Due to a Hemoglobin Variant, Alina G Sofronescu, Laurie M Williams, Dorinda M Andrews, Yusheng Zhu; Department of Pathology and Laboratory Medicine, MUSC.
128 Fli-1 Transcription Factor is Involved in Inflammatory Chemokine Production and Inflammatory Cell Infiltration In the Kidneys in Animal Models of Autoimmune Disease, Eiji Suzuki1, Sarah Williams2, Emmanuel Reyes-Cortes8, Eva Karam1, Gary Gilkeson1, John Zhang1; 1Rheumatology and Immunology, MUSC, 2Ralph H. Johnson VA Medical Center.

129 Increased Beta-Arrestin 1 and 2 Expression in a Murine Model of Rheumatoid Arthritis, Pengfei Li1, Hongkuan Fan1, Perry V Halushka2, James A Cook1; 1Neurosciences, MUSC, 2Cell and Molecular Pharmacology, MUSC.

130 The Role of Complement and the Use of Complement Inhibitors in a DSS Model of IBD, Jennifer Schepp-Berglind1, Carl Atkinson1, Fei Qiao1, Stephen Tomlinson2; 1Microbiology and Immunology, MUSC, 2Microbiology and Immunology, MUSC, Ralph H. Johnson VA Medical Center.

131 Evidence for Neurogenesis After Acute Auditory Nerve Injury in the Adult Mouse Inner Ear, Devadoss J Samuvel, Lauren Kilpatrick, Juhong Zhu, Bradley Schulte, Hainan Lang; Pathology, MUSC.

132 8-Isoprostane As a Biomarker of Oxidative Stress in Patients with Severe Traumatic Brain Injury, Charles M Andrews1, Keith T Borg1, Ed Jauch1, James Cook2, Perry Halushka3; 1Emergency Medicine, MUSC, 2Neurology, MUSC, 3Pharmacology and Experimental Therapeutics, MUSC.
Session 11: Undergraduate II: 11:45 – 3:15 pm – Room CHP 204

11:45 - 12:00
133 The Inhibition of Apoptosis By Melatonin Receptors Agonists in VSC 4.1 Motoneurons Exposed to Cytokines Released From Activated Microglia, Megan E Busch¹, Arabinda Das², Misty McDowell², Casey O'Dell², Joshua A Smith², Abhay K Varma², Swapan L Ray³, Naren L Banik³; ¹Erskine College, Due West, SC, ²Neuroscience, MUSC, ³Pathology, Microbiology, and Immunology, University of South Carolina, Columbia, SC.

12:00 - 12:15
134 Fabrication and Characterization of Neurospheres with Novel Method for Suppression of Immune Response in Vivo, Laila C Roudsari¹, Xiaowei Li², Xiaoyan Liu², Xuejun Wen²; ¹Clemson University, Clemson, SC, ²Bioengineering, Clemson-MUSC.

12:15 - 12:30
135 Association of Spasticity and Life Satisfaction in Spinal Cord Injured Patients, Dana L Westerkam¹, Krause S James², Lee Saunders³; ¹Psychology, Davidson College, ²Clinical Research, College of Health Professions, ³Health Science and Research, College of Health Professions.

12:30 - 12:45
136 Anti-telomere Antibody Levels and Vitamin D Deficiency in Systemic Lupus Erythematosus Patients, Laura M Tonks¹, Brett Hoffecker², Fahmin Basher², Diane Kamen², Tamara Nowling²; ¹Biology, UNC Chapel Hill, ²Rheumatology, MUSC.

12:45 - 1:00
137 Effects of Genetic Deletion of NOS3 or NOS3 on Atherosclerosis in a Lupus Nephritis Mouse Model, Jashalynn C German¹, Samar Hammad²; ¹Spelman College, Atlanta, GA, ²Regenerative Medicine and Cell Biology, MUSC.

1:00 - 1:15
138 Determination of the Conditions of a Fluorescent Lipofuscin Precursor in Retinal Rod Outer Segments, Alexander G Verderber¹, Yiannis Koutalos²; ¹Physics, College of Charleston, ²Ophthalmology and Neuroscience, MUSC.

1:15 - 1:30
139 Magnetic Resonance Scanner Stability and Its Relation to Scanner Use, Emily L Graczyk¹, Mark S George²; ¹Engineering, USC, ²Medicine, Psychiatry and Behavioral Sciences, MUSC.

1:30 – 1:45 Break

1:45 - 2:00
140 The Differential Effects of Sphingosine-1-Phosphate Receptor Inhibition on Phosphorylation of the Cytoskeletal Proteins Ezrin, Radixin and Moesin, Boyd B Lever¹, Alexa O Gandy², Lina M Obeid³; ¹Dartmouth College, ²Medicine, MUSC, ³Internal Medicine/Geriatrics, MUSC.
2:00 - 2:15

**141 Evaluating an Intervention to Improve Perceptions of Cancer Clinical Trials Among Racially Diverse Communities in South Carolina**, Ebonie M Fuller¹, Amy E Wahlquist², Rashell Blake³, June Streets⁴, Melanie S. Jefferson⁵, Heidi Varner⁶, Shannon Johnson⁷, Marvella E. Ford⁸; ¹South Carolina State University, Orangeburg, SC; ²Division of Biostatistics and Epidemiology and Biostatistics Shared Resource, Hollings Cancer Center, ³Vorhees College, ⁴Georgetown University, ⁵Program Coordinator, Cancer Disparities, Hollings Cancer Center, ⁶The Varner Town Indian Community Economic, Health, and Cultural Development Council, ⁷Early Detection Coordinator, South Carolina Cancer Alliance, ⁸Division of Biostatistics and Epidemiology, Cancer Disparities, Hollings Canc.

2:15 - 2:30

**142 Regulation of Nkx2.5 in the Second Heart Field**, Kyle A Doherty¹, Kyu-Ho Lee²; ¹College of Charleston, ²Regenerative Medicine and Cell Biology, MUSC.

2:30 - 2:45

**143 Tissue Engineered Heart Valve Leaflet From Tissue Spheroids**, Hleb Fedarovich¹, Agnes Nagy-Mehesz², Vladimir Mironov³; ¹CofC, ²Regenerative Medicine and Cell Biology, MUSC.

2:45 - 3:00

**144 Investigating the Molecular Basis for Congenital Heart Defects in Ets1ΔVII Mutant Mice**, X S Zhou¹, D D Spyropoulos², R Southgate³; ¹Biology, Yale University, New Haven, CT, ²Pathology, MUSC, ³Biology, College of Charleston.

3:00 - 3:15

**145 Autophagy and Microgravity Induced Osteoclastogenesis**, Molly T Townsend, Yuvaraj Sambandam, Sakamuri V Reddy; Charles P. Darby Children's Research Institute, Pediatrics, MUSC.

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**Session 12: Clinical-Professional-Masters IV: 11:45 – 3:15 pm – Room CHP 201**

11:45 - 12:00

**146 Ganoderic Acid DM in Prostate Cancer Therapy**, Benjamin M Johnson, Bently P Doonan, Faisal F Radwan, Azim Hossain, Azizul Haque; Microbiology/Immunology, Hollings Cancer Center, MUSC.

12:00 - 12:15

**147 Vitamin D and Leukocyte Telomere Length in Patients with Systemic Lupus Erythematosus**, Brett Hoffecker¹, Laura M Tonks², Tamara Nowling³, Diane Kamen³; ¹College of Medicine, MUSC, ²Biology, UNC Chapel Hill, ³Rheumatology, MUSC.

12:15 - 12:30

**148 Increased Presence of Dendritic Cells and Dendritic Cell Chemokines in the Sinus Mucosa of CRSwNP and AFRS**, Christopher M Ayers¹, Brendan P O'Connell², Carl Atkinson³, Ryan M Mulligan², Eric W Wang², Eugene R Sansoni², Jennifer J Mulligan², Rodney J Schlosser²; ¹Medicine, Otolaryngology-Head and Neck Surgery, MUSC, ²Otolaryngology-Head and Neck Surgery, MUSC, ³Microbiology and Immunology, MUSC.
12:30 - 12:45

149 Early Recognition of Lymph Node First Presentation of Kawasaki Disease, Elizabeth M Van Cott¹, John T Kanegaye², Jane C Burns³, Adriana Tremoulet⁴, Andrea Salgado⁵; ¹MUSC College of Medicine, ²University of California, San Diego, Pediatrics, Rady Children's Hospital, Emergency Medicine, ³University of California, San Diego, Pediatrics.

12:45 - 1:00

150 The Relationship of Impulsivity to Alcohol and Marijuana Expectancies in an Adolescent Psychiatric Sample, Danna K Hall, Kendra M Scott, Natalie Johnson, Deborah Deas; Psychiatry, MUSC.

1:00 - 1:15

151 Independent Effect of Site of Care on Health Literacy Levels in Adults with Diabetes: Comparison of Community Health Centers to an Academic Health Center, Ravi P Mishra, Joni Strom, Cheryl Lynch, Leonard E Egede; College of Medicine, MUSC and Ralph H. Johnson VA Medical Center.

1:15 - 1:30

152 Sociodemographic Correlates of Health Literacy in Adults with Diabetes, Craig Thomas, Joni Strom, Cheryl Lynch, Leonard E Egede; College of Medicine, MUSC and Ralph H. Johnson VA Medical Center.

1:30 – 1:45 Break

1:45 - 2:00

153 Effect of Health Literacy and Demographic Characteristics on Medication Adherence in Adults with Diabetes, Roxana Pourdeyhimi, Joni Strom, Cheryl Lynch, Leonard E Egede; College of Medicine, MUSC and Ralph H. Johnson VA Medical Center.

2:00 - 2:15

154 Effect of Health Literacy on Diabetes Knowledge and Self-care Behaviors in Adults with Diabetes, Leslie J Thomas, Joni Strom, Cheryl Lynch, Leonard E Egede; College of Medicine, MUSC and Ralph H. Johnson VA Medical Center.

2:15 - 2:30

155 Predictors of Glycemic Control in Adults with Diabetes At Academic and Community Health Clinics in Charleston, Bimal A Patel, Joni Strom, Cheryl Lynch, Leonard E Egede; College of Medicine, MUSC and Ralph H. Johnson VA Medical Center.

2:30 - 2:45

156 Differential Effects of Diabetes Knowledge on Glycemic Control Between Ethnic Groups in Adults with Diabetes, Jimmy Walker, Joni Strom, Cheryl Lynch, Leonard E Egede; College of Medicine, MUSC and Ralph H. Johnson VA Medical Center.

2:45 - 3:00

157 Differential Effect of Depression on Self-Care and Glycemic Control By Ethnicity in Adults with Diabetes, Ashley Noisette, Joni Strom, Cheryl Lynch, Leonard E Egede; College of Medicine, MUSC and Ralph H. Johnson VA Medical Center.
3:00 - 3:15

158 Varying Effects of Adherence to Medications and Self-Care Behaviors on Glycemic Control By Race in Adults with Diabetes, Renee Joseph, Joni Strom, Cheryl Lynch, Leonard E Egede; College of Medicine, MUSC and Ralph H. Johnson VA Medical Center.

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Session 13: PhD V: 12:30 – 2:30 pm – Room CHP 202

12:30 - 12:45

159 Racial Disparity in Impact of Maternal Obesity and Diabetes on Upper Quantiles of Birth Weight, Caitlyn N Ellerbe¹, Nicole M Marlow¹, Jill Mauldin², Jeffrey E Korte¹, Mulugeta G Gebregziabher¹; Kelly J Hunt¹; ¹Medicine, Biostatistics and Epidemiology, MUSC; ²Obstetrics-Gynecology, MUSC.

12:45 - 1:00

160 Presidential Scholars: Addressing Healthy People 2020 with a Interdisciplinary Mixed Methods Study of Wellness Indicators in North Charleston, South Carolina, Amy R Painter¹, Joseph Cheng², Katie Koval³, Lisa Murphy⁴, Ebony Merisier⁵, Andrew Reynolds⁶, Kate Robinette⁷, Alice Uflacker³; ¹Nursing, MUSC, ²Medicine, Graduate Studies, MUSC, ³Medicine, MUSC, ⁴Pharmacy, MUSC, ⁵Health Professions, MUSC, ⁶Dental Medicine, MUSC, ⁷Law, Charleston School of Law.

1:00 - 1:15

161 Hidden Markov Models (HMM) in Predicting Future Drinking Behavior While Simultaneously Accommodating the Effects of Several Alcoholism Medications, Behavioral Therapy, Baseline and Time Dependent Cova, Codruta C Chiuzan, Stacia M DeSantis; Biostatistics and Epidemiology, MUSC.

1:15 - 1:30

162 EDD: A Novel Therapeutic Target for Platinum-Resistant Ovarian Cancers, Amber T Bradley¹, Hui Zheng¹, Charles N Landen², Scott T Eblen¹; ¹Cell and Molecular Pharmacology and Experimental Therapeutics, MUSC; ²Obstetrics and Gynecology, University of Alabama Birmingham.

1:30 – 1:45 Break

1:45 - 2:00

163 Modification By SUMO-1 Alters the RNA-binding Activity of the Human Cancer-associated La Protein, Julia Kuhnert, Gunhild Sommer, Tilman Helse; Biochemistry, MUSC.

2:00 - 2:15

164 Estrogen Receptor Agonists Attenuate TNF-alpha Induced Cell Damage and Apoptosis in VSC4.1 Motoneurons, Joshua A Smith¹, Arabinda Das¹, Misty M McDowell¹, Swapan K Ray², Naren L Banik¹; ¹Neurosciences, MUSC, ²Pathology, Microbiology, and Immunology, USCSOM.

2:15 - 2:30

165 Overexpression of Melatonin Receptors Reduces Cell Death in Rat Astroglia and Motoneuron Cells After Exposure to Glutamate Excitotoxicity, Casey O’Dell¹, Arabinda Das¹, Megan E Busch¹, Joshua A Smith¹, Russel J Reiter², Abhay K Varma¹, Swapan K Ray³, Naren L Banik¹; ¹Neurosciences, MUSC, ²Cellular and Structural Biology, University of Texas, San Antonio, TX , ³Pathology, Microbiology and Immunology, University of South Carolina School of Medicine, Columbia, S.
12:15 - 12:30

166 New Insights Into Prymnesium Parvum Toxicity, Matthew J Bertin\textsuperscript{1}, Paul V Zimba\textsuperscript{2}, Kevin R Beuchesne\textsuperscript{3}, Peter DR Moeller\textsuperscript{4}.\textsuperscript{1}Marine Biomedicine and Environmental Sciences (MBES), MUSC, \textsuperscript{2}Center for Coastal Studies, Texas A&M Univeristy, Corpus Christi, TX, \textsuperscript{3}JHT in support of the Hollings Marine Laboratory, NOAA, Charleston, SC, \textsuperscript{4}MBES, MUSC, Hollings Marine Laboratory, Charleston ,SC, Toxin/Natural Product Chemistry, NOAA, NOS.

12:30 - 12:45

167 Transdermal and Oral Dl-methylphenidate – Ethanol Interactions in C57BL/6J Mice: Elevated D-MPH Concentrations and Ethylphenidate As a Biomarker, Guinevere H Bell\textsuperscript{1}, William C Griffin\textsuperscript{2}, Kennerly S Patrick\textsuperscript{1}.\textsuperscript{1}Pharmaceutical and Biomedical Sciences, MUSC, \textsuperscript{2}Psychiatry and Behavioral Sciences, MUSC.

1:00 - 1:15

168 Effective Dose and Radiation-induced Carcinogenic Risk At Body CT, Wenjun He\textsuperscript{1}, Walter Huda\textsuperscript{2}, Hai Yao\textsuperscript{1}.\textsuperscript{1}Clemson-MUSC Bioengineering Program, \textsuperscript{2}Radiology and Radiological Sciences, MUSC.

1:15 - 1:30

170 The Role of Fli1 in Breast Cancer Development and Progression, Melissa N Scheiber\textsuperscript{1}, Patricia M Watson\textsuperscript{2}, Victoria J Findlay\textsuperscript{1}, Tihana Rumboldt\textsuperscript{1}, Dennis K Watson\textsuperscript{3}.\textsuperscript{1}Pathology, MUSC, \textsuperscript{2}Medicine, MUSC, \textsuperscript{3}Pathology, Biochemistry, MUSC.

1:30 – 1:45 Break

1:45 - 2:00

171 HDL and Albumin Specific Effects on S1P-dependent Endothelial Barrier Enhancement, Brent A Wilkerson, Shane B Wing, W Scott Argraves, Kelley M Argraves; Regenerative Medicine and Cell Biology, MUSC.

2:00 - 2:15

172 Mechanisms Contributing to the Cardiovascular Phenotype of the Cartilage Link Protein Knockout Mouse, Marie M Lockhart\textsuperscript{1}, Elaine Wirrig\textsuperscript{2}, Muyi Li\textsuperscript{3}, Andy Wessels\textsuperscript{1}.\textsuperscript{1}Regenerative Medicine and Cell Biology, MUSC, \textsuperscript{2}University of Cincinnati, \textsuperscript{3}University of Pennsylvania.

2:15 - 2:30

173 Epigenetic Modification of RXRα in Human Colon Carcinomas By the Green Tea Polyphenol, EGCG, Vondina R Mosely\textsuperscript{1}, Jay Morris\textsuperscript{2}, Michael J Wargovich\textsuperscript{2}.\textsuperscript{1}MCBP, MUSC, \textsuperscript{2}Pharmacology, MUSC.

2:30 - 2:45

174 Movement of Activator of G-Protein Signaling 3 Within the Aggresomal Pathway, Ali Vural, Sukru Sadik Oner, Ningfei An, Violaine Simon, Dzwokai Ma, Joe B. Blumer, S.M. Lanier; Pharmacology, MUSC.
12:15 - 12:30

**175 Extracellular Electron Transfer in Gram Positive Bacteria for the Production of Bioenergy**, Chris W Marshall, Hal May; Microbiology and Immunology, MUSC.

12:30 - 12:45

**176 Celastrol Inhibits Aminoglycoside-Induced Ototoxicity and Hearing Loss**, Shimon P Francis¹, Lisa L Cunningham¹, Carlene S Brandon¹, Inga Kramarenko¹, Fu-Shing Lee²; ¹Pathology, MUSC, ²Otolaryngology, MUSC.

12:45 - 1:00

**177 Regulation of Human DihydroCeramide Synthase 1 (dhCerS1/LASS1) Gene in HNSCC**, Marisa Meyers, B Ogretmen; Biochemistry and Molecular Biology, MUSC.

1:00 - 1:15

**178 Targeting I2PP2A/SET Oncoprotein By FTY720 Relieves Ceramide/I2PP2A Signaling for CMyc Degradation and Suppression of Lung Tumor Growth**, Sahar Saddoughi, Archana Mukhopadhyay, Besim Ogretmen; Biochemistry, MUSC.

1:15 - 1:30

**179 Ceramide Mediated Mitophagic Growth Inhibition of Head and Neck Cancers**, R David Sentelle¹, Can Senkal², Suriyan Ponnusamy², Besim Ogretmen²; ¹CDM/CGS, Biochemistry and Molecular Biology,MUSC, ²Biochemistry and Molecular Biology, MUSC.

1:30 – 1:45  **Break**

1:45 - 2:00

**180 MAP Kinase Phosphatase-1 is Required for Vitamin D Signaling in Bone Marrow Stromal Cells**, Alfred C Griffin, Carlos Rossa Jr., Keith L Kirkwood; Craniofacial Biology, MUSC.

2:00 - 2:15

**181 The Role of Cubilin in HDL Homeostasis**, Obaidullah Aseem, Brian T Smith, Marloes MA Hensels, Marion A Cooley, Jeremy L Barth, Sandra C Klatt, William S Argraves; Regenerative Medicine and Cell Biology, MUSC.

2:15 - 2:30

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

2:30 - 2:45

**183 Effect of CerS6 Modulation on Cell Cycle and SL Metabolism in Colon Cancer Cells**, Tejas S Tirodkar, Christina Voelkel-Johnson; Microbiology and Immunology, MUSC.
12:15 - 12:30

184 N-Methyl-D-Aspartate Receptor Subunit NR3a Expression and Function in Principal Cells of the Collecting Duct, Adrian D Sproul\textsuperscript{1}, Darwin P Bell\textsuperscript{2}; \textsuperscript{1}Neuroscience, MUSC, \textsuperscript{2}Medicine, MUSC, Ralph H. Johnson VA Medical Center.

12:30 - 12:45

185 Role of RPE65 Protein Within Murine Cone Photoreceptors, Peter H Tang\textsuperscript{1}, Rosalie K Crouch\textsuperscript{2}; \textsuperscript{1}Neuroscience, MUSC, \textsuperscript{2}Ophthalmology, MUSC.

12:45 - 1:00

186 Calpain Inhibition Confers Histological and Functional Neuroprotection to Retinal Ganglion Cells in Experimental Optic Neuritis, Amena W Smith\textsuperscript{1}, Baerbel Rohrer\textsuperscript{8}, Mitsuyoshi Azuma\textsuperscript{8}, Jun Inoue\textsuperscript{8}, Naren L Banik\textsuperscript{2}; \textsuperscript{1}Microbiology/Immunology, MUSC, \textsuperscript{2}Neurosciences, MUSC.

1:00 - 1:15

187 A Peptide Mimetic of the Connexin43 Carboxyl-Terminus Increases Activity of Protein Kinase C Epsilon in a Substrate-Specific Manner, Joseph A Palatinus, Robert G Gourdie; Regenerative Medicine and Cell Biology, MUSC.

1:15 - 1:30

188 Secondary Stroke Prevention: A Report From a One Year Follow-up Survey of a Stroke Cohort, Andrea D Boan\textsuperscript{1}, David L Bachman\textsuperscript{2}, Robert J Adams\textsuperscript{2}, Daniel L Lackland\textsuperscript{2}; \textsuperscript{1}Epidemiology, MUSC, \textsuperscript{2}Neuroscience, MUSC.

1:30 – 1:45 Break

1:45 - 2:00

189 Evolution of 10-Formyltetrahydrofolate Dehydrogenase Catalysis, Kyle C Strickland, Natalia I Krupenko, Sergey A Krupenko; Biochemistry, MUSC.

2:00 - 2:15

190 Alterations in Immune Phenotype During the Development of Squamous Cell Carcinoma of the Head and Neck, Anna-Maria A De Costa\textsuperscript{1}, Travis D Reeves\textsuperscript{2}, David D Walker\textsuperscript{3}, Corinne A Schuyler\textsuperscript{4}, Young I Rita\textsuperscript{5}; \textsuperscript{1}MSTP, MBIM, Otolaryngology, MUSC, Medical Research Service, Ralph H. Johnson VAMC, \textsuperscript{2}Otolaryngology, MUSC, \textsuperscript{3}Otolaryngology, MUSC, Medical Research Service, Ralph H. Johnson VAMC, \textsuperscript{4}Medical Research Service, Ralph H. Johnson VAMC.

2:15 - 2:30


2:30 - 2:45

192 Regulation of Acid Ceramidase-mediated Prostate Cancer Cell Radiation Resistance, Joseph C Cheng\textsuperscript{1}, Thomas H Beckham\textsuperscript{1}, S. Tucker Morrison\textsuperscript{1}, Barry J Keane\textsuperscript{1}, Lorianne S Turner\textsuperscript{1}, Thomas E Keane\textsuperscript{2}, Xiang Liu\textsuperscript{1}, James S Norris\textsuperscript{1}; \textsuperscript{1}Microbiology and Immunology, MUSC, \textsuperscript{2}Urology, MUSC.
11:45 - 12:00

193 Looping Mediated Termination of DNA Replication in Schizosaccharomyces Pombe, Samarendra K Singh¹, Sarah Sabatinos², Susan Forsburg², Deepak Bastia¹; ¹Biochemistry and Molecular Biology, MUSC, ²Biological Sciences, University of Southern California.

12:00 - 12:15

194 Reduced Membrane Fluidity Leads to Decreased Virulence in Pseudomonas Aeruginosa, Souzan A. Abdel-Samie, Yong-Mei Zhang; Biochemistry & Molecular Biology, MUSC.

12:15 - 12:30

195 Reduced Redox-Regulating Thiol Levels Render Effector Memory Like T Cells Obtained After Repetitive TCR Stimulation More Susceptible to Activation Induced Cell Death, Amir A Al-Khami¹, Håkan R Norell¹, Naytej Kaur¹, Osama S Naga¹, Christina Voelkel-Johnson², Bijay Mukherji³, Michael Nishimura¹, Shikhar Mehrotra¹; ¹Surgery, MUSC, ²Microbiology & Immunology, MUSC, ³Medicine, University of Connecticut Health Center, Farmington, CT.

12:30 - 12:45

196 Decreasing Fli1 Levels in Lupus T Cells Has Effects on Serum Immunoglobulin Levels and T Cell Infiltration in the Kidney, Erin E Morris, Maribel Harrell, Xian K Zhang, Phillip Ruiz, Tamara M Nowling; Rheumatology and Immunology, MUSC.

12:45 - 1:00

197 Mouse Model of Ischemic Mitral Regurgitation: Involvement of Bone Marrow-Derived Cells, Zoltan Hajdu, Roger R Markwald, Christopher J Drake, Richard P Visconti; Regenerative medicine and Cell Biology, MUSC.

1:00 - 1:15

198 Inferior Frontal Activity During Speech Recognition is Modulated By Intelligibility, Kenny I Vaden, Noam I Keren, Kelly C Harris, Jane B Ahlstrom, Judy R Dubno, Mark A Eckert; Otolaryngology, MUSC.

1:15 - 1:30

199 The Effect of Upper Airway Surgery on CPAP Pressure: A Systematic Review, Ryan P Reddy, M. Boyd Gillespie, Shawn A Nguyen; Otolaryngology, MUSC.

1:30 – 1:45 Break

1:45 - 2:00

200 Very Long-Chain Fatty Acid Accumulation Causes Enhanced Production of Reactive Oxygen Species and Proinflammatory Cytokines in Astrocytes, Jaspreet Singh, Mushfiquddin Khan, Inderjit Singh; Pediatrics, MUSC.

2:00 - 2:15

201 Role of Estrogen Receptor Alpha in SLE: Modulation of Toll-like Receptor-induced Inflammation, Melissa Cunningham¹, Osama Naga¹, Jackie Eudaly¹, Patricia Bosnic², Gary Gilkeson³; ¹Div Rheumatology and Immunology, MUSC, ²College of Medicine, MUSC, ³Ralph H Johnson VA Medical Center, Rheumatology and Immunology, MUSC.
**202** A Novel Role of Inositol Phosphosphingolipid Phospholipase C Gene (ISC1) in Morphogenesis During Replication Stress, Kaushlendra Tripathi, Nabil Matmati, Jim W Zheng, Bidyut K Mohanty, Yusuf A Hannun; Biochemistry & Molecular Biology, MUSC.


**204** The SR Protein Kinase Clk1 Phosphorylates SPF45 and Regulates Its Localization and Alternative Splicing Activity, Yuying Liu, Adnan M Al-Ayoubi, Hui Zheng, Scott T Eblen; Cell and Molecular Pharmacology and Experimental Therapeutics, MUSC.

**205** ALDH1L2 Gene Encodes for Mitochondrial 10-formyltetrahydrofolate Dehydrogenase, Marianne E Dubard, Natalia I Krupenko, Natalia V Oleinik, Sergey A Krupenko; Biochemistry, MUSC.
ABSTRACTS

001 Developmental Progression of Cortical GABA Transmission is Disrupted in a Rat Model of Schizophrenia, Michael T Weingarten\textsuperscript{1}, Heather Trananth-Davidson\textsuperscript{2}, \textsuperscript{1}Biology, \textsuperscript{2}Neurosciences, MUSC.

Schizophrenia is a complex neuropsychiatric disorder that progressively impacts the prefrontal cortex (PFC) to produce positive and negative symptoms that are hallmarks of this devastating disorder. Cortical GABA transmission is significantly affected in adult schizophrenics and contributes directly to the cognitive disturbances exhibited by these patients. These differences become evident in early adolescence, long before the first psychotic episode, and progressively worsen due in part to evolving maladaptations to blunted GABA function during development. Our long-term objective is the identification of developmental and synaptic abnormalities in the PFC that will reveal effective therapeutic targets to minimize the severity of this disease. Thus, the goal of this project is to demonstrate that developmental neuroadaptations in PFC neurons of schizophrenic brain result from a deficiency in GABA during the critical prodromal phase that begins in early adolescence. Our preliminary studies indicate that the cellular location and composition of GABAergic receptors changes during adolescence. For example, we find that tonic GABA current increases by 25\% by the end of the adolescent period in normal animals and this developmental trajectory is abolished in the MAME17 rodent model of schizophrenia. Alterations in GABAergic neurotransmission in the PFC during the prodromal phase of schizophrenia (which occur during adolescence) are a direct cause of cortical dysfunction, which characterizes the disorder. Therefore, our results will be used to conduct future studies aimed at enhancing GABA transmission during the prodromal phase of the disorder, thus reducing the severity of the illness in adulthood. NIH R21 MH080774-02

002 Active Protease Involvement in Ethanol-Induced Apoptosis in Ventral Spinal Cord Motor Neurons, Kaushal S Patel, Stacy Roudabush, Nakul P Thakore, Jenna H Heissenbuttle, Varduhi H Knaryan, Stacy Roudabush, Supriti S Samantaray, Naren L Banik; \textsuperscript{1}CofC.

Long-term effects of alcohol are damaging to the Central Nervous System (CNS). Even social drinking can affect the neural components such as spinal motoneurons in the long run. Alcohol effects on cultured motoneuronal cells were simulated with doses of ethanol that causes diverse effects on CNS like, euphoria, talkativeness, relaxation (level 1); depression, impaired motor and sensory function, impaired cognition (level 2); decreased blood flow to brain (level 3); stupification, possible unconsciousness (level 4); possible death (level 5) and death (level 6) (Pohorecky et al.) Mechanisms of cell death exposed to ethanol was studied in ventral spinal cord motoneuronal cells. Morphological inferences of cell death as assessed by In situ Wright Staining were further confirmed with biochemical assays such as TUNEL labeling and DNA laddering along with profiles of death-markers such as caspase-3, 8, 9 involving both intrinsic and extrinsic apoptotic pathways. Expression and activity of multitude of proteases marked the degeneration of the ethanol-exposed motoneurons compared to the control cells. Hence, calpeptin, a potent calpain inhibitor, was used in a pre-treatment regimen to conclusively establish the involvement of active proteases in ethanol-exposed damage to the motoneurons. Overall, exposure to ethanol rendered the ventral spinal cord motoneuronal cells vulnerable and calpeptin rendered functional protection to these cells.

003 Calpain Inhibition Protects Against Ethanol-induced Degeneration in Astroglial Cells, Nakul P Thakore\textsuperscript{1}, Jenna H Heissenbuttle\textsuperscript{2}, Stacy Roudabush\textsuperscript{3}, Kaushal S Patel\textsuperscript{4}, Varduhi H Knaryan\textsuperscript{5}, Swapan K Ray\textsuperscript{6}, Supriti S Samantaray\textsuperscript{5}, Naren L Banik\textsuperscript{5}, \textsuperscript{1}CofC, \textsuperscript{2}Trident Tech, \textsuperscript{3}New College of Florida, Sarasota, Florida, \textsuperscript{4}CofC, Charleston, SC, \textsuperscript{5}Neurosciences, MUSC, \textsuperscript{6}USC.

Astrocytes are the predominant cells in the central nervous system that aid neurons in multiple functions including signaling. They protect the neurons against deadly mechanisms and promote regeneration following injury. However, they themselves may fall prey into chronic conditions like alcoholism. Present study was conducted in the astroglial cells C6 differentiated into astrocytic phenotype with cAMP. Cells were exposed to graded concentrations of ethanol (25–100mM) and the morphological and biochemical indices of cell damage were assessed. Quantitative assessment of cell death by MTT assay confirmed that only high doses of ethanol (≥50 mM) can cause cell death, however, in situ Wright Staining inferred that exposure to even lower concentrations of ethanol (25–50mM) can cause damaging effects to the cell morphology. Western blotting analysis revealed, a consistent up-regulation of the pro-apoptotic caspases such as early apoptotic marker annexin V, late apoptotic markers caspase-3 and 9, calcium-activated neutral protease calpain, along with the necrotic marker cathepsin-D. The extrinsic pathways were involved in addition to the intrinsic in this degeneration as indicated by significant up-regulation of the active bands of caspase-8. There was also a significant elevation of Bax:Bcl-2 ratio, following dose-dependent increase in ethanol concentrations. As several active proteases including calpain were found to play key role in this degeneration, wherein calpain is upstream of many of these deteriorating events, hence, calpeptin, a potent calpain inhibitor, was tested for its protective efficacy. Pretreatment with 100nM-5µM Calpeptin...
prevented the ethanol-toxicity whereas a post-treatment regimen (1, 2, and 4h after ethanol exposure) failed to do so, presumably, because the ethanol-exposed damaged had already been initiated. Further studies are being aimed at slices of brain and spinal cord to test the post-treatment paradigm of the inhibitor.

**004** Increased Beta-arrestin-1 Expression Inhibits Apoptotic Signaling Pathways Induced By Tumor Necrosis Factor-alph (TNF-alpha), Melissa N Youssef1, Alessandra Bitto2, Hongkuan Fan3, Keith T Borg4, Sarah Ashton5, Perry V Halushka6, James Cook2, Biology, Furman University, Neuroscience, MUSC, Graduate Studies, MUSC.

Beta-arrestins 1 and 2 are ubiquitous 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 adaptor proteins that inhibit inflammatory cytokine expression. Additionally, it has been suggested that Beta-arrestin-1 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. TNF-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 and differentially modulates apoptotic activity induced by TLR4 and TNF alpha through the inhibition of the cysteine proteases, Caspases 3, 7 and 8. Apoptotic signaling was induced in the cells by TNF-alpha stimulation and was quantified by assessing Caspase-3, 7, and 8 activation. Also, Annexin V Flow Cytometry analysis was performed following cell stimulation. To determine if Beta-arrestin-1 prevents apoptosis in cells following TNF-alpha activation, the cells were transfected with β-arrestin-1 or the empty vector pDNA. Western blot analysis demonstrated over-expression of Beta-arrestin-1 relative to 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. TNF-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. Similarly, TNFalpha stimulated caspase 8 activity was suppressed 50.36% (p<0.01, n=4) in Beta-arrestin-1 transfected cells. These results demonstrate that human embryonic kidney cells showing increased expression of Beta-arrestin-1 reduce apoptotic signaling pathways activated by TNF-alpha, but not with endotoxin. Understanding the role of Beta-arrestin-1 in preventing apoptosis in response to inflammation may lead to novel approaches in the treatment of sepsis. Supported by the lab of Dr. James A Cook, Department of Neurosciences, Medical University of South Carolina and by the Summer Undergraduate Research Program at MUSC. Work also supported by the grants: R25HL92611, and NIH GM27673.

**005** Assessing Vascular Comorbidities Among Hospitalized Parkinson's Disease Patients, Adam H Pearlman1, Kenneth J Bergmann8, Andrea D Boan1, Daniel T Lackland1; 1Neurosciences, MUSC, 2FDA.

Background: Parkinson’s disease (PD) is a common neurodegenerative disease ranking 2nd only to Alzheimer’s disease. It is estimated that at least 1.5 million people suffer from PD in the United States, which is thought to be an underestimate of the true prevalence rate. Diabetes mellitus (DM) is also a common disorder, estimated by the Centers for Disease Control to affect 23.6 million people in the U.S. in 2007. Other vascular related disorders such as stroke and hypertension are also extremely prevalent among the aging population. Even so, there are few studies examining the presence of comorbidities such as DM, stroke, and hypertension among Parkinson patients and previously reported results are inconsistent. Objective: The purpose of this study was to examine the diagnosis of DM, stroke, and hypertension among PD patients in South Carolina across age, race, and gender, in order to estimate the prevalence of PD hospital visits where DM, stroke, and hypertension are present. Methods: Data was gathered from the SC Office of Research Statistics Hospitalization and Emergency Department database for 1999-2009 consisting of patients aged 45 and older using ICD-9 codes 332.0-332.1 for PD, 250.xx for DM, 430-438 for stroke, and 401 for hypertension. Results: Among all PD hospital visits, 22.5% were found to also have diabetes mellitus. Within this cohort, 14.5% of visits were among those 45 to 64 years old and 85.5% were among those 65+ years old. The study also revealed that 76.8% percent of PD with diabetes were Caucasian and only 22.1% were African American. Gender data reported 52.3% male and 48.7% female PD patients with diabetes. The data also showed 20.0% of non-PD hospital visits coded for DM. Findings also included results for stroke and hypertension. Conclusions: This observational study showed a similar percentage of Parkinson’s Disease visits with diabetes present as a co-morbidity compared to non-Parkinson’s Disease visits. Among these Parkinson’s Disease visits, similar percentages of coding for DM were seen for Gender while Age and Race showed greater disparities. A similar percentage was also found between those with PD and hypertension and those without PD and hypertension. A slight increase was found between PD with stroke patients versus stroke without PD patients.
**006** Modafinil Reverses Methamphetamine-Induced Memory Deficits on an Object-In-Place Task in Rats, Lauren A Ramsey1, Carmela M Reichel1, M Schwendt2, J F McGinty2, Ronald E See5; 1College of Charleston, 2Neuroscience, MUSC.

Chronic methamphetamine (meth) often leads to cognitive deficits in humans and animals. We show that both contingent and non-contingent meth impairs memory on an object-in-place task, which measures the ability to detect an object relative to its location and surrounding objects. Further, we assessed whether modafinil would reverse this cognitive impairment. In the first experiment, male Long-Evans rats received saline or acute meth injections (4 x 4 mg/kg, 2 hr intervals). In a second experiment, rats self-administered i.v. meth (0.02 mg/infusion) on an FR1 schedule of reinforcement (7 days for 1 hr/day, followed by 14 days for 6 hr/day), or received yoked saline infusions. Following one week of withdrawal, rats interacted with four objects for 5 min in a closed chamber. Ninety min later, the location of two objects was switched to test memory for object location, and total time spent with each object was recorded. Our results showed that saline-treated rats spent more time interacting with objects in the changed locations. In contrast, rats with a history of contingent or non-contingent meth spent similar amounts of time at all objects, regardless of location. In a final experiment, rats received vehicle or modafinil (100mg/kg) after familiarization. Modafinil treatment in meth rats reversed the deficit, in that they spent more time interacting with objects in the new locations. These findings demonstrate both meth-induced cognitive deficits on an object-in-place task and the reversal of these deficits by modafinil. Comparisons of monoamine transporter levels and markers of meth toxicity in brain areas involved in meth addiction and memory tasks will be presented. Characterization of meth-induced dysregulation of monoamine transporters in frontal and temporal cortical regions and their subsequent modulation by modafinil may identify neurobiological substrates that underlie the behavioral effectiveness of modafinil and its potential use as a treatment in meth addiction. Supported by P2ODA022658, T32DA007288 and F32DA029344.

**007** Effects of Vasopressin and Corticotropin Releasing Factor on Corticosterone Levels in Rats, Melza R van Roijen, R Parrish Waters, Ronald E See; Neuroscience, MUSC.

We used a radioimmunoassay ($^{125}$I) to assess diurnal plasma corticosterone levels in rats housed in the Medical University of South Carolina’s animal facility (BSB 723). These data provided a baseline measure of plasma corticosterone, that we used to compare to levels following stimulation of the hypothalamic-pituitary-adrenal (HPA) axis with two endogenously active pharmacological agents, corticotropin releasing factor and arginine vasopressin, given either individually or simultaneously. These data will be utilized in subsequent studies performed by the See Lab that will examine the interactions of these compounds with the HPA axis and the effects that these interactions have on cocaine seeking behavior.

**008** Mechanisms of Epithelial-to-Mesenchymal Transition Mediated Radiation Resistance in Colorectal Cancer, Eric Moretz1, Victoria J Findlay2, Silvia G Vaena3, Michael S Ashenafi2, David T Marshall3, Dennis K Watson3, Ernest R Camp2; 1Surgery, MUSC, 2Pathology and Laboratory Medicine, MUSC, 3Radiation Oncology, MUSC, 4Surgery, MUSC, Charleston VAMC.

Mechanisms of radiation resistance in colorectal cancer (CRC) are poorly understood. Epithelial-to-mesenchymal transition (EMT), a molecular process in which cells acquire a more mesenchymal phenotype, has been associated with therapeutic resistance and worse clinical outcomes in many types of cancer. We hypothesize that overexpression of Snail, a transcriptional regulator of EMT, will enhance radiation resistance in CRC through suppression of p53-mediated apoptosis. Stable Snail-expressing (Snail DLD-1) and empty control (Empty DLD-1) cell lines were created by transfecting DLD-1 human colon cancer cells with pCMV-3Tag-1 vector (control or with Snail cDNA) followed by bacterial selection. Snail and E-cadherin expression was tested using real time RT-PCR and normalized to GAPDH. p53 expression was tested using Western Blot. Sulforhodamine B (SRB) cytotoxicity assay was performed to assess radiation sensitivity for both cell lines at radiation doses from 0-6 Gy, delivered using a Varian Clinac 21EX linear accelerator. Snail expression was shown to be over 900-fold greater in the Snail DLD-1 compared with Empty DLD-1, conversely E-cadherin expression was 63.7% lower in Snail DLD-1. Lower p53 expression was also evident in Snail DLD-1. Based on the SRB assay, Snail DLD-1 were 50.9% more resistant at 4 Gy when compared with Empty DLD-1 (P<0.001). Expression of the EMT transcriptional regulator Snail leads to radiation resistance in colon cancer cells possibly by inhibition of p53-mediated apoptosis. Therapeutic strategies targeting EMT may enhance conventional radiation treatment for CRC.

**009** Using CBPR to Asses Oral Health Disparities Among the Gullah Population of Hollywood, SC -Hollywood Smiles, Christine M Hudson1, Lynn West1, Elizabeth Carpenter1, Renata S Leite2; 1CDM, Center for Oral Health Research, MUSC; 2Hollywood, SC, Mayor’s Office, 3CDM, Periodontics/ Center for Oral Health Research, MUSC.

Using a community-based participatory research (CBPR) approach, a formative assessment of oral health needs and barriers to oral health care was
conducted in the town of Hollywood, SC to guide the design of a culturally sensitive oral health promotion intervention to help decrease oral health disparities found in this community. Twenty-one participants, over the age of 18, who are Gullah African Americans and reside in the town of Hollywood, SC, participated in four focus group sessions. The participants responded to surveys on demographics and social, medical and oral health history and then, participated in discussions where they were asked open-ended questions. All four sessions were digitally audio-recorded, professionally transcribed and the contents were analyzed using NVivo8. Access to oral health care was identified as the most common barrier. Tooth extraction appears to be the treatment of choice in this community. Cultural habits, dental phobia, and decreased oral health literacy were also prevalent results found among this unique population. The barriers in oral health are complex and addressing a single barrier may not lead to an improvement in oral health outcomes, but designing a culturally and locally relevant intervention may lead to a decrease in oral health disparities.

010 Could Versican, a Proteoglycan, Play a Role in Early Myocardial Differentiation?, LaShardai N Conaway1, L. Reyes2, R. A. Moreno-Rodriguez2, C. F. Wright2, E. L. Krug2, 1CSU, 2Regenerative Medicine and Cell Biology, MUSC.

The study of human development has been a hot topic in science for years. Interests in developmental biology range from understanding the uses of stem cells, to exploring the regulation of apoptosis in the limb buds. There is also great interest in the organization of embryonic organs, particularly in the formation of the heart. Cardiac development is a vital landmark in embryonic development and is crucial for the development of other systems in the embryo. One main event in heart formation is the differentiation of the myocardium into striated muscle. When using the chick embryonic heart as a model, employing Hamburger and Hamilton’s concept of developmental staging, it was found that myocardial differentiation is initiated between stages 16-18. During this time, the myocardium undergoes a significant loss of vimentin, an intracellular intermediate filament normally associated with fibroblast-like cells. However, certain regions of the myocardium, particularly the ventricular trabeculae, atrioventricular canal, and atrium, showed maintenance of vimentin. This lab recently showed that these regions, along with the atrioventricular cushions, express versican, a proteoglycan found in the extracellular matrix associated with the myocardium, during these stages, suggesting that there may be a relationship between vimentin and versican during early myocardial differentiation. This study seeks to explore the co-localization of vimentin and versican in specific regions during myocardial differentiation in later stages of chick heart development. It also seeks to reveal if versican is regulating the expression of vimentin in the developing heart. Through a series of immunohistochemical studies performed on stage 24 chick embryos, it was found that vimentin and versican expressions co-distribute throughout the outflow track and the ventricular trabeculae and cushions. However, it was also revealed that there are areas where vimentin and versican localization do not correlate, indicating that the expression of vimentin may be regulated through alternative pathways.


In the field of regenerative medicine, organ bioprinting is a newly emerging technology for scaffold-free tissue bioengineering. Adipose-derived stem cells (ADSCs) are a useful cell source organ bioprinting because they have the potential to differentiate to multiple lineage pathways. Presently, we are using ADSCs that have been induced to differentiate to the vascular smooth muscle cell (VSMC) lineage for biofabrication of three-dimensional vascular toroids (rings) for evaluation of their efficacy for bioprinting of vascular segments. In particular, we are investigating whether VSMCs differentiated from human ADSCs possess comparable phenotypic and biomechanical properties, specifically expression of VSMC markers and contractile capabilities, to that of native human aortic smooth muscle cells (HAoSMCs). To determine their suitability for vascular tissue engineering, we are constructing vascular rings using VSMCs differentiated from ADSCs and evaluating their ability to contract in response to administration to known effectors of VSMC contraction (angiotensin II and serotonin). Additionally, based on our previous studies, we predict that serotonin exposure during the VSMC-specific differentiation of ADSCs should upregulate the expression of TGF-β1. This upregulation of TGFβ1 should induce synthesis of fibrillar ECM (e.g., collagen) by the ADSC-derived VSMCs, thereby increasing the biomechanical properties of the ring constructs. Changes in the vascular rings are assayed using immunofluorescence microscopy RT-PCR. Combining rapid production of bioprinted building units with ‘maturegenic’ factors like serotonin will potentially provide the optimal conditions to expedite the tissue maturation of bioengineered constructs. Successful biofabrication of three-dimensional ADSC-derived VSMC vascular structures, with comparable biomechanical properties to native blood vessels, will be a major step forward for tissue bioengineering and will ultimately lead to the clinical application of tissue bioprinting in the future. Supported by grants P20-RR1-16434 and CO6 RR018823 from the NIH.
The developing heart is under the control of a variety of growth factors and small molecules such as TGFb2 and retinoic acid, and each act through specific signaling pathways. In the case of TGFb2, both Smad2 and p38 are activated upon exposure to TGFb2 (phosphorylated and translocated to the nucleus). The lab has previously shown in both isolated dispersed heart cells and NIH3T3 cells (embryonic fibroblast cell line), that retinoids can enhance TGFbeta2-mediated Smad2 phosphorylation (pSmad2), but that less Smad2 accumulates in the nucleus. However, the effects of retinoids on TGFb2-mediated p38 phosphorylation (p-p38) and localization are not known. This study was designed to determine the effect of retinoic acid on the TGFbeta2-induced phosphorylation and subcellular localization of p38 (p-p38) in dispersed embryonic heart cells. Further, since isolated dispersed heart cells contain multiple cell types, we also aim to compare the TGFb2 response in myocytes to non-myocytes. We previously showed by Western blot analysis in NIH3T3 cells that activation of p38 and Smad2 by TGFb2 alone was differentially regulated by lower (0.02ng/ml) or higher (0.2ng/ml) concentrations of TGFb2, respectively. We found that differences exist between myocytes and non-myocytes regarding their cellular response after exposure to TGFb2. For example, non-myocytes appeared to be more sensitive to p38 activation as compared to myocytes. These and other differences could have a profound effect on how the developing heart responds to local concentrations of endogenous of TGFb2. NIH R01 HL038116

Response of Bone Marrow-Derived Cardiac Fibroblasts to Angiotensin II Antagonism

In response to myocardial infarction, hematopoietic stem cell (HSC) derived cells have been shown to migrate to the heart and differentiate into cardiac fibroblasts. Cardiac fibroblasts are the cell type that is mainly responsible for the synthesis of the extracellular matrix proteins in the heart. The goal of our experiments was to develop an in vitro system to complement our in vivo evaluation of differences in response of bone marrow-derived and endogenous fibroblasts in the infarcted to Angiotensin II antagonism. To accomplish this, we used a chimeric mouse model in which the bone marrow of lethally irradiated wild type mice is repopulated with EGFP+ bone marrow cells, permitting lineage tracing of bone marrow-derived cells that engraft into the infarcted myocardium. In our experiments, cardiac fibroblasts were isolated from the infarct zone of chimeric mice that had been subjected to myocardial infarction by ligation of the left anterior descending coronary artery thirty days prior to sacrifice. Isolated cells were subjected to limited expansion to evaluate whether cardiac fibroblasts derived from bone marrow HSCs respond differently from endogenous fibroblasts to Angiotensin II antagonism in vitro. Cells were exposed to Angiotensin II (10-7M) subsequent to treatment with the AT1 receptor inhibitor, Losartan (1.0µM), or the ACE inhibitor, Enalapril (1.0µM). After this treatment, the cells were immunolabeled with antibodies to phospho-histone H3 and anti-active caspase 3 to evaluate differences in proliferation and apoptosis respectively in the bone marrow-derived versus endogenous fibroblasts. Finally, the cells were immunolabeled with antibodies to myofibroblast antigens to evaluate activated phenotype in the bone marrow-derived fibroblast population. Quantification of differential response of these two populations to Angiotensin II signaling may indentify bone marrow HSC-derived cardiac fibroblasts as an attractive target for post-infarction clinical targeting. Supported by grants P20-RR1-16434 and CO6 RR018823 from the NIH NCRR, Grant in Aid 0865325E from the AHA, grant EPS-0903795 from the NSF, and the Cardiac Developmental Biology Center

012 The Subcellular Localization of Activated P38 and Smad2 in Isolated Dispersed Embryonic Heart Cell Lineages in Response to TGFb2 and 9-cis RA

Fibroblasts to Angiotensin II Antagonism

In response to myocardial infarction, hematopoietic stem cell (HSC) derived cells have been shown to migrate to the heart and differentiate into cardiac fibroblasts. Cardiac fibroblasts are the cell type that is mainly responsible for the synthesis of the extracellular matrix proteins in the heart. The goal of our experiments was to develop an in vitro system to complement our in vivo evaluation of differences in response of bone marrow-derived and endogenous fibroblasts in the infarcted to Angiotensin II antagonism. To accomplish this, we used a chimeric mouse model in which the bone marrow of lethally irradiated wild type mice is repopulated with EGFP+ bone marrow cells, permitting lineage tracing of bone marrow-derived cells that engraft into the infarcted myocardium. In our experiments, cardiac fibroblasts were isolated from the infarct zone of chimeric mice that had been subjected to myocardial infarction by ligation of the left anterior descending coronary artery thirty days prior to sacrifice. Isolated cells were subjected to limited expansion to evaluate whether cardiac fibroblasts derived from bone marrow HSCs respond differently from endogenous fibroblasts to Angiotensin II antagonism in vitro. Cells were exposed to Angiotensin II (10-7M) subsequent to treatment with the AT1 receptor inhibitor, Losartan (1.0µM), or the ACE inhibitor, Enalapril (1.0µM). After this treatment, the cells were immunolabeled with antibodies to phospho-histone H3 and anti-active caspase 3 to evaluate differences in proliferation and apoptosis respectively in the bone marrow-derived versus endogenous fibroblasts. Finally, the cells were immunolabeled with antibodies to myofibroblast antigens to evaluate activated phenotype in the bone marrow-derived fibroblast population. Quantification of differential response of these two populations to Angiotensin II signaling may indentify bone marrow HSC-derived cardiac fibroblasts as an attractive target for post-infarction clinical targeting. Supported by grants P20-RR1-16434 and CO6 RR018823 from the NIH NCRR, Grant in Aid 0865325E from the AHA, grant EPS-0903795 from the NSF, and the Cardiac Developmental Biology Center

014 MiR-10A Down-Regulates Jarid2 Expression in the Second Heart Field

Jarid2 is an essential gene for cardiac outflow tract development, and is directly regulated by Nkx2.5. Nkx2.5 over expression represses Jarid2 expression, and levels of Jarid2 are abnormally high in Nkx2.5 null embryos, potentially leading to an outflow tract defect seen in Nkx2.5 mutants. In Nkx2.5 nulls it is also observed that the expression of the canonical homeobox transcription factor, HoxB4 is decreased. Embedded within this Hox family gene is a coding region for microRNA-10A (miR-10A). MicroRNAs are 20-23 base pair long RNAs that function as post-transcriptional regulators of gene expression. MicroRNAs decrease select target mRNA expression by destabilizing the mRNA or by inhibiting its translational ability. One predicted target of miR-10A is Jarid2, leading us to the hypothesis that an additional mode of Nkx2.5 repression of Jarid2 is through positive regulation of miR-10A. Here we present data exploring this hypothesis by examining both the ability of miR-10A to regulate Jarid2 expression and its potential regulation by Nkx2.5 in the second heart field.
progenitors of the cardiac outflow tract. MUSC’s SURP program

015 Mice Deficient in the Extracellular Matrix Protease ADAMTS5 Undergo Abnormal Endocardial Cushion Remodeling. Deidra L Weber1, Loren E Danese2, Suneel S Apte3, Christine B Kern2; 1Biology, College of Charleston, 2Regenerative Medicine and Cell Biology, MUSC, 3Biomedical Engineering, Cleveland Clinic.

During early cardiac valve formation, the chondroitin-sulfate proteoglycan versican is a critical component of the extracellular matrix (ECM), where it enables formation and cellularization of the endocardial cushions. However, during fetal development endocardial cushions undergo remodeling, and versican expression decreases and has a restricted distribution within the stratified ECM of adult valves. Previously our lab discovered that mice deficient in the ECM protease ADAMTS5 (A Disintegrin-like And Metalloprotease domain with Thrombospondin-type 1 motifs 5) developed severely myxomatous valves by embryonic day 17 (E17) with dramatically reduced versican cleavage. Here we investigated the early developmental onset of the myxomatous valve phenotype in Adamts5-/- mice. LacZ staining indicative of Adamts5 expression was detected in a subset of endocardial cells by E12.5. In serial sections at E12.5 we have identified subtle endocardial cushion contours in WT mouse that were absent in Adamts5-/- littermates and coincident with increased versican. In the endocardial cushions of Adamts5-/- mice increased versican also correlated with a loss of compaction of mesenchymal cells subjacent to the endocardium where Adamts5 is normally expressed. Analysis of E14.5 mice revealed similar findings and three-dimensional reconstructions of the developing valve cusps showed slight increases in cusp volume and shape contouring in the Adamts5-/- deficient mice. Immunohistochemistry revealed an increase in the Sox9 expression domain and intensity in developing cusps of Adamts5- compared to WT littermates at E14.5. Since Sox9 has been shown to upregulate versican transcription, these data suggest a positive feedback loop where reduction of versican cleavage due to loss of ADAMTS5 may result in an increase in its synthesis during early stages of cushion remodeling. These studies identify ADAMTS5 as a critical mediator in the initial remodeling of endocardial cushions and define the mechanism of versican cleavage as critical for normal cardiac valve development. Funding provided by: NIH COBRE (5P20 RR016434-09); American Heart Association: SDG (10SDG 2610168)

016 Cartilage Link Protein 1 and Its Effect on Versican and Hyaluronan Expression During Heart Development, Muyi Li1, Marie M Lockhart2, Andy Wessels3; 1University of Pennsylvania, 2Regenerative Medicine and Cell Biology, MUSC, 3Biomedical Engineering, Cleveland Clinic.

In order to expand our understanding of heart development, we studied versican and hyaluronan expression in the heart in both wild type and cartilage link protein 1 (Crtl1) knockout mice. Because Crtl1 stabilizes the interaction between versican and hyaluronan, two integral extracellular matrix (ECM) proteins, this comparison investigates the role that Crtl1 plays in cardiac development through the expression differences observed in versican and hyaluronan in Crtl1 knockout embryos. Using immunohistochemical procedures, we show that while versican and hyaluronan are co-expressed in the endocardial lining, the cushions, and the mesenchyme of the heart, the degree of expression differs in the Crtl1 wild type embryos and the Crtl1 knockout embryos. Versican isoform V1, and cleaved V0 and V1 isoforms are reduced in Crtl1 knockout embryos. However, no difference was observed in V2 isoform expression between Crtl1 wild type and knockout embryos. Additionally, V1 and cleaved V0/V1 isoforms are found in the endocardium and endocardial derived tissues while V2 is found in the myocardium. This variation in versican expression suggests that different forms of versican play different roles in cardiac development. Finally, the data displays that hyaluronan expression not only coincides with versican expression in the heart- namely V1, but is also reduced in the Crtl1 knockout embryos. Both the reduction of versican and hyaluronan found in Crtl1 knockout embryos may relate to the abnormalities found in those embryos. Overall, the finding from this study expands our knowledge of Crtl1 and asserts its importance in cardiac development. MUSC SURP Program NIH Summer Research Experience Program

017 Spasticity and Fatigue After Spinal Cord Injury: A Relationship with Socioeconomic and Demographic Factors, William H Bingham, James S Krause; MUSC.

Abstract not available.

018 The Relationship Between Prescription Medication Use and Ability to Ambulate Distances After Spinal Cord Injury, Ryan K Kohout1, James S Krause2, Lee L Saunders; 1College of Medicine, MUSC, 2Health Sciences and Research, College of Health Professions, MUSC.

Abstract not available.
019 Racial Disparities in Depression and Subjective Well-Being After Spinal Cord Injury: A Mediation Model, Simon A Brown1, Lee L Saunders2, James S Krause2; 1College of Medicine, MUSC, 2College of Health Professions, MUSC.

OBJECTIVE: The purpose of this study was to analyze the relationships between race and gender, with depression and subjective-well being (SWB) among patients with spinal cord injury (SCI). Furthermore, this study examined whether socioeconomic factors mediate the relationships between predictors and outcomes. DESIGN: A cross-sectional survey was done to collect data from participants. SETTING: All participants were selected a large specialty hospital in the southeastern United States. PARTICIPANTS: 1,549 participants met three inclusion criteria: 1.) traumatic SCI, 2.) 18 or older at assessment, and 3.) minimum of 1 year post-injury. MAIN OUTCOME MEASURES: The three satisfaction factors of Life Situation Questionnaire – Revised (LSQ-R): Home Life Satisfaction, Vocational Satisfaction, and Global Satisfaction; and The Older Health and Mood Questionnaire (OHAMQ), a 22-question set designed to assess depressive symptomatology according to Diagnostic and Statistical Manual of Mental Disorders (DSM III-R) criteria. RESULTS: MANOVA statistics revealed significant main effects for race outcomes with regards to three out of four dependent variables. Univariate analysis confirmed that black participants had significantly lower satisfaction scores compared to white participants, as well as significantly higher depression scores. The three-stage linear regression model proved that years of education and annual household income were both significantly correlated for mediating race effects in VOC (p<.001). In addition, annual household income was proven to have significant correlation for mediating the race effects in HLS (p<.05). CONCLUSIONS: Race is still a reliable risk predictor for depression or lower SWB among SCI patients with socioeconomic factors significantly accounting for this trend. The overall decline in disparities despite socioeconomic differences suggests that there are compensatory factors that need to be identified for improved rehabilitation efforts. Supported by NIDRR grants H133B090005 and H133G050165 from the Department of Education; and supported in part by NIH grant 1R01 NS 48117.

020 Does Abnormal Muscle Coactivity Decrease with Recovery Following Stroke?, Kathryn L Zettl1, Regan H Root1, Michelle L Woodbury1, 2; 1College of Health Professions, Occupational Therapy, MUSC, 2Ralph H. Johnson VA Medical Center.

Background: During forward-reach, the shoulder flexes, elbow extends and the trunk remains still; requiring simultaneous activation of arm muscles for mobility and trunk muscles for stability. Persons post-stroke display irregular muscle-activation associated with stroke-severity. When reaching forward, persons with severe-stroke simultaneously co-activate shoulder/elbow flexors. Persons with mild-moderate stroke display more normal shoulder-flexion and elbow-extension patterns. Abnormal shoulder-elbow muscle co-activation patterns can limit functional performance. Recovery is characterized by improved hemiparetic arm coordination associated with normalized shoulder-elbow muscle co-activity. Although shoulder-elbow muscle co-activity is well-studied, little is known about trunk-shoulder co-activity in persons with differing post-stroke severity. Objective: Compare trunk-shoulder muscle-activity patterns of less-impaired to more-impaired arms of persons with mild-moderate and severe stroke. Methods: Participants were recruited from VA Rehabilitation Research Center of Excellence, Gainesville FL. Inclusion criteria: participants having a single-stroke, having no pain, joint or visual limitations impeding participation-ability. Informed-consent was obtained and existing data analyzed according to protocols of University of Florida and MUSC IRBs. Surface-electromyographic (EMG) analysis was conducted during 5-trial sessions of seated reach-to-a-soda-can. Sensors were placed on infraspinatus, anterior-deltoid, and triceps according to SENIAM protocols. Data were cleaned, filtered, processed and analyzed. EMG onset/offset was defined as amplitude exceeding/falling below resting-amplitude +SSD. Results: Evaluations conducted on 55 individuals with stroke, ages 43-84, were 23-60 months post- stroke. Data-analysis comparing EMG of less-impaired arm to more-impaired arm is in-progress. We expect hemiparetic anterior-deltoid of mild-moderately impaired-persons will exhibit low co-activity with triceps, but high co-activity with infraspinatus; the same pattern seen in the less-affected arm. Hemiparetic anterior-deltoid of more severely impaired-persons will exhibit high co-activity with triceps and low co-activity with infraspinatus; opposite the pattern in the less-affected arm. Discussion: Results will show post-stroke muscle activity displayed by abnormal co-activity patterns thereby emphasizing the importance of patient-tailored rehabilitation, inform treatment, and defining post-stroke recovery expectations. Supported by the Veterans Affairs Office of Research and Development, Rehabilitation Research and Development Career Development 2 Award (Project #B6332W), PI: Michelle L. Woodbury

021 Does Active Range of Motion of Shoulder Flexion Recover Before Wrist Extension During Forward Reach in Individuals Post-Stroke?, Schayla D Ardis1, Ashley N Farina1, Jessica L Newton1, Michelle L Woodbury1,2; 1College of Health Professions, Occupational Therapy, MUSC, 2Ralph H Johnson VA Medical Center.

Objective: To compare active range of motion of shoulder-flexion to wrist-extension of the hemiparetic
arm post-stroke during forward reach. Background: Stroke is the main cause for persistent functional limitations. A primary focus of client-centered rehabilitation is improved function in the involved upper extremity. It is important to understand the pattern of upper extremity motor recovery post-stroke to provide optimal rehabilitation. Traditional views of recovery suggest movement is regained proximally to distally. However, there is evidence stroke equally affects active range of motion of proximal and distal segments of the upper extremity when isolated motions are compared. This suggests motor recovery does not follow a stereotypical gradient.

Methods: Participants were recruited from a VA Rehabilitation Research Center of Excellence in Gainesville FL. Inclusion criteria: single stroke, no pain, joint or visual limitations impeding ability to participate. Informed consent obtained and existing data analyzed according to protocols approved by University of Florida and MUSC IRBs. Kinematic analysis was conducted while subjects performed 5 seated reach-to-a-soda-can trials using an upper body biomechanical model validated in our lab. Shoulder and wrist joint excursions were calculated as the difference between 3-D joint angles from start to end movement. Active range of motion was calculated as a ratio of joint excursion of the more-involved to less-involved arm. Results: Evaluation conducted on 55 individuals: age range 43-84 years, 23-60 months post-stroke. Data analysis is in-progress. We expect post-stroke recovery of active range of motion does not follow a standard proximal-distal gradient. Therefore, we expect the shoulder and wrist will exhibit similar active range of motion limitations during forward reach. Discussion: It is important to validate or challenge traditional assumptions regarding post-stroke upper extremity recovery because rehabilitation is influenced by these ideas. If there is no stereotypical proximal-to-distal gradient of motor impairment, then rehabilitation must be individualized. Supported by the Veterans Affairs Office of Research and Development, Rehabilitation Research and Career Development Award (Project #B6332W).

023 Does Stroke Severity Influence Sensory-Feedback Needed for Reaching?, Kelly R Anderson1, Greg M Loftis1, Melissa K Turpin1, Michelle L Woodbury1,2; 1College of Health Professions, Occupational Therapy, MUSC, 2Ralph H. Johnson VA Medical Center.

Individuals post-stroke demonstrate reaching in a closed-loop system. This means sensory feedback is used to correct and ensure a successful reach. The reach has two components, feed-forward and feedback. Size, shape, and location of the object must be processed to formulate a motor plan. This feed-forward mechanism occurs before the reach. The feedback phase makes online adjustments by processing external stimuli during the reach to correct a faulty motor plan. Feed-forward processing corresponds to the acceleration phase of a reach, while feedback corresponds to deceleration. More severe strokes are associated with using more sensory-feedback and a longer deceleration phase. Objective: The purpose is to correlate time spent in deceleration phase with stroke severity. Methods: Participants were recruited from a VA Rehabilitation Research Center of Excellence in Gainesville FL.
Participants having a single stroke were included if having no pain, joint, or visual limitations impeding ability to participate. Informed consent was obtained and existing data analyzed in accordance with protocols approved by University of Florida and MUSC IRBs. Motion analysis was conducted while subjects performed 5 trials of seated reach-to-a-soda can using an upper body biomechanical model previously validated in our laboratory. Motion data were cleaned, filtered, processed, and analyzed using custom designed software programs. Time spent in deceleration phase was calculated as total movement time minus time to peak velocity. Results: Evaluation was conducted on 55 individuals ranging in age from 43-84 yrs who were 23-60 months post-stroke. Data analysis is in-progress. We hypothesize more time is spent in the deceleration phase for individuals with more severe strokes. Discussion: Results are clinically relevant because they influence rehabilitation. First, deceleration time provides a sensitive method quantifying post-stroke recovery. Second, therapists can design treatments to improve motor planning prior to reach. Supported by the Veterans Affairs Office of Research and Development, Rehabilitation Research and Development Career Development -2 Award (Project #B6332W), PI: Michelle L. Woodbury

024 Bedtime and Napping Behaviors in Preschool Children From a Low-Income Cohort, Saujanya Vadoothker1, Julie C Lumeng2; 1College of Medicine, MUSC, 2Center for Growth and Development, University of Michigan.

Sleep patterns change with age, and it is important to establish consistent nighttime routines in children at a young age to ensure they get an adequate amount of sleep. Sleep problems and disturbances that reduce sleep duration have been associated with obesity, behavior problems, and cognitive deficits. Few prior studies examining bedtime routines and napping behaviors in preschool children have been completed to date. Therefore, the objective of this study was to examine the prevalence of a range of bedtime routines and napping practices within a low-income cohort of preschoolers. The sleeping habits of 140 preschool children, aged 3 to 5, from Head Start, an early education program for at-risk families, in rural Michigan counties were studied. Mothers, or legal guardians, of the children completed detailed, standardized questionnaires (Children’s Sleep Hygiene Scale, General Sleep Information, and Child Sleep Wake Scale) concerning their child’s sleeping habits. This study found that a variety of bedtime routines exist. Responses were evaluated as always, sometimes, never, or as a time of day. Most children had a bedtime (86.43%, 0%, 13.57%) and a cold bedtime routine (35.25%, 56.83%, 7.91%). In a typical week, bedtimes ranged from 6:00 PM to 2:00 AM, and wake times ranged from 4:00 AM to 12:00 PM. Some evidence of poor sleeping habits at nighttime were found: trouble settling down at bedtime (7.14%), poor at falling asleep at “lights out” (12.86%), active 30 minutes before bedtime (39.39%), and co-sleeping with parents or a sibling every night (27.86%). Additionally, 23.57% reported that their child never takes a nap, and 16.43% reported their child naps 7 days/week. Thus, this information elaborates on the sleep practices of preschoolers in a low income, rural cohort and highlights the differences in this population as compared to previous studies completed with children from other backgrounds. American Pediatrics Society/Society for Pediatric Research

025 Dietary Habits of Community Dwelling Individuals with Severe and Persistent Mental Illness, Emily B Modlin, Dana M Blomquist, Shannon N Collie, Stephanie A Davidson, Shannon K Pouliot, Tara A Warner, Sarah C Wilkes, Nancy E Carson; Health Professions, Occupational Therapy, MUSC.

Depending on their living situation, individuals with severe mental illness (SMI) may not have an opportunity to engage in the occupational roles of meal planning and food preparation. Individuals with SMI have decreased behavioral capability as evidenced by greater difficulty obtaining or cooking food and unfavorable eating behaviors such as skipping meals (Chuang, et al., 2008; Kilbourne, et al., 2007; Brown, et al., 1999). Individuals with SMI may not have the skills to plan and purchase healthy foods or they may not have the skills needed to prepare their food. Their diet quality may be poor which can lead to obesity and related health problems. This is a concern as individuals with SMI experience higher obesity and mortality rates than the general population (Colton & Manderscheid, 2006) and their mortality risk for cardiovascular disease is significantly greater than expected (Brown, et al., 2000). A review of the literature regarding occupational role engagement for meal planning and food preparation for this population will be presented with a focus on required skills, skill performance, opportunity for engagement, and value to the individual. Surveys with participants of a community mental health center program were conducted to identify food habits and skills, and 24-hour food recalls were conducted to describe the dietary intake of these individuals. Descriptive data will be presented. For OTs working in community mental health, the focus on occupational roles such as meal planning and food preparation is essential to enabling the client to live as independently as possible.
026 Neurocognitive Functioning Among Bariatric Surgery Candidates, Andrea N Shipp\(^1\), Alok Madan\(^2\), Laura K Campbell\(^2\); \(^1\)College of Medicine, MUSC; \(^2\)Psychiatry and Behavioral Sciences, MUSC.

The incidence of obesity is growing and is associated with increased mortality, morbidity and healthcare cost. A growing literature suggests a link between obesity and neurocognitive dysfunction, including among bariatric surgery candidates; this relationship could plausibly be associated with health behaviors necessary for successful weight maintenance. The goal of this exploratory study was to add to the limited understanding of neurocognitive dysfunction among patients with Class III obesity (BMI>30) and to explore the implications of such dysfunction on historical health behaviors. In this retrospective chart review of individuals (N=12) seeking bariatric surgery who underwent comprehensive psychosocial evaluations (including neuro-cognitive testing) as part of routine pre-surgical evaluations, we examined their neurocognitive functioning and the relationship between attentional, memory and executive measures with medical variables and clinician-rated judgments of historical health behaviors and compliance. Descriptive analyses revealed that generally middle-aged Caucasian women with some college education, an average BMI of 51, and with one or more of the commonly associated comorbidities evidenced varying degrees of neurocognitive dysfunction across all tested domains. Correlational analyses revealed better performance on measures of attention (r=0.77, p<0.05) and executive functioning (r=0.73, p<0.05) were associated with historically better health behaviors. Lower IQ (r = -0.71, p<0.05) was associated with increased incidence of type II diabetes. Surprisingly, increasing BMI was associated with better performance on measures of visual/spatial construction (r=0.66, p<0.05). There appears to be subtle neurocognitive dysfunction among obese individuals considering bariatric surgery. Given the study design, directionality of the relationship between neurocognitive functioning and historical health behaviors is difficult to establish, especially from such a small study sample that may have limited generalizability to the population. Future research should examine the potential of surgically-mediated weight loss to improve neurocognitive functioning. DART Summer Research Fellowship

027 Health Behaviors Practiced by First-Year Health Professional Graduate Students at the Medical University of South Carolina, Lauren N Kohn, Hazel L Breland, Bailey H Mary, Hughes A Lauren, Rowell M Courtney, Tara L Scott; CHP, Division of Occupational Therapy.

Transitioning to post-secondary education often leads to the development of health-risk behaviors in areas such as alcohol, tobacco, nutrition, physical activity, and sleep patterns, placing students at an increased likelihood of developing long-term unhealthy behavior patterns. First-year health professional graduate students already have and will continue to acquire knowledge and exposure to health risks. Nonetheless, currently there is little known about the relationship between their knowledge and the health behaviors they actually practice. Given the prevalence of health-risk behaviors in the general college-age population, there is a need to gather preliminary information on the health and wellness of first-year health professional graduate students. This study examined health behaviors practiced by first-year health professional graduate students at the Medical University of South Carolina (MUSC) enrolled in occupational therapy (OT), physical therapy (PT), and physician assistant (PA) graduate clinical education programs. A survey of behavioral risk factors was adapted based on the Behavioral Risk Factor Surveillance System Survey Questionnaire (BRFSS) to examine the health behaviors practiced among first-year health professional students. The survey was administered to 83 first-year students enrolled in graduate clinical education programs in the College of Health Professions. Our anticipated results are that by the first-year health professional graduate students identifying their current practiced health behaviors, it will enhance their ability to facilitate health education as a means of promoting positive health behaviors of their future clients as well as enhance their personally practiced health behaviors.


Interpersonal communication styles and individual perceptions impact the effectiveness of healthcare delivery. To maximize patient-provider interactions among the elderly it is important to explore how the elderly communicate. With a national agenda for health promotion and an increasingly aged population, it is important for health professions students to understand the interaction of health, occupations, and health communication because the elderly are faced with the challenge of balancing all three. This qualitative study will explore the influences of health on the occupations of a multiethnic elderly cohort and examine patient health communication with community members versus trained health professions students. Recorded interviews and typed transcripts of conversation data collected during the Carolinas Conversation Collection (HR#17575) will be analyzed using summative content analysis. We anticipate the results will enhance the understanding of health influences on daily occupations and health
communication. In addition, the findings are expected to broaden health professions students’ perspective about patient-provider interactions to enhance communication for effective practice and health promotion. Thanks to Dr. Charlene Pope, PI of the Carolinas Conversation Collection for allowing us to serve as student interviewers as well as utilize the archived data for our research project.

029 Support Experiences in Individuals Coping with Advanced Colorectal Cancer, Elena I Gore1, Scott Cole1, Melanie B Thomas2, Katherine R Sterba1, Kristin Wallace1, 1Medicine, Biostatistics & Epidemiology, MUSC, 2Medicine, Hematology & Oncology, MUSC.

Background: While there is evidence demonstrating a link between social support and adaptive coping in cancer patients, less is known about support in the context of advanced cancer. An understanding of how support facilitates adaptive coping may inform interventions to improve outcomes after diagnosis. The purpose of this qualitative study was to explore experiences of support in patients coping with metastatic colorectal cancer at diagnosis, during care planning, and during treatment. Methods: Individuals with metastatic colorectal cancer (N=26, average age=58, 50% women, 35% African-American) were recruited in a regional cancer clinic. Participants completed telephone interviews using a structured interview guide and template analysis was used to explore themes in participants’ responses concerning support. Results: Support was consistently described as central to respondents’ coping experiences. Three major themes emerged: 1) faith, 2) friends and family, and 3) physicians. Faith in God’s omnipotence and the comfort of prayer provided ongoing emotional and spiritual support to patients. Family and friends offered both positive and negative emotional and instrumental support. For example, simply “being there” at diagnosis was viewed as supportive while pity was discouraging. Physicians conveyed instrumental and informational support through open communication. Notably “straight-forward and frank” communication from the physician with an acknowledgement that every patient is different, was seen as hopeful and encouraging. Patients reported a variety of support needs in the areas of nutrition, support groups, and improved communication with care providers. Conclusions: Frequent consideration of the social environment of patients with advanced cancer can help identify unmet needs at diagnosis and improve responses to changes along the care continuum. Future studies should investigate how to incorporate patients’ existing support resources into patient-centered models of care in an effort to improve quality of life. MUSC Center for Health Disparities Research

030 Barriers to HIV Testing: A Community Perspective, Brent A Boyer1, Dag Shapshak2, Bobby Navarro2, 1MUSC, 2MUSC, Emergency Department.

In South Carolina, the majority of newly identified HIV positive patients test late in their disease course when therapy is less effective and transmission is more likely to have occurred. Despite 2006 CDC recommendations for universal screening, many health care settings still don’t offer routine HIV testing. We developed a novel ‘hub and spoke’ testing paradigm to expand HIV testing into community healthcare clinics. This model incorporates a successful HIV testing infrastructure already in place at our MUSC emergency department, the hub. As a first step to implementing testing at spoke sites, we assessed if clinics in Charleston and Dorchester counties offer routine HIV testing and identified perceived barriers. Survey responses were collected from supervising clinicians at 20 primary care clinics. Respondents were identified from a volunteer list at a local free clinic comprised of physicians who provided input for their own practices as well as from the MUSC Go-Local website. Descriptive data collected include HIV testing practices, insurance status, and ranked responses of 13 perceived barriers to implementation of testing. Respondent rates were high from the Go-Local list 13/24 (54%) and volunteer list 7/8 (88%). Two clinics (10%) reported routine, HIV screening. Moderate to strong barriers for ‘uninsured’ clinics included linkage to specialist follow-up, testing time requirements, costs of the test devices, costs of confirmatory testing, and provider training. Respondents at clinics serving mostly uninsured patients recognized their patients as at risk for HIV and believed their patients would accept testing. Clinics serving mostly privately insured patients viewed the clientele as low-risk and unaccepting of HIV testing. These data suggest barriers at uninsured clinics were financial in nature. Our testing paradigm, which relies on available resources from multiple departments, may be well suitable for uninsured clinics as these resources overlap with their perceived barriers. Thanks to the MUSC Summer Health Professional Program funded by Dr. Edege’s Short Term Research Training for Health Professional Students.


OBJECTIVE: Traumatic Brain Injury (TBI) is a devastating epidemic in the pediatric population with significant long-term implications. There are few successful interventions after injury; therefore, we sought to better understand factors that contribute to this problem. METHODS: This was a retrospective cohort study, where data on pediatric TBI was
collected from all hospitals in South Carolina from 1998-2008. The SC TBI Surveillance System was established in 1992 and collects information on all TBI patients from all nonfederal in state acute care hospitals. Information was collected on 55,439 patients, including patient age, severity of TBI, insurance status, patient socioeconomic status (SES), and discharge disposition. SES was determined by analyzing both zip code and insurance status to categorize patients into low, middle, or high-income groups. RESULTS: Patient data was analyzed by developmental age groups (0-2, 3-7, 8-12, and 13-17 yrs). The 13-17 age group (n=17,090) had the highest representation (30.8%) of reported TBI. Although the largest group of patients was reported to have commercial insurance coverage (45.6%), the next two largest groups were supported through Medicaid (34.3%) or were uninsured (11.6%). This correlates to the fact that more than half of the reported TBI cases were patients from low-income families (56.4%). Utilizing SES we noted that 63% of the TBI patients in the 0-2 age group were from lower SES while only 12.8% of the patients were from higher SES. This pattern continues with lower SES comprising more than 50% of all TBI in all age groups. CONCLUSION: The incidence of pediatric TBI has been increasing over the last 10 years, primarily due to increased numbers of cases in the 0-2 age group. Safety and prevention measures should be targeted towards teenagers and infants from lower socioeconomic status, where the highest incidence of injury occurs. Further study is required to evaluate the level of hospital care provided to those with lower SES with respect to pediatric TBI. Supported by the South Carolina Clinical & Translational Research Institute, Medical University of South Carolina’s CTSA, NIH/NCRR Grant Number UL1RR029882 and KL2 Program Grant Number KL2RR029880.

032 Baseline Prevalence of Waterborne Parasites in Ugandan Communities As Part of a Cohort Study, Kevin M McElligott¹, James T McElligott¹, Christiana Naaktgeboren², Kristen Wolf², Andrea Summer², Jeffery L Deal², ¹Medical, Pediatrics, MUSC, ²Water Missions International.

An association between a water purification intervention and reduced stool parasite load was shown in cross sectional data from Honduras. To further explore this effect, the pre-intervention stage of a cohort study involving 6 communities in Uganda is presented. The objective is to compare parasite prevalence and explore community characteristics. We hypothesize that there will be no significant difference in baseline prevalence among the six communities. Communities were selected based on criteria of size, location, and access to water. Subjects were randomly selected using a stratified cluster sampling method. Subjects were interviewed and tested using a validated rapid test to determine parasitic load of E. histolytica/dispar, Giardia lamblia, and Cryptosporidium. The primary outcome was the presence of stool parasite. Independent variables of age, gender, diarrhea symptoms, profession, and water source were also collected. Significance was determined with chi square, Fisher’s Exact and multivariable analysis. A total of 308 out of 431 (71.5%) subjects returned samples. The median prevalence for the 6 communities was 0.16 (Range = 0.08 - 0.18). There were no significant differences for a positive (+) test between communities (p=0.63). Those who are younger (Age: <13) were more likely to be + (p=.02), and those who reported a fishing related occupation were less likely to be + (p<.01). Other variables analyzed revealed no significant differences. Logistic regression controlling for the independent variables reveals consistent results. Parasite prevalence among communities is similar, supporting the stated hypothesis. Sample size will be expanded for the post-intervention stages of the analysis to facilitate further subgroup analysis of trends, allowing for a greater understanding of the impact of the water purification intervention. Water Missions International

033 Effect of Reduced Marijuana Use on Cognitive Battery Performance Among Cannabis Dependent Adolescents, Candice S Whitaker¹, Kevin M Gray²; ¹College of Medicine, MUSC, ²Psychiatry, MUSC.

Marijuana is the most commonly used illicit drug among adolescents. While research studies have shown that heavy cannabis use has an effect on multiple domains of cognitive functioning in adolescents, it is less clear whether or not the deficits will subside with continued abstinence and what time point neurocognitive recovery occurs. The objective of the present work is to investigate the cognitive functioning of adolescent cannabis users at different stages of reduction and/ or abstinence from marijuana use. Cognitive functioning was assessed using CNS Vital Signs neurocognitive battery in 49 adolescent participants in a placebo-controlled trial of N-acetylcysteine in cannabis dependent adolescents. Participants completed a neurocognitive battery at 4 time points during the 12 week clinical trial and urine drug screens twice weekly. At baseline, neurocognitive battery performance did not significantly correlate with urine creatinine normalized tetrahydrocannabinol level. As urine creatinine normalized tetrahydrocannabinol levels decreased over the course of the trial, verbal memory performance improved at week 4 (p = .0182) and reaction time and social acuity improved at week 8 (p = .0500 and .0007), when compared to baseline performance. These are considered trend-level findings at this preliminary stage, and we predict that with an adequately powered analysis (goal N=134) there will be significance in the domains of verbal memory, reaction time, and social acuity. MUSC DART Program Summer Research Fellowship
Glioblastoma multiforme (GBM) is one of the deadliest brain tumors with an average survival of 12 months. The purpose of this retrospective study was to evaluate the efficiency of the Multidisciplinary Clinic (MDC) treatment method, and to evaluate the relationship between various treatment factors and ultimate patient survival outcomes at a regional teaching hospital. We reviewed and followed 53 patients treated at Greenville Memorial Hospital from the years 2001-2010 encompassing both pre- and post-MDC patients. Variables collected and analyzed included age, survival time, tumor size, tumor site, and extent of resection. Although the relatively small sample size of our study limited the statistical significance of many of our findings, the results of our study provided valuable insight into the effectiveness of a new GBM treatment model at a regional teaching hospital.

Neurosurgery in a Rural Sub-Saharan African Hospital: A Survey of Procedures and Outcomes, Joseph J Kavolus1, Jordan Magarik1, Joyce Nicholas2, Dilan Ellegala3, Emmanuel Nuwas4, 1College of Medicine, MUSC, 2Furman University, 3Wofford College, 4Greenville Hospital System University Medical Center.

036 Purkinje Fiber Response to Pressure Overload in an Underdeveloped Cardiac Conduction System, Amanda Northup1, Mary S Rackley2, Catalin F Baicu2, Brett H Harris3, Terrence X O’Brien2, 1College of Medicine, MUSC, 2MUSC Gazes Cardiac Research Institute, 3Ralph H. Johnson VA Medical Center, 3Regenerative Medicine and Cell Biology, MUSC.

Mutations of Nkx2-5 are known to cause congenital heart defects in humans. In mice, Nkx2-5 haploinsufficiency results in hypoplasia of the conduction system, and essentially an underdeveloped conduction system. In this study, the effects of pressure overload on an underdeveloped murine cardiac conduction system were examined by assessing changes in the expression of Connexin40 (Cx40), a gap junction protein. Clinically, the pressure overload model is representative of hypertension, atherosclerosis, aortic valve disease, and some cardiomyopathies. This study was designed to examine the effects of pressure overload on Cx40 expression in a hypoplastic conduction system. The mouse model was a heterozygous transgenic, created by crossing Cx40 EGFP/+ and Nkx2-5/- mice. Transverse aortic constriction (TAC) surgery was performed on the mice to induce pressure overload. Purkinje fibers were imaged, and Cx40 levels were quantified as a measure of gap junction expression. As expected, there was an increase of 77% in the expression of Cx40 in the TAC mice compared to the control. In addition, there was observable disorganization of Cx40 signal after TAC, suggesting gap junction remodeling. From this data, we can conclude that TAC in mice with hypoplastic conduction systems leads to increased expression and disorganization of Cx40. Clinically, this is important because increased levels of Cx40 may increase the risk for atrial and ventricular arrhythmias. Supported by Leonard E. Egede, MD, through the Short Term Research Training for Health Professional Students (grant number 5T35DK007431).
Introduction: tDCS is a non-invasive scalp-applied brain stimulation technique that has been shown to change cortical activity within the brain. Current directed into the brain runs from anode to cathode and changes cortical neuron activity such that there is activation under the anode and deactivation under the cathode. tDCS may be beneficial in the treatment of chronic pain, depression, epilepsy, and stroke (1). The aim of this study is to examine if tDCS is effective in the treatment of post-surgical pain in patients undergoing a total knee arthroscopy (TKA). Methods: Six patients undergoing unilateral TKA were randomized into either an active or sham treatment group. Patients received 2mA anodal stimulation over the knee-representation of the motor cortex and cathodal stimulation over the right prefrontal cortex. Patients received either four real or four sham treatments during the 48-hour period post-surgery. Hour-by-hour PCA use was documented as a measure of pain behavior, and VAS scales were used to assess pain, mood, and anxiety levels before and after each treatment. Results: There was a significant difference in the cumulative PCA usage at 48-hours post-surgery with patients receiving sham using 7.6 mg (SEM=.99) versus only 2.7 mg (SEM = .88) for patients receiving real treatment (t(4)=3.74, p=.02). Discussion: Patients receiving real tDCS treatment experienced less pain post surgery as measured by their consumption of pain medication in this preliminary pilot. More data is needed to permit definitive conclusions regarding the effectiveness of adjunctive brain stimulation for managing post-operative pain, and this trial is currently on going. (1) George George, M. S., & Aston-Jones, G. (2010). Noninvasive techniques for probing neurocircuitry and treating illness: vagus nerve stimulation (VNS), transcranial magnetic stimulation (TMS) and transcranial direct current stimulation (tDCS). Neuropsycho-pharmacology, 35, 301-316.

038 Hyperglycemia and Outcomes of Perfusion CT Guided Therapy in Patients Treated for Acute Ischemic Stroke, Jordan A Magarik1, Robert J Adams1, Marc Chimowitz2, Christine A Holmstedt3, Edward C Jauch2, Aquilla S Turk3, Daniel Lackland1, 1Neuroscience, MUSC, 2Emergency Medicine, MUSC, 3Interventional Neuroradiology, MUSC.

Stroke and diabetes are prevalent in the southeastern United States especially among African Americans in South Carolina. The treatment of acute ischemic stroke is multimodal and requires the consideration of factors such as: non-contrast CT and perfusion-CT findings, duration and extent of symptoms, as well as several risk factors and comorbid conditions like race, hypertension, hyperlipidemia, and diabetes mellitus. Furthermore, studies have suggested an increased risk of recurrent stroke in diabetic patients, as well as poorer outcomes in patients who are hyperglycemic during the immediate and 24-hour post stroke period. Additionally it has been suggested that hyperglycemic patients in the acute post stroke period experience worse outcomes with intravenous thrombolytic reperfusion than those who do not achieve reperfusion. To examine the effects of hyperglycemia on the extent of penumbral and infarcted neural tissue on perfusion-CT imaging and on patient outcomes measured using the National Institute of Health Stroke Scale (NIHSS), Rankin scale, and Barthel index scores. Patients admitted to the Medical University of South Carolina (MUSC) with the diagnosis of acute ischemic stroke from October 1, 2008 to September 30, 2009 and underwent CT-perfusion will be included in the study. Additional inclusion criteria include patients who received intravenous, intra-arterial, or no treatment. Data on serum glucose levels at admission and throughout treatment of the initial stroke event will be extracted from patient records. NIHSS, Rankin, and Barthel index scores will be utilized to assess outcome. Diabetic hyperglycemia will be considered separately from non-diabetic hyperglycemia during acute ischemic stroke to determine the role of chronic hyperglycemia in short and long-term outcome in stroke. Delineation of ischemic penumbra from infarcted neural tissue will be assessed. From multivariate regression analysis odds ratios will be calculated from stratified glucose levels, type of intervention (intravenous, intra-arterial, or medical therapy), perfusion CT finding, and outcome.

039 Early Motor Skill Patterns in Low and High Risk Infants, Beth A Bower, Katherine Bean, Kelsey Carn, Lindsey Mays, Sara Pender, Lindsay Rowland, Sarah Shell, Patricia Coker-Bolt; Occupational Therapy, MUSC.

The purpose of this pilot study is to collect prospective pilot data on the time course of motor skill development in low and high risk term, near term, and preterm infants using kinematic assessment, non-invasive muscle ultrasound imaging, and validated motor developmental tests in a completely novel application to detect motor skill changes occurring in the first year of life. We will collect data on muscle architecture to correlate these parameters with the Alberta Infant Motor Scale (AIMS) and the Test of Infant Motor Performance (TIMP) scores in low and high risk term, near term, and preterm infant groups at term, 6, and 12 weeks post-EDC. We will utilize video kinematic analysis to quantify aspects of motor activity during TIMP/AIMs testing and use specific tests of reflexes, head, body, arm and leg movements.Cerebral Palsy (CP)
has been newly defined as “a group of disorders of the development of movement and posture, causing activity limitations that are attributed to non-progressive disturbances that occurred in the developing fetal or infant brain.” (Bax, Goldstein, Rosenbaum, et al., 2005). This new definition of CP highlights abnormal motor development or the development of movement as the crux of CP that leads to activity limitation throughout the lifespan, despite the fact that the initial brain lesion is non-progressive. CP occurs in 3.6 per 1,000 live births or 1 in 278 children and is the most common physical disability originating in childhood. There are no quantifiable early markers of cerebral palsy (CP) in current clinical use. Even in a high risk population of infants, 18-24 months of age is the typical timeframe in which a reliable diagnosis of CP can be made. A detailed knowledge of what to expect for the motor skill development of low and high risk infants in the first year of life is a critical first step to improve outcomes for infants at risk for later diagnosis of CP.

**MUSC Specialized Center of Research (SCOR 2010-2011)**

### 040 Getting the Most Out of a 2D Ultrasound Measure of Muscle Thickness in Children with Cerebral Palsy

**Ashley P Dew, Noelle G Moreau; Health Professions, Physical Therapy, MUSC.**

**Background:** Muscle size is known to be directly proportional to the force generating capacity of skeletal muscle. Therefore, precise measures of muscle size are useful when investigating weakness in children with Cerebral Palsy (CP). Muscle thickness measurements taken at 50% of thigh length (MT50) are traditionally estimated as the maximum cross-sectional area of the quadriceps. Therefore, the purpose of this study was to determine agreement between MT50 (RF) and a maximal muscle thickness measurement (MaxMT) in children with CP. Methods: MT50 and MaxMT of the rectus femoris (RF) were obtained bilaterally using ultrasound imaging in 13 ambulatory children with CP (mean age: 14.4 ± 3.6 years). Video sequences were taken as the probe was slowly moved from the MT50 line towards the proximal insertion of the muscle. Muscle thickness was measured every 2 seconds until MaxMT was determined. Three MT50 measurements were obtained at 50% thigh length and averaged. Pearson’s correlation was used to calculate linear agreement, paired t-tests to evaluate mean differences, and a Bland Altman plot to determine agreement between measures. Results: MT50 and MaxMT were significantly correlated (r=0.98; p< .001). The Bland Altman plot showed all values fell within 95% limits of agreement, except for a single outlier. However, on average, MT50 was .09cm less (1.70± .46) than MaxMT (1.78± .48) (p< .001). Conclusions: Although MT50 and MaxMT were highly correlated, Bland Altman showed constant bias across values. On average, MaxMT was .09cm higher indicating maximal RF thickness is proximal to the standard 50% of thigh length in CP.

However, given the more time-consuming nature of obtaining MaxMT, the MT50 measurement may be a more feasible alternative when the true maximum is less relevant. Therefore, the researcher/clinician must determine whether the differences are clinically important, depending on the research question or clinical application. Funded by the Thrasher Research Fund and the Pedal-With-Pete Foundation

### 041 Chemotherapy Tolerance in Colorectal Cancer Patients Post Liver Resection: A 5-year Retrospective Study At a Regional Teaching Hospital

**Leah D Fryml1, William J Edenfield2, Elizabeth Bleed3, James M Mills4; 1College of Medicine, MUSC, 2Cancer Center of the Carolinas, 3Truman University, 4Wofford College.**

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

### 042 ETS1 Transcriptional Regulation of Prostate Cancer Progression

**Ashley M Smith1, Victoria J Findlay1, Angen Liu2, Emily Kistner-Griffin3, David P Turner2; 1Pathology, MUSC, 2Hollings Cancer Center, MUSC, 3Biostatistics & Epidemiology, MUSC.**

Androgen deprivation therapy (ADT) reduces the levels of male hormone (testosterone) in the body which inhibits the growth of prostate tumors by preventing the function of a protein known as the androgen receptor (AR). However, many cancers develop insensitivity to ADT as androgen receptor function is restored and the cancer progresses to the deadly castrate resistant prostate cancer (CRPC). The levels of expression of the E-Twenty-Six transcription factor family member ETS1 are significantly increased in clinical and latent prostate cancer relative to benign prostatic hyperplasia and normal prostate. This study examines the role of ETS1 transcriptional regulation in promoting prostate cancer progression and the CRPC phenotype. ETS1 loss of function and gain of function studies have been used to examine the role of ETS1 in promoting prostate cancer progression. ETS1 and AR RNA and protein levels were examined in human tissue samples as well as in a cell line progression model by q-PCR, immunohistochemical staining and
western blot analysis. Cellular growth was determined in 3D tissue recombination models and cellular localization defined by co-immunofluorescence. The effect of ETS1 modulation on target gene expression was analyzed using qPCR. Apoptosis Superarrays and promoter occupancy was determined by chromatin immunoprecipitation (ChIP) and q-PCR. Interestingly, over 70% of AR response elements are adjacent to ETS transcriptional binding sites. An in vivo analysis of ETS1 and AR levels in low grade (Gleason 5-6) and high grade (Gleason 7-9) human prostate tumor samples reveals a significant correlation between high ETS1 and low AR expression levels. ETS1 gene knockdown in 3D culture models inhibits spheroid formation both in the absence and presence of the stromal compartment. Using Dr. Leland Chung's LNCaP prostate cancer progression model this study correlates elevated ETS1 levels with the increased metastatic potential of the LNCaP derivative cell lines. Additionally, nuclear localization of the phosphorylated form of ETS1pThr38 is increased in the castrate resistant LNCaP C4-2 derivative cell line compared to the castrate sensitive parental cell line suggesting increased transcriptional activation.

In vitro ETS1 loss of function and gain of function studies demonstrate the altered expression of AR target genes and chromatin immunoprecipitation studies demonstrate that AR transcriptional activation leads to the recruitment of ETS1 to these promoters. These and published data indicate that ETS1-AR transcriptional co-regulation may function to promote prostate cancer progression. America Cancer Society - Institutional Research Grant; Center for Health Disparities Research (CHDR) - Pilot Research Grant

043 Management of Lobular Carcinoma in Situ (LCIS) and Atypical Lobular Hyperplasia Diagnosed By Core Needle Biopsy (CNB). Kristen N Arnold, Brian Boland, Christine MG Schammel, David P Schammel, Brian P McKinley. College of Medicine, Greenville Hospital System University Medical Center, Furman University, Pathology Associates of Greenville.

Introduction: Lobular Neoplasia (LN) encompasses a spectrum of diagnoses ranging from Atypical Lobular Hyperplasia (ALH) to Lobular Carcinoma in situ (LCIS). ALH is distinguished from LCIS based on the extent of proliferation of discohesive, atypical epithelial cells and distention of the lobular unit. The estimated prevalence of LN is 0.5 - 3.8% of otherwise benign breast biopsies. LN on core needle biopsy (CNB) is typically not associated with clinical or mammographic abnormalities but is associated with an increased risk of developing an invasive carcinoma: ALH 4-5X and LCIS 10X. Currently, no further surgical treatment is indicated after excisional biopsy (EB) and identification of LN. We reviewed cases of LN diagnosed by CNB and recorded subsequent surgical management and additional pathologic findings to determine if excision was warranted in the appropriate treatment of LN.

Results: Histologic/Mammographic concordance was present in 96% of all patients receiving CNB. Of all the patients in the cohort, 33/77 (43%) of patients received EB while 44/77 (57%) of patients did not receive EB. Of those receiving EB, 9/33 (27%) were upgraded, with 2/9 (22%) of demonstrating an invasive carcinoma on EB. Of the patients that did not receive EB, 39/44 (89%) had no ipsilateral disease progression while 5/44 (11%) developed further ipsilateral breast disease, 2/5 with an invasive lesion at the same site as their original CNB and 3/5 with Atypical Ductal Hyperplasia (ADH). Conclusion: The total percentage of CNB followed by EB (43%) is not impressive given current NCCN guideline recommendations to perform EB for LN. In those cases in which EB was performed, 27% were up-graded, and a total of 4 invasive lesions (5%) were identified at the same site as original CNB either immediately on EB or at a later point, supporting the conclusion that EB is necessary following a CNB diagnosis of pure LN. Thanks to the CUR2E Program and the Greenville Hospital System University Medical Center.

044 An Exploration of Sociodemographic, Clinical, and Psychosocial Functioning Variables in Newly Diagnosed Hollings Cancer Center Breast Cancer Patients. Kristina Andrijauskaite, Alok Madan, Jeff Borckhardt, Megan Baker, Kent Armeson, Katherine Sterba. Biochemistry, MUSC, Psychiatry, MUSC, Surgery, MUSC, Hollings Cancer Center, MUSC, Biostatistics and Epidemiology, MUSC.

Breast cancer is the most common form of female cancer in the United States. Women with breast cancer are at risk for depression and the prevalence of depression among cancer patients may be associated with disease severity and symptoms such as fatigue and pain. The goal of this study was to describe sociodemographic, clinical, and psychosocial functioning (depression and anxiety) variables in newly diagnosed Hollings Cancer Center (HCC) breast cancer patients who completed a self-administered questionnaire as part of the Outpatient Psychosocial Triage System (OPTS). We measured depression (CESD-10) and anxiety (State-Trait Anxiety Inventory) using validated instruments and assessed sociodemographic (age, race, marital status, insurance status) and clinical data (stage at diagnosis, treatment type, co-morbid health conditions) from the medical record. We used descriptive statistics, Pearson correlations, and ANOVA to conduct our analyses. The average age of study participants (n=39) was 61 years and participants were racially diverse (54% Caucasian, 39% African American). Initial stage at diagnosis ranged from DCIS to III (DCIS – 28.2%, I – 35.9%, II- 33.3%, III- 2.6%). The majority of patients (61.5%) were married and 61.5% had private insurance. In addition to cancer, participants reported an average
of 2.31 additional co-morbid health conditions. The average score on depression was 10.46 (SD=5.59) with 48.7% of patients meeting a cutoff score for clinical depression. The average score for trait anxiety was 45.95 (SD=5.48) with 74.4% meeting the OPTS program’s cutoff score for anxiety. Our findings indicate that a vast majority of newly diagnosed breast cancer patients at HCC reported a high level of depression and anxiety. No significant correlations were found between depression or anxiety and sociodemographic and clinical variables. Future larger studies should investigate these potential relationships further so that high-risk groups can be identified and referred for specialized services. MUSC Center for Health Disparities Research

045 Quantification of PLGF Via RT-PCR in Head and Neck Squamous Cell Carcinoma Cell Lines, Jackson M Condrey1, Brian Hoel1, Wei Sun1, Semyon Rubinchik2, Joshua Horning2, Marion B Gillespie2, Natalie Sukowski1, 1Microbiology and Immunology, MUSC, 2Otorlaryngology, MUSC.

Placental growth factor (PLGF) is a member of the VEGF family of growth factors and is an important factor in the promotion of pathogenic angiogenesis. PLGF levels are increased in certain types of cancer, such as stomach, breast, lung, and rectal cancer. Additionally, increased expression of PLGF in oral cancer is correlated with further progression of oral cancer. In our study, we hypothesize that PLGF levels would be elevated in various head and neck squamous cell carcinoma cell lines. The cell lines we analyzed were UM-SCC-1, UM-SCC-9, UM-SCC-12, UM-SCC-14A, UM-SCC-22A, UM-SCC-22B, and UM-SCC-40. These cell lines serve as predictors for clinical tumor sample PLGF levels. We performed RT-qPCR to quantify PLGF mRNA expression levels in the panel of cell lines. RNA was extracted from each cell line, which was then used to make cDNA. The PLGF levels were normalized against JAR, a human choriocarcinoma cell line known to express very high levels of PLGF. We found that all SCC cell lines expressed a detectable range of PLGF RNA. Furthermore, we found that the paired cell lines established from the same patient, UM-SCC-22A and UM-SCC-22B, expressed different levels of PLGF. Specifically, UM-SCC-22B, the metastatic origin line, expressed higher PLGF mRNA levels than the founding tumor line, UM-SCC-22A. Overall, our demonstration of PLGF expression in the HNSCC cell lines warrants further investigation with studies of HNSCC clinical tumor samples. Further studies with clinical tumor samples may suggest new methods to retard head and neck cancer growth by inhibiting pathogenic angiogenesis.

046 Assessment of Predictors for Survival: 3 Year Follow-up of H&N Cancer Patients, Robert J Yawn1, Joan Cunningham2, Nadia Duffy3, Elizabeth Garrett-Mayer4, Kathleen Cartmell5, Boyd Gillespie1, Terry Day1, Susan Reed1, 1Otorlaryngology- Head & Neck Surgery, MUSC, 2Medicine, MUSC, 3Center for Disease Control and Prevention, 4Holings Cancer Center, Biostatistics, MUSC, 5Holings Cancer Center, Cancer Prevention and Control, MUSC, 6Craniofacial Biology, MUSC.

The specific aim of this study is to determine whether or not baseline (pre-surgery) dietary data, oral microbial environment (including HPV status), tumor characteristics, alcohol and tobacco use, and social support domains predict 3-year survival outcomes in our patients with oro-pharyngeal cancer. Patients include the 19 well-characterized cases of the 2007 MUSC HCC Oral and Pharyngeal Cancer Case-Control Feasibility Study. Methods include case patient chart abstractions for treatment received, outcomes including recurrence, retreatment, and vital statistics. The existing baseline data are analyzed in context of these 3-year follow-up data. Descriptive statistics, regression models, and survival analyses are used to discern prognostic factors for survival of the head and neck cancer patients. The results of this follow-up study provide preliminary data for additional investigations into the relationships of diet, oral microbial environment, tumor characteristics, alcohol and tobacco use and social support domains for survival. Results will be used to guide survivorship research in our HCC population of oral cavity head and neck cancer patients. Funding by DHHS/PHS/CDC Grant No. H75/CCH424532-01-2, NIDCR/T32/DE017551, GCRC/RR01070. MUSC IRB HR #16253

047 The Impact of Surgical Diversion Prior to Neoadjuvant Therapy for Locally Advanced Rectal Cancer, Robert E Sweeney1, Norman R Harvey2, Deanna Mansker3, Amy Wahlquist4, David T Marshall4, David J Cole5, Elizabeth Hill3, Ernest R Camp2,5, 1College of Medicine, MUSC, 2Surgery, MUSC, 3MUSC, 4Radiation Oncology, MUSC, 5Ralph H. Johnson VA Medical Center.

Abstract not available.

048 Development of a Novel Hydrogel for Synthesis of Pancreatic Islets of Langerhans, Zachary J Coffman1, Xiaoyan Liu2, Xuejun Wen2, 1College of Medicine, MUSC, 2College of Graduate Studies, Clemson-MUSC Bioengineering Program, MUSC.

Type I diabetes is a disease characterized by autoimmune destruction of pancreatic β-cells. The destruction of these cells leads to decreased production of insulin resulting in poor glycemic control and secondary disease. A proposed treatment is to generate a β-cell seeded implant that would serve as an endogenous source of insulin and
would not be affected by the body's immune system. We evaluated the influence of altering the mechanical properties of hydrogels of different compositions on the viability of β-cells in 3D hydrogels. The different hydrogel ratios had different stiffness properties with optimal resistance pressures ranging from 100Pa to 1000Pa. Gels were seeded with MIN6 pancreatic β-cells at a concentration of 2x104 cells/150µL of hydrogel. Experiments were also formed with spheroids grown before addition to the hydrogel. Additionally, some plates had Laminin proteins added to their hydrogels to give a concentration of 40 or 100µg/mL. Cell viability and cell morphology was observed within the gels using a Leica® confocal microscope for acquiring images. Some gels from each sample were incubated in low and high glucose Krebs Ringer solutions for ELISA testing of insulin secretions. This was performed to determine β-cell function in the different hydrogel combinations and compared to their morphology and viability. This study revealed cellular viability and growth was greater in hydrogels with decreased stiffness. Cell function assays also revealed function in all hydrogels with inconsistent results between different hydrogels. Cell function however did increase in all hydrogels with increased incubation time. Dr. Egede’s Short Term Research Training for Health Professional Students

049 GILT Inhibits PAX-3 Protein Expression in Human Melanoma Cells, Jessica D Hathaway, Bently P Doonan, Azim Hossain, Lixia Zhang, Azizul Haque; Microbiology/Immunology, Hollings Cancer Center, MUSC.

Melanoma is an aggressive skin cancer and is the 6th most common malignancy in the United States. Treatments such as surgery, radiation, and chemotherapy have had some success, but often fail in treating late stage metastatic melanoma. Immunotherapy such as whole cell vaccines and peptides using melanoma antigens have also been employed in many forms with varied results. We have recently shown that the insertion of Gamma-Interferon-inducible Lysosomal Thiol Reductase (GILT) into melanoma cells favors HLA class II antigen processing and CD4+ T cell recognition of tumors. In this study, we show that GILT expression reduces angiogenic growth factors, inflammatory cytokines, and immune inhibitory molecules in melanoma cells. We also show that the paired box 3 (PAX-3) protein, implicated in late stage metastatic melanoma, is also downregulated by GILT expression. These data suggest that GILT-mediated reduction of PAX-3 could lead to a new target for devising chemotherapeutics. NIH, Hollings Cancer Center

050 A Retrospective Investigation of Lymph Node Occurrence Identified in Regional Lymph Node Dissections of Melanoma At a Regional Teaching Hospital, Alex D Gleason1, Hannah Bruch2, Christine Schammer1, Steven Trocha3; 1College of Medicine, MUSC, 2Cardiology, MUSC.

BACKGROUND: The objective of this analysis was to evaluate the number of lymph nodes dissected from each of the three nodal basins and the affect on the rate of recurrence in melanoma patients at Greenville Hospital within the last 10 years. METHODS: Patients admitted to Greenville Hospital with stage III melanoma from 1999-2009 and had at least one positive lymph node were identified from the tumor registry. The demographic data considered was age, gender, race, and body mass index. The pathologic data points were primary tumor location, whether a dissection occurred, the region of that dissection, the total number of lymph nodes dissected, the amount of positive lymph nodes, and the lymph node ratio. Laboratory data included the mitotic rate, Clark level, Breslow thickness, ulceration, and palpability. Adjuvant treatment received and diagnostic testing was also studied, as well as survival, including overall survival, disease specific survival, and whether or not recurrences occurred. RESULTS: The average number of lymph nodes dissected from the cervical, axillary, and inguinal regions at Greenville Hospital was 30.8, 20.8, and 14 nodes, respectively. 35.5% of our patients had a recurrence. Of the patients who had recurrences, the majority of them had local recurrence (72.7%). CONCLUSION: The surgical department at Greenville Hospital is removing more than twice the amount of lymph nodes from each of the three regions than the national recommendation. Of those patients who had less than the recommended number of lymph nodes removed at Greenville Hospital, all had local recurrences. Department of Surgery at Greenville Hospital and the CURE Program

051 Regulation of ERRs During Hypoxia, Alex T Damron1, Paul McDermott2; 1College of Medicine, MUSC, 2Cardiology, MUSC.

ERRα is a transcriptional activator that is regulated post-transcriptionally mainly by PGC-1α. When an organism is faced with a stressor that requires a shift in energy metabolism to maintain homeostasis, levels of PGC-1α increase, and, in the presence of PGC-1α, ERRα becomes a potent transcriptional activator for genes important in regulating lipid transport, FAO, oxidative phosphorylation, mitochondrial biogenesis, mitochondrial dynamics, and oxidative stress defense. PGC-1α acts as a ‘protein ligand’ for ERRα in cells with high metabolic needs and changes in energy requirements ultimately regulate the expression of ERRα in human kidney cells. ERRα and PGC-1α levels were measured in human kidney cells by Western Blot
and RT-PCR techniques at different exposure times to a hypoxic environment to test the correlation between ERRαs and PGC-1α and how they are regulated. SHP Program

052 The Role of Toll-like Receptor 6 in Collagen Processing “Mechanism for Intestinal Fibrosis”, Jacqueline A. Savage1, David P. Lebel1, Titus A. Reaves2; 1Medicine, MUSC, 2Regenerative Medicine & Cell Biology, MUSC.

Intestinal fibrosis is a major patho-physiological complication of Inflammatory Bowel Disease (IBD), dysregulated intestinal inflammation with an unknown etiology) that clinically presents as an over production of collagen leading to intestinal strictures and aberrant intestine function. Despite these observations, the development and progression of intestinal fibrosis is poorly understood. Interestingly, persistent intestinal fibrosis has been reported in Salmonella infections in mice and previously we show that toll-like receptor-6 (TLR-6), receptor for gram positive microbes) is expressed by intestinal fibroblast and removed from the surface of such fibroblasts following exposure to the inflammatory cytokine interleukin-6 (IL-6). For the current studies, we investigate the role of matrix metalloproteinase’s (MMPs), a group of zinc binding peptidases known to degrade collagens and other extracellular matrix components) in expression of TLR-6. In particular, following exposure of fibroblast to IL-6, results indicate that like TLR-6, MMP-2 (in media) is reduced. Using siRNA technology, we confirmed that both TLR-6 and MMP-2 are also reduced. In addition, we show that CD36, an extracellular glycosylated protein that is a receptor for collagen and an indicator of inflammation; is expressed by fibroblast but only after exposure to IL-6. CD36 mediated inflammation is through the interaction of TLRs 2, 4 or 6 in immune cells, and previously not shown in intestinal fibroblast. Taken together, the down regulation of TLR-6 appears to be essential before the decrease MMP-2 and the increase in CD36. Lastly, we examined expression of procollagen (precursor to collagen) under conditions of reduced expression of TLR-6 and results strongly suggest an increase in procollagen. These results potentially identify a novel pathway leading to an over activation of intestinal fibroblast and dysregulated production of collagen that may lead to intestinal fibrosis. Graduate Student Summer Health Professions Program, Grant number: 5R25HL096316-02

053 Function Studies of Quinolone Response Protein PqsE of Pseudomonas Aeruginosa, Mo Wei Yang, Yong-mei Zhang; Biochemistry and Molecular Biology, MUSC.

Pseudomonas aeruginosa (PA) is a gram-negative rod-shaped bacterium ubiquitous in soil and water. It is a particularly aggressive opportunistic pathogen and is responsible for 10% of all nosocomial infections. PA exists in both planktonic and biofilm form, and is naturally resistant to many antibiotics. Intercellular communication plays a key role in PA pathogenicity, allowing it to simultaneously regulate virulence gene expression through a complex quorum-sensing (QS) network. The Pseudomonas QS network consists of three main systems, each with its own unique signal molecules, synthases and cognate regulators. The Las and Rhl systems rely upon acyl-homoserine lactones (AHLs) as their signal molecules while the signal for the third system uses a unique alkyl quinolone molecule, commonly known as PQS (Pseudomonas Quinolone Signal). PQS synthetic enzymes are encoded by the first four genes of the pqsABCDE operon. PqsE is the last gene of the operon, and while it is not required for PQS synthesis, it is essential for activating downstream production of a multitude of virulence factors, most notably pyocyanin. Our aim is to elucidate the exact functions and molecular mechanism of PqsE. Our preliminary studies show that the expression of PqsE is dependent on PQS signal, whereas the function of PqsE in the activation of pyocyanin production is independent of PQS. Spectrophotometric analysis of PqsE enzymatic activity showed that PqsE is capable of hydrolyzing the β-lactam Nitrocefin. HPLC and proton NMR analyses revealed that PqsE is also capable of hydrolyzing butyryl-homoserine lactone (C4-HSL), which is the signal of the Rhl QS system. These data provide the first evidence of PqsE activity, and suggest a role of PqsE in connecting PQS and Rhl signaling systems. Funding provided by the National Institutes of Health COBRE in Lipidomics and Pathobiology at the Medical University of South Carolina P20 RR017677 (Y-M. Z.)

054 Ethanol Inhibits Metabolic Clearance of Methylphenidate and Potentiates Pharmacodynamics, Owen T. Reeves1, Hilary Bernstein2, Malcom Robert3, Kennerly S. Patrick3; 1South Carolina College of Pharmacy, 2Psychiatry and Behavioral Sciences, MUSC, 3Pharmaceutical and Biomedical Sciences, MUSC.

The persistence of attention-deficit hyperactivity/disorder (ADHD) into adulthood has been increasingly recognized and dl-methylphenidate (dl-MPH) remains the pharmacotherapy of choice, with enantiopure d-MPH also a treatment option. We have previously established that ethanol elevates plasma d-MPH concentrations after concomitant dl-MPH administration. This elevation is accompanied by the enzymatic formation of l-ethylphenidate. Further, this drug combination increases pleasurable effects relative to dl-MPH alone, especially in women, and increases the potential for abuse and cardiovascular accidents. The present study examines the ethanol – MPH interaction in the context of dl-MPH versus d-MPH. A randomized 4-way crossover study design was used with healthy volunteers (12 M/12F) dosed...
with dl-MPH (0.30mg/kg) or d-MPH (0.15mg/kg), with or without alcohol (0.6g/kg). Subjective effects were recorded using periodic visual analog scale questionnaires and cardiovascular effects were recorded. Plasma was collected over 12 h, then enantiospecifically analyzed for MPH and EPH by LC-MS/MS. Ethanol elevated d-MPH exposure (AUC and Cmax) when dosing with either dl-MPH or d-MPH. Ethanol also increased hemodynamic responses and positive subjective effects, including drug likability, when compared to MPH administered alone. Pharmacological sex dimorphisms were evident. Statistical analysis is in progress. The present clinical findings regarding dl-MPH and d-MPH interactions with ethanol contribute to evidence-based criteria for specific drug selection in the individualized treatment of adult ADHD patients with comorbid alcohol use disorder. For instance, the ADHD drugs atomoxetine and guanfacine are not expected to metabolically interact with ethanol, nor should they predispose the patient to drug abuse. Supported by RO1AA016707, the MUSC CTRC and TL1RR029881 from NCRR (NIH).

055 Cytokine-driven Bone Resorption with Aggregatibacter Actinomyctecomitans, Joni Dunmyer, Qian Kay Kang, Xiaoyan Liu, Bou Zhou; College of Medicine, MUSC, Orthopedics, MUSC, MUSC-Clemson Bioengineering.

Previous studies from the project laboratory have shown that bacterial constituents, such as gram-negative derived lipopolysaccharide can initiate an induction of host-derived inflammatory cytokines (J Perio 78(3), 2007). Periodontal diseases are initiated by periodontal pathogens that elicit host-immune response which result in alveolar bone loss around the dentition as a consequence of osteoclast activation and alveolar bone resorption. Objective: To identify host immune response post A. actinomyctecomitans calvarial stimulation to better understand consequences of whole bacterial stimulation with periopathogenic microbes. Methods: NR8383 rat macrophage cell line (1 x 106) exposed with 100CFU or 400CFU of formalin-fixated A. actinomyctecomitans and harvested at 0.5, 1, 2, 4, 8 hours post stimulation. Inflammatory cytokine levels were measured via ELISA from cell culture supernatant. Sprague Dawley rats were injected in the mid sagal suture area with 1 x 109 or 1 x 108 in PBS (control) in the supraperiosteal region of the rat calvarium. Harvested calvaria were scanned into a computerized micro-tomography to observe changes in calvarial bone resorption. Differentiated osteoclasts were determined by tartrate-resistant acid phosphatase (TRAP) staining. Results: Rat macrophage cells expressed statistically significant increased levels of TNF-alpha, IL-6, and IL-10 inflammatory cytokines respectively, post A. actinomyctecomitans stimulation compared to control treated cells. Bone resorption lacunae dominated the injection site of the rat calvarium post two week A. actinomyctecomitans injection. Histologically, a marked increase in lymphocyte infiltration was observed as well as osteoclast formation in sample groups stimulated with A. actinomyctecomitans compared with controls. Conclusion: Host immune response post A. actinomyctecomitans calvarial stimulation results in inflammation bone resorption supporting a role for this microbe to elicit a pathogenic process of focal bone loss consistent with human periodontitis.

056 Inhibited Biofilm Formation On Albumin-Coated Biomaterial Surfaces, Thomas E Niemeier, Qian Kay Kang, Xiaoyan Liu, Bou Zhou; College of Medicine, MUSC, Orthopedics, MUSC, MUSC-Clemson Bioengineering.

Over one half of the two million hospital acquired infections each year occur on biomaterial prosthetic surfaces. In orthopedic surgery, bacterial infections following total knee and hip arthroplasty occur at a frequency of 1-4% leading to prolonged hospitalization, amputation, and possibly death. Currently, many strategies have been employed to prevent bacterial colonization, yet infection rates remain steady over the past decade. Previous work in our lab has shown cross-linking albumin to biomaterial surfaces prevents bacterial adherence. In this study, we evaluate the long-term durability of cross-linked albumin with carbodiimide in preventing biofilm formation. Coated titanium alloy samples were incubated in an open channel bacterial flow chamber containing Staphylococcus epidermidis, a microbe notorious in orthopedic infections. By continuously flowing media past the samples, the flow chamber attempted to mimic in vivo conditions while maintaining bacteria in optimal growth conditions. Preliminary data after five days show an 85% reducing in the number of viable bacteria on the albumin coated sample versus an uncoated control. This relationship was confirmed through the use of confocal fluorescent microscopy at 1, 3, 5, 7, and 10 days. MUSC Health Professionals Research Program

057 Abnormal Dental Morphology in Orpk Mice, Ben T Wietecha, Courtney J Haycraft; Medicine, Nephrology, MUSC.

Oak Ridge Polycystic Kidney (orpk) mice have a genetic mutation leading to defects in primary cilia. As a result, they exhibit many of the same conditions seen in human ciliopathies, including polydactyly, craniofacial abnormalities, cleft palate and supernumerary teeth. To further the understanding of this mutation, mutant enamel, dentin, predentin and cementum widths were compared at various ages to wild type control mice. Specimens were also used to compare pulp chamber width and root length. The data indicates dentin width is significantly smaller in orpk mice of all ages measured, while only early predentin width is significantly smaller. Mutant enamel measured at p7
is also significantly smaller, but p30 cementum did not prove significantly smaller. Additionally, mutant pulp chamber widths were significantly smaller, but not after controlling for overall tooth size. Root length, however, was significantly smaller with and without controlling for overall mandible size. These results may indicate an early delay in predentin activity leading to perpetually smaller dentin, enamel and root length. Center for Oral Health Research

058 Comparison of Digital Imaging Methods for Recording Developmental Defects of Enamel, Jeanette S Wingate1, Susan G Reed2, Carol L Wagner3, Lydia A King4, Mallika Murali5, Bruce W Hollis6, Thomas Hulsey3; 1Dental Medicine, MUSC, 2Craniofacial Biology, MUSC, 3Pediatrics, MUSC, 4George Washington University.

Developmental defects of enamel (DDE) are characterized as hypoplasia, opacities, and post-eruptive breakdown by the Enamel Defects Index (EDI). To optimize the visualization of DDE, two digital imaging methods – fixed focal length, hand-held light microscope (ProScope™) and macro single lens reflex camera (Nikon D90) with ring flash – were evaluated to determine the better method to document DDE in children. The maxillary central incisors of children (ages 2-5 years) were imaged using the microscope (50x and 100x magnifications) and the camera. Aim 1 was to determine which imaging method better captured the DDE by evaluating the images for focus and EDI score. Aim 2 was to determine which method was more acceptable for use by evaluating the operator and child acceptance and time needed to make the images. Digital images for 35 children with a mean age 3.6 years SD 1.0, age range 2-5 years were compared. The mean image focus score for the microscope was 3.4 SD 1.5 and camera was 4.2 SD 1.1 (0-5 scale with "5" as best focus). The frequency of defects detected by the microscope was 62 (50x) and 45 (100x), and the camera was 58. Operator acceptability scores averaged 4.6 and 4.1 (5 maximum) for the microscope and camera, respectively. Child acceptance scores were 4.5 for both the microscope and the camera. The average time to capture images for the microscope was 88 seconds and 53 seconds for the camera. Findings support the use of the camera and hand held microscope (50x) as comparable when recording images of developmental defects of enamel of young children’s teeth. Support in part from: American Association for Dental Research Student Research Fellowship Award, MUSC College of Dental Medicine, CDM Center for Oral Health Research

059 Prrx Homeodomain Proteins, Key Regulators of Extracellular Matrix Expression During Secondary Palate Formation, K, Bryan Wingate2, Michael J Kern3, Christi B Kern2; 1College of Dental Medicine, MUSC, 2Regenerative Medicine and Cell Biology, MUSC.

Abstract not available.

060 Porcine TMJ Retrodiscal Tissue Under Tensile Forces, Jon Petersen1, Hai Yao2, Greg Wright2; 1College of Dental Medicine, MUSC, 2Clemson/MUSC Bioengineering.

Objective: Temporomandibular joint disorders (TMDs) pose a significant national health problem, afflicting more than 10 million people in the US. While the exact cause of TMDs is unclear, Temporomandibular joint (TMJ) disc displacement is central to many TMDs. To better understand, predict, and treat TMDs, we examined the TMJ retrodiscal tissue’s tensile properties due to its primary role in the joint. Methods: We tested the tensile biomechanical properties of twenty porcine TMJ retrodiscal tissues. Tension was applied to the specimens by means of a Bose table top tensile-testing machine. The specimens were rigidly gripped by the posterior band of disc and the most posterior section of the tissue by machined clamps. The specimens were then stretched with a ramp-strain input to eight strain levels: 5, 10, 15, 20, 30, 40, 50, and 60%. Both the superior and inferior retrodiscal lamina were tested in the anterior/posterior direction, as well as the medial/lateral direction, while Poisson’s ratio was measured simultaneously using reflective markers. Finally, at each strain level a stress-relaxation test was conducted over a 2.5-min period. Results: The inferior and superior retrodiscal lamina exhibited a higher elastic modulus in the anterior/posterior direction than in the medial/lateral. The inferior retrodiscal lamina also proved more resistant to tensile forces than the superior retrodiscal lamina. Conclusions: The Porcine TMJ retrodiscal tissue proved to 1) have a capacity for energy dissipation and display significant resistance to tensile forces, and 2) exhibit transverse isotropic behavior, as seen in other collagenous tissues. Our findings correlate directly with the current histological literature which finds the inferior lamina more collagenous and the superior lamina more elastin rich. These characteristics of the TMJ retrodiscal tissue contribute directly to maintaining the position of the disc relative to the condyle during mandibular function. NIH T32DE017551 and R03DE018741, MUSC Craniofacial Biology Department, Clemson-MUSC Bioengineering Department
061 Hematopoietic Stem Cell-Derived Fibroblasts Promote Tumor Cell Migration and Invasion, Lindsay T McDonald1,2,3, Daniel J Neitzke1, Amanda C LaRue2,3,4, 1College of Graduate Studies, MUSC, 2Pathology and Laboratory Medicine, MUSC, 3Ralph H. Johnson VAMC, 4Hollings Cancer Center, MUSC.

Carcinoma associated fibroblasts (CAFs) are the primary stromal component of solid tumors. Our previous studies based on a single hematopoietic stem cell (HSC) transplantation model demonstrate that a portion of CAFs are derived from HSCs and can be identified as circulating fibroblast precursors (CFPs) in peripheral blood. We have shown that CFPs preferentially migrate and differentiate in response to tumor both in vitro and in vivo. Inhibition of CFPs during tumor development also results in decreased tumor size. While these findings suggest that CFPs serve as a circulating intermediate between the bone marrow HSC and CAFs, the exact role of HSC-derived CFPs/CAFs in tumor progression has not yet been examined. Given that the HSC-derived fibroblasts comprise 8-10% of the stromal fibroblasts in solid tumors, the HSC-derived fibroblast population represents an important therapeutic target. It is our hypothesis that HSC-derived CAFs play an important role in the tumor microenvironment by promoting angiogenesis, inhibiting immune response and increasing tumor cell proliferation, migration and invasion. To begin to address this hypothesis, we first examined the ability of HSC-derived fibroblasts to affect tumor cell migration and invasion in vitro. Fibroblasts were established from peripheral blood and bone marrow of normal mice. The effects of conditioned media from these fibroblast populations on tumor cell migration and invasion was then examined in chemotactic transwell migration assays and matrigel-based invasion assays, respectively. A Lewis lung carcinoma cell line (LLC) was used for these studies and currently, these assays are being expanded to include additional cancer cell lines. Data show that conditioned media from HSC-derived fibroblasts significantly increases migration and invasion of LLC cells as compared to control. These findings suggest that the HSC-derived fibroblasts promote tumor cell migration and invasion. Ongoing studies are directed at identifying the mechanisms by which HSC-derived fibroblasts mediate these effects.

062 Gamma-Glutamyl Transpeptidase Activity in Cancer Cell Lines, Thomas J Sadowski, Anna-Lisa Nieminen; Pharmaceutical & Biomedical Sciences, MUSC.

The diagnosis of pancreatic cancer can equal almost certain death due to pancreatic cancer's re-sistance to radiation, surgery, and chemotherapy. Resistance to conventional chemotherapy may result from the hypoxic tumor core resulting from rapid tumor growth with insufficient angio-genesis. Intracellular antioxidants, such as glutathione (GSH) may also explain the increased resistance to chemotherapy. Indeed, many chemotherapeutic agents can be scavenged by GSH. Intracellular GSH content can be increased by two mechanisms: N-acetyl-L-cysteine (NAC) diffuses freely across the plasma membrane. Once inside cells L-cysteine is utilized to synthesize GSH. Alternatively, gamma-glutamyl transpeptidase (GGT), located on the plasma membrane, utilizes GSSG to increase intracellular GSH. In order to fight against the chemotherapeutic agents, certain cancerous cells increase their GGT activity. The aim of this study was to determine the levels of GGT activity in 3 different pancreatic cancer cell lines. The cell lines chosen for this experiment were Mia PaCa-2, BxPC-3, and PANC-1. GGT activities were measured in cell lysates using an established enzymatic assay. The assay was performed at 37ºC on 96-well plate using a plate reader (λ=405 nm). Mia PaCa-2 cells had the highest GGT activity (52.5 mU/mg of cellular protein). BxPC-3 and PANC-1 cells had very low GGT activity (0.00125 mU/mg of cellular protein). To determine whether hypoxia affects GGT activity, cells were exposed to hypoxia (0.5% oxygen) for 16 h. There was no difference in GGT activity between normoxic and hypoxic cells. In conclusion, GGT activity greatly varies in pancreatic cancer cell lines. Cells with high GGT activity have capability of increasing intracellular GSH content and thereby making them more resistant to chemotherapy. SHP Grant

063 Hypoxia-Induced Cleavage of Hur is a Critical Regulator of C-Myc Mrna Stability in Head and Neck Squamous Cell Carcinoma (HNSCC), Brittany Carroll1, Sudha Talwar1, Angen Liu3, Boyd M. Gillespie2, Imed E. Gallouzi2, Viswanathan Palanisamy1; 1Craniofacial Biology, MUSC, 2Otolaryngology- Head and Neck Surgery, MUSC, 3Biochemistry, McGill University, Montreal, QC, CANADA.

The human ELAVL1 alias HuR stabilizes a subset of cellular mRNAs containing AU-rich elements in their 3' untranslated region. It has recently been shown that in response to severe stress, HuR undergoes cleavage in a caspase-dependent manner, generating two cleavage products (CPs). However, there has been no reported clinical data on HuR expression related to its cleavage. Our Western blot data indicates that HuR is significantly over-expressed and cleaved in oral cancer tissues compared to the normal adjacent tissues. We have also observed that events leading to HuR cleavage are dependent on signals generated from hypoxic conditions in oral cancer cells in a caspase-dependent manner. Our observation of a protein band at 24 kDa in tumor tissues and hypoxic cells is known to be CP-1 of HuR. In addition, Immunohistochemistry analysis for HuR, HIF-1α and VEGF reveal a strong cytoplasmic staining of HuR in tumors tissues. To our knowledge, this is the first
observation showing that HuR is cleaved in hypoxic tumors. Interestingly, our Immuno-localization studies indicate that HuR is localized in the nucleus and cytoplasm of the hypoxic cancer cells, whereas almost all of the HuR is localized in the nucleus or perinuclear of normoxic cancer cells. These studies indicate that in hypoxic oral cancer cells, HuR is exported to cytoplasm and cleaved. Next, we tested specific HuR-associated genes and their stability under hypoxia. The quantitative-PCR analysis revealed that hypoxia promotes c-Myc stability. To confirm HuR-CF1 is responsible for the stabilization, we over-expressed HuR-CF1 in UM74B cells and found that it promotes up regulation of c-Myc; although these studies need to be further confirmed. Currently, we are investigating how c-Myc is regulated under hypoxia with cleaved HuR. Thus, HuR may be part of a pro-apoptosis regulatory pathway that controls the stability of a subset of mRNAs under hypoxia.

064 Effect of Dendrimer Nanoparticles on Pseudomonas Aeruginosa Biofilms, 
Jordon D Gruber, Yong Mei Zhang; Biochemistry, MUSC.

Antibiotic resistance of bacterial pathogens is one of the greatest threats to human health. Infections now occur that are resistant to all available treatment options. Therefore, there is an urgent need for new antibiotics and new delivery methods of the currently available drugs. The versatile human pathogen Pseudomonas aeruginosa is responsible for persistent lung infections and mortality in cystic fibrosis patients, and hospital-acquired infections in the immunocompromised. P. aeruginosa infections are difficult to treat because of the ability to acquire resistance mutations, efflux pumps and permeability barriers afforded by its outer membrane and biofilm formation. Bacterial biofilms (which Pseudomonas takes advantage of) have been shown to use an elaborate communication system of quorum sensing molecules to coordinate with their bacterial neighbors biofilm formation and differential gene expression. Once the quorum signals have built up in the environment, the biofilm alters genes for metabolism, adhesion, survival, and virulence. Dendrimers (dendri = tree, -mer = branching) are made up of hyperbranched NH2 groups and serve as key building blocks of nanotechnology. Their internal hydrophobic cavities allow for encapsulation of hydrophobic small molecules, and the surface functional groups are available for chemical modification and conjugation for drug delivery. PAMAM dendrimers exhibit antimicrobial properties against planktonic P. aeruginosa, but their effects on biofilm formation and the viability of mature biofilm are unknown. Using a static pegged-lid method for biofilm attachment, we found that generation five PAMAM dendrimers inhibited biofilm formation in a dose-dependent manner. This result suggests that dendrimers are excellent drug carriers of antimicrobials, which are ineffective against P. aeruginosa biofilm when given alone. Complexation of antibiotics to dendrimers could re-establish antibiotic susceptibility of P. aeruginosa because of the inhibition of drug-resistant biofilm formation.

065 The Effects of Lupus Plasma on Endothelial Nitric Oxide Synthase Activity in HAECs, 
Joy J N Buie¹, Ann F Hofbauer², Thomas A Morinelli³, James C Oates²,⁴; ¹Graduate Studies, Microbiology & Immunology, MUSC, ²Medicine, Rheumatology & Immunology, MUSC, ³Medicine, Nephrology, MUSC, VA, ⁴Ralph H Johnson VA Medical Center

Introduction/Rationale-Endothelial nitric oxide synthase (eNOS) generates the diatomic radical nitric oxide (NO). NO is responsible for maintaining vascular tone and inhibiting platelet aggregation, expression of adhesion molecules (ICAM-1, VCAM-1, E-selectin), and MCP-1 production. eNOS polymorphisms resulting in loss of function have been linked to endothelial dysfunction and immune-complex mediated glomerulonephritis severity. Whether lupus plasma derived immune complexes have a direct effect on eNOS activity remains unclear. We hypothesized that plasma from patients with SLE would inhibit bradykinin induced eNOS activity in human aortic endothelial cells (HAECs). Methods-Confluent monolayers of HAECs in 96 well plates were incubated with plasma samples from 2 lupus patients with positive anti-dsDNA readings and 1 normal (healthy) control for one hour at 37°C. After one hour, cells were stained with a nitric oxide sensitive fluorescent dye, DAF-FM (4-Amino-5-methylamino-2',7'-difluorofluorescein) Diacetate, to directly measure the effects of lupus plasma on nitric oxide production. Changes in fluorescence were analyzed using FLIPRTetra® technologies. Cells were treated with bradykinin or calcium ionophore A23287 and images were captured every 4-24s for 90 minutes at 37°C. Results- Exposure of human aortic endothelial cells for one hour to lupus plasma at varying concentrations significantly reduced NO production in response to bradykinin (n=3, p<.05) and the calcium ionophore A23187 (n=3, p<.05) when compared to buffer controls. However, no difference was detected in NO production between normal and lupus plasma exposed groups. Conclusion- Lupus patients develop endothelial dysfunction (ED) prematurely. Mechanisms of ED are suspected to be inflammatory in nature leading to subsequent eNOS inhibition and endothelial damage. However, we cannot conclude that lupus plasma, under these conditions, inhibits NO production when compared to normal human plasma. Department of Veterans Affairs, VA Research Enhancement Award Program (REAP), Initiative for Maximizing Student Diversity (IMSD), 5R01AR045476-11 from the National Institute of Arthritis and Musculoskeletal and Skin Diseases
Shining the Light on Relapse Neurocircuitry: Modulating the Reinstatement of Drug-Seeking Behavior Using an Optogenetic Approach, Michael T Stefanik, Khaled Moussawi, Karl Deisseroth, Peter W Kalivas, Ryan T LaLumiere; Neuroscience, MUSC, Bioengineering and Psychiatry, Stanford University.

With the recent development of the field of optogenetics (the use of genetically targeted transfection of light-activated channels and transporters) we are now capable of selectively modulating projections within individual circuits in a cell specific manner. Previous work manipulating the neurocircuitry involved in the reinstatement of drug seeking behavior implicates the dorso-medial prefrontal cortex (dmPFC) in the initiation of cocaine-seeking. Pharmacological inhibition of the dmPFC attenuates drug-seeking behavior, but these studies lack the specificity to adequately define the projections to and from the PFC, making it difficult to determine the crucial connections between the dmPFC and other structures during drug-seeking. As a first step in using optogenetics to analyze these pathways, the present experiments optically inhibited the dmPFC and, later, the basolateral amygdala (BLA) during the reinstatement of drug-seeking. Male Sprague-Dawley rats underwent surgeries for viral microinjections, implantation of bilateral guide canulas (20 ga) aimed at the dmPFC or BLA, and implantation of intra-jugular venous catheters. During surgery, microinjections of adeno-associated virus (AAV) containing the coding sequence for halorhodopsin (either eNpHR or eNpHR3.0) with either a CaMKII or synapsin promoter was made into the dmPFC or BLA. Halorhodopsin is a fast light-activated electrogenic Cl- pump, which, when activated by the appropriate wavelength of light, produces hyperpolarization of the transfected neurons. Animals then went through 12 days each of cocaine self-administration followed by extinction training (2 hr/day). Following extinction, animals underwent cue-induced or cocaine prime-induced reinstatement along with the presence/absence of optically induced inhibition via laser light (561 nm) provided through a fiber optic cable, terminating 2 mm beyond the tip of the guide cannula. Cocaine-induced, but not cue-induced, reinstatement was reduced with optical inactivation of the dmPFC. Confocal microscopy was utilized to verify virus expression in dmPFC, BLA, and their afferent targets. As cue-induced reinstatement is known to involve the BLA, current experiments are investigating whether optically induced inhibition of BLA activity reduces drug-seeking behavior. Following training, the behavioral responses (reinstatement of drug seeking behavior) to both cue and cocaine-induced reinstatement were examined. The results of these studies seek to validate/refute previous work using pharmacological inactivation techniques.

Behavioral Responses to Ethanol in NMDA Receptor Knock-in Mice, Carolina R den Hartog, Corigan T Smothers, Gregg E Homanics, John J Woodward; Neuroscience, MUSC, Anesthesiology and Pharmacology, University of Pittsburgh.

The N-Methyl-D-Aspartate receptor (NMDAR) subtype of ionotropic glutamate receptors has been implicated as an important mediator of the behavioral effects of ethanol in the central nervous system. NMDARs are tetrameric complexes assembled from NR1 and NR2 (A-D) subunits and receptor composition can alter its sensitivity to ethanol inhibition. In addition, a variety of other factors including cytoskeletal interactions and phosphorylation influence the receptor’s overall sensitivity to ethanol. Despite these findings, the molecular site(s) of action for ethanol on the receptor remains unknown. Previous mutagenesis studies in our laboratory identified a residue (phenylalanine, F) in the TM3 domain of the NR1 subunit that significantly reduces the ethanol sensitivity of the receptor in recombinant expression systems. Recently, we generated a novel knock-in mouse that expresses the F639A mutation in the NR1 subunit and hypothesize that these mice will show diminished behavioral responses to ethanol as compared to wild-type mice. In initial studies, mice were given one of three doses of ethanol (0.75, 1.5, 3.0 g/kg), prior to placing them in locomotor activity boxes. In general, mice heterozygous for the NR1(F639A) allele showed less effect of ethanol on horizontal locomotor activity and this effect was most pronounced at the 1.5 g/kg dose. In addition, NR1(F639A) mice showed greater amounts of time spent in the center of the test box than control mice especially following injection of 1.5 or 3.0 g/kg ethanol. Studies currently underway include assessment of drinking behavior using a 2-bottle choice assay and analysis of ethanol-induced sedation. These studies are the first to use genetically modified mice to test the role of NMDA receptors in the behavioral actions of ethanol. Supported by R37AA009986.

Reduced Histone Deacetylase Activity Protects the Retina From Ischemic Injury, Oday Alsarraf, Santhosh K Mani, Donald R Menick, Craig E Crosson; Graduate Studies, MUSC, Medicine, MUSC, Ophthalmology, MUSC.

Purpose: Protein acetylation is an essential mechanism for regulating transcriptional and inflammatory events. The current studies investigate if reduced histone deacetylase (HDAC) activity via administration of exogenous inhibitors or endogenous events can limit ischemic retinal injury. Methods: To investigate if administration of HDAC inhibitors can reduce ischemic retinal injury, rats were treated with valproic acid (100 mg/kg; i.p.), trichostatin-A (TSA) (2.5 mg/kg; i.p.), or vehicle, 1 hour prior to and 3 hours following, 45 minutes of retinal ischemia. To investigate if endogenous
events can alter HDAC activity and reduce ischemic injury, retinal neuroprotection was induced by 5 minutes of an ischemic preconditioning (IPC) event, 24 hours prior to the ischemic injury. Morphometric and electroretinogram (ERG) analyses were used to assess differences in retinal structure and function, 7 days following ischemic injury. Protein acetylation, HDAC expression and TNF-α levels were evaluated by Western blot analysis. Results: In vehicle-treated animals, ERG a- and b-waves from ischemic eyes were significantly reduced compared to contralateral responses by 46.3% and 67.4%, respectively. Histologic examination of these eyes demonstrated extensive degeneration of the ganglion cell and inner plexiform layers. In rats treated with valproic acid or TSA, ERG a- and b-waves from ischemic eyes were significantly increased, and normal inner retina morphology was preserved. Ischemia also increased retinal TNF-α, which was blocked by pretreatment with HDAC inhibitors. Both neuroprotection and reduced TNF-α were associated with an increase in retina protein acetylation. In animals receiving a preconditioned stimulus, retina protein acetylation was increased and retinas exhibited significant preservation in functional and structural endpoints. Conclusions: These studies provide evidence that reductions in histone deacetylase activity with the resulting hyperacetylation of retina proteins can protect the retina from ischemic injury. Decrease in HDAC activity and expression also plays a role in the development of ischemic preconditioning in the retina. Supported in part by NIH/NEI EY-09741; EY-14793; and Research to Prevent Blindness, NY.

069 K63-Linked Ubiquitinated HDAC5 Remains Nuclear and Upregulates Ncx1 in Cardiac Hypertrophy, Denise M Kimbrough1, Santhosh K Mani2, Donald R Menick2. 1College of Graduate Studies, Molecular and Cellular Biology &Pathobiology, MUSC, 2Medicine, Division of Cardiology, MUSC.

Class I and II histone deacetylases (HDACs) play a role in the regulation of the sodium calcium exchanger (Ncx1) gene, which is upregulated in cardiac hypertrophy and failure. Acetylated Nkx2.5 is associated with the Class I/II HDAC complex, HDAC5/1/2 at the Ncx1 promoter. Deacetylated Nkx2.5 is associated with the transcriptional activator and histone acetylase, p300 in a mutually exclusive manner. Inhibition of HDACs by the Class I/II inhibitor, trichostatin A (TSA) prevents the deacetylation of Nkx2.5 and recruitment of p300 to the Ncx1 promoter, thereby repressing Ncx1 upregulation. Our hypothesis is that the HDAC5/1/2 complex regulates Ncx1 upregulation in cardiac hypertrophy. Multiple studies have elegantly shown that hypertrophic stimulation results in phosphorylation of HDAC5 at serine 259/498 resulting in its export from the nucleus. However, we discovered that a portion of HDAC5 undergoes Lys(K)63-linked ubiquitination and not phosphorylation in isolated adult cardiac myocytes. K48-linked ubiquitination targets proteins for proteasome-degradation. However, K63-linked ubiquitination of proteins is not associated with degradation but rather affects activity, stability, cellular localization and interaction with other proteins. Immunohistochemistry demonstrates that K63-linked ubiquitinated HDAC5 is sequestered in the nucleus. ChIP analysis demonstrates that ubiquitinated HDAC5 remains associated with chromatin with hypertropic stimuli in isolated adult cardiac myocytes. Importantly, in pressure overloaded ventricles, the K63-linked ubiquitinated HDAC5 remains in the nucleus associated with the Ncx1 promoter. Therefore, in cardiac hypertrophy, non-ubiquitinated HDAC5 is phosphorylated and exported out of the nucleus, but K63-linked ubiquitinated HDAC5 remains in the nucleus and regulates Ncx1 expression. Kevin Schey; Mass Spectrometry Research Center, Vanderbilt University, Nashville, TN American Heart Association 09GRNT2020202 (DRM) NIH grants: NIH RO1 HL066223 (DRM) and PO1 HL48788 (DRM)

070 Akt3 Promotes Nuclear Retention of PGC-1 and ER Alpha By Regulation of the Major Nuclear Export Protein, CRM-1, Daniel G Corum1, Robin C Muise-Helmericks2, 1Molecular and Cellular Biology &Pathology, MUSC, 2Regenerative Medicine & Cell Biology, MUSC.

Findings from our laboratory have demonstrated a clear role for Akt3 in facilitating mitochondrial biogenesis in primary endothelial cells. We show that this was due to the ability of Akt3 to indirectly affect subcellular localization of peroxisome proliferator-activated receptor gamma co-activator 1 alpha (PGC-1 alpha), a well established master regulator of mitochondrial biogenesis. Our studies show that knockdown of Akt3 expression by RNAi results in an up-regulation of Chromosomal Region Maintenance 1 (CRM-1) protein expression. This is not due to changes in mRNA levels or translation, but is instead due to increased CRM-1 protein stabilization. These findings suggest that Akt3 inhibition results in a CRM-dependent export of PGC-1 alpha. In addition, the PGC-1 associated protein, estrogen receptor (ER) alpha’s subcellular localization is similarly affected by Akt3 inhibition. Leptomycin B, a specific CRM-1 inhibitor blocks the affect of Akt3 RNAi on the cytoplasmic shift in PGC-1 alpha localization. In silico sequence analysis shows two putative nuclear export sequences (NES1 and NES2) contained within PGC-1 alpha and one within ER alpha. Site directed mutagenesis of PGC-1 NES2 results in accumulation of PGC-1 alpha in the nucleus even under conditions of Akt3 blockade, as shown by immunofluorescence and cytoplasmic/nuclear fractionation. Taken together these findings suggest that Akt3 controls the transcriptional activity of both ER alpha and PGC-1 alpha by modulation of their nuclear/cytoplasmic
localization. Future studies will confirm the role of the putative NES sequence in ER alpha subcellular localization and its transcriptional activity as regulated by Akt3. NIH R01 # 84565-02

071 Fibulin-1 Regulation of Neural Crest-dependent Morphogenesis, Victor M Fresco, Marion A Cooley, Waleed O Twal, Jeremy L Barth, W Scott Argraves; Regenerative Medicine & Cell Biology, MUSC.

DiGeorge syndrome (DGS) is a complex and variable disorder that includes defects of the cardiovascular system, pharyngeal glands and head. Most of the tissues affected in DGS are derived from the pharyngeal arches, which are populated by migrating neural crest cells (NCCs). Fibulin-1 (Fbln1) is an extracellular matrix protein required for motility, guidance and survival of NCCs contributing to the pharyngeal arches. Deficiency of Fbln1 in mice leads to defects of the heart, pharyngeal glands and head that resemble abnormalities of human DGS. A number of genes have been identified that produce DGS-like phenotypes in mice. These genes can be integrated into a pathway that involves forkhead transcription factor (e.g., Foxa2, Foxc1 and Foxc2) activation of Tbx1 expression which in turn promotes expression of Fgf8 whose interaction with FgfRs induces activation of Map kinase pathway intermediates and cellular responses including NCCs survival and migration. Using a combination of DNA microarray and qPCR analysis we have evaluated the impact of Fbln1 deficiency on the expression of genes in this pathway. We find that Foxa2, Foxc1 and Foxc2 and Tbx1 mRNAs are decreased in pharyngeal arch tissues from Fbln1-deficient embryos. Likewise, the expression of Fgf8 and Fgfr mRNAs are also decreased. Furthermore, phosphoErk1/2 levels are decreased in pharyngeal arch-containing tissues from Fbln1-deficient embryos. Together, these findings lead to the hypothesis that Fbln1 is a novel component of the molecular pathway that regulates NCC-dependent development of the pharyngeal arch and the formation of its derivative structures through regulation of Fgf8 signaling.

072 Improvement in Treatment of Hypoplastic Left Heart Syndrome- Key Component to Mortality Reduction, Joseph Sistino, Heather Bonilha; College of Health Professions, MUSC.

This poster will review the key changes that have enhanced the survival of patients born with hypoplastic heart syndrome. From diagnosis to surgical repair there have been major advances that have dramatically reduced the mortality in this population. Surgical techniques such as RV to PA conduit improve RV function. Perfusion techniques including low prime circuits and selective antegrade cerebral perfusion reduce morbidity. The progression of these developments will be highlighted in this presentation.

073 The Role of Estrogen-Related Receptors in Cardiomyocyte Metabolic Adaptation to Oxidative Stress, Kathryn F Cribben¹, Paul J McDermott²; ¹Graduate Studies, MUSC, ²Cardiology, MUSC.

Introduction: In the heart, hypoxia limits oxygen availability to contracting cardiomyocytes in the myocardium. Cardiomyocyte metabolic adaptation to hypoxia is critical to sustain myocardial structure and function. These metabolic adaptations are determined by Estrogen-Related Receptors, ERRs, a family of transcription factors regulating genes involved in fatty acid metabolism, oxidative phosphorylation, and mitochondrial biogenesis. Preliminary studies indicate that hypoxia induces gene expression of the ERR isoform alpha by transcriptional and translational mechanisms in cardiomyocytes. However, regulation of the ERR-beta and -gamma isoforms has not been elucidated. We hypothesize that changes in expression of ERR isoforms elicit a cardioprotective effect in hypoxic myocardium by regulating expression of genes required for energy metabolism. Methods: Adult feline cardiomyocytes in primary culture were subjected to normoxia, hypoxia, or hypoxia/reoxygenation conditions. Expression of ERR isoforms and target genes was measured by QRT-PCR. Distribution of mRNA-ribosomal complexes was measured by fractionation of polysomes on a linear sucrose gradient. SABiosciences QRT-PCR arrays provided a high throughput tool for prospective target gene identification. Results: Expression of ERR isoforms alpha and beta isoforms was significantly altered in response to 24 hours of hypoxia followed by 24 hours of reoxygenation, as compared to normoxic controls. In response to hypoxia, ERR-alpha expression was induced 3.5-fold over 24 hours. In contrast, hypoxia induced ERR-beta expression 11-fold by 12 hours, and increased expression was maintained over the entire 24 hours. Subsequent reoxygenation resulted in a partially sustained ERR-alpha increase (2.5-fold), but quickly depleted the ERR-beta increase to baseline levels. Additionally, PGC-1alpha, a verified ERR target gene, also increased expression in response to hypoxia followed by a reduction of that increase during reoxygenation. Conclusions: 1) Hypoxia in cardiomyocytes induced increases in expression of ERR isoforms alpha and beta at different rates and magnitudes; 2) ERR-alpha expression was sustained during reoxygenation, but ERR-beta expression declined rapidly. Funded by the NIH Predocotoral Fellowship Training Grant to Improve Cardiovascular Therapies, and the Merit Review Award of the Department of Veterans Affairs.
074 IL-12 Stimulation of CD8+ T Cells Alters Ceramide Metabolism But These Changes Are Not Required for Development of IL-12-Mediated Effector Function, C. Bryce Johnson, David H Craig, Colleen A Cloud, Mark P Rubinstein, Besim Ogretmen, David J Cole; 1Surgery, MUSC, 2Biochemistry, MUSC.

After exposure to antigen, naive CD8+ T-cells undergo a rapid clonal expansion to develop into memory and effector cells. One of the cytokines mediating this transition is IL-12; however, the mechanisms by which IL-12 exerts its actions are largely unknown. Recent studies found that exposure of Jurkat T-cells to fumonisin B1, an inhibitor of ceramide synthesis, results in an increase in proliferation. Therefore, we studied the impact of IL-12 on ceramide metabolism and found that IL-12 increases the concentration of ceramides produced by CerS2 (C14 and C16 ceramide) and reduces the concentration of the major ceramide species produced by CerS6 (C24 ceramide). Despite these changes, IL-12-mediated stimulation of primary mouse T-cells to proliferate, develop effector function and persist in vivo were not affected by fumonisin B1. These results suggest that the changes observed in ceramide metabolism after IL-12 exposure do not play a significant role in IL-12’s ability to improve anti-tumor efficacy of CD8+ cells.

075 Effects of Fli-1 on T Cell Function in Systemic Lupus Erythematosus, Fahmin Bashir, Maria Harrell, Erin Morris, Tamara Nowling, 1Microbiology & Immunology, MUSC, 2Medicine-Rheumatology, MUSC, 3Ralph H. Johnson VA Medical Center.

Lupus, or systemic lupus erythematosus (SLE), is an autoimmune disease affecting primarily women and minorities. The disease is characterized by abnormal activation of T and B cells, resulting in proliferation of these cell types targeted towards self-antigens and subsequent production of autoantibodies. In human SLE patients, T cells are one of the primary cell types infiltrating the kidney and are part of the pathogenesis of lupus nephritis. Fli-1 is a transcription factor that plays a major part in embryogenesis and development and is highly expressed in lymphoid tissues. Reduction of Fli-1 expression has been demonstrated to result in decreased T cell infiltration in the kidney, decreased renal pathology and inflammation and increased survival in lupus-prone mice. The goals of this project include determining the effects of heterozygosity at the Fli-1 locus, resulting in decreased Fli1 expression, on proliferation and apoptosis of non-autoimmune prone and lupus prone T cells after exposure to mitogens such as phorbol myristate acetate (PMA) and ionomycin, which are known activators of T cells. In addition, chromatin immunoprecipitation (ChIP) will be used to identify target genes in human and mouse T cells located proximal to the Fli-1 promoter, including cytokines, chemokines and associated receptors, and transcription factors, that are involved in the inflammatory response and could be used as targets for downregulating Fli-1 expression. VA Merit Review IO1 BX000115, NIAMS R03 AR053376

076 Differences in Kappa:Lambda Ratios Identified By Proteomic Analysis of Plasma Exosomes Predict Severe Acute Graft-Versus-Host Disease, Joseph L Alge, Michael Janeczko, John Schwacke, John Arthur, Luciano Costa; 1Medicine, MUSC, 2Medicine, Nephrology, MUSC, 3Ralph H. Johnson VA Medical Center, 4Medicine, Biostatistics & Epidemiology, MUSC, 5Hematology-Oncology, MUSC, Hollings Cancer Center.

Abstract not available.

077 Glt1 Regulation in the Nucleus Accumbens of Cocaine Dependent Rats Following Cortical BDNF Administration, Benjamin J Newcomb, Timothy W Whitfield, Jacqueline F McGinty; MUSC.

During cocaine addiction and relapse, glutamate homeostasis in the mesolimbic reward pathway is altered. Specifically, extracellular glutamate levels in the nucleus accumbens (NAc) are depressed during cocaine addiction and elevated during relapse. It has been shown that intracranial administration of brain-derived neurotrophic factor (BDNF) into the dorsomedial prefrontal cortex (dmPFC) normalizes glutamate levels in the NAc and attenuates relapse behavior in rats. TrkB signaling, through the MAPK/ERK cascade, has been implicated in the mediation of the BDNF signal from the dmPFC to the NAc where extracellular glutamate levels are normalized. Since the glutamate transporter 1 (Glt1) is largely responsible for maintaining glutamate homeostasis in the NAc, the current study investigated the regulation of Glt1 in the NAc after 10 days of cocaine self-administration followed by an intra-dmPFC infusion of BDNF. Rats were trained to self-administer cocaine (0.2 mg/0.05 ml) in a lever-pressing task in daily 2 hr sessions for 10 days. Immediately after the last self-administration session, recombinant human BDNF was infused into the dmPFC and rats were euthanized 2 hrs later. Although BDNF was able to normalize cocaine-induced decreases in p-CREB and p-ERK in the dmPFC 2 hrs after the end of cocaine self-administration, Glt1 levels in the NAc were not altered at this timepoint. Glt1 levels in the NAc will be investigated at longer intervals after cocaine self-administration and BDNF infusion. Supported by P50 DA 015369 and MUSC MSTP.
078 SPARC/Osteonectin-Null Mice Have Increased Bone Loss and Decreased Periodontal Ligament Collagen Content in Response to LPS-Induced Periodontitis, Jessica M Trombetta, Hong Yu, Daniela N Arias, Carlos Rossa, Keith L Kirkwood, Amy D Bradshaw, Craniomaxillofacial Biology and Center for Oral Health Research, Erskine College, Ralph H. Johnson VA Medical Center.

Periodontal diseases affect at least 30% of the American population, with higher incidence associated with increasing age. Chronic periodontitis is initiated by a microbial biofilm and is exacerbated by the recruitment of inflammatory cells. Periodontal disease progression results in loss of supporting structures of teeth including the gingiva, periodontal ligament (PDL), and alveolar bone. The PDL is composed of fibrous connective tissue that connects to the cementum of the tooth to the alveolar bone of the socket. PDL fibroblasts maintain this collagenous ECM with high rates of collagen turnover. SPARC (osteonectin/BM40) is a collagen binding protein that is highly expressed within the PDL, cementum, and alveolar bone. Previous work demonstrated that SPARC-null mice exhibited decreased collagen content in the PDL in young and aged mice. To address whether SPARC plays a significant role in PDL-derived collagen turnover, SPARC-null and wild type (WT) mice were subjected to an established experimental model of periodontal disease. Periodontal pathogen derived lipopolysaccaride (LPS), was micro-injected into the maxilla of WT and SPARC-null mice three times a week for a 4-week period. Results indicate that SPARC-null mice exhibited significantly greater loss of PDL collagen versus WT PDL. In addition, the loss of alveolar bone, as measured by micro-computed tomography analysis, was two-fold higher in SPARC-null animals than in WT. Interestingly, LPS injected SPARC-null PDL exhibited decreased inflammatory cell infiltrate in comparison to that of injured WT PDL. These results indicate that expression of SPARC preserves PDL collagen content and alveolar bone in response to chronic inflammation and supports a critical role of SPARC in PDL homeostasis and disease. National Institute of Health Grants T32DE017551 (JMT), R25 HL092611 (DNA), 2P20RR017696, HL094517 (ADB), R01DE018290 (KLK), and a Veteran’s Administration Merit Award (ADB).

079 The Terminal Pathway of Complement in Hepatic Ischemia/Reperfusion Injury and Regeneration, Keely L Morris, Song He, Carl Atkinson, Paul Morgan, Stephen Tomlinson, Microbiology and Immunology, MUSC, Radiology, MUSC, Ralph H. Johnson VA Medical Center.

Liver resection is the most common surgical procedure performed on the liver, mostly for removal of malignant tumors, and ischemia and reperfusion injury (IRI) is unavoidable in the vast majority of liver resections performed. The complement system has a dual role in liver recovery following resection in that it causes injury following ischemia and reperfusion (IR), but is important in the regenerative response. It is known that the early complement activation products C3a and C5a are important for stimulating regeneration, but it is not clear how regeneration is impacted by IRI and the role of complement in this process. We investigated the role of the terminal complement pathway and the membrane attack complex (MAC) in hepatic IRI and regeneration using a novel targeted murine complement inhibitor, CR2-CD59. For characterization in surgical models, mice were treated with CR2-CD59, CR2-Cry (C3 inhibitor) or PBS after total warm IR, 70% partial heptectomy (Phx) or 90% Phx. CR2-Cry protected against IRI, but significantly impaired regeneration in the 70% Phx model. CR2-CD59 was as effective as CR2-Cry at protecting from IRI, but significantly did not impair regeneration after 70% Phx. In fact, regeneration and various markers of the proliferative response were increased in CR2-CD59 treated mice compared to PBS controls. Similar results were obtained using C6 deficient mice. CR2-CD59 was also protective after 90% Phx, a model of acute liver failure. Remarkably, CR2-CD59 improved long term survival from 0% to 70%, accompanied by significantly reduced markers of injury and increased markers of cell proliferation. CR2-Cry had no effect. These studies indicate that the MAC has a clear-cut and pivotal role between injury and regeneration, and that pharmacological inhibition of the MAC is a potential therapy for use in the clinical setting of liver resections where IRI and regeneration are factors in morbidity and mortality.

080 Connexin 43 Heterogeneity is Increased in the Hearts of Mice Overexpressing Cardiac-Specific Angiotensin Converting Enzyme, Erik G Strungs, Jane Jourdan, Joe Palatinus, Rob Gourdie; Regenerative Medicine & Cell Biology, MUSC.

Activation of the Renin-Angiotensin System (RAS) has been associated with arrhythmogenesis. Renin, released in response to decreased blood volume, cleaves angiotensinogen to form angiotensin I (AngI). AngI is cleaved by angiotensin converting enzyme (ACE) to form angiotensin II (AngII). AngII exerts its effects both directly, by binding cell surface receptors (Type I or Type II cell surface receptors), or indirectly, through induction of aldosterone production. Transgenic mice overexpressing cardiac-specific ACE (ACE 8/8 mice) have been used to study the impact of AngII overproduction in the heart. Hearts of ACE 8/8 mice have been shown to express less of the gap junction protein connexin 43 (Cx43). Cx43 is a channel protein that allows the electrochemical linkage of neighboring ventricular myocardial cells. Due to its important role in action potential propagation across ventricular myocardium, the decrease in Cx43 expression may provide a mechanism to describe the increased arrhythmogenesis seen in ACE 8/8 mice. In this
study, we used confocal microscopy and immunohistochemistry to generate short-axis images of Cx43 expression in hearts of wild type and ACE 8/8 mice, both in the presence and absence of an AngII Type I receptor antagonist (losartan) and an ACE inhibitor (captopril). Images where analyzed to quantify the heterogeneity of Cx43 expression. Hearts of mice overexpressing ACE, treated with losartan, were shown to have increased heterogeneity of Cx43 expression compared to wild-type mice treated with losartan, suggesting a role for the activation of Type II angiotensin receptors in arrhythmogenesis.

081 Potential Impact of Common Dosing References on Vancomycin Efficacy and Toxicity in Patients with Varying Degrees of Renal Function: A Monte Carlo Analysis, Heather R Hummel, Margarita Taburyanskaya, Robert V DeClue, Roger White; Pharmacy, SCCP, Pharmaceutical and Biomedical Sciences, SCCP.

Purpose: Increasing MRSA vancomycin (V) MICs require higher doses to reach AUC/MIC targets associated with improved clinical outcome. To compensate, many clinicians are adapting by using higher V doses; however, patients are more susceptible to nephrotoxicity. Many common references suggest different empiric V dosing regimens that may not reflect this increase in dose. Monte Carlo analysis (MCA) can be used to evaluate efficacy and toxicity of these dosing regimens. Methods: We performed MCA on empiric V dosing regimens from 5 dosing references to assess potential efficacy and toxicity in a hospital patient population. Pharmacokinetic simulations were done for 1,000 patients with our institution’s creatinine clearance (CrCl) distribution (mean=67ml/min, weight=70kg, volume=0.7L/kg, and CrCl vs CL (Matzke) regression. Steady state serum concentration time profiles were simulated for Facts and Comparison (F&C), Lexicomp high dose long interval (Lexi1) and low dose short interval (Lexi2), package insert (PI), and Matzke’s nomogram (Matzke) dosing schemes. Our institution’s MRSA MIC distribution (50%=1, 50%=2) was used to conduct the MCA. Target attainment (TA) for efficacy (AUC/MIC ≥400, V troughs of 15-20mg/L) and possible nephrotoxicity (troughs ≥15 and ≥20) were calculated from the MCA. Results: Percent of the population (F&C/Lexi1/Lexi2/PI/Matzke) with AUC/MIC ≥400 were 50/76/78/54/43, with troughs 15-20 were 27/25/11/0/6, with troughs ≥15 were 44/89/90/0/6, and troughs ≥20 were 17/64/79/0/0. Conclusion: Different references have empiric dosing regimens that would likely produce a wide range of efficacy and potential nephrotoxicity in hospital patient populations. Some dosing regimens are more aggressive and achieve high percent target attainment, but at the expense of higher possible nephrotoxicity. Other regimens pose little probability of nephrotoxicity, but do not obtain targets associated with clinical success.Clinicians should be aware of these variations and use dosing regimens cautiously. Empiric V dosing regimens that could potentially increase efficacy and reduce nephrotoxicity should be assessed.

082 Impact of Patient Populations with Varying Degrees of Renal Function on Vancomycin Potential Efficacy and Toxicity, Margarita Taburyanskaya, Haether R Hummel, Robert V DeClue, Roger White; Pharmacy, SCCP, Pharmaceutical and Biomedical Sciences, SCCP.

Purpose: Higher vancomycin (V) dosages are being used to reach AUC/MIC targets associated with better clinical outcomes. Since creatinine clearance (CrCl) affects V concentrations, empiric regimens should consider differences in population renal function. Monte Carlo analysis (MCA) can be used to assess potential efficacy and toxicity of V regimens in these populations. Methods: MCA was performed on: 3 CrCl distributions (mean ml/min, our institution =67, skewed high=82, skewed low=48), 2 V dosing regimens (1-2 g doses, V1 and V2) with these dosing intervals (hrs): CrCl>60 ml/min, 12; 31-60, 24; 15-30, 48; and <15, 72, 3 V MRSA MIC distributions (our institution=50% MICs 1 and 2, MICs=1, and MIC=2). Population PK values (CrCl - regression, volume) were used to simulate steady-state population PK profiles. MCA was performed to assess target attainment (TA) for efficacy at (AUC/MIC ≥400, V troughs of 15-20) and potential nephrotoxicity (troughs ≥15). Results: TA at MIC=2 was 0% for V1 and 79-87% for V2; however, for MIC=1, TA was 79-87% for V1 and 100% for V2. Percentages of the population with troughs of 15-20 were 25-32% and 15-19% for V1 and V2, respectively. TA(%) at AUC/MIC ≥400 (our institution MICs) and percentage of troughs ≥15mg/L (%/%) were:

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Although one might assume that efficacy and toxicity endpoints would always be higher in populations with lower CrCls, specific CrCl distributions and dose/dosing interval adjustments at specific CrCls have a large impact. Conclusions: CrCl distributions in patient populations had a minimal impact on assessment of efficacy (AUC/MIC targets or troughs of 15-20 mg/L); however, the impact on potential nephrotoxicity is much greater. Institution-specific CrCl distributions should be considered in the selection of empiric V dosing regimens.
083 The Role of Mitogen-Activated Protein Kinase Phosphatase-1 in Tumor Progression, Xiaoyi Zhang1, Hong Yu1,2, Keith L Kirkwood1,2, 1Craniofacial Biology, MUSC, 2Dental Medicine, MUSC.

Head and neck cancer accounts for approximately 6% of diagnosed malignancies in the United States, with an estimated 35,000 incidences and over 7,000 deaths every year, the most common form being head and neck squamous cell carcinoma. Despite ongoing research, survival rates remain lower than other more common malignancies. Cytokines and pro-inflammatory factors have been shown to have a critical role in the various steps of malignant transformation, including tumor growth, survival, invasion, angiogenesis, and metastasis. Mitogen-activated protein kinases (MAPK), such as p38, JNK, and ERK, relay information from extracellular signals to the effects which control these diverse cellular processes. These kinases are negatively regulated by MAPK phosphatases that dephosphorylate MAPK proteins, the founding member of this class being mitogen-activated protein kinase phosphatase-1 (MKP-1). Initial studies revealed significant over-expression of MKP-1 in a range of human epithelial tumors including prostate, colon, and bladder, seen only in the early phases of disease with levels of MKP-1 expression falling progressively in tumors of higher histological grade and in metastases. We hypothesize low levels of MKP-1 in the HNSCC tumor microenvironment generate high levels of inflammation which promote tumor development and progression. To address how MKP-1’s regulation of inflammatory cytokine expression via MAPK activity may affect HNSCC development and progression, we have examined the effects of MKP-1 deficiency on a well-characterized model for oral squamous cell carcinoma. MKP-1 deficient and wild-type mice were treated with 4-nitroquinoline 1-oxide, a surrogate for tobacco exposure, in drinking water for 16 weeks and monitored for an additional 12 weeks. Our preliminary studies show a significant increase in tumor development, characterized by onset of disease, tumor size, histological grade, and inflammation. Further work will be done to assess levels of MAPK activity as well as pro- and anti-inflammatory cytokines in the epithelial tumor tissue as well as the surrounding stroma. Understanding the role of inflammatory mediators in the tumor microenvironment in head and neck cancer progression may yield novel therapeutic targets, such as MKP-1, for prevention and treatment. NIH 1R01DE018290, P20 RR017696 NIH 5T32ES012878 South Carolina Electric and Gas Fellowship

084 Evaluating the Impact of Acid Ceramidase Overexpression on Activation of and Addiction to the PKB/Akt Pathway, Thomas H Beckham, Joseph C Cheng, Xiang Liu, James S Norris; Microbiology and Immunology, MUSC.

We have previously found that acid ceramidase is overexpressed in a majority of prostate and head and neck cancers and that overexpression of acid ceramidase in prostate cancer cells causes chemotherapy resistance, increased proliferation, increased migration, and increased xenograft growth. Acid ceramidase deacylates ceramide species, shifting the sphingolipid balance from a pro-apoptotic ceramide-dominated signal to an anti-apoptotic sphingosine-1-phosphate dominated signal. The PKB/Akt pathway is frequently activated in human cancers, and aberrant activation can cause increased cell proliferation, growth, and resistance to apoptosis. Previous studies have shown that sphingolipids modulate PKB/Akt signaling: ceramide by causing dephosphorylation of Akt whereas sphingosine-1-phosphate activates Akt by stimulation of PI3K through interaction with extracellular receptors. We therefore sought to determine if the aggressive phenotype of acid ceramidase overexpressing cells was caused by activation of the PKB/Akt pathway resulting from alterations in bioactive sphingolipids. Here we report that overexpression of acid ceramidase causes activation of Akt in multiple cancer cell lines with changes in targets of Akt downstream consistent with Akt activation. Acid ceramidase induced sphingolipid alterations may be responsible for activation of Akt. Interestingly, acid ceramidase overexpressing prostate cancer cells are more sensitive to Akt inhibition than control cells, indicating that acid ceramidase overexpressing cells may be addicted to increased signaling through the oncogenic PI3K/Akt signaling pathway. Thus, we propose that acid ceramidase overexpression activates PKB/Akt by altering endogenous sphingolipids and that the aggressive phenotype of acid ceramidase overexpressing cells is due to activation of this pathway. In addition to casting light on the oncogenic properties of acid ceramidase, we propose that the PI3K/Akt pathway may be a druggable target for acid ceramidase overexpressing tumors. NIH 5P01CA097132-07 NIGMS Medical Scientist Training Program, MUSC Hollings Cancer Center Wachovia Scholarship

085 Evaluating the Use of LCL124 to Circumvent Gemcitabine Resistance in Pancreatic Cancer, Sarah T Marrison1, Clayton S Lewis2, Xiang Liu1, James S Norris1, Microbiology and Immunology, MUSC, 2Pharmaceutical and Biomedical Sciences, MUSC.

Abstract not available.
**086** **VDR and RXRα Expression in Chemically Induced Acute Colitis**, Rebecca J Weber, Jay Morris, Vondina Moseley, Michael Wargovich; Pharmacology, MUSC.

Vitamin D, whose functionality is controlled by its signaling through the VDR, plays a role in numerous pathways within the human body including regulating inflammation. To properly signal, VDR must heterodimerize with its signaling partner, RXRα. When the signaling capability of Vitamin D goes awry, inflammation is unchecked and cells are free to proliferate and release inflammatory signaling molecules. Inflammation and dysregulated Vitamin D signaling have been implicated in allowing the progression of colitis to cancer and encouraging the proliferation of colon cancer cell lines. As Vitamin D has been implicated in the causation of colon cancer, it appears likely that its dysregulation may be present in colitis, a state of inflammation that is a precursor to cancer. Human colitis samples have been examined and demonstrated a decreased expression of VDR in the nucleus versus their normal colon mucosa. This expression decreases even further as the colitis progresses into dysplasia and later into cancer. Expression of RXRα is decreased in high-grade dysplasia and further decreased in adenomas and adenocarcinomas. When RXRα is downregulated, it is unable to interact with VDR and thus inflammation can proceed unchecked to colitis and potentially cancer. Green tea constituents have shown to restore RXRα's expression and thus, allow its interaction with VDR. With a better understanding of the roles Vitamin D and RXRα play in regulating inflammation, better treatment modalities may be developed to treat colitis and prevent its progression to colon cancer. To examine the interplay between VDR and RXRα expression in colitis, DSS was utilized to induce an acute form of colitis in a murine model. Upon sacrifice, the colons were harvested, the degree of colitis was scored and expression levels of VDR and RXRα were examined via IHC. MUSC MSTP Program

**087** **Requirement for Akt1 in the Regulation of Anti-Bacterial Effects of Poly-N-Acetylglicosamine Nanofibers (sNAG) in Cutaneous Wound Healing**, Haley B Lindner1, Aiguo Zhang2, Juanita Eldridge3, Marina Demcheva3, Philip Tsichlis4, Arun Seth5, John C. Vournakis3, Robin C. Muise-Helmericks1; 1Regenerative Medicine & Cell Biology, MUSC, 2Sunnybrook Research Institute, 3Marine Polymer Technologies, Inc., 4Tufts University.

Recent findings show that treatment of cutaneous wounds with poly-N-acetyl-glucosamine nanofibers (pGlcNAc/sNAG), 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. We show that in addition to its effects on endothelial cell migration, sNAG treatment results in increased expression of both alpha- and beta-type defensins in endothelial cells and the beta-type defensins in keratinocytes. Defensins are small antimicrobial peptides that are part of the innate immune response. Both pharmacological inhibition of the PI3K/Akt1 pathway and Akt1 knockdown using lentiviral shRNAs delivery results in decreased expression of these factors in endothelial cells. In an Akt1-null animal model of cutaneous wound healing, we show that sNAG stimulation of defensin expression is Akt1-dependent. We show that sNAG treatment decreases bacterial infection of cutaneous wounds infected with Staphylococcus aureus in wild type control animals but not in similarly treated Akt1 null animals. Importantly, Akt1 null animals present with a wound healing delay that is not rescued by sNAG treatment. Application of defensin peptide mimics the effects of sNAG on bacterial clearance in wild type animals. Furthermore, sNAG treatment of S. aureus infected wounds show an early increase in beta-defensin 3 expression that is not mimicked by bacterial infection. Taken together our findings suggest a central role of Akt1 in the regulation of cutaneous wound healing and in the stimulation of innate immunity responsible for bacterial clearance. Additionally, these findings support the use of sNAG nanofibers as a novel and effective method for enhancing both wound closure while simultaneously decreasing wound infection. Marine Polymer Technologies, Inc. # 86319

**088** **Regulation of P38-delta By Gba: Mechanistic Insights and Implications for Disease**, David Perry1, Kazuyuki Kitatani1, Patrick Roddy1, Masayuki Wada1, Yusuf Hannun1; 1Biochemistry, MUSC, 2Tottori University.

Sphingolipids have long been implicated in stress responses while molecular mechanisms have been more elusive to delineate, particularly for ceramide. Complexity of sphingolipid/ceramide biology arises from several factors: structural diversity within a given class, subcellular restriction of the sphingolipid-metabolizing enzymes, and intricate metabolic pathways involving the enzymes and sphingolipids. Therefore, studying ceramide in the context of a specific enzyme is important as this may dictate its function and downstream target. One such enzyme is Gba (glucosylceramidase, EC-3.1.2.45), which is proposed to have an anti-inflammatory role, distinguishing it from other ceramide-producing enzymes. Previous work from our lab has shown that loss of Gba results in decreased ceramide formation leading to hyperphosphorylation of p38 and overproduction of IL-6 in breast cancer cells, with indirect evidence that the p38δ isoform is preferentially hyperphosphorylated by loss of Gba. In an effort to identify novel targets of Gba-derived ceramide, we discovered PP2Cδ (PPM1A), a stress-related phosphatase, to be activated by ceramide. Interestingly, both IL-6 and p38 are proposed to have pro-migratory and pro-metastatic roles in
breast cancer, and conversely, PP2Cδ has been reported to be a negative regulator of migration. Our overall hypothesis is that Gba-derived ceramide activates PP2Cδ to dephosphorylate p38α as part of a negative feedback mechanism in stress signaling, which plays a role in suppressing invasiveness of breast cancer cells. **GAAN Grant Abney Foundation SCE&G**

**089 Fibulin-1 Binds Both HB-EGF and EGF Receptor/ErbB1 and Controls HB-EGF-dependent Proliferation**, Keerthi Harikrishnan, Marion A Cooley, Victor F Fresco, Waleed O Twal, W Scott Argraves; Regenerative Medicine & Cell Biology, MUSC.

Abstract not available.

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

Abstract not available.

**091 The Modeling of the Extracellular Processing of Angiotensin in Cultured Mouse Podocytes: A Proposed Mass Action Model**, Christian G Spainhour, Juan Carlos O Velez, Michael G Janech, John H Schwacke; 1Biochemistry, Bioinformatics, MUSC, 2Medicine, Nephrology, MUSC, 3Ralph H Johnson VA Medical Center.

The Renin-Angiotensin system (RAS) is an important component of the endocrine system that primarily regulates blood pressure and ion balance through a variety of G-protein coupled receptors. Dysfunction of this system has been documented in the progression of multiple diseases such as hypertension, diabetes, and kidney disease. RAS is also a part of several normal physiological processes including blood pressure regulation, angiogenesis, apoptosis, neuronal growth, and oxidative stress response. The extracellular portion of RAS can be described as signal pre-processing network where the signaling molecule, Angiotensin I (Ang I), is cleaved by a combination of enzymes into different length fragments. This occurs after Ang I is cleaved from its precursor Angiotensinogen. Depending on how Ang I is cleaved, the signal it delivers changes by binding to different G-protein coupled receptors. The signal pre-processing creates a profile of angiotensin fragments that can be changed depending on the expression of the associated enzymes in a given tissue, thus altering the desired signal. Our research focuses on the development of a mathematical model of the peptidase network responsible for RAS pre-processing. Our objective is to develop a model that is predictive of the response of the pathway under selective inhibition of its steps. Herein a mass action model of the pre-processing network is implemented and refined. This model was constructed using a current understanding of RAS and data obtained from experiments with isolated rat glomeruli measuring the degradation of Angiotensin I and the production of various Angiotensin fragments under various protease inhibitors using AQUA mass spectrophotography. The model was then tested against similar data generated from similar experiments using mouse podocytes and human glomerular endothelial cells.

**092 Transcriptomic Changes Associated with Elastogenesis Induced in Arterial Smooth Muscle Cells By the Proteoglycan Versican Variant V3**, Erin L Pardue, Kathleen R Braun, Jeremy L Barth, Waleed O Twal, Thomas N Wight, W Scott Argraves; 1Regenerative Medicine & Cell Biology, MUSC, 2The Hope Heart Program, Benaroya Research Institute, Virginia Mason.

Arterial smooth muscle cells (ASMCs) produce significant quantities of elastin when transduced with the proteoglycan versican splice variant V3. To identify changes in gene expression that may underlie V3 induced elastogenesis, we used both microarray expression analysis and real-time polymerase chain reaction to quantify shifts in mRNA levels in V3 transduced and control ASMCs. Analysis of DNA microarray expression profiling data revealed that V3 up-regulated the expression of elastin (Eln) (3.3 fold) as well as a number of genes previously shown to be critical for elastogenesis including fibulin-5 (Fbln5) (7 fold) and fibulin-2 (Fbln2) (2 fold). Several other genes known to promote elastogenesis were down-regulated in V3 transduced ASMCs including transforming growth factor beta 1 (Tgfβ1) (-1.5 fold) and microfibrillar associated protein 5 (Mfap5/Magp-2) (-2.4 fold). There were a number of other elastin-related genes for which no change was detected in the expression of transcripts including lysil oxidase (Lox), Lox-like protein (Loxl), loxl2, fibulin-3, fibulin-4, fibrillin-1, fibrillin-2, Magp1, Mfap1, Ltbp4, emlin-1 and Igf-1. Together, these data demonstrate that versican V3 induces significant changes in mRNA expression of genes associated with elastogenesis. **Supported by NIH grant HL095067 (W.S.A.), National Science Foundation Engineering Research Center Grant #EEC-9529161 (T.N.W.), NIH grants HL18645 (T.N.W.), DK95929161 (T.N.W.), and AHA Predoctoral Fellowship Award 10PRE4020031 (E.L.P.).**

**093 A Novel Murine Pancreatic Cancer Metastatic Model Allowing Continuous Evaluation of Tumor Burden**, Elizabeth C Little, Lisa Sun, Patricia Watson, Dennis Watson, David Cole, Ramsay Camp; 1Microbiology & Immunology, MUSC, 2Surgery, MUSC, 3Hematology - Oncology, MUSC, 4Pathology, MUSC.

Introduction: With 5-year survival less than 6%, pancreatic adenocarcinoma is one of the most deadly cancers in America. The lack of relevant preclinical models is a major barrier in the search for
novel therapeutics. We have developed an immunocompetent mouse model of metastatic pancreatic cancer; incorporating bioluminescent imaging (BLI) to assess tumor growth and hepatic metastasis development. Experimental Design: Murine Panc02 cells were stably transfected with a luciferase plasmid under G418 antibiotic selection (Pan02luc). 1x106 Panc02luc cells in 0.1mL PBS were injected directly into the tip of the exteriorized spleen. BLI was performed weekly to track tumor growth using Xenogen optical imaging device with D-luciferin at a concentration of 140mg/kg in 0.2mL, intra-peritoneal (i.p.). On days 12, 15, and 18 mice received an i.p. injection of either saline (n=7) or 40mg/kg Gemcitabine (n=11). Mice were monitored daily and animals were sacrificed as they became moribund. Results: The pattern of metastases in this model was predominately hepatic with occasional intraperitoneal and splenic tumor deposits, consistent with the clinical pattern of this disease. Saline-treated animals became moribund between days 13 and 22 post-Panc02luc injection. BLI established no significant differences in tumor size prior to treatment at day 7 (p=0.25, average BLI flux was 1.43x106 photons/s in the saline group and 5.89x105 photons/s in the Gemcitabine group) or after one round of treatment at day 14 (p=0.80, BLI flux averaged 3.13x106 photons/s in the saline group and 3.49x106 photons/s in the Gemcitabine group). While most mice in the saline control were sacrificed by day 21, the Gemcitabine group maintained consistent tumor growth with an average BLI flux of 4.59x106 photons/s at day 21. Ultimately, the Gemcitabine-treated group demonstrated a median survival of 25.5 days post-tumor injection compared to 18.3 days in the control saline-treated cohort, marking a significant survival advantage (p<0.001).

**094 Redox Modulation of Interleukin-6 Production in MRL/lpr Mesangial Cells**, Ahmad K Mashmoushi1, Ann F Hofbauer2, James D Crapo3, Gary S Gilkeson2, Jim C Oates2; 1Microbiology and Immunology, MUSC; 2Medicine, MUSC; 3Medicine, National Jewish Medical and Research Center.

Introduction: Lupus nephritis (LN) is an immune-complex glomerulonephritis with glomerular inflammation and cellular proliferation. Interleukin-6 (IL6), released by LN mesangial cells (MC), is an important mediator of inflammation. High levels of reactive intermediates are associated with proliferative LN. Although IL6 production was shown to be controlled by a redox sensitive pathway in macrophages, little is known about the effect of oxidative stress on IL6 production by mesangial cells. We hypothesized that reactive intermediates in proliferative murine LN modulate MC IL6 production. Methods: Immortalized MRL-MpJFASlpr (MRL/lpr – murine model of LN) MCs were stimulated with lipopolysaccharide (LPS)(100ng/ml)/IFNγ(10U/ml) in the presence of different concentrations of a superoxide dismutase mimetic (MnTE-2-PyP5+) and hydrogen peroxide (H2O2). After overnight culture, supernatants were analyzed for IL6 by ELISA. Three replicates in duplicate were normalized to a percentage of stimulated cells with no treatment. Results: Stimulation of MRL/lpr MCs with LPS/IFNγ increased IL6 production by 18.5 fold. H2O2 at concentrations higher than 25µM had a cytotoxic effect and increased cell death. MnTE-2-PyP at concentrations ranging from 5µM to 34µM had no effect on baseline IL6 production by stimulated MCs, but it had a protective effect against H2O2 cytotoxicity. IL6 production increased in LPS/IFNγ stimulated MCs incubated with both MnTE-2-PyP (34µM) and H2O2 in a dose dependent manner. The following results of IL6 production were obtained: MCs with MnTE-2-PyP + H2O2 5 µM IL6: %148±4, p=0.0003 MCs with MnTE-2-PyP + H2O2 10 µM IL6: %167±5, p=0.0003 MCs with MnTE-2-PyP + H2O2 25 µM IL6: %229±7, p=0.0004 MCs with MnTE-2-PyP + H2O2 50 µM IL6: %322±7, p=0.0005 MCs with MnTE-2-PyP + H2O2 100 µM IL6: %917±4, p=0.0003 Conclusion: IL6 production and cell survival in stimulated MRL/lpr MCs appear to be redox sensitive. The signaling for IL6 production may be dependent on H2O2, H2O2 products that are not scavenged by MnTE-2-PyP, or effect of MnTE-2-PyP on redox signaling that is dependent on H2O2; while H2O2 derived oxygen free radicals scavenged by MnTE-2-PyP may induce cell death.

**095 Extracellular Hsp90 Serves As a Co-Factor for KSHV-Associated Activation of NF-κB During De Novo Infection**, Michael DeFee1, Qin Zhiqiang2, Dai Lu2, Bryan Too3, Jennifer S Isaac4, Chris Parsons4; 1Microbiology and Immunology, MUSC; 2Craniofacial Biology, MUSC; 3Medicine, MUSC; 4Regenerative Medicine & Cell Biology, MUSC, 5Pharmacology, MUSC.

Abstract not available.

**096 Bcr-abl Regulates Activity of Sphingomyelin Synthase in Chronic Myelogenous Leukemia Cells**, Tara A Burns, P Meier, A Bai, X Yang, Y Hannun, D Zhou, Chiara Luberto; Biochemistry, MUSC.

Sphingomyelin synthase (SMS) is an important class of enzymes regulating sphingolipid metabolism. In particular, SMS transfers the phosphorylcholine moiety from phosphatidylycholine (PC) onto ceramide forming sphingomyelin and diacylglycerol. Because of the ability to modulate in opposing directions the level of ceramide, a negative regulator of cell growth, and DAG, a well-established mitogenic factor, SMS activity has been proposed to play a significant role in the regulation of those processes associated with aberrant cell proliferation. Through analysis of a variety of different cell lines, a chronic myelogenous leukemia/Bcr-abl positive cell line (K562) was identified displaying a dramatic
upregulation of SMS activity. Furthermore, stable transfection of Bcr-abl causes a dramatic increase of SMS1 activity, expression, and translation. In addition, expression analysis by quantitative real time RT-PCR and modulation of gene expression by siRNA treatment suggested that enhanced expression of SMS1, and not SMS2 was responsible for increased SMS activity in bcr-abl-positive versus negative cells. Functionally, inhibition of SMS/SMS1 activity to levels approaching bcr-abl regulates SMS1 transcription in order to better understand the potential contribution of SMS1 on maintaining the undifferentiated, pro-proliferative phenotype of Bcr-abl positive cells. GAAN fellowship to TB COBRE in lipidomics and ACS-IRG to CL Abney Predoctoral fellowship

097 Regulation of Telomerase By Sphingosine Kinase 2/ Sphingosine-1-Phosphate in Human Lung Adenocarcinoma Cells, Shanmugam Panneer Selvam, Besim Ogretmen; Biochemistry and Molecular Biology, MUSC.

Sphingosine Kinases (SphK) are enzymes catalyzing the conversion of sphingosine to sphingosine-1-phosphate, a second messenger playing key roles in inflammation, angiogenesis and cancer. Two isoforms of this enzyme- SphK1, SphK2 are known to exist. The role of SphK1 generated S1P has been well elucidated, whereas SphK2 is often understudied. The goal of this study is to identify/establish intracellular targets of SphK2 involved in supporting tumor growth / progression. Telomerase, a ribonucleoprotein extends the ends of chromosomes, (telomeres) allowing cancerous cells to become immortal, and hTERT (human telomerase reverse transcriptase), the catalytic subunit of telomerase predominantly localizes to nucleus to carry out this function. We postulate that hTERT could be one of the downstream targets for SphK2/S1P signaling in the nucleus in lung cancer cells. RNA interference mediated knockdown of SphK2 showed decreased hTERT protein levels whereas SphK1 knockdown did not have any significant effect. Moreover, treatment of A549 cells with ABC294640, a SphK2 specific inhibitor downregulated hTERT protein in a time and dose dependent manner. ABC294640 mediated hTERT degradation was rescued by exogenous addition of S1P to A549 cells in a dose dependent manner indicating a direct intracellular role for S1P. Mechanistically, our data suggests that SphK2 inhibition results in caspase 3 activation which in turn mediates hTERT degradation. Indeed, pretreatment with caspase 3 inhibitor prevented ABC294640 dependent hTERT degradation.

Similarly, treatment of wt MEF’s with ABC294640 resulted in apoptotic cell death whereas caspase 3/- MEF’s were resistant to ABC294640. In addition, SCID mice bearing A549 lung tumor xenografts showed decreased tumor growth compared to controls. In summary, the preliminary data indicates an intracellular role for S1P generated selectively by SphK2 in the nucleus by stabilizing hTERT in human lung adenocarcinoma (A549) cells and thus targeting SphK2 appears to be an attractive new strategy for treatment of human lung cancers.

098 Development of Selective Small Molecule Inhibitors of Heterotrimeric G-Protein Signaling for the Treatment of Ovarian Cancer, Kevin J Bigham, Yuri K Peterson, Starr E Hazard, Joe B Blumer; Pharmaceutical & Biomedical Sciences, MUSC, Pharmaceutical, MUSC.

G-protein coupled receptors (GPCRs) are a widely expressed class of cell surface receptors that are frequently overexpressed in tumor cells. Their ligands are also commonly found in high concentrations at metastatic sites. Overactive signaling at the level of hormone, receptor, or G-protein can initiate and potentiute cellular transformation and other diseases. Heterotrimeric G-proteins, the immediate downstream effectors of GPCRs, present an attractive approach to regulate GPCR signaling cascades. We hypothesize that direct inhibition of overactive G-protein signaling is cytotoxic to ovarian cancers and will reverse their malignant phenotype. We describe the development of selective small molecule inhibitors which bind to and stabilize the GDP-bound form of the Galpha1. Preventing nucleotide exchange of the alpha subunit will in turn inhibit downstream G-protein signaling. This type of inhibition has the advantage of circumventing the need to directly address the genetic component of GPCR signaling in cases of mutations, polymorphisms, and expression-related defects often seen in cancer. Initial inhibitors were identified using computational high throughput docking of a 280,000 small molecule database to Galpha1. Fluorescent nucleotide exchange assays have verified selective G-protein inhibition. This inhibition was supported by live cell bioluminescence resonance energy transfer (BRET) experiments measuring the interaction of Galpha1 with the regulatory protein AGS4 in HEK293 cells. Inhibition of G-proteins also decreased cell viability in SKOV3 ovarian cancer cells. Targeting G-protein subunits rather than their receptors is expected to provide improved efficacy by targeting the regulatory molecule for a number of different GPCRs. Pharmacologic regulation of both receptor dependent and independent signaling through specific heterotrimeric subunits will provide a unique window into a major signaling axis while providing data and compounds for the treatment of many refractory diseases including cancer, inflammatory disease, and neurological disorders. Heidi Hamm,
Vanderbilt University School Of Medicine; John Hildebrandt, MUSC; Kate Appleton, MUSC

099 High Throughput Virtual Drug Discovery for Novel and Future Compounds That Cause Mitochondrial Toxicity, Richard E Trager, Lauren Willis, Christopher Lindsey, Craig Beeson, Rick Schnellmann, Yuri Peterson; Pharmaceutical and Biomedical Sciences, MUSC.

Many environmental, pharmaceutical, and industrial compounds negatively affect human health by exerting toxic effects on mitochondrial function. Currently there are no reliable methods for predicting mitochondrial toxicity. We hypothesize that there are distinct classes of chemotypes that can be identified and used to predict previously unrecognized and future mitochondrial toxicants. A novel respirometric assay was used to develop a database of mitochondrial toxicants. A set of 1760 diverse compounds were tested using primary cultures of rabbit renal proximal tubule cells (RPTCs) on the Seahorse Biosciences Extracellular Flux (XF) analyzer. The screen revealed 22 compounds that diminish uncoupled mitochondrial respiration. Based on chemical similarity, five chemical clusters of three or more compounds were identified from these 22 compounds. Clusters were computationally modeled using 3D pharmacophore and 2D electronic descriptor based quantitative structure-activity relationship (QSAR) analysis. These toxicophore models have identified a preliminary group of chemical structures related to mitochondrial toxicity. A search of a small molecule diversity library of 50,000 compounds revealed 91 potential toxicants to be tested on the XF analyzer. These descriptive and predictive models are being used to probe vast amounts, on the order of millions, of virtual small molecule chemical space to discover previously unknown scaffolds for mitochondrial toxicity. Novel predictive models have been created and will be experimentally validated using primary kidney cell respirometry. These validated predictive models will allow for continued identification of compounds that cause mitochondrial toxicity. NIH

100 Structural and Functional Implications of HIV-1 Rev Oligomerization, Fabio Casu, Stuart Parnham, Marco Marenchino, Mirko Hennig; Biochemistry and Molecular Biology, MUSC.

Rev is a regulatory protein essential in the HIV-1 replication cycle, which promotes the nuclear export of unspliced and incompletely spliced viral RNA transcripts. Rev is known to oligomerize both in the absence and in the presence of viral RNA, and oligomerization on its target sequence, the Rev Responsive Element (RRE), is critical to its biological function. Previous investigations have advanced our understanding of Rev-dependent nuclear export of viral, intron-containing RNA, yet many structural and mechanistic details remain to be unraveled. We hypothesize that monomeric Rev is an intrinsically unstructured protein and is able to adopt his fully functional folded state and form export-competent protein-RNA complexes through self-association and protein-RNA interactions. In order to investigate the role of Rev oligomerization, we studied the wild-type protein and Rev mutants L18T, V16D, I55N, V16DI55N using a combination of biochemical and biophysical techniques including chemical cross-linking, circular dichroism (CD) spectroscopy, tryptophan fluorescence spectroscopy, and nuclear magnetic resonance (NMR). Additionally, structural changes concerning Rev's arginine-rich RNA binding domain (Rev ARM) were monitored using a peptide spanning helix 2, the characterization of which has been shown to be particularly difficult in the full-length protein. We demonstrate that oligomerization in combination with electrostatic interactions involving helix 2 allows the mostly random-coiled Rev monomers to undergo significant conformational changes and allow it to adopt the export-competent protein conformation in the context of the oligomeric Rev-RNA complex. A better characterization of the role of Rev oligomerization in complex with the RRE RNA will allow for identification of possible new targets and therefore the development of new therapeutic agents for the treatment of HIV infection.

101 A Study of Determinants of Coping in Childhood Cancer Survivors, Lea H Soderstrom1, Michelle Hudspeth2, Michelle Vandermaas3, Katherine Sterba1, Elizabeth Garrett-Mayer1, Anthony Alberg1, 1Biostatistics and Epidemiology, MUSC, 2Pediatrics-Hematology/Oncology, MUSC, 3Child Life, MUSC.

Abstract not available.

102 Impaired Pro-neurotrophin Processing is Associated with Cholinergic Degeneration and Cognitive Impairment Observed in Down Syndrome, Ashley M Fortresss, Mona Buhusi, Ann-Charlotte Granholm; Neurosciences, MUSC.

Individuals with Down syndrome (Trisomy 21; DS) develop Alzheimer’s-like neuropathology and cognitive impairments by the fourth decade of life. One such neuropathological hallmark is the degeneration of the basal forebrain cholinergic neurons (BFCNs), which has been characterized in the Ts65Dn mouse model of DS. BFCNs use the NGF/TrkA signaling complex to promote cholinergic signaling to the hippocampus and loss of NGF availability results in degeneration of these neurons. Although retrograde transport of NGF is disrupted in Ts65Dn mice, the mechanism by which the NGF signal is lost is not well understood. Recent evidence in the Alzheimer’s field has suggested that pro-NGF, the un-cleaved precursor to mature NGF, interacts with p75/sortilin to promote pro-apoptotic pathways, leading to BFCN degeneration - however this has not yet been examined with respect to DS. Plasmin, and hence also plasminogen, is involved in
cleavage of pro-NGF and may therefore alter cleavage processes, especially with aging and/or degenerative disease. Therefore, we used four age groups across the lifespan of the Ts65Dn mouse and performed cognitive testing using the 12-day water radial arm maze followed by analyses of the ratio of pro-NGF:mature NGF, TrkA: p75, and plasminogen:plasmin in the hippocampus and basal forebrain. Our goal was to establish an understanding of the role of upstream mechanisms regulating mature NGF production with aging and DS. Preliminary findings suggest that pro-NGF cleavage and plasmin pathways are altered in DS and may lead to a loss of NGF availability and ultimately, BFCN degeneration and cognitive impairment. Supported by NIA grant AG12122.

103 MPTP Neurotoxicity in Nigrostriatal Dopamine Neurons is Exacerbated in Gdnf Heterozygous Mice, Bok Soon Go, Heather A Boger, Jacqueline F McGinty; Neuroscience, MUSC.

Parkinson's disease (PD) is a progressive neurodegenerative movement disorder characterized by a progressive degeneration of nigrostriatal dopamine (DA) neurons. Genetic vulnerability and exposure to environmental neurotoxins during aging have been implicated as risk factors for PD. Glial cell line-derived neurotrophic factor (GDNF) is reduced in the substantia nigra of PD patients, suggesting that GDNF reduction contributes to DA neuronal cell loss. We have previously shown that mice with a partial deletion of Gdnf (Gdnf+/−) mice exhibited lower motor activity and less striatal TH expression than wild type (WT) mice during aging and that methamphetamine-induced toxicity is exacerbated in Gdnf+/− mice. Similarly, GDNF reduces damage to the midbrain DA system of mice from 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP). MPTP is a DA neuron-specific neurotoxin known to induce parkinsonism. Acute exposure to MPTP does not sufficiently mimic the main features and symptoms of PD. But combined with probenecid, which slows the clearance of MPTP, the duration of MPTP's toxic effect is extended. Therefore, in this study, male Gdnf+/− and WT mice at 7-8 months of age were injected with probenecid (250 mg/kg, i.p.) 30 min before MPTP (20 mg/kg, s.c.) biweekly for five weeks. Two weeks after the end of MPTP injections, locomotor activity was tested and one week later, the mice were perfused with 4% paraformaldehyde for immunohistochemistry. Total distance traveled was less in saline-treated Gdnf+/− mice and MPTP-treated Gdnf+/− mice than in saline- and MPTP-treated WT mice, respectively. Further, the level of striatal TH-ir was less and the induction of dihydrothidium-induced fluorescence, a marker of radical oxygen species, was greater in nigral cells of Gdnf+/− mice than in WT mice treated with MPTP. These data indicate that GDNF is neuroprotective for nigrostriatal dopamine neurons after a chronic MPTP challenge. Supported by P01 AG023630.

104 Long-Term Treatment with a High Fat/High Cholesterol Diet in Young and Aged Rats: Inflammatory Response, Blood-Brain-Barrier Breakdown, and Cognitive Impairment, Linnea R Freeman, Ann-Charlotte Granholm; Neurosciences, MUSC.

Consumption of mainly saturated fats and cholesterol in the diet has been proven to be damaging to organs such as the heart and liver, particularly through inflammatory mechanisms. However, the effects of a high saturated fat and cholesterol diet (HFHC diet) on the brain are not currently well understood. We hypothesize that long-term treatment with this type of diet may be damaging to the brain, especially the hippocampus, a vulnerable region to ischemia and hypoxia. We also hypothesize that aged subjects exhibit an enhanced response to this diet compared to young subjects due to increased inflammation and ensuing alterations to the blood brain barrier (BBB) permeability. Previous work from our laboratory demonstrated that a 10% hydrogenated coconut oil and 2% cholesterol diet (HFHC diet) resulted in impaired performance on the 12-day water radial arm maze, increased circulating cholesterol and triglyceride levels, increased microgliosis, and decreased dendritic microtubule associated protein 2 (MAP2) staining in the hippocampus after only 8 weeks on the diet. Our current study has further evaluated long-term effects of the HFHC diet on cognition and hippocampal morphology using the same HFHC diet for 6 months starting at the age of 4 months (young) or 14 months (aged) in male Fischer 344 rats. In this long-term study, serum was collected in order to analyze triglyceride and cholesterol levels, water radial arm maze behavior was performed, and immunofluorescence studies on the hippocampus have been conducted. These experiments revealed impaired working and reference memory, a compromised BBB, increased microgliosis, and dendritic damage in HFHC treated rats compared to control rats. Alterations in cognitive and morphological measures were exacerbated in aged vs. young rats, suggesting enhanced sensitivity to this diet with aging. Together, this provides novel evidence for a role of inflammation in diet-induced neurodegeneration. Supported by the Nutrition Council of South Carolina and NIA grant AG04418.

105 Relationship Between Repetitive Traumatic Brain Injury and Substance Use Disorders Among a Female State Prison Offender Population, Monica E Cornelius, Pamela F Ferguson, E E Pickelsimer; Medicine, Biostatistics and Epidemiology, MUSC.

Background: Female offender populations often have high rates of traumatic brain injury (TBI) and substance use disorder (SUD). TBI is an important cause of physical and mental disability and may contribute to SUD. Repetitive TBI (RTBI) may have
106 Inferring Novel Genes and Pathways That Modulate the Sphingolipid Pathway From a Novel Yeast Gene Network Derived From Ontology Fingerprints, Tingting Qin¹, Lam C Tsoi¹, Nabil Matmati², Bidyut K Mohanta³, Andrew B Lawson³, Yusuf A Hannun², Jim Zheng³; ¹Bioinformatics Graduate Program, Biochemistry and Molecular Biology, MUSC, ²Biochemistry and Molecular Biology, MUSC, ³Biostatistics and Epidemiology, Medicine, MUSC.

Abstract not available.

107 Distribution and Elimination of Brevetoxin Metabolites, Tod Leighfield¹,², John Ramsdel²; ¹MCBP-Marine Biomedicine, ²NOAA National Ocean Service.

Abstract not available.

108 Proteome Changes Associated with Salinity Stress and DMSP Accumulation in Fragilariopsis Cylindrus, Barbara R Lyon¹, Peter A Lee², Giacomo DiTullio³, Michael G Janeczko; ¹Marine Biomedicine and Environmental Science, MUSC, ²Hollings Marine Lab, College of Charleston, ³Nephrology, MUSC, Ralph H. Johnson VA Medical Center.

Abstract not available.

109 Post-transcriptional Regulation of the Cell Cycle in the Red Tide Dinoflagellate, Karenia Brevis and a Potential Role for Cyclin-Dependent Kinase, Stephanie A Brunelle³, Frances M Van Dolah²; ¹Marine Biomedicine, MUSC, ²Marine Biotoxins Program, CCHEBR, NOS, NOAA.

The dinoflagellate, Karenia brevis, produces harmful algal blooms in the Gulf of Mexico that cause extensive marine animal mortalities and human illness nearly annually. The molecular mechanisms controlling cell cycle entry in this dinoflagellate are important because bloom development occurs through vegetative cell division. Microarray and qPCR studies have demonstrated that, unlike typical eukaryotes, dinoflagellate cell cycle genes are not regulated at the transcriptional level, including genes that code for replication fork proteins, typically activated by the E2F transcription factor at the G1/S transition. Post-transcriptional control of these genes is also suggested by the presence of a trans-spliced leader sequence on their transcripts. Sequence analysis and protein modeling were used to develop custom antibodies for Western blotting to investigate the abundance of replication fork proteins over the cell cycle and whether they are regulated at the translational or post-translational level. The K. brevis replication fork proteins, PCNA, RFC, RPA and RnR2 were shown to change over the cell cycle, with highest expression at S-phase, suggesting translational control. PCNA also appears to be modified post-translationally, either by ubiquitin or SUMO concurrent with S-phase. Immunolocalization of PCNA showed that it is present in the nucleus throughout the cell cycle in cells actively traversing the cell cycle. However, PCNA showed a pattern of nuclear location that changes between a chromatin bound form and a pool that is peripheral. Cell cycle inhibition at the G1/S transition with the CDK2 specific inhibitor, fascaplycin or the pan-CDK inhibitor Olomoucine specifically inhibited the expression of PCNA protein. These results lead us to propose a novel mechanism of translational control of cell cycle entry as opposed to transcriptional control which is seen in most eukaryotes. Marine Biotoxins Program, NOAA, Charleston, SC.
110 C-Myc is a Downstream Target of CXCL13 to Stimulate RANK Ligand Expression in Bone Marrow Stromal/Preosteoblast Cells, Yuvaraj Sambandam1, William L Ries2, James S Norris3, Sakamuri V Reddy1; 1Charles P. Darby Children's Research Institute, Pediatrics, MUSC, 2College of Dental Medicine, MUSC, 3Microbiology & Immunology, BSB, MUSC.

Chemokine ligand-13 (CXCL13) has been implicated in oral squamous cell carcinomas (OSCC) tumor progression and osteolysis. We recently demonstrated that NFATc3 transcription factor plays a role in CXCL13 stimulated RANK ligand (RANKL) expression, a critical osteoclastogenic factor in OSCC cells. We hypothesized that CXCL13 production by OSCC cells stimulates RANKL expression in stromal/preosteoblast cells in the bone microenvironment. Interestingly, treatment of human bone marrow derived stromal cells (SAKA-T) and murine preosteoblast cells (MC3T3) with conditioned media (20%) obtained from SCC14a cells significantly increased RANKL expression while incubation with an antibody against CXCL13 specific receptor, CXCR5 markedly decreased RANKL expression in these cells. Western blot analysis demonstrated that recombinant hCXCL13 treatment (0-15 ng/ml) of SAKA-T and MC3T3 cells for a 6 h period increased (5-fold) RANKL expression. Realtime RT-PCR analysis identified a dose-dependent stimulation of CXCR5 mRNA expression in these cells. CXCL13 stimulation of SAKA-T and MC3T3 cells transiently transfected with hRANKL gene promoter-Luc reporter plasmid demonstrated a 3.5 and 3.0-fold increase in RANKL gene promoter activity, respectively. Further, CXCL13 stimulation significantly increased p-ERK1/2 levels in SAKA-T and MC3T3 cells. Transcription factor array screening by real-time RT-PCR identified high levels of c-Myc and NFATc3 mRNA expression in CXCL13 stimulated SAKA-T cells. Western blot analysis revealed that CXCL13 dose-dependently increased the levels of c-Myc and NFATc3 expression in these cells. We also showed that CXCL13 increased the phosphorylation of c-Myc in SAKA-T (10-fold) and MC3T3 (7-fold) cells. Furthermore, siRNA suppression of c-Myc expression markedly decreased CXCL13 stimulated RANKL and NFATc3 expression in bone marrow stromal cells. Chromatin-immuno precipitation (ChIP) assay confirmed c-Myc binding to the hRANKL promoter region (-1315 bp to -1435 bp). In summary, CXCL13 production by OSCC cells stimulates RANKL expression in bone marrow stromal/preosteoblast cells and that c-Myc 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.

111 Role of P38/Akt Signaling Pathway in the Regulation of Sodium/Calcium Exchanger Expression in Adult Cardiomyocytes, Olga Chernysh1, Santhosh K Mani1, Paige Snider2, Simon J Conway3, Donald R Menick1; 1Medicine, MUSC, 2Indiana University School of Medicine, Indianapolis, IN.

Introduction: The sodium/calcium exchanger (NCX1) is regulated at the transcriptional level in cardiac hypertrophy and heart failure. Upregulation of NCX1 affects sarcoplasmic reticulum calcium loading and directly contributes to contractile dysfunction of failing myocardium. In animal models, it has been demonstrated that pharmacological inhibition of NCX1 may be beneficial in heart failure and during ischemia/reperfusion. However, most studies have focused only on the acute effects of NCX1 inhibitors on calcium homeostasis, and there is little information available on the potential risks and benefits of chronic therapeutic inhibition of NCX1. Previous work from our laboratory has shown that prolonged treatment with NCX1 inhibitor, KB-R7943 results in the upregulation of Ncx1 gene expression in both isolated adult cardiomyocytes and intact mouse hearts. This upregulation is mediated via the activation of p38 and formation of a NCX1-p38 complex. However, the signaling pathway leading to the increase in Ncx1 gene expression remains to be elucidated. Hypothesis: NCX1, whose activity is acutely sensitive to cytosolic calcium, sodium and membrane potential, can also regulate its own expression in an activity-dependent manner as part of a macromolecular signaling complex. Results: To identify potential downstream targets of p38, we treated isolated adult feline cardiomyocytes with KB-R7943 in the presence of p38 inhibitor, SB203580, which resulted in the inhibition of Akt kinase activation. Co-immunoprecipitation studies also showed that Akt was in complex with NCX1. Conclusion: Our results suggest that p38/Akt pathway plays a role in regulating Ncx1 gene expression in response to pharmacological inhibition of the exchanger. NIH: RO1 HL095696 AHA: 09GRNT2020202

112 A Novel Pathway Modulates FGFR1 Signaling By Controlling the Receptor Trafficking to the Plasma Membrane, Jagadish kummetha Venkata, Claire Hinsch, Venkatesababa Sammanna, Vincent Dammai; Pathology, MUSC.

Abstract not available.

113 HSP70 Inhibits Aminoglycoside-Induced Activation of JNK and Downstream Signaling, Inga I Kramarenko, Carlene S Brandon, Lisa L Cunningham; Pathology and Lab Med, MUSC.

Exposure to aminoglycosides results in hair cell death that is mediated by specific apoptotic proteins, including c-Jun N-terminal kinase (JNK). Constitutive expression of heat shock protein 70 (HSP70) inhibits
aminoglycoside-induced cochlear hair cell death and hearing loss in vivo. In order to examine the molecular mechanism(s) underlying the protective effect of HSP70 against aminoglycoside-induced hair cell death, we have analyzed the effects of HSP70 on aminoglycoside-induced JNK activation. Utricles from adult CBA mice were heat shocked in vitro and were exposed to neomycin for 12 hours. Protein analysis indicates that neomycin exposure results in robust activation (phosphorylation) 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 express HSP70 (and their wild-type littermates) were treated with neomycin for 12 hours. Western blot data indicate that HSP70 constitutive expression 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. Specific substrates for activated JNK include the transcription factors c-Jun (phosphorylated by JNK on Ser63) and ATF-2 (phosphorylated by JNK on Thr71) and the pro-apoptotic Bcl-2 family member BimEL (phosphorylated by JNK on Ser65). Our recent data indicate that HSP70 constitutive expression inhibits neomycin-induced BimEL phosphorylation. In addition, heat shock inhibits neomycin-induced c-Jun activation. 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 and downstream BimEL activity. Supported by NIH NIDCD R01 DC007613 and DC07613-S2. Additional support was provided by NIH/NCRR extramural research facilities construction (C06) grants C06 RR015455 and C06 RR14516 from the National Center for Research Resources.

113.1 Extracellular Heat Shock Protein 90 (Ehsp90): A Novel Modulator of the Tumor Microenvironment in Prostate Cancer, Jessica E Bohonowycz, Michael W Hance, Jennifer S Isaacs; Medicine, Cell and Molecular Pharmacology, MUSC.

Abstract not available.

114 ZO-1 Regulates Cx43 Function Via The Connexon Switch Mechanism In A Novel Perinexal Region Of The Plasma Membrane, J Matthew Rhett, Jane Rhett Jourdan, Robert G Gourdie; Regenerative Medicine & Cell Biology, MUSC.

Gap junctions (GJs) uniquely provide a conduit for the passage of solutes and signals between the cytoplasm of cells. These structures are large aggregates of intercellular channels composed of protein subunits called connexins. Prior to entering GJ plaques, connexins exist as hexameric half-channels called connexons or hemichannels that have been shown to play roles in signaling events, volume control, and membrane polarization under both physiological and pathological conditions. One isoform of the connexin protein family, connexin43 (Cx43), is of particular importance given that is widely expressed in mammalian tissues, and is the primary isoform expressed in ventricular myocardium where it is responsible for propagation and syncronization of the myocardial action potential. Our work has previously shown that Cx43-GJ size is regulated through an interaction between Cx43 and the scaffolding protein, ZO-1. The mechanism of ZO-1-mediated GJ size regulation appears to occur through limiting the rate at which cell-surface hemichannels are allowed to accumulate into GJ plaques. The data presented here indicate that this mechanism sets up a balance between intercellular channels and hemichannels that correlates to functional changes in GJ-mediated and hemichannel-mediated communication. Most recently, we have used biochemical and immunofluorescent methods to more rigorously describe the mechanism of GJ size control. Specifically, fractionation of Cx43 into junctional and nonjunctional pools followed by IP for ZO-1 and immunoblotting for Cx43 shows that ZO-1 interacts with both hemichannels and intercellular channels. Additionally, we have used the novel DuoLink system to describe the subcellular locale at which Cx43/ZO-1 interaction takes place. Our findings indicate that ZO-1 directly interacts with Cx43-hemichannels in a previously undescribed region surrounding the GJ plaque, which we have termed "The Perinexus." These results underpin studies of molecular therapies aimed at pathologies such as arrhythmia already under way. Supported by a grant from the South Carolina Space Grant Consortium (to J.M.R.) and National Institute of Health Grants HL56728-10A2, HL082802-01, and DE019355-01 (to R.G.G.).

115 Regulation of the AGS3 - G(α)i Signaling Complex By a Seven-Transmembrane Span Receptor, Sukru S Oner¹, Ningfei An², Ali Vural¹, Billy Breton³, Michel Bouvier⁴, Joe B Blumer⁵, Stephen Lanier⁶; ¹Pharmacology, MUSC; ²Pathology, MUSC; ³Biochemistry, Université de Montréal.

G-protein signaling modulators (GPSM) play diverse functional roles through their interaction with G-protein subunits. AGS3 (GPSM1) contains four G-protein regulatory motifs (GPR) that directly bind G(α)i free of G(βγ) dimer providing an unusual scaffold for the "G-switch" and signaling complexes, but the mechanism by which signals track into this scaffold are not well understood. We report the regulation of the AGS3 - G(α)i signaling module by a cell surface, seven-transmembrane receptor. AGS3 and G(α)i tagged with Renilla luciferase or yellow fluorescent protein expressed in mammalian cells exhibited saturable, specific bioluminescence resonance energy transfer indicating complex formation in the
cell. Activation of alpha2-adrenergic receptors or mu-opioid receptors reduced AGS3-RLuc - G(alpha)1-YFP energy transfer by over 30%. The agonist-mediated effects were inhibited by pertussis toxin and co-expression of RG54, but were not altered by G(1) sequestration with the carboxyl terminus of GRK2. G(1)-dependent and agonist-sensitive bioluminescence resonance energy transfer was also observed between AGS3 and cell-surface receptors typically coupled to G(1) and/or G(0) indicating that AGS3 is part of a larger signaling complex. Upon receptor activation, AGS3 reversibly dissociates from this complex at the cell cortex. Receptor coupling to both G(beta gamma) and GPR-G(1) offer additional flexibility for systems to respond and adapt to challenges and orchestrate complex behaviors. Supported by grants from the National Institutes of Health [NS24821 (SML), DA025896 (SML), GM086510 (JBB)] and the Canadian Institutes of Health Research (MB). MB holds a Canada Research Chair in Signal Transduction and Molecular Pharmacology.

116 Activator of G-protein Signaling 3 Null Mice II: Exploring the Functional Roles of AGS3 in the Immune System. Melissa Branham-O'Connor1, Xian Xhang2, Stephen M Lanier3, Joe B Blumer1; 1Pharmacology, MUSC, 2Medicine, MUSC.

Abstract not available.

117 HSP70 Induced By Lipoprotein Immune Complexes Sequester Lipids in The Endosomal Compartment: Impact on Oxidative Stress and Macrophage Survival. Mohammed M Al Gadban1, Kent J Smith1, Dezirea Jones1, Virella Gabriel2, Lopes-Virella F Maria3, Hammad M Saman4, 1Regenerative Medicine & Cell Biology, MUSC, 2College of Graduate Studies/ SURP, 3Immunology, MUSC, 4Endocrinology, MUSC.

Oxidized low-density lipoproteins (oxLDL) and oxLDL-containing immune complexes (oxLDL-IC) contribute to formation of lipid-laden macrophages. We have previously shown that knockdown of HSP70B' protects cells from cytotoxic effects of oxLDL. Oxidative and nitrosative stresses have been shown to be induced by oxLDL in macrophages. We have recently shown that mitochondrial membrane potential was decreased and generation of reactive oxygen and nitrogen species was increased in U937 cells treated with oxLDL compared to oxLDL-IC. We proposed that HSP70/70B' through co-localization with internalized lipids in the endosomal compartment could influence the differential intracellular trafficking of oxLDL and oxLDL-IC. This study examines whether HSP70/70B' are necessary for the differential oxidative and nitrosative stresses in response to oxLDL and oxLDL-IC. U937 cells were transfected with siRNAs specific to HSP70/70B' then treated with oxLDL, oxLDL-IC, KLH-IC or IMDM control in combination with DCF-DA for H2O2, DAF-FM plus l-arginine for nitric oxide (NO), and Mito Tracker for mitochondrial membrane potential and visualized using confocal microscopy. Knockdown of HSP70B' resulted in a significant decrease in NO production in response to oxLDL compared to control-transfected cells; knockdown of HSP70 resulted in an intermediate reduction in NO generation. Knockdown of HSP70 or HSP70B' resulted in no significant decrease in H2O2 production in response to oxLDL. The knockdown of HSP70 and HSP70B' resulted in no change in either H2O2 or NO production in response to oxLDL-IC compared to control-transfected cells. The mitochondrial membrane potential was not affected by oxLDL-IC in cells transfected with either HSP70 siRNA or HSP70B' siRNA compared to control-transfected cells. However, mitochondrial membrane potential was significantly decreased in response to oxLDL compared to oxLDL-IC regardless to HSP70 siRNA or HSP70B' siRNA transfection. In conclusion, these findings suggest that HSP70 and HSP70B' expression regulates the nitrosative but not oxidative stress response induced by oxLDL in macrophages. Supported by NIH grant HL079274, NIH (ARRA) grant R01 HL079274-04S1, and the South Carolina COBRE in Lipidomics and Pathobiology (P20 RR17677 from NCRR) to SMH, and NIH grants P01 HL55782, R01 DK081352 and R01 DK081352-02S1 (ARRA) to MLV

118 Maintenance of Genome Stability By Intra-S Phase Checkpoint Protein Tof1 and Other Fork-associated Proteins As Measured By Ty1 Retro-transposition and Karyotypic Changes. Narendra K Bairwa1, Bidyut K Mohanty2, Radostina Stemenova2, Joan Curcio3, Deepak Bastia1; 1Biochemistry, MUSC, 2Laboratory of Molecular Genetics, Wadsworth Center Albany, NY.

We have previously shown that the intra-S checkpoint proteins Tof1 and Csm3 of S. cerevisiae counteract the helicase Rrm3 to modulate fork arrest not only at the replication termini but also at non-histone protein binding sites elsewhere in the genome. In the present work, our goal was to investigate whether the checkpoint proteins acted either antagonistically or in synergy with Rrm3 to control genome stability. We measured genome stability in various genetic backgrounds by measuring the rate of Ty1 retro-transposition, karyotype analysis and telomere length maintenance. We show here that Tof1 is a key player in suppressing promiscuous retro-transposition in collaboration with two fork-associated proteins namely the helicase Rrm3 and the F box protein Dia2. In rrm3Δ tof1Δ or dia2Δtof1Δcells, ultrahigh frequency of retro-transposition was unleashed (up to ~350 fold above the WT levels). Complementation with either Rrm3 or Dia2 brought the frequency down to normal levels. We also show that mutations in these genes cause karyotype instability as measured by the relative migrations of the individual chromosomes in
pulsed field gels (CHEF) in comparison with the WT chromosomes. The mobility changes were RNaseH resistant and therefore probably not caused by extensive R-loop formation. These mutations also caused changes in the lengths of telomeres. However any of these events alone could not account for the magnitude of karyotypic instability. We conclude that Tof1 in collaboration with either Rrm3 or Dia2 represses various intermediate steps of Ty1 retro-transposition that together lead to stringent negative regulation of the process in normal cells. Supported by the grants GM049264 and GM049264-17S1 to DB and by GM52072 to MJC.

120 Placenta Growth Factor (PLGF) As a Potential Therapeutic Target in Head and Neck Squamous Cell Carcinoma, Brian D Hoel1, Wei Sun1, Kenneth J Byrd2, Isaac Dingle3, Boyd M Gillespie2, Natalie A Sutkowski1; 1Microbiology and Immunology, MUSC, 2Otolaryngology, MUSC, 3Medicine, MUSC.

Abstract not available.

121 Role of mGluR5 During Conditioned Hyperactivity in Differentially Reared Rats, Margaret J Gill1,2, Mary E Cain1; 1Neuroscience, MUSC, 2Psychology, Kansas State University.

Environmental enrichment decreases amphetamine self-administration and amphetamine sensitization at low unit doses. Glutamate contributes to the changes that occur during differential rearing and the response to psychostimulants. This has been demonstrated as enriched condition (EC) rats have greater levels of glutamate in the NAcc following amphetamine than impoverished condition (IC) rats (Rahmen & Bardo, 2008). Additionally, 3-(2-Methyl-1,3-thiazol-4-yl)ethyl)pyridine hydrochloride (MTEP), an mGluR5 antagonist, attenuates cue- and methamphetamine-induced reinstatement, as well as methamphetamine self-administration (Gass et al., 2009). Further, group II mGluR antagonists have been shown to attenuate conditioned hyperactivity in an amphetamine-associated environment (Kim, Vezina, & Kim, 2008). The current study examined if MTEP pretreatment attenuates expression of amphetamine-induced conditioned hyperactivity in EC, IC, and social condition (SC) rats. Male Sprague Dawley rats arrived in the lab at 21 days of age and were randomly assigned to EC, IC, or SC conditions in which they were reared for 30 days. Rats were then assigned to the Paired (amphetamine in both locations), Unpaired (saline prior to session; amphetamine in home cage), or Control (saline in both locations) condition. Rats received repeated amphetamine (0.3 mg/kg) or saline injections immediately prior to 5 training sessions. For the conditioned hyperactivity test, rats were pretreated with MTEP (1.0 mg/kg) or saline 30 minutes prior to the session. Rats then received a saline injection immediately prior to the conditioned hyperactivity test. During acquisition EC rats displayed attenuated locomotor activity compared to IC and SC rats. During the conditioned hyperactivity test, conditioned hyperactivity was observed in IC and SC, but not EC rats. However, in the MTEP pretreatment group, conditioned hyperactivity was observed in EC, IC, and SC rats. Additionally, pretreatment with MTEP attenuated locomotor activity in IC and SC, but not EC rats. These results suggest that mGluR5 contributes to the expression of conditioned hyperactivity in EC rats. USPHS DA021359 and Kansas State University

122 Excitotoxic Lesions of the Dorsolateral Caudate-Putamen Impair Cocaine-primed Reinstatement in an Animal Model of Relapse, Amanda Gabriele, Ronald See; Neurosciences, MUSC.

Recent evidence suggests that cocaine addiction may involve progressive drug-induced neuroplasticity of the dorsal striatum. The dorsolateral caudate putamen (dlCPu), which has been implicated in habit learning, may be a key substrate of habitual drug-seeking in addiction, and prior studies have demonstrated the involvement of the dlCPu during relapse to cocaine-seeking following abstinence. Here, we examined the effect of dlCPu lesions on acquisition and maintenance of cocaine self-administration, extinction of responding, and subsequent reinstatement of cocaine-seeking. We predicted that pre-training dlCPu lesions would not affect acquisition or maintenance of cocaine self-administration, but would affect reinstatement of cocaine-seeking. Male Sprague-Dawley rats received bilateral excitotoxic lesions of the dlCPu with N-methyl-D-aspartate (NMDA, 0.12 M, 0.6 ml per side) or a sham lesion and underwent jugular catheter surgery. Animals self-administered cocaine (0.2 mg/50 ul infusion, i.v.) along an FR1 schedule in daily 2 hr sessions for 10 days, whereby lever presses resulted in cocaine infusions and presentation of a paired light-tone stimulus complex. After 14 days of abstinence, animals were returned to the self-administration chamber and lever responding was recorded, but had no programmed consequences (relapse test). Animals then underwent extinction trials for a minimum of 7 days and a series of reinstatement tests. Animals reinstated responding in the presence of conditioned cues, after a cocaine priming injection (10 mg/kg), or with the combination of cues and cocaine prime. Rats with dlCPu lesions showed no differences from sham controls during self-administration and extinction. While dlCPu lesioned rats showed no differences in responding during the relapse test or the cued reinstatement test, cocaine-seeking was significantly impaired during cocaine-primed reinstatement as compared to sham controls. These results demonstrate the critical involvement of the dlCPu in cocaine-primed reinstatement, perhaps via changes in cocaine activated stimulus-response learning. NIH grant DA10462
Stress is a primary factor in relapse to drug-seeking and drug-taking in human addicts and in animal models of addiction. To date, few stressors have demonstrated consistent and reliable efficacy to induce reinstatement to drug-seeking in animal models. Previous evidence demonstrates that the anxiogenic stressor, yohimbine, produces reliable reinstatement of cocaine-seeking. Here we tested the anxiogenic GABA inverse agonist, FG7142, for its ability to reinstate cocaine-seeking in rats with a trained to self-administer cocaine. Male, Sprague-Dawley rats underwent jugular catheter surgery and then self-administered cocaine (0.2 mg/50 μl infusion) in daily 2 hr sessions for 2 weeks, whereby lever presses resulted in cocaine infusions and presentation of a paired light-tone stimulus complex. Animals then underwent extinction trials for a minimum of 7 days. On reinstatement test days, animals received injections of either FG7142 (1.0 – 10mg/kg, IP) or saline vehicle prior to testing. We observed no effects of FG7142 alone on reinstatement of cocaine-seeking. However, in a subset of animals, prior FG7142 exposure led to a potentiated response to yohimbine in subsequent reinstatement trials. We also determined the effects of FG7142 on plasma corticosterone and anxiotypic behavior in the elevated plus maze and defensive burying test in both cocaine naïve and cocaine trained animals. While cocaine naïve animals exhibited the expected increased corticosterone and anxiotypic behavioral responses to FG7142, we observed no behavioral or corticosterone response to FG7142 in cocaine trained animals. Our data demonstrate that FG7142-induced anxiogenic stress does not drive reinstatement to cocaine-seeking, and that animals with a history of cocaine intake may show blunted responses to the anxiogenic effects of FG7142. These studies were conducted in accordance with the Guide for the Care and Use of Laboratory Animals, as adopted and promulgated by the National Institutes of Health. This research was supported by NIH grant RO1 DA21690.

124 Sex Differences in Orexin 1 Receptor Mediation of Cocaine-induced Locomotion and Cocaine-seeking in Rats, Luyi Zhou, Ronald E See; Neurosciences, MUSC.

Prior studies have demonstrated sex differences in locomotor and reward-associated behaviors with cocaine. The orexin/hypocretin system has recently been implicated in the conditioned-cued reinstatement of cocaine-seeking in male rats. Although female rats express higher levels of orexin A peptide and orexin 1 receptor (OX1R) in the hypothalamus when compared to male rats, it has not yet been determined if the orexin system shows sexual dimorphism in response to cocaine or cocaine-seeking. Therefore, we assessed the effects of the selective OX1R antagonist, SB-334867 (SB), on locomotion and on cue-induced reinstatement of cocaine-seeking. All male and female rats were administered SB (10, 20, or 30 mg/kg, i.p.) or vehicle 30min prior to tests. First set of rats were tested for both basal and acute-cocaine (10mg/kg, i.p.) induced locomotion over a period of 4 hr using photobeam equipped test chambers. Another set of rats experienced daily sessions (2 hr/day for 10 days) of lever pressing for intravenous cocaine (0.6 mg/kg/infusion) paired with stimulus cues. Then rats underwent daily extinction trials for at least 7 days. Following SB treatment, reinstatement of cocaine-seeking was then triggered by presentation of previously cocaine-paired cues. In males, 20 and 30 mg/kg SB reduced basal locomotor activity; cocaine-induced hyperlocomotion was blocked by all three SB doses. In female rats, only the 20mg/kg SB reduced cocaine-induced locomotion. SB pretreatment significantly attenuated cue-induced reinstatement in males, but not females. Taken together, these data suggest that male rats are more sensitive to the effects of OX1R blockade for locomotion than female rats. Orexin regulation of cocaine-seeking produced by conditioned cues occurs in males, but not females. These sex differences may be due to intrinsic differences in hypothalamic orexin-mediated signaling. A greater understanding of sex differences in the orexin/hypocretin system will lead to improved treatment of cocaine addiction. Supported by NIH grant P50 DA16511 (Specialized Center of Research on Sex and Gender Factors Affecting Women’s Health).

125 Loss of Object Recognition Memory Produced By Extended Access to Methamphetamine Self-Administration is Reversed By Positive Allosteric Modulation of Metabotropic Glutamate Receptor 5, Carmela Reichel, Marek Schwendt, Jacqueline F McGinty, Ronald E See; Neuroscience, MUSC.

Methamphetamine (meth) abuse can lead to persisting cognitive deficits. Here, we utilized a long-access meth self-administration (SA) protocol to assess recognition memory and metabotropic glutamate receptor (mGluR) expression, and the possible reversal of cognitive impairments with the mGluR5 allosteric modulator, CDPPB. Male, Long-Evans rats self-administered i.v. meth (0.02 mg/infusion) on an FR1 schedule of reinforcement or received yoked saline infusions. After 7 daily 1-h sessions, rats were switched to 6-h daily sessions for 14 days, and then underwent drug abstinence. Rats were tested for object recognition memory one week after meth SA at ninety min and 24 hour retention intervals. In a separate experiment, rats underwent the same protocol, but received either vehicle or CDPPB (30 mg/kg, s.c.) after familiarization. Rats were sacrificed on day 8 or 14 post-SA and brain tissue was
obtained. Meth intake escalated over the extended access period. Additionally, meth-experienced rats showed deficits in both short- and long-term recognition memory, as demonstrated by a lack of novel object exploration. This deficit was reversed by CDPPB treatment. On day 8, meth intake during SA negatively correlated with mGluR expression in the perirhinal cortex and mGluR5 receptor expression was decreased 14 days after discontinuation of meth. This effect was specific to mGluR5 levels in the perirhinal cortex, as no differences were identified in the hippocampus, or in mGluR2/3 receptors. These results from a clinically-relevant animal model of addiction suggest that mGluR5 receptor modulation may serve as a potential treatment of cognitive dysfunction in meth addiction. Supported by NIH grants P20DA022658 (RES), F32DA029344 (CMR), T32DA007288 (CMR), R01DA024355 (MFO), and C06 RR015455. The authors thank Shannon Ghee, Lauren Ramsey, and Stacey Sigmon for technical assistance.

126 Ethanol Effects on the Discriminative Stimulus Properties of Methylphenidate, Robin L. McGovern1,2, Kennerly S Patrick1, William C Griffin, III1, 1Pharmaceutical Sciences, MUSC, 2Psychiatry and Behavioral Sciences, MUSC.

RATIONALE: Methylphenidate (MPH; Ritalin®) remains the drug of choice for treatment of attention-deficit hyperactivity disorder (ADHD). Widespread abuse of MPH has prompted studies into the pharmacology/toxicology of this stimulant, especially when MPH is combined with ethanol. Ethanol elevates d-MPH plasma concentrations through inhibition of carboxylesterase 1. Importantly, ethanol also enhances euphoric effects of MPH. We have shown that C57BL/6J (C57) mice model aspects of this MPH – ethanol interaction. HYPOTHESES AND METHODS: A drug discrimination task was used to test if 1) MPH produces interoceptive cues that effectively support discrimination in C57 mice, and if 2) ethanol potentiates discriminative effects of MPH. RESULTS AND CONCLUSIONS: 1) C57 mice learned to discriminate cues produced by 5 mg/kg MPH and dose-response tests established appropriate reductions in discrimination with declining dose. One half the mg/kg dose of d-MPH generalized completely for dl-MPH doses in substitution tests, consistent with the d-isomer solely possessing the pharmacological activity of the racemic drug. Accordingly, mice can learn to discriminate the cues produced by 5 mg/kg dl-MPH or 2.5 mg/kg d-MPH. 2) In C57 mice trained to discriminate 5.0 mg/kg dl-MPH, the combination of 1.0 g/kg ethanol and MPH produced a significant leftward shift in the ED50 (p<0.05) of the MPH dose response curve at low doses of MPH (1-2 mg/kg). Importantly, these mice failed to recognize ethanol when given alone as having MPH-like interoceptive cues. These ethanol-potentiated interoceptive properties of MPH in C57 mice give support to the leftward response shift being based on the inhibition of carboxylation 1 by ethanol, resulting in elevated concentrations of d-MPH as seen in clinical studies. Future studies will examine the neurobiological mechanism of MPH discrimination and the mechanism by which ethanol alters the discriminative cues produced by MPH. Supported by NIH grant R01AA016707 and the MUSC-Claflin Cooperative for Postdoctoral Academic Career Development 5K12GM081265-03

127 Spurious Elevation of Hemoglobin A1c Due to a Hemoglobin Variant, Alina G Sofronescu, Laurie M Williams, Dorinda M Andrews, Yusheng Zhu; Department of Pathology and Laboratory Medicine, MUSC.

Hemoglobin A1c (HbA1c) results from a non-enzymatic addition of a glucose molecule to the first N-terminal valine residue of the β-chain of HbA. In non-diabetic patients, the normal level of HbA1c is < 6.0%. The presence of different hemoglobinopathies may interfere with HbA1c testing and can lead to falsely increased or decreased levels. The objective of this study is to identify potential hemoglobin variants that cause a spurious HbA1c level in an automated cation-exchange HPLC (CE-HPLC) HbA1c assay (Bio-Rad VARIANT II TURBO Link). The initial method used for the analysis of HbA1c was a charge-based CE-HPLC, followed by a turbidimetric inhibition immunoassay (TINIA, SIEMENS). The former measured the A1c fraction of only hemoglobin A, while the latter measured all hemoglobinbs that are glycated at the b-chain N-terminus with epitopes identical to that of HbA1c. Hb variants analysis was performed using Bio-Rad Classic Variant CE-HPLC β-thalassemia short program, acid gel Hb electrophoresis, and DNA sequencing of the β-globin genes. Results: CE-HPLC HbA1c assay showed an aberrant level of HbA1c (115.8%). Analysis of hemoglobin variants revealed the absence of HbA and presence of HbS (37.4%) with normal HbA2 (3.2%) and HbF (<1.0%). Another large peak (53%), identified as P2, eluting earlier than HbA, was evident. This suggested the presence of a Hb variant with a chromatographic retention time virtually identical to that of HbA1c. Subsequent Hb electrophoresis at pH 6.0 (QuickGel Acid, Helena Laboratories) identified HbS and another abnormal band with a mobility similar to HbF. DNA sequence analysis of the patient’s β-globin genes identified a substitution at codon 6 (GAG to GTG or Glu to Val) corresponding to HbS on one allele, and a substitution at codon 1 (GTO to GCG or Val to Ala) corresponding to Hb Raleigh on the other allele. HbA1c level determined by TINIA was normal (4.1%). The spurious elevation of HbA1c determined by the CE-HPLC method is due to the co-elution of Hb Raleigh with HbA1c. This case indicates that HbA1c assays are prone to interference of certain Hb variants. When an aberrant HbA1c value is produced, interferences caused by Hb variants should be considered. In this case, HbA1c values should be interpreted based on
Background and Purpose: Fli-1 expression levels, a member of the Ets family of transcription factors, are a mitigating factor in the development of nephritis in murine models of systemic lupus erythematosus (SLE). Lupus nephritis is a major cause of death in both animal models and human patients, and is characterized by immune complex formation and inflammatory cell infiltration. Expressions of monocyte chemotactic protein-1 (MCP-1) and Chemokine (C-C motif) ligand 5 (CCL5, also known as RANTES) play an important role in the inflammatory cell infiltration. Overexpression of the Fli-1 protein in transgenic mice resulted in the development of a lupus-like disease with nephritis. Expression of Fli-1 in SLE patients and animal models of lupus is higher compared to normal controls. In this study, we examined the role of expression of Fli-1 on chemokine production and inflammatory cell infiltration in conjunction with nephritis development in NZM2410 mice, an animal model of SLE. Methods: We generated Fli-1 heterozygous knockout NZM2410 mice (Fli1+/−; Fli-1 homozygous knockout is embryonic lethal) and wild-type (WT) littermate (Fli1+/+) mice for use as controls. The expression levels of monocyte chemotactic protein-1 (MCP-1) and Chemokine (C-C motif) ligand 5 (CCL5, also known as RANTES) in the kidneys from 18-week-old mice were analyzed by real-time PCR. Pathological scores of the kidneys from 34-week-old mice were assessed and the number of macrophages, neutrophil granulocytes, T cells and B cells in the kidneys were stained with specific antibodies and counted in 10 random high power fields (HPF). These numbers were averaged and directly compared between WT and Fli1+/− NZM2410 mice. The MCP-1 in serum was measured by ELISA. Small interfering RNA (siRNA) was used to inhibit Fli-1 expression in endothelial cells and production of MCP-1 and CCL5 in these cells were investigated. Results: Since expression of CCL5 and MCP-1 was demonstrated to initiate inflammatory cell infiltration in the kidneys of lupus mice, we first examined the expression of MCP-1 and CCL5 in the kidneys from both Fli-1+/− and WT controls. Expression of MCP-1 and CCL5 in the kidneys from 18-week old Fli-1+/− NZM2410 mice was significantly decreased compared to that from WT littermates. Fli-1+/− NZM2410 mice also had significantly reduced renal pathology scores compared to those from WT littermates (WT mouse: 6.846 ± 0.9635; Fli-1+/− mouse: 3.882 ± 1.043, p< 0.05). The number of macrophages, neutrophil granulocytes, T cells and B cells in the kidneys from Fli-1+/− NZM2410 mice decreased by 44 - 75% compared to WT littermate controls. The serum MCP-1 levels in Fli-1+/− NZM2410 mice were significantly lower at the age of 34 weeks compared with WT littermates (WT mouse: 118.9 ± 17.7 pg/ml; Fli-1+/− mice: 67.7 ± 7.1 pg/ml, p< 0.01). The productions of MCP-1 and CCL5 in endothelial cells transfected with specific Fli-1 siRNA were significantly reduced compared to cells transfected with negative control siRNA (MCP-1, Fli-1 siRNA: 18.7 ± 2.1 ng/ml; negative control: 36.5 ± 3.9 ng/ml, p< 0.01, CCL5, Fli-1 siRNA: 3.55 ± 4.2 ng/ml; negative control: 8.65 ± 1.7 ng/ml, p< 0.05). Conclusion: Our data indicate that Fli-1 play an important role in production of inflammatory chemokine MCP-1 and CCL5, and inflammatory cell infiltration in the kidneys. The lower expression of Fli-1 results in decreased expression of CCL5 and MCP-1 in the kidneys with significantly reduced infiltration of inflammatory cells, which leads to lower overall kidney pathological scores in NZM2410 mice. Therefore, Fli-1 plays an important role in the development of nephritis in NZM2410 mice.

128 Fli-1 Transcription Factor is Involved in Inflammatory Chemokine Production and Inflammatory Cell Infiltration In the Kidneys in Animal Models of Autoimmune Disease, Eiji Suzuki1, Sarah Williams2, Emmanuel Reyes-Cortes3, Eva Karam4, Gary Gilkeson5, John Zhang6, 1Rheumatology and Immunology, MUSC, 2Ralph H. Johnson VA Medical Center.

In chronic inflammatory diseases such as rheumatoid arthritis (RA), beta-arrestins are multifunctional scaffolding proteins involved in the regulation and function of G-protein coupled receptors and cytokine receptor signaling. Our laboratory demonstrated that beta-arrestins are involved in the regulation of inflammation and the immune response. We hypothesized that beta-arrestin 1 and 2 are involved in regulation of inflammation and the immune response. Western blot analysis was used to examine the beta-arrestin 1 and 2 expression. Our data demonstrate that the beta-arrestin 1 expression in the hind knee joint tissue from CIA mice was significantly increased at 8, 10 and 12 weeks and beta-arrestin 2 expression was also significantly increased at 4 and 6 weeks compared to the control mouse. In spleen tissue from arthritic mice, beta-arrestin 1 expression was increased at 12 weeks and the beta-arrestin 2 expression was increased at 8 weeks compared to the control mouse. In subsequent studies, the FLS cells were isolated.

129 Increased Beta-Arrestin 1 and 2 Expression in a Murine Model of Rheumatoid Arthritis, Pengfei Li1, Hongkuan Fan2, Perry V Halushka3, James A Cook1, 1Neurosciences, MUSC, 2Cell and Molecular Pharmacology, MUSC.

Chronic inflammation is a key component of autoimmune diseases such as rheumatoid arthritis (RA). RA is characterized by chronic inflammation of synovial joints leading to cartilage damage and ultimately total joint destruction. Pro-inflammatory cytokines and chemokines play critical roles in autoimmune diseases. Recently, it has been reported that ubiquitously expressed adaptor proteins beta-arrestin 1 and 2 are involved in regulation of inflammation and the immune response. We hypothesized that Beta-arrestin 1 and 2 expression are altered in spleen and joint tissue and fibroblast-like synoviocytes (FLS) in a murine model of Rheumatoid arthritis. The spleen and hind knee joint tissue were collected from DBA/1J wild type mouse and the Collagen-induced arthritis (CIA) mouse at 4, 6, 8, 10, and 12 weeks after collagen injection. Western blot analysis was used to examine the beta-arrestin 1 and 2 expression. Our data demonstrate that the beta-arrestin 1 and 2 expression are altered in spleen and joint tissue and fibroblast-like synoviocytes (FLS) in a murine model of Rheumatoid arthritis.
from the CIA mouse and the wild type mouse. Our data demonstrate that Beta-arrestin 1 and 2 expression were augmented in FLS in the CIA mouse at 4 weeks. Our findings demonstrate for the first time that Beta-arrestins are increased in the murine model of arthritis. Understanding of the role of beta-arrestin 1 and 2 in the CIA model will provide insight into the pathogenesis of arthritis as well as has potential novel therapeutic approaches. Supported by NIH GM 27673, AI 079248.

130 The Role of Complement and the Use of Complement Inhibitors in a DSS Model of IBD, Jennifer Schepp-Berglind1, Carl Atkinson1, Fei Qiao1, Stephen Tomlinson1,2, 1Microbiology and Immunology, MUSC, 2Ralph H. Johnson VA Medical Center.

Complement plays a central role in the pathophysiology of many inflammatory and autoimmune diseases, but there is surprisingly little data available on the role of complement in the pathogenesis of inflammatory bowel disease (IBD). Previous studies have shown that C3b is deposited in IBD lesions in humans, and studies in rodent models have shown that DAF deficiency increases susceptibility to colitis whereas treatment with C5a receptor antagonist is protective. We utilized complement deficient mice and wild type (wt) mice treated with complement inhibitors to investigate the role of different complement activation pathways in dextran sulfate sodium (DSS)-induced colitis. In an acute model (5% DSS for 5 days), DSS treatment of wt mice resulted weight loss, diarrhea, shortening of colons, massive increase in neutrophil and mononuclear cell infiltration and epithelial cell destruction. All of these parameters were significantly improved in C3 and fB deficient mice, but not in C1q/MBL deficient mice after acute DSS treatment. There were also significantly decreased levels of the inflammatory cytokines TNFa, IFNy and IL-12 in colon samples from C3 and fB deficient mice compared to wt and C1q/MBL deficient mice. Treatment of wt mice with the C3 inhibitors CR2-Crry (inhibits all pathways) or CR2-fH (inhibits alternative pathway) resulted in an outcome similar to that seen in C3 and fB deficient mice. Interestingly, in a chronic model of DSS-induced colitis (repeating cycles of DSS administration and rest period), C3 deficiency and to a lesser extent fB deficiency, resulted in a significantly worse outcome compared to PBS treated controls, with 50% and 25% mortality in C3 and fB deficient mice, respectively (0% in wt). In contrast, however, complement inhibition in the chronic model was protective, with no mortality and significantly reduced inflammation and injury scores for both CR2-Crry and CR2-fH treated mice compared to PBS treated controls. The data indicate a key role for the alternative pathway of complement in the inflammatory reaction following DSS-induced colitis. However, the data also suggest a dual role for complement in the pathogenesis of IBD, possibly due to complement-dependent contributions to mucosal repair mechanisms and host defense (sepsis), areas currently under investigation. Crohn’s and Colitis Foundation

131 Evidence for Neurogenesis After Acute Auditory Nerve Injury in the Adult Mouse Inner Ear, Devadoss j Samuvel, Lauren Kilpatrick, Juhong Zhu, Bradley Schulte, Hainan Lang; Pathology, MUSC.

Spiral ganglion neurons (SGNs) are primary auditory afferent neurons that deliver signals from the inner ear to the brain. Loss of SGNs can occur with exposure to ototoxic drugs and noise, genetic mutations and age, resulting in permanent sensorineural hearing loss. Recent studies have shown that neural stem cells are able to be isolated from vestibular and auditory sensory epithelia, and spiral ganglia of postnatal mice. However, it unknown whether the neural stem/progenitor cells are present in the adult auditory nerve. The transcription factor Sox2 is predominantly expressed in proliferation and undifferentiated neural stem/progenitor cells during neurogenesis. Our previous study showed that ouabain induced SGN degeneration while sparing hair cell function. In this study, we examined Sox2 expression in the auditory nerve after ouabain treatment and the capability of neurogenesis in adult mouse inner ear using both in vivo and in vitro approaches. Three and 7 days after ouabain exposure, there is an upregulation of Sox2 expression and an increased cell proliferation seen in the injured auditory nerve. In addition, more neurospheres-like clusters were generated when cultured from the injured mice than normal mice and the cells derived from these cluster were stained positively for nestin, a neural stem/progenitor cell marker. The majority of the cells in the clusters were also BrdU positive indicating their ability of self-renewal. These results suggest that neurogenesis occurs in the adult inner ear and the acute SGN injury enhances this activity.

132 8-Isoprostane As a Biomarker of Oxidative Stress in Patients with Severe Traumatic Brain Injury, Charles M Andrews1, Keith T Borg1, Ed Jauch1, James Cook2, Perry Halushka3; 1Emergency Medicine, MUSC, 2Neurology, MUSC, 3Pharmacology and Experimental Therapeutics, MUSC.

Oxidative stress after traumatic brain injury (TBI) produces significant pathology. The gold standard measure of oxidative stress measures is the oxidized product of arachadonic acid, 8-Isoprostane (8-IsoP). We sought to determine whether 8-IsoP levels correlated with severity of injury and outcome in patients with TBI. Patients with severe TBI (GCS<9) who receive ventriculostomies for clinical care were recruited into the study. Samples of CSF, plasma and urine for 8-IsoP analysis were taken at time of ventriculostomy placement (within 6 hours of injury) and 24 hours later. Levels of 8-IsoP were
measured by enzyme immunoassay (EIA). Recruitment is ongoing for the study. Seven TBI patients and seven control ED CSF samples (from patients receiving LP for other reasons) have been recruited. Initial data from 8-IsoP EIA analysis shows ten-fold elevations in 8-IsoP (peak at 200pg/ml) with most patient samples decreasing 50% by 24 hours. The patients with the highest levels had more resultant disability at discharge and the patient with lowest level was discharged with no neurological deficit. Additional patient recruitment, plasma analysis and control patient analysis of 8-IsoP are ongoing. Oxidative stress causes significant pathology in patients with TBI. Preliminary data suggest that levels are highest in patients with more severe TBI and that patients with lower levels or faster decrease have better outcomes. Research is ongoing, but the basis and timing for successful antioxidant therapies may be found in better understanding the pathophysiology and time course of oxidative stress in patients with TBI.

133 The Inhibition of Apoptosis By Melatonin Receptors Agonists in VSC 4.1 Motoneurons Exposed to Cytokines Released From Activated Microglia, Megan E Busch1, Arabinda Das2, Misty McDowell3, Casey O'Dell2, Joshua A Smith2, Abhay K Varma1, Swapan L Ray1, Naren L Banik2; 1Erskine College, 2Neuroscience, MUSC, 3Pathology, Microbiology, and Immunology, University of South Carolina.

Abstract not available.

134 Fabrication and Characterization of Uniform-Size Neurospheres, Laila C Roudsari1, Xiaowei Li2, Xiaoyan Liu2, Xuejun Wen2; 1Clemson University, 2Bioengineering, Clemson-MUSC.

Uniform size neurospheres can be a very good model to study neural biology and regeneration in vitro and in vivo. Neurospheres may also provide a source for replacing neurons in the brain that are lost in many neurodegenerative diseases. Protocols were developed to control the size of neurospheres using different methods. Neurosphere morphology and differentiation was evaluated by measuring neurite outgrowth on polyethylene glycol hydrogels of varying stiffness and hollow fibers with different topography. Analysis was performed using immunocytochemistry and confocal microscopy. Once neurospheres were characterized in vitro, an in vivo study was performed in the rat striatum to compare the effects of size on neurosphere differentiation and viability using immunohistochemistry. Data showed that neurite outgrowth is dependent upon hydrogel stiffness whereby outgrowth is larger on less stiff hydrogels because these hydrogels undergo hydrolysis more quickly. The in vivo studies are currently in progress. Overall, neurospheres show potential benefits for the treatment of neurodegenerative diseases. Clemson University

135 Association of Spasticity and Life Satisfaction in Spinal Cord Injured Patients, Dana L Westerkam1, Krause S James2, Lee Saunders3; 1Psychology, Davidson College, 2Clinical Research, College of Health Professions, MUSC, 3Heath Science and Research, College of Health Professions, MUSC.

Abstract not available.

136 Anti-telomere Antibody Levels and Vitamin D Deficiency in Systemic Lupus Erythematosus Patients, Laura M Tonks1, Brett Hoffecker2, Fahmin Bashser3, Diane Kamen2, Tamara Nowling2; 1Biology, UNC Chapel Hill, 2Rheumatology, MUSC.

Systemic lupus erythematosus (SLE) is a chronic autoimmune disorder affecting multiple organ systems. Many SLE patients suffer from vitamin D deficiency, perhaps contributing to disease progression. Another hallmark of SLE is the presence of antibodies to double stranded DNA. Recent studies have indicated that the presence of anti- double stranded DNA antibodies specific to telomeric DNA may be a more sensitive test for SLE than the presence of general anti-double stranded DNA antibodies. Low vitamin D levels have been correlated with shorter telomeres in the general population, but it is not known whether vitamin D deficiency is connected to anti- telomere antibody levels in SLE patients. We hypothesized that levels of serum 25-hydroxyvitamin D3 (25D) in SLE patients will inversely correlate with levels of anti-telomere antibodies. To address this hypothesis, anti-telomere antibody levels were measured by ELISA in lupus patients and unaffected control subjects from the Sea Island Gullah African American population. These values were compared to 25D levels. The study examined fifty-seven female patients and age- and gender-matched unrelated controls; twenty five of these patients had samples from two time points, allowing us to look at changes in anti-telomere antibody levels and vitamin D levels over time. SLE patients have higher levels of anti-telomere antibodies compared to controls, with 50.8% of the SLE population tested being positive compared to 4% of the control population. However, there is little correlation between anti-telomere antibody levels and vitamin D levels in this patient population, though there does appear to be a correlation between anti-telomere antibody levels and disease activity. Supported in part by VA Merit Review I01 BX000115 awarded to T. Nowling, NIAMS K23 AR052364 awarded to D. Kamen, and the MUSC SCTR voucher awarded to T. Nowling. Thanks also go to the Summer Undergraduate Research Program at MUSC.
Effects of Genetic Deletion of NOS3 or NOS3 on Atherosclerosis in an Lupus Nephritis Mouse Model, Jashaayn C German1, Samar Hammad2, Spelman College, Regenerative Medicine and Cell Biology, MUSC.

Autoimmune diseases, such as lupus are characterized by accelerated atherosclerosis. We have previously shown that MRL/lpr lupus mice with a genetic deletion of inducible nitric oxide synthase 2 (NOS2) had higher atherosclerotic plaque scores, increase in levels of plasma sphingolipids including sphingosine-1-phosphate (S1P), and higher levels of plasma triglycerides, and total and HDL cholesterol compared to counterpart controls. We also determined that advanced vascular disease in NOS2 KO mice was mediated by activated endothelium and macrophages. In this study, we examined how the genetic deletion of the endothelial nitric oxide synthase 3 (NOS3) affects the severity of atherosclerosis in the MRL/lpr lupus mouse model. We used an immunohistochemical approach in addition to lipid profiling and determination of levels of plasma cytokines. We first performed gross examination and plaque scoring on aortas from NOS3 knockout mice and counterpart controls. Previously formalin-fixed aortas were opened longitudinally, stained with Sudan IV and plaque scores (1 lowest to 3 highest) were recorded. Hematoxylin and eosin staining was performed for general screening. Immunohistochemical analysis of inflammatory markers in the arterial wall was conducted on serial paraffin sections. Sections were probed with antibodies for macrophage marker, activated endothelial cells and platelets, oxidized low density protein (oxLDL), reactive nitrogen species and sphingosine kinase 1 (SK1). Cytokine levels in plasma from NOS2 and NOS3 models were determined using multiplex technology. Cytokines of interest included interleukin 1 alpha and beta, interleukin 6, interleukin 10, interferon gamma, and tumor necrosis factor alpha. Atherosclerotic plaques were more severe in NOS2 and NOS3 knockout mice compared to their counterparts. However, the mean score of NOS3/-/ mice was lower than the mean score of NOS2/-/ mice. NOS3/-/ mice showed a trend of higher levels of total cholesterol, high density lipoproteins, triglycerides and glucose compared to counterpart controls. However, NOS3/-/ mice and their counterparts showed approximately 25% higher levels of total cholesterol than NOS2/-/ mice and their counterparts. Gene deletions resulted in an increase in inflammatory cytokines. Inflammatory cytokines were significantly higher in NOS2 compared to NOS3 mice. Levels of reactive nitrogen species were higher in the NOS2 knockout compared to NOS3 knockout mice. NOS2 knockout displayed higher levels of oxLDL compared to NOS3 knockout mice. Levels of SK1 were higher in NOS2 knockout compared to NOS3 knockout mice. Genetic deletion of NOS2 or NOS3 leads to an increase presence of macrophages in the tissue. NIH: The National Heart, Lung and Blood Institute R25 HL092611

Determination of the Conditions of a Fluorescent Lipofuscin Precursor in Retinal Rod Outer Segments, Alexander G Verderber1, Yiannis Koutalos2, Physics, College of Charleston, Ophthalmology and Neuroscience, MUSC.

A fluorescent precursor to lipofuscin accumulation in retinal pigment epithelium lysosomes has been observed in the form of an orange fluorescence (600-620 nm) within living rod photoreceptor outer segments with a 488 nm excitation light. This orange fluorescence has not been observed in purified rod outer segment (ROS) membranes when subject to the same excitation light. The fluorescence emission spectra of phospholipid solutions and purified ROS membranes were measured with a fluorescence microscope and a constant 488 nm excitation light. The effects of photobleaching on ROS membrane fluorescence emission spectra were observed over time. The photobleaching of rhodopsin in the ROS membranes releases all-trans retinal. Within 4 hours after photobleaching, ROS membranes with all-trans retinal concentrations between 100 microM and 400 microM showed the potential to have maximum fluorescence emission at wavelengths longer than 550 nm. The source of the orange fluorescence may be A2PE, a compound formed from an initial reaction between all-trans retinal and the membrane phospholipid, phosphatidylethanolamine (PE). Solutions containing the purified ROS membrane components PE, phosphatidylcholine (PC), and all-trans retinal were prepared with the same concentrations as comparable photobleached ROS membranes. These photobleached ROS membranes displayed significantly lower fluorescence at lower concentrations compared to corresponding PC-PE all-trans retinal solutions which fluoresced near 600 nm. Exogenous all-trans retinal was added to photobleached ROS membranes to see if doubling the overall ROS all-trans retinal concentration could generate an orange fluorescence. The addition of exogenous all-trans retinal to ROS membranes led to a consistent fluorescence emission in the 590-620 nm region; a region greater than that seen for the majority of photobleached ROS samples containing only endogenous all-trans retinal. This suggests that there may be a component in ROS membranes preventing endogenous all-trans retinal from taking part in an interaction with PE that would generate an orange fluorescence. Storm Eye Institute

Magnetic Resonance Scanner Stability and Its Relation to Scanner Use, Emily L Graczyk1, Mark S George2, Engineering, USC, Medicine, Psychiatry and Behavioral Sciences, MUSC.

Functional Magnetic Resonance Imaging (fMRI) is increasingly being used in research as a way to measure the location of brain activation in response
to stimuli. Therefore, it is important to verify that the MR scanner itself does not introduce variation into the data gathered. Other studies have noted so-called “warm-up effects” (Friedman and Glover 2006) and other instances where scanner performance changes in relation to duration of scanner functioning (Shimada, Kocbaya et al. 2008). I hypothesize that prolonged scanner use will induce more scanner instabilities, as measured by increases in variation of stability measurements, than would be present after no scanner use. Two datasets were collected. For the first, four QA scans of a 17 cm agar phantom were taken on a Siemens Tim Trio 3T MR Scanner: before and after 3 hours of continuous use, and before and after 3 hours of no use. Corresponding scans were taken at the same time of day on two consecutive days. For the second dataset, the QA protocol was run using the previously listed equipment repeatedly six times within a 3 hour interval. Software published by the Biomedical Informatics Research Network (BIRN) was used to analyze the stability of the scanner during each of these QA scans. The SNR, SFNR, percent fluctuation, drift, driftfit, and RDC values of each of these scans were evaluated. Results indicate that the relationship between scan-time accumulation and scanner performance could pose problems for some types of fMRI studies and should be more extensively investigated. Summer Undergraduate Research Program, MUSC; Palmetto Academy, SC Space Grant Consortium

140 The Differential Effects of Sphingosine-1-Phosphate Receptor Inhibition on Phosphorylation of the Cytoskeletal Proteins Ezrin, Radixin and Moesin, Boyd B Lever1, Alexa O Gandy2, Lina M Obeid3; 1Dartmouth College, 2Medicine, MUSC, 3Internal Medicine/Geriatrics, MUSC.

Sphingosine-1-phosphate (S1P) is a bioactive lipid with roles in cellular proliferation, inflammation, angiogenesis and protection from apoptosis. Levels of S1P are tightly regulated by sphingosine kinase (SK), the enzyme responsible for conversion of sphingosine to S1P. Sphingosine kinase 1 has been shown to be activated by numerous ligands, including pro-inflammatory cytokines and growth factors. S1P achieves many of its effects by including pro-inflammatory cytokines and growth factors.

Pharmacological inhibition of S1PR2 knockdown using siRNA in HeLa cells also inhibited phosphorylation of ERM, further solidifying S1PR2 involvement in S1P-mediated phospo-ERM. In summary, our results implicate S1PR2 as an essential component of the ERM phosphorylation pathway in glioma and HeLa cells, potentially affording a point of therapeutic intervention in human cancer. In the future these experiments should be extended to other cell lines and other models (i.e. Receptor knockout mice) to assess the specificity of our results and how they may be applied to human cancers. Supported with resources and the use of facilities at the Ralph H. Johnson VA Medical Center, Charleston, South Carolina and a NIH/NCI R01 CA09713 (to LMO).

141 Evaluating an Intervention to Improve Perceptions of Cancer Clinical Trials Among Racially Diverse Communities in South Carolina, Ebonie M Fuller1, Amy E Wahlquist2, Rashell Blake3, June Streets4, Melanie S. Jefferson5, Heidi Varner6, Shannon Johnson6, Marvella E. Ford2; 1South Carolina State University, 2Hollings Cancer Center, 3Vorhees College, 4Georgetown University, 5The Varner Town Indian Community Economic, Health, and Cultural Development Council, 6South Carolina Cancer Alliance.

Objective. To conduct a cancer clinical trials education intervention with racially diverse groups in South Carolina. Methods. The study was conducted at ten different sites in eight counties in South Carolina. The intervention consisted of a 30-minute cancer clinical trial educational presentation. Participants were recruited primarily by community partners. Pre- and post-intervention surveys were administered. The survey instrument included seven items. Sample items included the following: "Do you think that patients should be asked to take part in medical research?" and "Would you be prepared to take part in a study where treatment was chosen at random?" Analyses were completed using SPSS 16.0, SAS 9.1.3, and R v2.6.1. Results. The study sample consisted of 195 predominantly African American participants (n=195). The majority of the 190 participants who reported age were 50+ years (57.4%). Among those who reported income (n=182), 66.6% had an annual household income < $60,000. For each of the seven survey items assessing perceptions of cancer clinical trials, respectively, 9%, 24%, 38%, 20%, 18%, 14% and 13% of the participants changed to more favorable responses on the post-test vs. pre-test (p<.001). Conclusions. Providing cancer clinical trials information to racial and ethnic minorities led to more positive perceptions of cancer clinical trials. Future research studies could incorporate a longer follow-up period to assess the behavioral impact of the intervention and whether short-term gains are sustained over time. Department of Defense, South Carolina State University, Louis Stokes South
Regulation of Nkx2.5 in the Second Heart Field, Kyle A Doherty, Kyu-Ho Lee; College of Charleston, Regenerative Medicine & Cell Biology, MUSC.

Tissue Engineered Heart Valve Leaflet From Tissue Spheroids, Hleb Fedarovich, Agnes Nagy-Mehesz, Vladimir Mironov; CoFC, Regenerative Medicine & Cell Biology, MUSC.

The tissue engineering of the natural-like heart valve leaflet for the pediatric patient is one challenge of the cardiovascular tissue engineering. There are artificial heart valve grafts used for cardiovascular implantation in pediatric patients. However, they do not last and require substitution endangering the life of the patient. We hypothesize that in order to achieve a transplantable heart valve, heart valve leaflet must have the ability to grow and natural-like bio-mechanical properties. Adipose stem cells derived from human fat tissue were taken as the cell source. Using the hanging drop method we produced tissue spheroids. Then, tissue spheroids were put in engineered mold to self assemble into an aggregate. We incubated the aggregate with TGF to speed up tissue maturation. As the result, we showed the ability of self-assembled tissue spheroid leaflet to grow and some improvement in bio-mechanical properties of the leaflet. It is closer step to in vivo practical application of scaffold free tissue engineering. However, there are still many challenges to engineering of the natural-like heart valve.

Investigating the Molecular Basis for Congenital Heart Defects in Ets1ΔVII Mutant Mice, X S Zhou, D D Spyropoulos, R Southgate; Biology, Yale University, Pathology, MUSC, Biology, College of Charleston.

Autophagy and Microgravity Induced Osteoclastogenesis, Molly T Townsend, Yuvaraj Sambandam, Sakamuri V Reddy; Charles P. Darby Children's Research Institute, Pediatrics, MUSC.

Long term space flight has been hampered due to the physiological stresses that the weightlessness/microgravity environment has imposed on the astronauts. Microgravity (μXg) leads to a 10-15% loss of bone mass in astronauts during space flight. Osteoclast is the multinucleated bone resorbing cell. We used the NASA developed ground based Rotating Wall Vessel Bioreactor (RWV), Rotary Cell Culture System (RCCS) to simulate μXg conditions and demonstrated a significant increase in osteoclastogenesis compared to normal gravity control (Xg). Autophagy is a cellular self-consumption process greatly increased in starvation, metabolic stress, hypoxia and radiation exposure conditions to degrade proteins, organelles to recycle the macromolecular nutrients such as amino acids, fatty acids and nucleotides for cellular survival. However, the role of autophagy in μXg induced osteoclastogenesis is unknown. In this study, we used RT-PCR and Western blot analysis to demonstrate autophagy proteins such as Atg5 and LC3-II expression is upregulated in preosteoclast cells under μXg conditions compared to normal gravity. Confocal microscopy analysis further confirmed LC3-II expression in preosteoclast cells under μXg conditions. In summary, modeled μXg modulates autophagy in osteoclasts and could be a potential therapeutic target to prevent bone loss in astronauts during space flight missions. Supported by South Carolina EPSCoR (NGT5-40099) Consortium REU (Dr. W. Scott Argraves) and EPSCoR Consortium REU (Dr. Reddy).

Ganoderic Acid DM in Prostate Cancer Therapy, Benjamin M Johnson, Bently P Doonan, Faisal F Radwan, Azim Hossain, Azizul Haque; Microbiology/Immunology, Hollings Cancer Center, MUSC.

Prostate cancer is the most commonly diagnosed cancer in men and accounts for significant morbidity and mortality in the western world. While traditional therapies are effective at clearing early stage cancer, they often fail to treat late stage metastatic disease. Thus, an effective therapy that targets prostate tumor growth and metastasis is desired for alleviating the disease and improving patient outcomes. Natural extracts have been the focus of recent investigation, particularly those with reduced cellular toxicity to healthy tissue. One potential natural therapeutic agent is ganoderic acid DM (GA-DM), an extract from the Ganoderma lucidum mushroom. Previous studies have shown that GA-DM inhibits the activity of 5α-reductase and competitively binds to the androgen receptor (AR), preventing binding of dihydrotestosterone (DHT). My study suggests that GA-DM shows dose-dependent cytotoxicity in both androgen-dependent and androgen-independent prostate cancer cell lines. Mechanistic studies also suggest that GA-DM treatment activates caspases and other apoptotic proteins while downregulating the anti-apoptotic protein Bcl-2. These data suggest that GA-DM could be a new alternative chemotherapeutic in the treatment of prostate cancer, particularly the advanced, metastatic form of the disease. NIH, Hollings Cancer Center.
Background: The aim of this study was to determine if there is a link between local DCs and various subtypes of chronic rhinosinusitis (CRS); chronic rhinosinusitis with nasal polyposis (CRSwNP), subtypes of chronic if there is a link between local DCs and various subtypes of chronic rhinosinusitis (CRS); chronic rhinosinusitis with nasal polyposis (CRSwNP), and allergic fungal rhinosinusitis (AFRS). Once DC presence was established we considered possible mechanisms for DC recruitment to the sinuses. Methods: Biopsy specimens were taken from the osteomeatal complex during endoscopic sinus surgery in patients with AFRS (n=5), CRSsNP (n=6) and CRSwNP (n=5). Control patients (n=5) were undergoing either tumor resection or repair of cerebrospinal fluid leak and had no radiographic or endoscopic evidence of inflammatory sinus disease. Tissue samples were immunohistochemically stained for DC marker, CD209, costimulatory molecules, CD80 and CD86, and chemokine receptors CCR2 and CCR6. Sinus tissue lysates were examined for levels of the DC chemoattractants, CCL2 and CCL20. Results: Analysis of sinus tissue from AFRS and CRSwNP revealed elevated numbers of cells staining positive for CD209, CD80, CD86, CCR2 and CCR6 compared to controls. CCL2 and CCL20 levels were elevated in AFRS and CRSwNP compared to controls, similar to increases in their receptors, CCR2 and CCR6, respectively. Although there were increases in all markers in CRSsNP none of them were statistically significant. Conclusion: AFRS and CRSwNP have increased numbers of DCs displaying costimulatory molecules, DC chemoattractants and their corresponding receptors in the sinus mucosa compared to controls. These differences represent a possible mechanism for increased numbers of DCs with a Th2 skewed profile seen in CRSwNP and AFRS. Supported in part by grants from the American Academy of Otolaryngic Allergy to BOC and grants from the Flight Attendant Medical Research Institute to RJS and JKM.

148 Increased Presence of Dendritic Cells and Dendritic Cell Chemokines in the Sinus Mucosa of CRSwNP and AFRS, Christopher M Ayers1,2, Brendan P O’Connell1,2, Carl Atkinson2, Ryan M Mulligan2, Eric W Wang2, Eugene R Sansoni2, Jennifer J Mulligan2, Rodney J Schlosser2, 1Medicine, MUSC, 2Otolaryngology-Head and Neck Surgery, MUSC, 3Microbiology and Immunology, MUSC.

Background: The aim of this study was to determine if there is a link between local DCs and various subtypes of chronic rhinosinusitis (CRS); chronic rhinosinusitis with nasal polyposis (CRSwNP), subtypes of chronic if there is a link between local DCs and various subtypes of chronic rhinosinusitis (CRS); chronic rhinosinusitis with nasal polyposis (CRSwNP), and allergic fungal rhinosinusitis (AFRS). Once DC presence was established we considered possible mechanisms for DC recruitment to the sinuses. Methods: Biopsy specimens were taken from the osteomeatal complex during endoscopic sinus surgery in patients with AFRS (n=5), CRSsNP (n=6) and CRSwNP (n=5). Control patients (n=5) were undergoing either tumor resection or repair of cerebrospinal fluid leak and had no radiographic or endoscopic evidence of inflammatory sinus disease. Tissue samples were immunohistochemically stained for DC marker, CD209, costimulatory molecules, CD80 and CD86, and chemokine receptors CCR2 and CCR6. Sinus tissue lysates were examined for levels of the DC chemoattractants, CCL2 and CCL20. Results: Analysis of sinus tissue from AFRS and CRSwNP revealed elevated numbers of cells staining positive for CD209, CD80, CD86, CCR2 and CCR6 compared to controls. CCL2 and CCL20 levels were elevated in AFRS and CRSwNP compared to controls, similar to increases in their receptors, CCR2 and CCR6, respectively. Although there were increases in all markers in CRSsNP none of them were statistically significant. Conclusion: AFRS and CRSwNP have increased numbers of DCs displaying costimulatory molecules, DC chemoattractants and their corresponding receptors in the sinus mucosa compared to controls. These differences represent a possible mechanism for increased numbers of DCs with a Th2 skewed profile seen in CRSwNP and AFRS. Supported in part by grants from the American Academy of Otolaryngic Allergy to BOC and grants from the Flight Attendant Medical Research Institute to RJS and JKM.
University of South Carolina, Institute of Psychiatry Youth Division were recruited for this study. The study was approved by Medical University of South Carolina's Institutional Review Board. Parents gave consent and adolescents gave assent for participation in the study. All participants completed the alcohol expectancy questionnaire, the marijuana expectancy questionnaire, and the demographic profile. The timeline follow back for alcohol and marijuana use was administered to the adolescent for use during the past 30 days. Results: There was a moderate correlation ($r = .49; p = .04$) between the alcohol expectancy total score and the urgency subscale of the impulsivity scale. The drivers of the correlation were: global positive change, sexual enhancement, and relaxation/tension reduction. There was a robust correlation ($r = .65; p = .01$) between the marijuana expectancy total score and the urgency subscale of the impulsivity scale. The most significant driver was the perceptual and cognitive enhancement subscale. Conclusions: In this sample of adolescents, alcohol and marijuana expectancies were only correlated with the impulsivity urgency subscale.

151 Independent Effect of Site of Care on Health Literacy Levels in Adults with Diabetes: Comparison of Community Health Centers to an Academic Health Center, Ravi P Mishra, Joni Strom, Cheryl Lynch, Leonard E Egede; College of Medicine, MUSC and Ralph H. Johnson VA Medical Center.

Background: Health literacy has significant impact on medication adherence, self-care behaviors and health outcomes. Few studies have examined variations in health literacy across different sites of care. The objective of this study was to compare health literacy levels of adults with diabetes seen at two sites: an academic medical center (AMC) and a Federally Qualified Health Center (FQHC) and to determine if site of care was independently associated with lower health literacy levels.

Methods: Data on 378 subjects with type 2 diabetes recruited from the MUSC Internal Medicine Clinic and the Franklin C. Fetter Health Center was examined. Health literacy was assessed with the S-TOFHLA and treated as a continuous variable. Covariates included race (non-Hispanic White, non-Hispanic Black), age (18-49, 50-64, 65+), gender, marital status (married vs. not married), education (high school graduate), employment (employed vs. unemployed), insurance status (insured vs. uninsured), income ($<10,000, $10,000-$24,999, $25,000+), and health status (worse than last year, same as last year). Multiple linear regression was used to identify independent factors associated with health literacy. Results: 83% were NHB, 69% were women, 22% were 65 year or older, 68% were not married, 26% had high school education had 4 points higher (95% CI 0.4, 6.8) health literacy compared to those with high school education and income $>10,000 were associated with increased health literacy. Supported by Grant #T35DK007431 from the National Institute for Diabetes, Digestive and Kidney Disease

152 Sociodemographic Correlates of Health Literacy in Adults with Diabetes, Craig Thomas, Joni Strom, Cheryl Lynch, Leonard E Egede; College of Medicine, MUSC and Ralph H. Johnson VA Medical Center.

Background: Previous studies have shown that low health literacy is associated with poor health outcomes in diabetes. The objective of this study was to identify individual socio-demographic factors associated with low health literacy in order to identify targets for literacy interventions in adults with diabetes. Methods: Data on 378 subjects with type 2 diabetes recruited from the MUSC Internal Medicine Clinic and the Franklin C. Fetter Health Center was examined. Health literacy was assessed with the S-TOFHLA and treated as a continuous variable. Covariates included race (non-Hispanic White, non-Hispanic Black), age (18-49, 50-64, 65+), gender, marital status (married vs. not married), education (high school graduate), employment (employed vs. unemployed), insurance status (insured vs. uninsured), income ($<10,000, $10,000-$24,999, $25,000+) and health status (worse than last year vs. better/same as last year). Multiple linear regression was used to identify independent factors associated with health literacy. Results: 83% were NHB, 69% were women, 22% were 65 year or older, 68% were not married, 26% had high school education had 4 points higher (95% CI 0.4, 6.8) health literacy compared to those with high school education and income $>10,000 were associated with increased health literacy. Supported by Grant #T35DK007431 from the National Institute for Diabetes, Digestive and Kidney Disease

153 Effect of Health Literacy and Demographic Characteristics on Medication Adherence in Adults with Diabetes, Roxana Pourdeyhimi, Joni Strom, Cheryl Lynch, Leonard E Egede; College of Medicine, MUSC and Ralph H. Johnson VA Medical Center.

Background: Studies have shown that low health literacy is associated with poor health outcomes in diabetes. However, few studies have examined the effect of health literacy on medication adherence. The objective of this study was to examine the independent effect of health literacy on medication adherence.
adherence in adults with diabetes controlling for relevant socio-demographic characteristics. Methods: Data on 378 subjects with type 2 diabetes recruited from the MUSC Internal Medicine Clinic and the Franklin C. Fetter Health Center was examined. Medication adherence was assessed with the 4-item Morisky scale dichotomized as adherent vs. non-adherent. Health literacy was assessed with the S-TOFHLA dichotomized as adequate vs. marginal/inadequate. Covariates included race (non-Hispanic White, non-Hispanic Black), age (18-49, 50-64, 65+), gender, marital status (married vs. not married), education (high school graduate), employment (employed vs. unemployed), insurance status (insured vs. uninsured), income (<$10,000, $10,000-$24,999, $25,000+) and health status (worse than last year vs. better/same as last year). Multiple logistic regression was used to assess the independent effect of health literacy on medication adherence controlling for covariates. Results: 45% were adherent and 86% had adequate health literacy. 83% were NHB, 69% were women, 22% were 65 year or older, 68% were not married, 26% had < adherence. medication independently insurance having Older significantly was 3.2). 1.1, 1.9 95% 1.8, (OR 5.0) 2.3, 65+ 4.1), 1.2, 2.2, Significant 2.8), 0.7, 1.4, adherence>Supported by Grant #T35DK007431 from the National Institute for Diabetes, Digestive and Kidney Disease

154 Effect of Health Literacy on Diabetes Knowledge and Self-care Behaviors in Adults with Diabetes, Leslie J Thomas, Joni Strom, Cheryl Lynch, Leonard E Egede; College of Medicine, MUSC and Ralph H. Johnson VA Medical Center.

Background: Although there is evidence that poor health literacy is associated with glycemic control, few studies have examined the effect of health literacy on intermediate outcomes such as diabetes knowledge and self-care behaviors. The objective of this study was to examine the independent effect of health literacy on diabetes knowledge and self-care behaviors (diet, exercise, blood sugar testing and footcare) in adults with diabetes controlling for relevant socio-demographic characteristics. Methods: Data on 378 subjects with type 2 diabetes recruited from the MUSC Internal Medicine Clinic and the Franklin C. Fetter Health Center was examined. Health literacy was assessed with the S-TOFHLA and treated as a continuous variable. Diabetes knowledge was assessed with the 24-item diabetes knowledge questionnaire (range 0-24) and self-care behaviors were assessed with the Summary of Diabetes Self-care Scale (range 0-7 for each behavior). Covariates included race, age, gender, marital status, education, employment, insurance status, income and health status. Pearson’s correlation was used to assess the associations between health literacy and knowledge and health literacy and self-care behaviors. Multiple linear regression was used to assess the independent effect of health literacy on diabetes knowledge and self-care behaviors controlling for covariates. Results: 83% were NHB, 69% were women, 22% were 65 year or older, 68% were not married, 26% had < independently significantly was covariates. relevant for adjusting after persisted findings. These behaviors. self-care correlated but knowledge, diabetes modestly (p=0.002), "knowledge pSupported by Grant #T35DK007431 from the National Institute for Diabetes, Digestive and Kidney Disease

155 Predictors of Glycemic Control in Adults with Diabetes At Academic and Community Health Clinics in Charleston, Bimal A Patel, Joni Strom, Cheryl Lynch, Leonard E Egede; College of Medicine, MUSC and Ralph H. Johnson VA Medical Center.

Background: Few studies have examined variations in glycemic control across different sites of care. The objective of this study was to compare glycemic control for adults with diabetes seen at two sites: an academic medical center (AMC) and a Federally Qualified Health Center (FQHC) and to identify differences in independent factors associated with poor glycemic control at both sites. Methods: Data on 378 subjects with diabetes recruited from the MUSC Internal Medicine Clinic and the Franklin C. Fetter Health Center was examined. Glycemic control was assessed with Hemoglobin A1c (HbA1c). Covariates included race (White and Black), age (18-49, 50-64, 65+), gender, marital status (married vs. not married), education (high school graduate), employment (employed vs. unemployed), insurance status (insured vs. uninsured), income (<$10,000, $10,000-$24,999, $25,000+) and health status (worse than last year vs. better/same as last year). Multiple linear regression was used to identify independent factors associated with glycemic control in the whole sample and across the two sites controlling for covariates. Results: 122 subjects were from MUSC and 256 subjects were from the FQHC. In adjusted model for the full sample, individuals seen at the FQHC had 1.1% higher HbA1c compared to those seen at MUSC. In contrast, individuals aged 65 years and older had 1.0% lower HbA1c compared to those aged 18-49 years and those with better/same health status had 0.6% lower HbA1c compared to those with worsening health status. In adjusted models for MUSC, individuals with >high school education, insured individuals and those with better/same health status had 1.0%, 1.4% and 1.2% lower HbA1c respectively. In adjusted models for the FQHC, individuals 65 years or older had 1.4% lower HbA1c. Conclusion: In this sample, glycemic control was better at the academic medical center and the predictors of control varied by clinical site. Supported by Grant #T35DK007431 from the National Institute for Diabetes, Digestive and Kidney Disease
Differential Effects of Diabetes Knowledge on Glycemic Control Between Ethnic Groups in Adults with Diabetes, Jimmy Walker, Joni Strom, Cheryl Lynch, Leonard E Egede; College of Medicine, MUSC and Ralph H. Johnson VA Medical Center.

Background: Evidence suggests that ethnic minorities have poorer glycemic control. However, few studies have examined ethnic differences in diabetes knowledge and whether these differences account for the ethnic differences in glycemic control. The objective of this study was to examine ethnic differences in both diabetes knowledge and glycemic control and to determine whether diabetes knowledge had differential impact on glycemic control in Blacks compared to Whites. Methods: Data on 378 subjects with type 2 diabetes recruited from the MUSC Internal Medicine Clinic and the Franklin C. Fetter Health Center was examined. Diabetes knowledge was assessed with the 24-item diabetes knowledge questionnaire (range 0-24). Glycemic control was assessed with Hemoglobin A1c (HbA1c) abstracted from the medical records. Race was defined as non-Hispanic Black and non-Hispanic White. Mean diabetes knowledge and HbA1c were compared by ethnicity using t-test. Linear regression was used to assess the effect of ethnicity on diabetes knowledge and HbA1c. Then separate linear regression models were run for Blacks and Whites to assess the differential effect of knowledge on HbA1c by race. Results: 83% were NHB. Mean knowledge score was significantly lower in Blacks (15.3 vs. 18.5, p<0.001). Mean HbA1c was marginally higher in Blacks (8.5 vs. 7.7, p=0.05). In univariate regression models, diabetes knowledge was not associated with HbA1c while Blacks had 0.7% higher HbA1c (p=0.05). In a model with both ethnicity and diabetes knowledge, ethnicity remained significant with Blacks having 0.95 higher HbA1c (p=0.03), while diabetes knowledge was not significant. In separate models by ethnicity, diabetes knowledge was not significantly associated with HbA1c in Whites (p=0.262), but was marginally associated with HbA1c in Blacks (p=0.06). Conclusion: In this sample, the relationship between diabetes knowledge and glycemic control varies by ethnicity. In Whites there is no significant association, whereas in Blacks, increased knowledge is associated with decreased HbA1c.

Supported by Grant #T35DK007431 from the National Institute for Diabetes, Digestive and Kidney Disease

Varying Effects of Adherence to Medications and Self-Care Behaviors on Glycemic Control By Race in Adults with Diabetes, Renee Joseph, Joni Strom, Cheryl Lynch, Leonard E Egede; College of Medicine, MUSC and Ralph H. Johnson VA Medical Center.

Background: There is strong evidence that adherence to medications and self-care improves glycemic control. However, few studies have examined differential effect of medication and self-care adherence on glycemic control by race. The objective of this study was to determine whether adherence to medications, diet, exercise, blood sugar testing and foot care were independently associated with glycemic control after adjusting for sociodemographic factors and whether this effect differed by race. Methods: Data on 378 subjects with type 2 diabetes recruited from the MUSC Internal Medicine Clinic and the Franklin C. Fetter Health Center was examined. Glycemic control was assessed with Hemoglobin A1c (HbA1c). Ethnicity was defined as non-Hispanic Black and non-Hispanic White. Mean self-care and HbA1c were compared by depression status using t-test. Linear regression was used to assess the independent effect of depression on self-care and HbA1c and the differential effect by ethnicity. Results: 83% were NHB and 24% had depression. HbA1c was not different by depression status (8.6 vs. 8.2, p=0.259). Mean scores for diet (3.8 vs. 4.5, p=0.006), exercise (2.1 vs. 3.0, p=0.003), and foot care (3.6 vs. 4.6, p=0.002) were lower in depressed individuals, but not different for blood sugar testing. In regression models, depression was not associated with HbA1c or blood sugar testing and the effects did not differ by ethnicity. However, depression was associated with poor diet, exercise, and foot care behaviors and in separate models by ethnicity, depression was associated with poor diet, exercise and foot care in Blacks but not in Whites. Conclusion: In this sample, depression was not associated with glycemic control and the effects did not differ by ethnicity. In contrast, depression was significantly associated with diet, exercise and foot care behaviors and this effect was primarily due to the negative effects of depression on self-care in Blacks.

Supported by Grant #T35DK007431 from the National Institute for Diabetes, Digestive and Kidney Disease
Racial Disparity in Impact of Maternal Obesity and Diabetes on Upper Quantiles of Birth Weight

This study investigates the impact of maternal obesity and diabetes status during pregnancy on racial disparities in birth weight. Data representing the years 2004-2008 from South Carolina birth certificates, hospital discharge, and Medicaid or state health insurance prenatal care were collected. The study is restricted to live singleton births of 140,128 non-Hispanic white and 82,492 non-Hispanic black mothers. Diabetes prevalence was 10.24% in whites and 12.02% in black Hispanic black mothers. Diabetes prevalence was 140,128 non-Hispanic white and 82,492 non-Hispanic black mothers. Diabetes prevalence was 10.24% in whites and 12.02% in blacks. Mean delivery BMI, calculated from birth certificate reported delivery weight and height, was 32.9 (SD ±7.53) in blacks and 31.2 (SD ± 6.29) in whites. Quantile regression was used to model birth weight since it allows adjustment for obesity and diabetes status during pregnancy on the effects of medication and self-care adherence on HbA1c for the full sample and stratified by race. Results: 83% were NHB, 69% were women, 22% were 65 year or older, 68% were not married, 26% had high school education (beta=-2.6, p=0.04) and insurance (beta=-1.6, p=0.024) were significantly associated with HbA1c; whereas in the stratified models for Blacks, only medication nonadherence (beta=0.3, p=0.08) was marginally associated with HbA1c. Conclusion: In this sample, medication adherence was the only behavior associated with glycemic control. In stratified analyses by race, medication adherence was not significant in Whites, but was marginally significant in Blacks. Supported by Grant #T35DK007431 from the National Institute for Diabetes, Digestive and Kidney Disease

160 Presidential Scholars: Addressing Healthy People 2020 with a Interdisciplinary Mixed Methods Study of Wellness Indicators in North Charleston, South Carolina, Amy R Painter1, Joseph Cheng2, Katie Koval3, Lisa Murphy4, Ebony Merisier5, Andrew Reynolds6, Kate Robinette7, Alice Uflacker2; 1Nursing, MUSC, 2Medicine, Graduate Studies, MUSC, 3Medicine, MUSC, 4Pharmacy, MUSC, 5Health Professions, MUSC, 6Dental Medicine, MUSC, 7Law, Charleston School of Law.

South Carolina ranks 45th out of 50 states for all social determinants of health. A team of 11 interdisciplinary Presidential Scholars at the Medical University of South Carolina was challenged to address the Healthy People 2020 goals of "achieving health equity, eliminating disparities, and creating environments that promote health for all". The team partnered with an ongoing community based research project at the MUSC College of Nursing. The study's purpose was to assess access to healthful foods, safe environments, and healthcare around two elementary schools in North Charleston, SC. The team applied the Social Ecological Model and designed a mixed methods study. Store observations were used to assess food accessibility. Fresh food, carbonated beverages and alcohol were classified according to availability, shelf space used, and cost. An active neighborhood safety survey captured quantitative and qualitative data about built environment inhibitors and inducers to active lifestyles. Additionally, key informant interviews gathered the perspectives of community members on barriers to mental health care, wellness, and resources. The following conclusions revealed the complexity of factors across the social ecological model affecting community members' health. Accessibility and advertising of alcohol was more prominent than fresh food. There is a lack of access to fresh food within walking distance. Urban design inhibitors could be modified to improve accessibility for health active living choices. Data on barriers to mental health care, needed wellness promoting resources, and images of wellness or illness in were compiled and categorized. Data was presented at the groundbreaking of the Eat Smart Move More coalition and is currently being utilized by community members to affect change. Clearly,

control was assessed with Hemoglobin A1c (HbA1c) abstracted from the medical records. Self-care behaviors were assessed with the Summary of Diabetes Self-care Scale (range 0-7 for each behavior). Covariates included race, age, gender, marital status, education, employment, insurance status, income and health status. Multiple linear regression was used to examine the independent effects of medication and self-care adherence on HbA1c for the full sample and stratified by race. Results: 83% were NHB, 69% were women, 22% were 65 year or older, 68% were not married, 26% had high school education (beta=-2.6, p=0.04) and insurance (beta=-1.6, p=0.024) were significantly associated with HbA1c; whereas in the stratified models for Blacks, only medication nonadherence (beta=0.3, p=0.08) was marginally associated with HbA1c. Conclusion: In this sample, medication adherence was the only behavior associated with glycemic control. In stratified analyses by race, medication adherence was not significant in Whites, but was marginally significant in Blacks. Supported by Grant #T35DK007431 from the National Institute for Diabetes, Digestive and Kidney Disease

159 Racial Disparity in Impact of Maternal Obesity and Diabetes on Upper Quantiles of Birth Weight, Caitlyn N Ellerbe1, Nicole M Marlow1, Jill Mauldin2, Jeffrey E Korte3, Mulugeta G Gebregziabher1, Kelly J Hunt1; 1Medicine, Biostatistics and Epidemiology, MUSC, 2Obstetrics-Gynecology, MUSC.

This study investigates the impact of maternal obesity and diabetes status during pregnancy on racial disparities in birth weight. Data representing the years 2004-2008 from South Carolina birth certificates, hospital discharge, and Medicaid or state health insurance prenatal care were collected. The study is restricted to live singleton births of 140,128 non-Hispanic white and 82,492 non-Hispanic black mothers. Diabetes prevalence was 10.24% in whites and 12.02% in blacks. Diabetes was defined as present if reported on birth certificate, coded in inpatient hospital discharge records or during prenatal care. Mean delivery BMI, calculated from birth certificate reported delivery weight and height, was 32.9 (SD ±7.53) in blacks and 31.2 (SD ± 6.29) in whites. Quantile regression was used to model birth weight since it allows assessment of cofactors not only at the mean but also across the distribution of birth weights, specifically for high birth weight babies. Adjusted for baby's sex, mom's age, gestational age, prenatal care, parity, smoking, and hypertension babies of white non-diabetic mothers had a birth weight of 2739.69g, 3291.60g, 3854.09g for 10th, 50th, and 90th quantiles respectively. At the 90th quantile, for a baby with gestational age of 38 weeks and a maternal BMI of 35, exposure to diabetes in utero was associated with an excess birth weight of 71.5g in whites and 122.3g in blacks. This racial difference between diabetic and non-diabetic babies exists across the distribution of birth weights with the difference in diabetes impact between blacks as compared to whites being 47g at the 50th quantile, 55g at the 75th quantile, and 51g racial difference at the 90th quantile. These data suggest the negative effects of diabetes combined with obesity during pregnancy may be greater in blacks than whites. Compared to ordinary-least-squares regression these estimates are more extreme for upper quantile weights. Biostatistics Training for Basic Biomedical Research Training Grant(BTBBR) provided by National Institute of General Medical Sciences (1T32GM074934-01), R01 MD004251 (Mayorga/Hunt) provided by NCMDH/NIH.
interprofessional collaboration amongst community members, business leaders, policymakers, and clinical/public health experts committed to sharing information, resources and negotiating priorities are needed to design and implement effective goal oriented interventions and achieve positive outcomes.

161 Hidden Markov Models (HMM) in Predicting Future Drinking Behavior While Simultaneously Accommodating the Effects of Several Alcoholism Medications, Behavioral Therapy, Baseline and Time Dependent Covariates. Codruta C Chiuzaun, Stacia M DeSantis; Biostatistics and Epidemiology, MUSC.

Current research on alcoholism is exploring underlying causes and ways to treat this disorder. The Combined Pharmacotherapies and Behavioral Interventions (COMBINE) was the largest randomized clinical trial conducted by the NIAAA between 2001 – 2004, among 1383 recently alcohol-abstinent volunteers from 11 US academic sites. We are undertaking secondary analyses of the data to develop a multi-state hidden Markov Model (HMM) for longitudinal categorical and continuous drinking outcomes, and assess the effect of different combinations of alcoholism treatments on transitional drinking behavior. In this model, each time dependent outcome is assumed to represent an underlying latent trajectory for the individual. The premise of this modeling procedure is that subjects transition through states over time and that their transition behavior is influenced by underlying time dependent covariates such as treatment assignment, psychiatric state, comorbidities as well as other fixed and time dependent covariates. Estimation of parameters for the HMM model will be undertaken using a Bayesian framework, with the unobserved drinking state (heavy or low) following a Markov chain. The primary drinking outcome is represented by the daily number of drinks recorded by the TLF calendar assessment. Treatment assessments include medications (acamprosate and naltrexone), behavioral therapy (moderate and minimal), and their combinations. The set of covariates to be considered contains: demographics (age, gender, ethnicity), baseline covariates (history of psychiatric disease, severity of alcohol dependence), and time-dependent covariates (pre-study drinking behavior, class of concurrent medication, and medication non-compliance). Compared to the generalized linear models, our approach generates a better fit, offers graphical descriptions of treatment-specific transition behavior, and provides straightforward interpretation of covariate effects on the probability of transitioning among drinking states. Most importantly, our statistical model is capable of identifying subgroups of patients who are at higher risk of heavy transitional drinking; these subgroups can be targeted in future studies.

162 EDD: A Novel Therapeutic Target for Platinum-Resistant Ovarian Cancers, Amber T Bradley¹, Hui Zheng², Charles N Landen², Scott T Eblen¹; ¹Cell and Molecular Pharmacology and Experimental Therapeutics, MUSC, ²Obstetrics and Gynecology, University of Alabama Birmingham.

Ovarian cancer is treated with a combination of surgery and chemotherapeutics, including taxol and platinum agents. A major difficulty in eradicating these tumors is the selection of drug resistant cells, which are more difficult to treat upon cancer recurrence. Mechanisms for cisplatin resistance in tumors are numerous and poorly understood. EDD (E3-ubiquitin ligase identified by Differential Display) is a 300 kDa E3 ubiquitin ligase that is overexpressed in 84% of recurrent, chemoresistant ovarian cancers, but is rare in benign in borderline tumors. This correlation with chemoresistant ovarian cancers suggests that EDD may be involved in mediating cisplatin resistance and/or tumor survival. Several papers have shown that EDD has a role in regulating DNA damage repair, transcription, translation, and genomic stability, in addition to its role in protein degradation. We demonstrate that transient or stable knockdown of EDD in ovarian cancer cells increases cisplatin sensitivity. Cisplatin sensitization correlated with activation of the extrinsic apoptotic pathway and was accompanied by a decrease in Bcl-xl protein. Importantly, EDD overexpression in Cos-7 cells was sufficient to promote cisplatin resistance and the induced resistance was dependent upon EDD ubiquitin ligase activity. Interestingly, siRNA mediated knockdown of EDD alone induced apoptosis in vitro and in vivo in ovarian cancer cells that expressed high levels of EDD, suggesting roles for EDD in both cell survival and cisplatin resistance. Mouse xenograft studies demonstrated that liposomal delivery of EDD siRNA in combination with cisplatin treatment significantly reduced tumor volume compared to either control siRNA treatment or cisplatin treatment alone. Our working hypothesis is that siRNA therapy targeting EDD will provide a beneficial therapy for most ovarian tumors, both alone and in combination with cisplatin.

163 Modification By SUMO-1 Alters the RNA-binding Activity of the Human Cancer-associated La Protein, Julia Kuhnert, Gunhild Sommer, Tilman Heise; Biochemistry, MUSC.

The post-translational modification by SUMO (small ubiquitin-like modifier) regulates cellular activities, such as cell cycle regulation, gene transcription and differentiation. The SUMOylation pathway involves an enzymatic cascade that attaches one or more of the SUMO paralogs to lysine residues in target proteins. Although the steady-state SUMO modification of a protein is usually less than 1%, it causes dramatic cellular effects. The cancer-associated RNA-binding protein La is implicated in the translation of 5'-TOP mRNAs encoding...
ribosomal proteins. Recently we published that La regulates the internal ribosome entry site (IRES)-dependent translation of cyclin D1 in cancerous cells. Further, we found that La protein is overexpressed in several human tumor tissues, that rat La is SUMO-modified and that this modification controls its retrograde transport in sensory axons. Herein, we hypothesize that SUMO-modification effects the RNA-binding activity of La and its function in IRES-dependent cyclin D1 mRNA translation. To test our hypothesis we developed an efficient in vitro sumoylation system resulting in 5% SUMO-modified recombinant La protein (SUMO-La). To test whether the RNA-binding activity of SUMO-La and La was different electrophoretic mobility shift assays using fluorescence labeled 5'-TOP RNA oligonucleotides were employed. The results strongly suggest that SUMO-modification of La facilitates its RNA-binding activity. Currently, we are studying the binding of SUMO-La and La to the CCND1 IRES and aim to demonstrate that SUMOylation of La impacts IRES-dependent cyclin D1 translation. In conclusion our data suggest that SUMO-La binds RNA more effectively. RNA-binding of La affects the translation of cellular key factors, like 5'-TOP encoded ribosomal proteins, cyclin D1 (stimulates G1/S-phase transition), Mdm2 (negative regulator of the tumor suppressor p53) and XIAP (X-linked inhibitor of apoptosis). Our promising results suggest that the balance between SUMO-La and La has a major impact on its functions and might contribute to its role in tumorigenesis.

164 *Estrogen Receptor Agonists Attenuate TNF-alpha Induced Cell Damage and Apoptosis in VSC4.1 Motoneurons*, Joshua A Smith, Arabinda Das, Misty M McDowell, Swapan K Ray, Naren L Banik, 1Neurosciences, MUSC, 2Pathology, Microbiology, and Immunology, USCSOM.

Abstract not available.

165 *Overexpression of Melatonin Receptors Reduces Cell Death in Rat Astroglia and Motoneuron Cells After Exposure to Glutamate Excitotoxicity*, Casey O'Dell, Arabinda Das, Megan E Busch, Joshua A Smith, Russel J Reiter, Abhay K Varma, Swapan K Ray, Naren L Banik, 1Neurosciences, MUSC, 2Cellular and Structural Biology, University of Texas, San Antonio, 3Pathology, Microbiology, and Immunology, University of South Carolina School of Medicine.

Abstract not available.

166 *New Insights Into Prymnesium Parvum Toxicity*, Matthew J Bertin, Paul V Zimba, Kevin R Beauchesne, Peter DR Moeller, 1Marine Biomedicine and Environmental Sciences, MUSC, 2Center for Coastal Studies, Texas A&M University, 3Hollings Marine Laboratory, NOAA, 4Toxin/Natural Product Chemistry, NOAA, NOS.

Abstract not available.

167 *Transdermal and Oral DI-methylphenidate – Ethanol Interactions in C57BL/6J Mice: Elevated D-MPH Concentrations and Ethylphenidate As a Biomarker*, Guinevere H Bell, William C Griffin, Kennerly S Patrick, 1Pharmaceutical and Biomedical Sciences, MUSC, 2Psychiatry and Behavioral Sciences, MUSC.

We tested the hypothesis that C57BL/6J mice will model human metabolic interactions between di-methylphenidate (MPH) and ethanol, placing an emphasis on the MPH transdermal system (MTS). Specifically, we asked: (1) will MTS facilitate the systemic bioavailability of I-MPH; (2) will I-MPH enantioselectively interact with ethanol to yield I-ethylphenidate (EPH); and (3) will ethanol increase d-MPH concentrations? Mice were dosed with MTS (¼ of a 12.5 cm2 patch on shaved skin) or a comparable oral MPH dose (7.5 mg/kg), with or without ethanol (3 g/kg), and then placed in metabolic cages for 3 h. MPH and EPH isomer concentrations in blood, brain, and urine were analyzed by GC-MS monitoring of N-(S)-prolylpireridyl fragments. As in humans, MTS greatly facilitated the absorption of I-MPH in this mouse strain. Similarly, ethanol led to the enantioselective formation of I-EPH and to an elevation in d-MPH concentrations with both MTS and oral MPH. While only guarded comparisons between MTS and oral MPH can be made due to route-dependent drug absorption rate differences, MTS was associated with significant MPH – ethanol interactions. Ethanol-mediated increases in circulating concentrations of d-MPH carry toxicological and abuse liability implications should this animal model hold for ethanol consuming ADHD patients or co-abusers. Supported by the NIH RO1 AA016707

168 *Effective Dose and Radiation-induced Carcinogenic Risk At Body CT*, Wenjun He, Walter Huda, Hai Yao, 1Clemson-MUSC Bioengineering Program, 2Radiology and Radiological Sciences, MUSC.

Purpose: To convert effective doses to radiation-induced carcinogenic risks for adults undergoing body CT. Materials and Methods: Adult organ doses and the corresponding effective doses were computed using the ImPACT Dosimetry Calculator. Doses to 11 radio-sensitive organs were converted in radiation risks using the age and gender-specific patient risk values provided in BEIR VII Report. Calculations were performed for five types of body CT examination, as well as for uniform whole body irradiation. Risk factors were expressed for radio-sensitive organs per mSv effective dose. The contribution of the remained organs to the total patient risk was also estimated. Results: For males, the highest age averaged carcinogenic risk factor was for pelvis CT examinations (8.9 x 10-5 mSv-1).
Breast cancer is the second most common cancer-related death among women in the US. The majority of the breast cancer-related deaths are due to tumor progression. A multitude of changes in gene expression are required for the cancer cell to acquire the ability to invade and migrate. The transcriptional activation or repression of these cancer-associated genes is not clearly understood, however many ETS family members have been considered good candidates. Friend leukemia virus integration 1 (Fli1) is an ETS protein that is aberrantly expressed in retrovirus-induced hematological tumors, and is found to be rearranged in Ewing’s sarcoma and related primitive neuroectodermal tumors characterized by a t(11;22)(q24;q12) translocation. Limited attention has been directed towards elucidating the potential role of Fli1 in epithelial-derived cancers, including breast cancer. Our preliminary immunohistochemical analyses show that Fli1 protein is decreased in human invasive breast tumors compared to normal breast tissue. A decrease of Fli1 mRNA and protein was also demonstrated in breast cell cancer cell lines through Real Time RT-PCR and western blot, respectively. We used adenovirus to examine the effects of Fli1 expression in two invasive breast cancer cell lines (MDA MB 231 and MDA MB 157). Re-expression of Fli1 in both MDA MB 231 and MDA MB 157 inhibited cell growth, mainly due to a decrease in cellular proliferation. Fli1 expression also inhibited the motility and invasiveness of breast cancer cell lines, determined by the use of Transwell inserts coated with fibronectin or Matrigel, respectively. We hypothesize that the loss of Fli1 is a critical step for breast cancer progression. Loss-of-function studies using shRNA are being performed to complement the above gain-of-function studies. Future studies will investigate potential downstream targets of Fli1. Inhibiting the reduction of Fli1 or regulating its downstream targets may be to be unique targets of breast cancer therapy.

169 Mechanisms of HSP-mediated Protection Against Cisplatin-induced Hair Cell Death, Tiffany G Baker, Inga I Kramarenko, Shimon P Francis, Carlene S Brandon, Fu-Shing Lee, Lisa L Cunningham; Pathology, MUSC.

Cisplatin is an effective chemotherapeutic drug used to treat 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 sensory hair cells. We have previously shown that heat shock inhibits cisplatin-induced hair cell death in the adult mouse utricle in vitro. The molecular 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. 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 (phosphorylation) of both p53 and STAT-1. 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 activation of both p53 and STAT-1, and that heat shock inhibits activation of both molecules. Surprisingly, our data using uricules from p53 knockout mice indicate that p53 is not required for cisplatin-induced hair cell death. Confocal images of cisplatin-treated uricules support these data, showing that p53 accumulation does not occur in hair cells or supporting cells, but accumulation of the protein does occur in underlying stroma. Supported by NIDCD 5R01DC07613 and F30DC010522.

170 The Role of Fli1 in Breast Cancer Development and Progression, Melissa N Scheiber\textsuperscript{1}, Patricia M Watson\textsuperscript{2}, Victoria J Findlay\textsuperscript{1}, Tihana Rumboldt\textsuperscript{1}, Dennis K Watson\textsuperscript{1,3}, \textsuperscript{1}Pathology, MUSC, \textsuperscript{2}Medicine, MUSC, \textsuperscript{3}Biochemistry, MUSC.

Fli1 is an ETS family member that is overexpressed in 15% of invasive breast cancers, including breast cancer cell lines. Previous studies by the Wessels’ lab have demonstrated that Hyaluronan and Proteoglycan binding Link Protein 1 (Hapln 1 or cartilage link protein 1/Crtl1) is involved in heart development. Crtl1 is an extracellular matrix (ECM) protein that is involved in the extracellular environment of cancer cells in vitro and in vivo, implicating the pro-survival role of Hapln 1/Crtl1 in breast cancer progression. Loss of Fli1 is a critical step for breast cancer progression and may serve as a novel target for breast cancer therapy.
stabilizes the interaction between hyaluronan and versican and is expressed in endocardial and endocardially derived cells in the developing heart, including cells in the atrioventricular (AV) and outflow tract (OFT) cushions. Crt1 knockout mice have a range of cardiovascular malformations such as thin myocardium, atrioventricular septal defects (AVSD), and decreased trabeculation. Histological analysis of Crt1 knockout mice reveals there is decreased expression of the Crt1 binding-partners versican and hyaluronan and that reduced expression of these ECM proteins may contribute to the cardiovascular malformations observed. Investigations into the transcriptional regulation of the Crt1 gene have resulted in the finding that the cardiac transcription factor Mef2c may bind to the Crt1 promoter to regulate its expression in the endocardium. Funding for this project is provided by NIH-HLBI 1R01-HL084285 and NIH 5T32-HL007260-34

173 Epigenetic Modification of RXRα in Human Colon Carcinomas By the Green Tea Polyphenol, EGCG. Vondina R Mosely¹, Jay Morris², Michael J Wargovich³; ¹MCBP, MUSC; ²Pharmacology, MUSC.

Abstract not available.

174 Movement of Activator of G-Protein Signaling 3 Within the Aggresomal Pathway, Ali Vural, Sukru Sadik Oner, Ningfei An, Violaine Simon, Dzwokai Ma, Joe B. Blumer, S.M. Lanier; Pharmacology, MUSC.

AGS3, a receptor independent activator of G-protein signaling, is involved in unexpected functional diversity for G-protein signaling systems. AGS3 has seven tetricopeptide (TPR) motifs upstream of four G-protein regulatory (GPR) motifs, each of which bind and stabilizes the GDP bound conformation of Gia. The positioning of AGS3 within the cell and the intra-molecular dynamics between different domains of the proteins are likely key determinants of their ability to influence G-protein signaling. We report that AGS3 enters into the aggresome pathway and this positioning of the protein is differentially regulated by the AGS3 binding partners Gia and mInsc. Gia rescues AGS3 from the aggresome, whereas mInsc augments the aggresomal distribution of AGS3. The distribution of AGS3 to the aggresome is dependent upon the TPR domain and it is accelerated by disruption of the TPR organizational structure or introduction of a non-synonymous single nucleotide polymorphism. These data present AGS3, G-proteins and mInsc as candidate proteins involved in regulating cellular stress associated with protein processing pathologies.

175 Extracellular Electron Transfer in Gram Positive Bacteria for the Production of Bioenergy, Chris W Marshall, Hal May; Microbiology and Immunology, MUSC.

Abstract not available.

176 Celastrol Inhibits Aminoglycoside-Induced Ototoxicity and Hearing Loss, Shimon P Francis¹, Lisa L Cunningham¹, Carlene S Brandon¹, Inga Kramarenko¹, Fu-Shing Lee²; ¹Pathology, MUSC, ²Otolaryngology, MUSC.

Aminoglycoside antibiotics are among the most commonly used antibiotics worldwide, but side effects include irreversible hearing loss and/or balance disorders. Aminoglycoside-induced sensory cell death is associated with the induction of apoptotic signaling pathways, including JNK phosphorylation. Our previous work has shown that heat shock inhibits aminoglycoside-induced sensory cell death in the adult mouse utricle in vitro. Heat shock leads to robust upregulation of several heat shock proteins, including HSPs -32 and -70. Methods for inducing heat shock protein expression in human inner ears are available, but poorly tolerated. A recent screen for pharmacological inducers of heat shock proteins resulted in the identification of celastrol as a potent inducer of HSP’s. We examined the effect of celastrol on aminoglycoside-induced sensory cell death and found that treatment with celastrol results in robust upregulation of HSP70 and HSP32. Celastrol also inhibited aminoglycoside-induced sensory cell death across the dose-response curve (Two-way ANOVA, F1,39 = 13.12, p< .001, n=25). Pretreatment with celastrol also inhibited pro-apoptotic, aminoglycoside-induced JNK phosphorylation. We used utricles from Hsf-1/- mice to examine the role of HSP’s in celastrol-mediated protection. The protective effect of celastrol was retained in utricles from Hsf-1/- mice (3-way ANOVA F1,59 = 34.24, p < .001, n=57). mRNA analysis indicates that HSP32 expression is induced in the absence of Hsf-1, and HSP32 inhibitor ZnPPIX abolishes the protective effect of celastrol (One-way ANOVA, F1,29 = 26.35, p< .0001, n=30). These data indicate that HSP32 is the primary mediator of celastrol-mediated protection against aminoglycoside-induced hair cell death. In vivo analysis by Auditory Brainstem analysis (ABR) showed that mice treated with celastrol had significantly less hearing loss than mice treated with aminoglycoside alone(RM-ANOVA, F3,12 = 104.77, p< .0001, n=16). These data suggest celastrol may represent a viable approach to clinical prevention of aminoglycoside-induced hair cell death and hearing loss. Supported by NIH R01 DC07613; F31 DC010559
Abstract not available.
**180** MAP Kinase Phosphatase-1 is Required for Vitamin D Signaling in Bone Marrow Stromal Cells, Alfred C Griffin, Carlos Rossa Jr., Keith L Kirkwood; Craniofacial Biology, MUSC.

Abstract not available.

**181** The Role of Cubilin in HDL Homeostasis, Obaidullah Aseem, Brian T Smith, Marloes MA Hensels, Marion A Cooley, Jeremy L Barth, Sandra C Klat, William S Argraves; Regenerative Medicine & Cell Biology, MUSC.

Cubilin is a multiligand 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 show that cubilin haploinsufficiency results in >20% decrease in blood levels of HDL. The underlying mechanism for this effect is not yet known. While cubilin is not expressed in liver, the major site of HDL biosynthesis, it is expressed in two other HDL producing tissues, kidney and intestine. Kidney and intestine are both capable of de novo synthesis of HDL and apoA-I. In addition, the kidney also salvages apoA-I from the glomerular filtrate. In light of these observations, the decreased blood levels of HDL observed in cubilin haploinsufficient mice may be due to decreased biosynthesis of HDL in the intestine and kidney or decreased salvage of apoA-I/HDL in the kidney. We observed increased urinary loss of apoA-I in cubilin haploinsufficient mice with no significant change in the levels of apoA-I mRNA extracted from liver, kidney or intestine. Therefore, we hypothesize that renal cubilin-mediated endocytosis of apoA-I and associated cholesterol from the glomerular filtrate functions as an apoA-I salvage pathway, which has a significant role in maintaining HDL plasma levels. NIH Grant RO1 HL61873 (WSA) AHA Predoc fellowship (10PRE3870038)

**182** Regulation of Invadopodia Dynamics By Emmprin (CD147), Daniel Grass, Momka Bratoeva, Bryan P Toole; Regenerative Medicine & Cell Biology, MUSC.

Abstract not available.

**183** Effect of CerS6 Modulation on Cell Cycle and SL Metabolism in Colon Cancer Cells, Tejas S Tirodkar, Christina Voelkel-Johnson; Microbiology and Immunology, MUSC.

Abstract not available.

**184** N-Methyl-D-Aspartate Receptor Subunit NR3a Expression and Function in Principal Cells of the Collecting Duct, Adrian D Sproul\(^1\), Darwin P Bell\(^2\); \(^1\)Neuroscience, MUSC, \(^2\)Medicine, MUSC, Ralph H. Johnson VA Medical Center.

**185** Role of RPE65 Protein Within Murine Cone Photoreceptors, Peter H Tang\(^1\), Rosalie K Crouch\(^2\); \(^1\)Neuroscience, MUSC, \(^2\)Ophthalmology, MUSC.

Abstract not available.

**186** Calpain Inhibition Confers Histological and Functional Neuroprotection to Retinal Ganglion Cells in Experimental Optic Neuritis, Amena W Smith\(^1\), Baerbel Rohrer\(^2\), Mitsuyoshi Azuma\(^3\), Jun Inoue\(^5\), Naren L Banik\(^2\); \(^1\)Microbiology/Immunology, MUSC, \(^2\)Neurosciences, MUSC.

Abstract not available.

**187** A Peptide Mimetic of the Connexin43 Carboxyl-Terminus Increases Activity of Protein Kinase C Epsilon in a Substrate-Specific Manner, Joseph A Palatinus, Robert G Gourdie; Regenerative Medicine & Cell Biology, MUSC.

Abstract not available.

**188** Secondary Stroke Prevention: A Report From a One Year Follow-up Survey of a Stroke Cohort, Andrea D Boan\(^1\), David L Bachman\(^2\), Robert J Adams\(^3\), Daniel L Lackland\(^2\); \(^1\)Epidemiology, MUSC, \(^2\)Neuroscience, MUSC.

Background: South Carolina has long been recognized as a geographic area of high prevalence and mortality for stroke. Hypertension, diabetes, and dyslipidemia are established, independent predisposing risk factors for developing cerebrovascular disease, thus treatment of stroke related co-morbid conditions are of important consideration. Objective: To examine behaviors, treatments, quality indicators, and related risk factors with stroke from a one year follow up survey of a stroke cohort. Methods: This study utilized the Stroke Education and Prevention – South Carolina (STEP-SC) database in conjunction with a 1-year follow up telephone interview of stroke patients, at least 45 years of age, who were discharged with a primary diagnosis of stroke (ICD 9 codes 430 – 438) between October 1, 2008 and September 30, 2009 from the Medical University Hospital. The survey included demographic, health status, medication/treatment, and quality of life questions on 384 individuals with a primary diagnosis of stroke. Results: A total of 384 out of a possible 509 surveys were completed resulting in a 75% response rate. The average age for this cohort was 65.55 (± 11.37). The percent of stroke patients with hypertension (64.4%), diabetes (24.9%), dyslipidemia (43.7%), and myocardial infarction (80.9%) were considerably greater than the general population. 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. Conclusion: The goal of this study was to identify factors associated with stroke
and other underlying causes of stroke with a focus on recurrent stroke. This study is significant as the factors associated with second and multiple strokes in the high risk population of the Southeast are unclear. The results will be used to design interventions for improved stroke care focused on secondary stroke prevention. Stroke Education & Prevention in SC STEP-SC Funding: Health Sciences SC; PI: David Bachman, MD Clinical Translational Science Award, National Center for Research Resources (NCRR), National Institutes of Health Grant No: TL1RR029881 REGARDS Study

189 Evolution of 10-Formyltetrahydrofolate Dehydrogenase Catalysis, Kyle C Strickland, Natalia I Krupenko, Sergey A Krupenko; Biochemistry, MUSC. 10-Formyltetrahydrofolate dehydrogenase (FDH, ALDH1L1) is an abundant cytosolic enzyme involved in the regulation of folate metabolism. It catalyzes the irreversible conversion of 10-formylTHF to tetrahydrofolate (THF) and CO2 in a NADP+-dependent manner, a reaction regulating folate-dependent biosynthetic processes. We have recently discovered a mitochondrial isoform of the enzyme, which is the product of a separate gene, ALDH1L2, and shares 74% sequence similarity with FDH. This enzyme is distinguished from FDH as it contains an N-terminal mitochondrial targeting sequence of 23 amino acids. A phylogenetic analysis demonstrated that the mitochondrial isoform appeared later in evolution as a result of a duplication of the ALDH1L1 gene. In the current study, we report the cloning, E. coli expression and characterization of mtFDH. We have demonstrated that recombinant mtFDH, similar to the cytosolic enzyme expressed in E. coli, requires a post-translational modification, in which a 4′-phosphopantetheine group is covalently attached to a specific serine residue. This modification is necessary for mtFDH to perform 10-formylTHF dehydrogenase catalysis. Both isoforms also catalyze the hydrolysis of 10-formylTHF, a reaction which produces formate instead of CO2, and we found that mtFDH possesses about 7-fold higher hydrolase activity than the cytosolic enzyme. Surprisingly, these studies revealed that mtFDH does not catalyze an aldehyde dehydrogenase reaction, which was previously believed to be essential to the mechanism of 10-formylTHF dehydrogenase catalysis. A recent study has shown that cytosolic FDH, from more ancient organisms, also does not have aldehyde dehydrogenase activity. Overall, our findings imply that the isoforms of FDH have evolved to augment the compartmentation of folate metabolism. We further hypothesize that during evolution the mitochondrial enzyme retained the catalytic properties of ancient FDH enzymes while the cytosolic isoform gained its aldehyde dehydrogenase function, a property which may enhance 10-formylTHF dehydrogenase activity at the expense of hydrolase catalysis. Supported by the National Institutes of Health grant DK054388 (SAK) and a Ruth L. Kirschstein National Research Service Award for Individual Predoctoral MD/PhD Fellows F30DK083215 (KCS).

190 Alterations in Immune Phenotype During the Development of Squamous Cell Carcinoma of the Head and Neck, Anna-Maria A De Costa, Travis D. Reeves, David D. Walker, Corinne A Schuyler, Young I Rita, Kyle C Strickland, Anna Maria De Costa; Otolaryngology, MUSC, Medical Research Service, Ralph H. Johnson VAMC, Otolaryngology, MUSC. Head and neck squamous cell carcinoma (HNSCC) is an aggressive malignancy associated with extensive immune inhibition. This local and systemic immunosuppressive environment is a significant obstacle to effective immunotherapeutic intervention. One way to avoid this obstacle would be to initiate therapy prior to establishment of immunosuppression, yet little is known about the development of immune inhibition during the transition to malignancy. The present study aimed to further investigate the phenotype of the immune system during progression to HNSCC by determining the local and systemic expression of various cytokines and angiogenic factors in tissue biopsies and plasma samples from patients bearing premalignant oral lesions, patients with HNSCC, and normal controls. All factors measured in the plasma did not differ between premalignant samples and controls, signifying a lack of systemic immunosuppression at this stage. At the tissue level, Th1 cytokines IL-2, IFN-γ, and TNF and the Th17 cytokine IL-17A were found to be elevated in premalignant samples compared to normal controls, indicating an ongoing inflammatory reaction in response to neoplastic transition that is restricted to the local environment. Each of these cytokines, with the exception of TNF, decreased to normal levels in HNSCC tissue. In addition, levels of the angiogenic factors IL-8 and VEGF in premalignant tissue remained near levels in controls while these factors were increased in HNSCC tissue, suggesting that this aspect of conversion to a pro-tumorigenic local environment occurs after malignant transformation. The lack of systemic immunosuppression and increase in local inflammation during the premalignant stages of HNSCC indicate that immunotherapy implemented at this point may have greater potential to produce a strong anti-tumor immune response. Supported by the Medical Research Service of the Department of Veterans Affairs and grants NIH/NCI RO1 CA128837 and RO1 DE018268 to MRIY.
Projections for prostate cancer in the United States predict over 210,000 new diagnoses and 32,000 deaths in 2010, which emphasize the sizable therapeutic challenge that the disease poses. A mainstay of treatment for localized disease, radiation therapy is performed through various protocols and modalities that have proven efficacious. However, the subset of prostate cancer cells that remain resistant to therapy and lead to relapse prompt investigation of the molecular mechanisms at the root of radiation resistance with the goal of, ultimately, generating novel therapeutic strategies. Work in our lab examines cellular responses to therapy through the metabolism of the pro-apoptotic bioactive sphingolipid, ceramide, into the mitogen sphingosine-1-phosphate. We have previously demonstrated that exposure to ionizing radiation (IR) induces over-expression of the lysosomal ceramide-hydrolyzing enzyme, acid ceramidase (AC), resulting in prostate cancer cell resistance to IR-induced cell killing independent of sphingosine kinase status. Here, we demonstrate this effect occurs as a result of transcriptional activation of the AC gene, ASA1H, which is mediated by ceramide generation. Dissection of the pathways of IR-induced ceramide generation reveal that transcriptional control of ASA1H occurs through a fumonisin-sensitive pathway. Transcription factor binding arrays demonstrate increased activity of activator protein 1 (AP-1) upon exposure to either IR or exogenous ceramide. Prostate cancer cells expressing the c-Jun dominant negative mutant, TAM67, fail to up-regulate AC expression upon exposure to IR. Finally, irradiation of prostate cancer cells reveals sensitization by TAM67-mediated AP-1 deficiency to IR-induced clonogenic cell death which is rescued, in part, by reconstitution of AC over-expression via adenoviral transgene expression. Taken together, these results demonstrate a key role for acid ceramidase in cell survival through radiation-induced AP-1 activation, and lend support for further investigation into their development as targets for cancer therapy. NIH/NCI PO1 CA-097132, NIGMS Medical Scientist Training Program

DNA transactions driven by long range protein-mediated inter and intra-chromosomal interactions have been reported to influence gene expression. Here, we report that site-specific replication termination in Schizosaccharomyces pombe is modulated by protein-mediated interactions between pairs of Ter sites located either on the same or on different chromosomes. The dimeric Reb1 protein catalyzes termination and mediates interaction between Ter sites. The Reb1-dependent interactions between two anti-parallel Ter sites in cis caused looping out of the intervening DNA in vitro and enhancement of fork arrest in vivo. A Ter site on chromosome 2 interacted pair-wise with two Ter sites located on chromosome 1 by chromosome kinking. Mutational inactivation of the major interacting Ter site on chromosome 1 significantly reduced fork arrest at the Ter site on chromosome 2, thereby revealing a cooperative mechanism of control of replication termination. Supported by the grants GM 049264 and GM049264-17S1 to DB.

Membranes are important barriers between bacterial cells and the environment. To survive under various conditions, it is essential for bacteria to regulate the membrane fluidity for the optimal functioning of various membrane-associated processes. The membrane of the versatile human pathogen Pseudomonas aeruginosa contains both saturated fatty acids (SFAs) and monounsaturated fatty acids (UFAs). UFA cis-vaccinate (C18:1) is the major determinant of membrane fluidity in P. aeruginosa. The pathogenicity of P. aeruginosa is determined by various extracellular virulence factors that damage host cells in addition to multi-cellular group behaviors such as quorum-sensing, biofilm, and motility. Genome-wide screen of motility defective mutant of P. aeruginosa identified fabF1 as an essential gene for swarming motility, which is a rapid and coordinated group movement over semisolid surfaces. FabF1 is an elongation condensing enzyme with predicted function in UFA biosynthesis. Analysis of the membrane fatty acid composition showed that the fabF1 mutant produced significantly reduced level of cis-vaccinate comparing to the wild-type (WT) strain. The fabF1 mutant also exhibited decreased membrane fluidity and impaired growth at low temperature. Complementation of the fabF1 mutant with a plasmid completely restored cis-vaccinate level and membrane fluidity. Further phenotypic characterization showed that fabF1
mutant was deficient in biofilm formation and pyocyanin production, and these deficiencies were also rescued by the fabF1 plasmid. Consistent with these results, supplementation of UFA oleate (C18:1) in the medium increased membrane fluidity and enhanced the virulence phenotypes. In addition, antibiotic survival assays showed that human bronchial epithelial S9 cells engulfed twice the number of fabF1 mutant compared with the WT strain, demonstrating the reduced virulence of the mutant, which was supported by the decreased levels of tissue-damaging extracellular proteins secreted by the fabF1 mutant. Taken together, our findings suggest that reduced membrane fluidity results in attenuated virulence in P. aeruginosa. Supported by National Institutes of Health COBRE in Lipidomics and Pathobiology at the Medical University of South Carolina P20 RR017677 (Y.-M.Z.)

195 Reduced Redox-Regulating Thiol Levels Render Effector Memory Like T Cells Obtained After Repetitive TCR Stimulation More Susceptible to Activation Induced Cell Death, Amir A Al-Khami, Häkan R Norell, Navtej Kaur, Osama S Naga, Christina Voelkel-Johnson, Bijay Mukherji, Michael Nishimura, Shikhar Mehrotra

Human antigen-specific CD8+ T lymphocytes have a heterogeneous phenotype that includes functionally distinct populations programmed in response to strength and duration of stimulation. Ex vivo-expanded CD8+ T cells used for adoptive immunotherapy generally acquire an effector memory (TEM)-like phenotype that exhibit impaired in vivo persistence and thus reduced anti-tumor efficacy. Our data show that cytotoxic T lymphocytes (CTLs) with the TEM-like phenotype (CD62LloCCR7loCD45ROhi) obtained after repetitive T cell receptor (TCR) stimulation exhibit increased sensitivity to activation induced cell death (AICD) induced by cognate antigen re-exposure as compared to CTLs with a central memory (TCM)-like phenotype (CD62LhiCCR7hiCD45ROlo). Interestingly, the CTLs with TEM-like phenotype have reduced expression of intracellular glutathione compared to T cells with TCM-like phenotype. This decrease in key redox-regulating thiols proteins was inversely proportional to the extent of CD8+ T cell proliferation and accompanied by a decrease in the antioxidant protein thioredoxin. Importantly, it was also associated with lower expression of the anti-apoptotic proteins bcl2 and bclxl. Pretreatment of both tumor epitope-specific primary and TCR-transduced T cells with the thiol donor N-acetyl cysteine increased cellular thiols and rescued T cells from TCR stimulation-mediated AICD, without impairing their functional capacity. In conclusion, our results suggest that T cell expansion upon cognate antigen encounter affects both the replicative history and the CTL quality by decreasing its antioxidant capacity. Since increasing the antioxidant capacity prevented AICD, it may increase the persistence of T cells and have translational implications for immunotherapy. Supported by grants from NIH R21CA137725 and NIH R01CA138930 to SM; NIH RO1 CA117254 and CA88059 to BM, and R01CA104947 to MN.

196 Decreasing Fli1 Levels in Lupus T Cells Has Effects on Serum Immunoglobulin Levels and T Cell Infiltration in the Kidney, Erin E Morris, Maribel Harrell, Xian K Zhang, Phillip Ruiz, Tamara M Nowling; Rheumatology and Immunology, MUSC

Purpose: Systemic lupus erythematosus (SLE) is an autoimmune disease caused by genetic predisposition, environmental factors, and abnormalities in cells of the immune system including B and T cells. SLE is characterized by production of autoantibodies, chronic inflammation, and deposition of immune complexes in target organs, most commonly the kidneys. Overexpression of the transcription factor Fli1 in non-autoimmune prone mice led to the development of a lupus-like phenotype while global reduction in Fli1 expression in lupus mouse models improved disease measures. The role of Fli1 in immune cell abnormalities and in lupus pathogenesis is not understood. In this study we investigate the hypothesis that decreasing Fli1 levels specifically in lupus T cells will decrease measures of disease. Methods: T cell populations infiltrating the kidneys of MRL/lpr mice with normal levels of Fli1 and 50% reduced levels of Fli1 (MRL/lpr Fli1+/−) were characterized by flow cytometry. T and B cells from MRL/lpr lupus mice with normal levels of Fli1 and 50% reduced levels of Fli1 (MRL/lpr Fli1+/−) were mixed in different combinations and adoptively transferred into Rag1−/− mice. Serum IgM and IgG levels in recipient Rag1−/− mice were measured by ELISA. Specific effects on kidneys of Rag1−/− recipients were analyzed by quantification of T cell infiltration using immunohistochemistry and scoring of pathological changes. Results: Comparison of MRL/lpr and MRL/lpr Fli1+/− mouse kidneys demonstrated that lowering Fli1 levels specifically in lupus T cells will decrease measures of disease. Methods: T cell populations infiltrating the kidneys of MRL/lpr mice with normal levels of Fli1 and 50% reduced levels of Fli1 (MRL/lpr Fli1+/−) were mixed in different combinations and adoptively transferred into Rag1−/− mice. Serum IgM and IgG levels in recipient Rag1−/− mice were measured by ELISA. Specific effects on kidneys of Rag1−/− recipients were analyzed by quantification of T cell infiltration using immunohistochemistry and scoring of pathological changes. Results: Comparison of MRL/lpr and MRL/lpr Fli1+/− mouse kidneys demonstrated that lowering Fli1 levels specifically in lupus T cells will decrease measures of disease. Methods: T cell populations infiltrating the kidneys of MRL/lpr mice with normal levels of Fli1 and 50% reduced levels of Fli1 (MRL/lpr Fli1+/−) were mixed in different combinations and adoptively transferred into Rag1−/− mice. Serum IgM and IgG levels in recipient Rag1−/− mice were measured by ELISA. Specific effects on kidneys of Rag1−/− recipients were analyzed by quantification of T cell infiltration using immunohistochemistry and scoring of pathological changes. Results: Comparison of MRL/lpr and MRL/lpr Fli1+/− mouse kidneys demonstrated that lowering Fli1 levels specifically in lupus T cells will decrease measures of disease. Methods: T cell populations infiltrating the kidneys of MRL/lpr mice with normal levels of Fli1 and 50% reduced levels of Fli1 (MRL/lpr Fli1+/−) were mixed in different combinations and adoptively transferred into Rag1−/− mice. Serum IgM and IgG levels in recipient Rag1−/− mice were measured by ELISA. Specific effects on kidneys of Rag1−/− recipients were analyzed by quantification of T cell infiltration using immunohistochemistry and scoring of pathological changes. Results: Comparison of MRL/lpr and MRL/lpr Fli1+/− mouse kidneys demonstrated that lowering Fli1 levels specifically in lupus T cells will decrease measures of disease.
Ischemic mitral regurgitation (IMR) is mitral valve insufficiency caused by post-infarction remodeling of the left ventricle. Recently, our collaborators have used a sheep model of IMR to demonstrate that the mitral leaflets undergo adaptive remodeling during which their thickness and surface area are increased. We have previously reported, using our chimeric mouse model, in which the bone marrow of lethally irradiated mice is replaced with donor EGFP+ repopulating cells, that recruitment and differentiation of bone marrow-derived cells (BMDCs) in the adult mouse heart valves is a homeostatic process. Based on our observations using this model of increased EGFP+ cell engraftment in the mitral leaflets during post-infarction IMR, we sought to determine the specific contribution of BMDCs to post-ischemic remodeling of the mitral valve. Our initial analyses of the post-infarction mitral valve demonstrated increased thickness and surface area of the mural (or posterior) mitral leaflet, increased EGFP+ cell engraftment and proliferation, increased interstitial collagen deposition, and increased expression of myofibroblastic markers by BMDCs. In an effort to understand the mechanisms that lead to increased BMDC engraftment and activation in the ischemic mitral valve, we compared levels of expression of effectors of cell recruitment and ECM turnover in the mitral leaflets of sham-operated hearts with hearts subjected to LAD ligation. Using immunofluorescence, we detected increased levels of IL6, TGFbeta and MMP1, MMP2, MMP9 and MMP13 in the infarcted mitral valves. Importantly, MMP1 and MMP13 expression is largely limited to BMDCs. We additionally found upregulation of CD34, ICAM-1 and vWF in the valvular endocardium and a disruption of the subendocardial basement membrane, suggesting that endocardial activation might lead to increased transmigration of BMDCs. A more comprehensive understanding of the mechanisms that lead to recruitment and activation of BMDCs in the post-infarction mitral valve could yield new therapeutic strategies for modulation of IMR. Supported by grants from the NIH RO1-HL080168 (CJD), RO1-HL033756 (RRM), the NCCR P20-RR1-16434 (RRM) and CO6 RR018823, the AHA 0865325E (RPV), the NSF EPS-0903795 (RRM), and the Cardiac Developmental Biology Center.

Abstract not available.
Abcd1 (ALDP) and Abcd2 [adrenoleukodystrophy-related protein (ALDRP)] genes in mice primary astrocyte cultures resulted in accumulation of VLCFA and induction of an inflammatory response characteristic of human cALD. Correction of the metabolic defect using monoenoic FAs in Abcd1/Abcd2-silenced cultured astrocytes decreased inducible nitric oxide synthase and inflammatory cytokine expression, suggesting a link between VLCFA accumulation and inflammation. Although mechanisms of VLCFA-mediated induction of the inflammatory response have been investigated here in vitro, the in vivo mediators remain elusive. These results suggest for the first time that VLCFA accumulation in astrocytes may contribute to the pathogenesis of inflammatory diseases through the enhancement of inflammatory and oxidative responses. NS-22576, NS-34741, NS-37766, NS-40810, C06 RR018823, and C06 RR015455

201 Role of Estrogen Receptor Alpha in SLE: Modulation of Toll-like Receptor-induced Inflammation, Melissa Cunningham1, Osama Naga1, Jackie Eudaly1, Patricia Bosnic2, Gary Gilkeson1,2; 1Rheumatology and Immunology, MUSC, 2College of Medicine, MUSC, 3Ralph H Johnson VA Medical Center.

Systemic lupus erythematosus (SLE) is a disease that disproportionately affects women and minorities. The mechanisms underlying the 9:1 female predominance in this question is a key unanswered question. The cause is likely multifactorial, including differences in the sex hormones and their receptors. Previously, we showed that estrogen receptor alpha (ERα) knockout lupus-prone mice have significantly less pathologic renal disease and proteinuria, and significantly prolonged survival, despite increased serology of autoantibodies. These findings led to the hypothesis that the primary impact of ERα deficiency in lupus nephritis is on the response of the kidney to immune activation. Investigating a role for toll-like receptors (TLRs), which are critical in determining the innate immune response, revealed that kidney mesangial cells have a blunted response to TLR3/7 activation in B6 ERα-/- mice as measured by IL-6 and MCP-1 compared with wild-type littermates. Dendritic cells (DCs), which are potent antigen presenting cells that express high levels of TLRs, were also examined. Similarly, production of IL-6 and MCP-1 by DCs from female (B6 and lupus prone) ERα-/- mice is also reduced in response to TLR7/9 agonists compared with wild type. Interestingly, in the setting of ERα deficiency, mRNA from IL-1β, IL-23, and IL-23R, which are all key in the activation and stabilization of Th17 cells, were also reduced in response to TLR stimulation in ERα-/- mice, suggesting that not only is ERα required for a robust response to TLR stimulation of immune cells, but may also be necessary for maintenance of dysregulated DCs that favor the production of Th17 cells, a pro-inflammatory phenotype. Further experiments are needed to determine the mechanism by which ERα impacts TLR signaling pathways, however, these data indicate that the immune response to specific TLR ligands is significantly impacted by the presence or absence of ERα, which may explain the renal-protective effect of ERα deficiency in lupus-prone animals, and may partially explain the gender bias in this disease. NIH T32 AR 50958-05; Dept of VA BLRD Scientific Merit Award

202 A Novel Role of Inositol Phosphosphingolipid Phospholipase C Gene (ISC1) in Morphogenesis During Replication Stress, Kaushlendra Tripathi, Nabil Matmati, Jim W Zheng, Bidyut K Mohanty, Yusuf A Hannun; Biochemistry & Molecular Biology, MUSC.

ISC1 encodes the only known inositol phosphosphingolipid phospholipase C protein in Saccharomyces cerevisiae that converts complex sphingolipids into ceramides. Deletion of ISC1 causes sensitivity to hydroxyurea (HU) and methyl-methane sulfonate (MMS), and G2/M arrest. Here we show that replication stress by hydroxyurea (HU) and methyl-methane sulfonate (MMS) in isc1Δ cells induces morphological and cellular aberrations such as elongated buds, chains of cells, accumulation of high levels of chitin in cell walls, and loss of depolymerization of actin. Mechanistically, loss of Isc1 led to overexpression of Swe1p whereas deletion of Swe1p abolished these morphological aberrations in isc1Δ cells, thus implicating Swe1p as a key mediator of the effects of Isc1 loss. Moreover, expression of a non-phosphorylatable form of Cdk1 largely reduced the morphological defects whereas deletion of the formin gene BNI1 partially reduced the defects in the isc1Δ cells. Simultaneous deletions of ISC1 and a replication checkpoint mediator genes MRC1, TOF1 or CSM3 that is needed to keep the DNA replication machinery intact in the cell upon HU treatment, caused synthetic sickness, and morphogenetic and cellular aberrations. These results implicate for the first time, a sphingolipid pathway gene in the morphogenesis checkpoint under replication stress or replication defect. Supported by the South Carolina COBRE in Lipidomics and Pathobiology (P20 RR17677 from NCCR) for BKM and WJZ, an ACS-IRG grant (IRG – 97-219-08) grant from Hollings Cancer Center, MUSC for BKM, a PhRMA foundation starter grant WJZ, and NIH grants GM 43825 and GM 63265 for YAH.
**203** The Effects of 1,25-dihydroxy Vitamin D3 on Tumor-associated Immunosuppression in Squamous Cell Carcinoma of the Head and Neck, Travis D Reeves, de Costa Anna-Maria, Walker D David, Schuyler Corrine, Young I Rita, Otologygology-Head and Neck Surgery, MUSC, MBIM, MUSC, Medical Research Service, Ralph H. Johnson VAMC.

Squamous cell carcinoma of the head and neck (HNSCC) is an aggressive cancer with well-established immunosuppressive activities that evade the host immune system through a number of different mechanisms. In patients with HNSCC, 1,25-dihydroxy vitamin D3 (vitamin D3) has been shown to promote the differentiation of immune inhibitory immature CD34+ progenitor cells into activated antigen-presenting cells (APC). However, the effects of vitamin D3 have not been well-characterized with respect to downstream immune system effects as a result of these activated APCs. This is particularly unclear with respect to systemic versus local (intra-tumoral) effects. The objective of this study is to evaluate the role of vitamin D3 in modulating tumor-associated immunosuppression in HNSCC. In order to compare the peripheral versus local immune status of patients treated and untreated with vitamin D3, we analyzed cytokine and growth factor levels in previously collected plasma and tissue samples from normal controls, patients with HNSCC, and patients with HNSCC treated with vitamin D3. Vitamin D3 treatment results in a systemic increase in Th2-associated cytokines, IL-6 (p-value = 0.01), IL-8 (p-value = 0.02) and IL-10 (p-value = 0.01), when compared to untreated patients with HNSCC. However, there is a reverse trend in the analysis of the tumor homogenates suggesting that systemic markers may not be indicative of the immunologic status of the local tumor environment. These findings are surprising, for the anticipated anti-neoplastic effects of vitamin D3, seen in numerous contexts, does not seem to be associated with the expected Th1 response. This may have implications for systemically administered immunotherapy which requires a certain immune milieu to sustain an effective anti-tumor response. Immunohistochemical staining that is underway will help to elucidate the cellular context for this paradoxical role of vitamin D3 at the level of the tumor's interaction with the host immune system. *Supported by the Medical Research Service of the Department of Veterans Affairs and grants NIH/NCI RO1 CA128837 and RO1 DE018268 to MRIY*.

**205** ALDH1L2 Gene Encodes for Mitochondrial 10-formyltetrahydrofolate Dehydrogenase, Marianne E Dubard, Natalia I Krupenko, Natalia V Oleinik, Sergey A Krupenko; Biochemistry, MUSC.

Folate metabolism is essential for maintaining key biochemical reactions of nucleotides and amino acid biosynthesis. In eukaryotic cells, folate reactions and corresponding enzymes are compartmentalized between cytosol and mitochondria. One of the well-characterized folate enzymes, 10-formyltetrahydrofolate dehydrogenase (FDH, ALDH1L1), an abundant protein in liver cytosol, catalyzes the conversion of 10-formyltetrahydrofolate to tetrahydrofolate and CO2 in an NADP+-dependent manner. This reaction removes one-carbon groups from folate pool and thus controls the availability of folate derivatives for biosynthetic reactions. We have recently identified a gene in the human genome (ALDH1L2), which protein product shares 74% similarity with FDH. This novel protein has extra 23 amino acid residues at its N-terminus, a sequence recognized as a putative mitochondria leader. In the present study, we have proven that this protein translocates into mitochondria. We have further purified the product of ALDH1L2 gene (it was assigned the name mtFDH) from pig liver and confirmed that it is a functional 10-formyltetrahydrofolate dehydrogenase/hydrolase. Unlike the cytosolic enzyme, which is not detectable in cancer cells, the presence of mtFDH has been demonstrated in several human cancer cell lines by conventional and real time PCR and by Western blot assays. In support of this observation, our recent study has indicated that the two FDH isoforms might have different functions in tumorigenesis. Overall, we propose that mitochondrial and cytosolic FDH enzymes work in concert to regulate the folate pool of one-carbon groups. We further hypothesize that in some conditions these two enzymes may become redundant allowing the cell to rely only on one to fulfill corresponding metabolic function. *NIH grant DK 54388*.

**204** The SR Protein Kinase Clk1 Phosphorylates SPF45 and Regulates Its Localization and Alternative Splicing Activity, Yuying Liu, Adnan M Al-Ayoubi, Hui Zheng, Scott T Ebben; Cell and Molecular Pharmacology and Experimental Therapeutics, MUSC.

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