2013 SOMA Abstracts and Poster Competition

The Student Osteopathic Medical Association (SOMA), with support of the American Osteopathic Association (AOA), is committed to expanding research involvement and opportunities for osteopathic medical students. The 17th Annual National SOMA Research Symposium and Student Poster Competition, which was held as a part of the 55th annual AOA Research Conference during the 2013 Osteopathic Medical Conference and Exposition in Las Vegas, Nevada, with the theme "From Bench to Bedside," was impressive. The posters demonstrated students' originality, osteopathic pride, and dedication to research. The posters covered a variety of research fields, including bench, clinical, and osteopathic manipulative medicine. The AOA and SOMA recognize the role that clinical and basic science research plays in bridging the gap between the laboratory and the bedside.

This year's abstracts were organized into the following categories:

On October 1, 2013, judges met with the student presenters to discuss and review their research. Judges identified 3 first-place winners, who received $500 each, and 6 second-place winners, who received $250 each. The 9 winners are as follows:

First Prize

- Amanda King, OMS II, from the Midwestern University/Chicago College of Osteopathic Medicine for abstract S16, "Voluntary Exercise Reduces Intestinal Content of *Lactobacillaceae* in a Model of Diet-Induced Obesity" (see page e21)
- Amanda W. Liu, OMS IV, the from Touro University California, College of Osteopathic Medicine for abstract S5, "High Yield of Doppler Ultrasound Arteriogram of Lower Extremity in Diabetics Suggests New Screening Modality and Criteria for PAD Surveillance" (see page e10)
- Artur Schander, OMS IV, from the University of North Texas Health Science Center Texas College of Osteopathic Medicine for abstract F4, "Development of a Novel Osteopathic Animal Modality of Inflammatory Bowel Disease: Preliminary Findings and Clinical Implications" (see page e4)

Second Prize

- Kathleen M. Vazzana, OMS III, from the New York Institute of Technology College of Osteopathic Medicine for abstract S60, "Effect of Osteopathic Manipulative Medicine Thoracic Cage Techniques on Parkinson Disease Patients" (see page e7)
- Jessica Diane Lapinski, OMS III, from the A.T. Still University-Kirksville College of Osteopathic Medicine for abstract S9, "Examining the Doctor-Patient Relationship: Clinical Rotations and Health Care Delivery for LGBT Patients" (see page e12)
- Vishnu Mudrakola, OMS II, from the Midwestern University/Chicago College of Osteopathic Medicine for abstract B15, "Receptor Physiology in the MDH Responsible for the Diving Reflex" (see http://www.jaoa.org/content/113/8/e1.full)
- Ryan R. Kahl, OMS III, from the West Virginia School of Osteopathic Medicine for abstract S58, "Multidisciplinary Approach to Characterizing Cardiac Function in Aging BALB/c Mice" (see page e43)
- Meredith Loh, OMS III, from the New York Institute of Technology College of Osteopathic Medicine for abstract S17, "Role of Tight Junction Proteins in Mediating Oxidative Damage of Renal Epithelial Cells" (see page e22)
- Kenna Schnarr, OMS II, from the Kansas City University of Medicine and Biosciences' College of Osteopathic Medicine for abstract S33, "Investigation of the Role of Carcinoma-Associated Fibroblasts in Tumor Angiogenesis" (see page e30)

Abstracts submitted through SOMA appear on the following pages. The winning abstracts are noted with "♦".

Angela Parsons, OMS IV

SOMA research and development director; Midwestern University/Chicago College of Osteopathic Medicine, Downers Grove, Illinois

Editor's Note: Student poster competition participants submitted their abstracts through either the AOA's Council on Research or the Student Osteopathic Medical Association (SOMA). Abstracts submitted through the American Osteopathic Association's Council on Research were published in the August 2013 issue of *The Journal of the American Osteopathic Association* (*JAOA*) and are available online at http://www.jaoa.org/content/113/8/e1.full.

Abstracts have been edited for basic *JAOA* style only. The content has not been modified; information provided reflects information that was submitted by the primary author. Neither SOMA nor the *JAOA* assume responsibility for the abstracts' content.

SOMA Research Fellowship

SF1

Lipoxin A4 Improves Survival From Sepsis by Enhancing the Phagocytic Index and Viability of Free Radical Producing Blood Neutrophils

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Introduction: Sepsis is an important cause of human disease. Neutrophils play a pivotal role in control of bacterial infections by degrading phagocytized pathogens via hydrogen peroxide, and by stimulation of adaptive immune cells. A paradoxical role for immune system dysregulation has been implicated in the pathogenesis of severe sepsis. Premature neutrophil activation and delayed neutrophil apoptosis are associated with this immune dysregulation. We have previously demonstrated that injection of lipoxin A4 (LX) improved survival of rats in the cecal ligation and puncture (CLP) model of sepsis. In this study we investigate the effects of LX on blood neutrophils by measuring their (i) index of phagocytosis, (ii) free radical production, and (iii) percentage apoptosis.

Hypothesis: That LX treatment of septic rats will increase (i) blood neutrophil phagocytosis index (ii) free radical production, and (iii) percentage of apoptotic neutrophils.

Methods: Sprague-Dawley rats were treated with: (i) Sham control, (ii) CLP+vehicle saline, or (iii) CLP+LX. All rats were sacrificed 24 hours post-CLP and whole blood collected via cardiac puncture. Lysis of red blood cells, and leukocyte count were performed prior to surface marker staining for rat granulocytes (clone RP-1) in preparation for flow cytometry (FACS) functional assays. Phagocytosis was assessed by incubating total blood leukocytes with pH rodo red and green *E coli* bioparticles. Neutrophil free radical production was quantified by incubating leukocytes with dihydrorhodamine 123 (DHR). Phorbol myristate acetate (PMA) stimulation was used as positive control. For detection of apoptosis, Annexin V (Anx V) was used after leukocytes were incubated with DHR and PMA. All samples were analyzed by BD Accuri C6 or LSR Fortessa flow cytometers. FACS analysis was gated on granulocytes, only (RP-1+cells).

Results: LX treatment significantly increased percentage of blood neutrophils ingesting *E coli* bioparticles when compared to CLP+saline or sham control ($P<.0001$, ANOVA). Furthermore, LX significantly increased the phagocytic index of blood neutrophils, measured by percentage of neutrophils with ingested particles multiplied by mean channel fluorescence ($P=.0001$, ANOVA). Although LX did not decrease free radical production as quantified by DHR, the percentage of apoptotic DHR+, Anx V+ neutrophils was significantly reduced ($P=.0051$, ANOVA).

Conclusion: In vivo administration of LX enhances phagocytosis by peripheral blood neutrophils in a clinically relevant sepsis model, and reduces the percentage of circulating, free-radical producing neutrophils undergoing apoptosis. These findings help to explain our published results demonstrating decreased blood bacterial load in CLP+LX treated animals, and suggest that future efforts to elucidate the role of apoptotic vs nonapoptotic free radical producing neutrophils is warranted.

AOA Research Fellowship

F2

Pilot Study Comparing 2 Variations of Occipitomastoid Suture (OMS) Release and Their Effects on Blood Pressure and Pulse Rate in Prehypertensive and Hypertensive Individuals Compared With Normotensive Controls

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Introduction: The number of hypertensive patients is increasing every year. Oftentimes hypertension (HTN) is managed using pharmacological modes of treatment (tx), but occasionally finding an effective tx can be quite challenging. When this happens, a nonpharmacologic approach to tx which focuses on a structural rather than chemical solution may be the answer. Using osteopathic manipulative treatment (OMT) is such a tx; in particular, a cranial technique called occipitomastoid suture (OMS) release technique. This technique could be used as an adjunct to current hypertensive medications in hypertensive patients.

Hypothesis: The OMS release will decrease blood pressure (BP) and normalize pulse rate (PR) in prehypertensive/hypertensives, regardless of the technique version used, while not altering BP in healthy patients. The OMS release technique with more focal fingertip contact will decrease BP in the population with elevated BPs better than the version using a broader, longer contact. Finally, the OMS release in controls will lower PR in subjects without OMS dysfunction but increase PR in those where preexisting OMS dysfunction is successfully removed.

Methods: Twenty prehypertensive/hypertensive subjects and 30 control subjects were randomized into each of the 2 variations of OMS tx: (1) broad contact parallel with the OMS; (2) focused fingerpad contact at dysfunctional sites along OMS while directing fluid wave from opposite frontal region. The subjects will be enrolled for 4 weeks with their BP, and PR recorded weekly and OMT evaluation and tx once a week. Hypertensives returned 1 month after the fourth tx for outcome measurements only.

Results: An overall improvement in systolic BP ($P \leqslant .0001$) and diastolic BP ($P = .0005$) was observed in hypertensives. Among hypertensives, it was noted that the focal fingerpad variation lowered systolic BP ($P = .025$) and diastolic BP better when compared to the broad contact variation. Preliminary data for pulse rates show slight increase in pulse rates immediately after tx among hypertensives, but a slight overall decrease in pulse rates over time in hypertensives. Controls did not show much overall change in pulse rates.

Conclusion: OMS release techniques are successful in lowering blood pressures (predominately systolic BP) in hypertensives when treated over time. Tx 2 (fingertip) is noted to be more effective than tx 1 (broad base) at lowering BP in hypertensives. Neither tx definitively lowered pulse rates.

F3

Manual Therapy and Exercise to Prevent Posttraumatic Osteoarthritis in a Eat Model of Impact Injury

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Introduction: Osteoarthritis affects millions of people and can have a significant effect on everyday activities. Posttraumatic osteoarthritis (PTOA) manifests years to decades after the initial traumatic event. Osteopathic manipulation or exercise to prevent PTOA may be low cost interventions for this condition. In preclinical trials, forced exercise

has worsened outcomes, but immobility is not recommended after injury. There may be a dose effect of exercise, or a passive (vs active) mobilization may improve outcome. Our long-term goal is to determine the efficacy of osteopathic manipulation and exercise in preventing the onset and advancement of PTOA. Therefore, we used a drop tower device to create an impact injury in rats, which would progress to PTOA, modeling the "dashboard injury" common in motor vehicle accidents. We tested the hypothesis that manual therapy and exercise prevent PTOA.

Hypothesis: Exercise and manual therapy are effective in preventing PTOA.

Methods: The right knee of 3-month-old, anesthetized female Lewis rats was injured with the drop tower. Rats were randomly assigned to receive manual therapy (flexion and extension of the injured knee), voluntary exercise (access to activity wheels), or no treatment during the week after injury. Eight weeks after injury, both left and right knees were harvested and processed histologically. Progression of PTOA was assessed by 2 independent scorers.

Results: In the sedentary group, the injured knees had more severe PTOA than uninjured knees (2.3 vs 1.6 grade, $P=.003$). This difference disappeared with manual therapy treatment (1.8 vs 1.8 grade, $P=.92$), but not with exercise (1.9 vs 1.4, $P=.05$). Exercise and manual therapy lessened the magnitude of the difference between injured and uninjured knees relative to control, but not at statistically significant level ($P=.37$ and $P=.06$, respectively).

Conclusion: Our data suggest that osteopathic manipulative therapy may reduce PTOA in this animal model. Voluntary exercise, which can be considered a lower 'dose' than forced exercise, had no effect on outcome. We speculate that damaged cartilage may respond positively to low-weight bearing mobilization due to enhanced circulation of soluble nutrients through the cartilage matrix and the mechanostimulation of chondrocytes, resulting in improved cartilage health after impact injury. Further investigation to optimize joint mobilization following injury is warranted.

♦ Abstract that won first or second place in the 2013 SOMA Student Poster Competition.

♦ F4

Development of a Novel Osteopathic Animal Modality of Inflammatory Bowel Disease: Preliminary Findings and Clinical Implications

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University of North Texas Health Science Center Texas College of Osteopathic Medicine, Fort Worth

Introduction: Osteopathic clinicians have reported some success in the treatment of Inflammatory Bowel Disease (IBD) patients; however, objective evidence-based research exploring mechanisms and efficacy of OMT in IBD is lacking, in part due to the lack of an osteopathic IBD animal model. Therefore, the purpose of these experiments was to establish such a model and lay a foundation for future studies. Preliminary results can be used and expanded upon in future studies to evaluate the safety and efficacy of lymphatic pump techniques (LPT) in IBD, to create treatment regimens and guidelines for the application of LPT, and to test this intervention as an adjunct therapy with currently used pharmacological interventions.

Hypothesis: We hypothesize that the application of LPT will reduce signs and severity in experimental colitis in a rat model of IBD, which is induced by dextran sodium sulfate (DSS) polymers in their drinking water.

Methods: Colitis in male, Wistar rats, weighing around 275 grams, was induced by replacing normal drinking water with water containing 3.5% DSS for 10 days (days 0-9). Treatment was performed daily on days 3-8, which allowed for 3 days of IBD induction by DSS. To minimize stress to both animals and animal handlers, 2-5% isoflurane gas was administered to LPT or sham rats prior to and during treatment. This was done daily for 6 days (days 3-8). Experiments included an LPT group (DSS+ISO+LPT), a sham group (DSS+ISO+light touch), a disease control group (DSS only), and a healthy control group (no treatment and no DSS). Weights and clinical signs of

disease were monitored daily. On day 9, rats were sacrificed.

Results: Daily treatment with DSS decreased body weight in both DSS and DSS+ISO groups, with a statistically significant difference to the control group on days 7-9. This decreased weight gain was not due to changes in fluid status, as all groups consumed roughly the same amount of fluid. Daily clinical assessment of general health and inflammation is represented by the Disease Activity Index (DAI). The DAI score increased over time, without any changes between DSS and DSS+ISO groups. Mucosal damage was assessed using the macroscopic inflammatory scoring system. We found a statistically significant increase in colonic tissue damage at days 6 and 9 in DSS and DSS+ISO groups when compared to the control group at respective days. LPT significantly decreased DAI as compared to sham and DSS+ISO controls. Of interest, application of LPT restored the weight of the colon still containing fecal contents similar to levels seen in the healthy control group. In addition, LPT also restored stool consistency similar to what was seen in the healthy control group. This is of significance because decreases in filled colon weight are indicative of colonic hypermotility; thus, colons from animals with severe colitis can be seen to be nearly devoid of fecal contents. These results show that LPT influences colonic motility and effects school consistency, thus applying this treatment in a clinical setting could significantly alleviate the symptoms experienced by patients.

Conclusion: The results shown in this presentation confirm that the proposed DSS induction model does in fact present a disease model with clinical measurable variables, such as weight changes and DAI. We further showed that LPT had a significant decrease on disease severity and was able to reverse clinical symptoms of IBD.

Osteopathic Manipulative Medicine/Osteopathic Principles and Practice

S3

Effect of Osteopathic Manipulative Treatment on Blood Lactate Clearance After High Intensity Exercise

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Introduction: Increased reliance on anaerobic glycolysis to meet metabolic energy demand (eg, intense exercise) results in elevated tissue and blood lactate/H+ levels. While lactate is an important gluconeogenic substrate, excess accumulation is associated with muscle fatigue and clinical lactic acidosis conditions (eg, heart failure). This study examined whether osteopathic manipulative treatment (OMT) can influence blood lactate clearance after high intensity exercise.

Hypothesis: We hypothesized that postexercise OMT normalizes blood lactate more rapidly compared to other recovery protocols by optimizing ventilation and shifting core blood distribution and lymphatic flow to facilitate metabolic lactate clearance.

Methods: After determining resting blood lactate, subjects completed a high intensity exercise regimen: 3 sets of progressive resistance recumbent cycling to maximum effort; 2-minute rest between sets. Following set 3, subjects underwent 1 of 3 post-exercise recovery protocols: (PR) Passive Recovery (rest-sitting position), (AR) Active Recovery (20 minutes low resistance cycling; rest-sitting position), or (OR) OMT Recovery (20 minutes OMT; rest-supine position). OMT was prescribed to increase thoracic excursion and to shift tissue and core blood distribution and lymphatic flow through neural reflex manipulation. Lactate was measured immediately after exercise and at 5-10 minute intervals for 60 minutes. Time course

of lactate clearance was determined for each recovery protocol and statistically analyzed for differences. TUC-IRB approval M-0412.

Results: High intensity cycling increased blood lactate 7.5-fold (10.5 mM ±0.6 SEM) relative to resting levels. Postexercise, the 3 recovery protocols displayed distinct time course patterns of lactate clearance. Consistent with other studies, AR group (n=10) lactate levels tended to be lower than PR values (n=12) through the observation period. Interestingly, OR subjects (n=5) displayed a consistent transient rise in lactate 5 minutes after initiation of OMT that declined thereafter; following a pattern that lagged behind AR subjects at certain time points ($P<.05$).

Conclusion: Proposed mechanisms for this observation are hypothesized including supine position effects and our hypothesis that OMT may facilitate channeling of intramuscular lactate into the blood through lymphatics. Data may lead to a better understanding of mechanisms underlying lactate clearance, exercise recovery, and OMT.

S6

Transcending the International Osteopathic Identity: Cross-Sectional Analysis of Osteopathic Principles and Practice in Peru

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Introduction: Due to the success of statewide workshops in Michigan, medical students of Michigan State University College of Osteopathic (MSUCOM) decided to conduct workshops in Peru, where they have conducted medical missions since 2009. These workshops aimed to educate and expand knowledge of Osteopathic Principles and Practices (OPP).

Hypothesis: It was postulated that OPP can be integrated into these missions to achieve long term health promotion after the mission ended. The purpose of this study was to identify current perceptions among Peruvian physicians and patients to better determine the barriers to integration of OPP in Peru.

Methods: MSUCOM students presented case studies, clinical research papers, and OMM/OMT demonstrations at 2 interactive OPP workshops in Lima, Peru. The first was at the Colegio Medico del Peru, the national medical licensure and accreditation institution of Peru. The second event was held at Cayetano Heredia University, a health system in Peru. Research design included a cross-sectional investigation of health perceptions using an optional 1-5 before and after survey. OMM/OMT was also administered by students during the medical mission in Mala, Peru from August 6-9, 2012. Patient perception to clinical OMM/OMT was measured using a cross-sectional pre- and posttreatment survey. Treatment response was assessed with a subjective pain scale of 0-10.

Results: The workshops involved 150 subjects with an overall response rate of 29.3%, omitted answers were excluded. The majority of the participants (91.2%) reported no prior knowledge of osteopathic medicine. Participants (100%) left understanding a new osteopathic concept. Responses to implementation were generally positive and overall osteopathic principles were well received. 78.2% expressed interest in implementing OMT/OMM. Subjective pain response was measured in 57 clinical patients before and after integration of clinical OMM/OMT services. 100% (n=51) of the patients reported a reduction in pain with a mean reduction of 3.4 points. Patients stated they would seek out OMT again.

Conclusion: Knowledge disparity is one of the main barriers to implementation of OPP. The short-term impact of these workshops has been substantial and generated immeasurable national interest in the news as well as the Ministry of Health. The long term impact is that this model has tremendous potential in both improving medical missions and providing sustainable treatment options.

S57

Changes in Biomechanical Dysfunction With Osteopathic Manual Treatment in Patients With Chronic Low Back Pain According to Diabetes Mellitus Status

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Introduction and Objective: To assess the relationship between changes in Greenman's "dirty half dozen" biomechanical dysfunctions after osteopathic manual treatment (OMT) in patients with chronic low back pain, with and without diabetes mellitus.

Hypothesis: We hypothesized that improvements in chronic low back pain with OMT may be mediated by different factors in patients with and without diabetes mellitus. Consequently, we used changes in Greenman's "dirty half dozen" dysfunctions to test this hypothesis.

Methods: This subgroup analysis of data from the OSTEOPATHIC Trial focused on changes over time in Greenman's "dirty half dozen" dysfunctions in patients who received OMT, according to diabetes mellitus status. The OSTEOPATHIC Trial studied OMT and ultrasound therapy (UST) for the treatment of chronic low back pain in 455 patients in the Dallas-Fort Worth metroplex. Subjects who met all eligibility criteria were randomized to 1 of 4 treatment groups based on a 2×2 factorial design with active and sham treatment alternatives. Treatment providers assessed the presence or absence of Greenman's "dirty half dozen" dysfunctions prior to interventions at weeks 0, 1, 2, 4, 6 and 8.

Results: Changes in each of the 6 somatic dysfunctions between weeks 0 and 8 were measured in 230 patients who received OMT. There were no significant changes in the status of Greenman's "dirty half dozen" in patients with diabetes mellitus; however, there were significant improvements in patients without diabetes mellitus (decreased psoas tenderpoint $P=.003$; decreased lumbar non-neutral dysfunction $P\leq.001$; decreased innominate shear $P=.03$; and decreased pubic shear $P<.001$).

Conclusion: The OMT effects in patients with chronic low back pain and diabetes mellitus do not appear to be mediated by changes in biomechanical dysfunctions. However, these negative findings may be attributable to inadequate statistical power and other confounders in our subgroup analyses. A subsequent trial is planned to more adequately test this hypothesis.

♦S60

Effect of Osteopathic Manipulative Medicine Thoracic Cage Techniques on Parkinson Disease Patients

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Introduction: Parkinson disease (PD) is the second most prevalent progressive neurodegenerative disorder. It is a disabling disease frequently associated with pulmonary dysfunction. Pulmonary function test (PFT) and maximal voluntary ventilation (MVV), which has been associated with PD severity, are used to assess respiratory status. Osteopathic Manipulative Medicine (OMM) on the thoracic cage and diaphragm is used clinically to address myofascial imbalances to improve thoracic cage excursion. Prior research has demonstrated that manual approaches to the thoracic cage yield improvements in lung function. These findings have not been applied to the treatment of PD patients.

Hypothesis: Performing thoracic cage OMM on PD subjects will improve PFT, MVV, and chest expansion.

♦ Abstract that won first or second place in the 2013 SOMA Student Poster Competition.

Methods: 22 subjects with PD were randomly assigned to an OMM protocol (N=10) or light touch (LT) control (N=12) group for 1 session. The OMM protocol consisted of 5 techniques (thoracic spine/rib articulation, diaphragm doming, thoracic outlet release, and pectoral traction). Maximal and minimal chest circumferences, PFTs, and MVV were measured pre and post OMM/LT protocol. Statistical analysis was performed using analysis of covariance to assess the changes in each of the measured variables.

Results: The 3-way interaction effect of time, protocol, and PD severity found a significant difference for lower chest expansion (P=.02) with a large effect size. The change in MVV pre/post treatment was significant in the OMM and LT groups (P=.004). The difference between the groups was marginally significant (P=.06). No significant difference between OMT and LT was found for the PFTs.

Conclusion: This pilot study suggests the potential benefit of utilizing OMM for PD patients. Significant improvements were found in MVV for both groups. This could be attributed to the effort-dependent nature of the MVV. Future studies need to be performed to further assess the potential benefit of OMM in PD patients.

Clinical Studies

S1

Comparison of Various Contemporary Methods to Prevent a Wet Cast

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Introduction: Avoiding contact with water is a customary recommendation made for patients treated with a non-waterproof cast. Many traditional methods and commercially available products are available to prevent a wet cast, however there is a paucity of literature regarding the optimal strategy.

Hypothesis: Traditional cast protecting methods (trash bag and duct tape) will be as effective and more cost efficient than professional methods.

Methods: Using a synthetic a leg model, a short leg cast was applied and 6 different methods were tested. Group A (Glad Press and Seal), Group B (plastic bag with rubber band), Group C (plastic bag with duct tape), Group D (double plastic bag with duct tape), Group E (CVS Reusable Cast Protector) and Group F (Dry Corp Dry Pro Cast Cover). Casts were submerged in water for 2 minutes and weighed. Each group had 10 individual trials. Effectiveness was measured by calculating amount of water absorption using cast weights before and after submersion. Comparison data, cost analysis, and ease of application were evaluated.

Results: The percentage of water absorption prevention ranged from 62% to 100% with Groups A and B being the least effective and Groups D, E, and F being the most effective. The range of costs for 6 weeks of cast care was between $8.24 (Group B) and $38.00 (Group F). There was considerable variation in simplicity of use. Groups C, D, and E were found to be simple to use with increasing difficulty in Groups A, B, and F.

Conclusion: Our findings conclude that the 6 methods tested are effective in preventing the majority of water saturation. Although abstaining from contact with water is the most prudent approach, if a cast cover is to be used, we found that double plastic bags with duct tape (100% prevention, $13) or the CVS cast cover (100% prevention, $13) are the preferred contemporary methods to prevent a wet cast.

S2

Current Tobacco Use May Not Correlate With Increased Risk of Peripheral Arterial Disease in Poorly Controlled Diabetics

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Introduction: Peripheral arterial disease (PAD) causes significant morbidity and mortality. Tobacco use, hypertension, hyperlipidemia, and type 2 diabetes significantly and independently correlate with PAD. 96% of PAD patients have at least 1 of the risk factors.

Hypothesis: Concurrent tobacco use and DM compound the risk for PAD, so that PAD is more prevalent in diabetics who smoke compared to those who do not smoke.

Methods: A retrospective cross-sectional study was conducted on patients older than 40 years treated as in patients at Chino Valley Medical Center during 5/1/12-5/13/13 (N=4877). All diabetics were screened for PAD with Doppler Ultrasound Arteriogram Lower Extremity (DUSALE.) The effects of risk factors on PAD development were calculated as proportions in these groups: controlled DM nonsmokers (CDNS); uncontrolled DM nonsmokers (UDNS); nondiabetic smokers (NDS); controlled DM smokers (CDS); uncontrolled DM smokers (UDS). The prevalence of PAD in nondiabetic nonsmokers (NDNS) was calculated as the control.

Results: Mean PAD risk of all subjects including the control is 07612; standard deviation is 093693. Prevalence of PAD in controlled diabetic smokers (8.22%) exceeds that of controlled diabetic nonsmokers (7.036%). Surprisingly, prevalence of uncontrolled diabetic nonsmokers (26.33%) exceeds that of uncontrolled diabetic smokers (20.74%). The Z scores provide additional support for this observation. PAD prevalence is lowest as expected in nondiabetic nonsmokers at 0.2809%; PAD prevalence is 4.545% in nondiabetic smokers. Furthermore, binary-logistic regression model (smoking is assigned value of 1; no-smoking 0) reveals: smoking without diabetes positively correlates with PAD; smoking with controlled diabetes positively correlates with PAD, though less than smoking alone; smoking with uncontrolled diabetes negatively correlates with PAD.

Conclusion: Smoking correlates with a higher risk of developing PAD in controlled diabetics. However, current tobacco use may decrease a poorly controlled diabetic's chance of developing PAD. This paradox may parallel the protective nature of tobacco use against ulcerative colitis exacerbations. This finding and nondiabetic smokers' low risk of developing PAD at 4.545% may result from one limitation of the study: smokers asymptomatic for PAD were not screened for PAD with DUSALE. In future studies, we can screen all smokers for PAD and investigate the impact of history of smoking.

S4

Alarming Prevalence of Lower Extremity Peripheral Arterial Disease in Young Diabetics With Poor Glycemic Control Suggests This Group May Need Earlier PAD Screening

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[1]Touro University California, College of Osteopathic Medicine, Vallejo; [2]Chino Valley Medical Center, Chino, California

Introduction: The 2011 American College of Cardiology/American Heart Association Peripheral Arterial Disease Guidelines advise a resting Ankle Brachial Index for screening lower extremity PAD in patients with 1 or more of the following: exertional leg symptoms, nonhealing wounds, age 65 years and older, or 50 years and older with a history of smoking or diabetes. Furthermore, Selvin et al found a positive, graded, and independent association between hemoglobin A1c and PAD risk in diabetic adults.

Hence, diabetes out of control (DMOOC) may pose a higher risk of developing PAD than that of age-matched controlled diabetes (CD).

Hypothesis: The percentage of DMOOC subjects with concurrent PAD exceeds that of CD subjects with PAD in age-stratified comparison among those who deny current tobacco use.

Methods: A cross-sectional study was done on diabetic subjects selected based on diagnostic abstracts from in-patient setting at CVMC during 02/01-04/30/13. Tobacco use, a potential confounder, was partially accounted for by limiting the study to diabetics who denied current use. All diabetics were screened for Lower Extremity-PAD with Doppler Ultrasound Arteriogram Lower Extremity; reports of stenosis, biphasic or monophasic waveform constituted a diagnosis of PAD. PAD cases included new diagnoses and PAD on admission. DMOOC (diabetics with A1c >6.3) and CD subjects (diabetics with A1c <6.3) were age-stratified and the percentage of DMOOC subjects with PAD and those with CD were compared.

Results: Across all age groups, PAD cases with DMOOC (38.95%; 148 in 380) were more than double those with CD (17.07%; 14 in 82). Ages 20-30, 28.57% DMOOC had PAD vs 0% with CD; ages 31-40, 17.56% DMOOC had PAD vs 0% with CD; ages 41-50, 20% DMOOC had PAD vs 0% with CD; ages 51-60, 44.64% DMOOC had PAD vs 16.67% with CD; over age 61, 43.8% DMOOC had PAD vs 20.69% with CD.

Conclusion: PAD is more prevalent in DMOOC than CD patients across all age groups. Moreover, the prevalence of poorly-controlled younger diabetics with PAD is alarming. This finding may forecast a dire prognosis for these patients as they age and warrants a more stringent screening protocol than current literature suggests. Delaying PAD screening of DMOOC patients until age 50 may cause a missed opportunity to prevent serious complications. We may examine additional correlation with levels of micro-albuminuria, a known early indicator of atherosclerosis. Limiting the study to only lifetime-non-smoking diabetics can eliminate tobacco usage as a confounder.

♦ Abstract that won first or second place in the 2013 SOMA Student Poster Competition.

♦ S5

High Yield of Doppler Ultrasound Arteriogram of Lower Extremity in Diabetics Suggests New Screening Modality and Criteria for PAD Surveillance

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Introduction: Based on the literature consensus on the impact of hyperglycemia and potentially hyperinsulinemia on peripheral arterial disease, Chino Valley Medical Center (CVMC) started screening all diabetic patients for PAD with Doppler Ultrasound Arteriogram of Lower Extremity (DUSALE) in May 2012.

Hypothesis: In PAD-symptom-free diabetics, the percentage of PAD diagnosed with DUSALE is higher than that of PAD diagnosed with ankle brachial index <.90 based on 2011 American College of Cardiology/American Heart Association PAD guidelines.

Methods: 311 subjects received DUSALE during 3/29-6/4/13 at CVMC. Subjects were grouped by diabetic status (no diabetes, controlled diabetes, uncontrolled diabetes,) indications for DUSALE, and positive vs negative findings of PAD on DUSALE. Stenosis, or monophasic, or biphasic waveforms on DUSALE constitute a positive PAD finding. The percentages of positive PAD findings per DUSALE studies were calculated among various groups. Results are compared to literature-stated percentages of ABI-diagnosed PAD per 2011 American College of Cardiology/American Heart Association guidelines.

Results: The yield of positive PAD findings on DUSALE: in diabetics of all ages asymptomatic for PAD and without prior diagnosis of PAD is 68.11% (126 of 185); in diabetics age 50-69 is 65.51% (57 of 87); in diabetics age 50-69 asymptomatic for PAD and without prior diagnosis of PAD is 64.6% (42 of 65).

Conclusion: In the PAD Awareness, Risk, and Treatment: New Resources for Survival (PARTNERS), the prevalence of PAD in individuals at high risk for PAD (50 to 69 years of age and diabetes mellitus or >10 pack-year history of smoking, or >70 years of age) was 29%. Our results suggest that the prevalence of PAD may have been underestimated under current guideline and screening methods. Furthermore, literature states that those with asymptomatic PAD have a risk of cardiovascular events (eg, myocardial infarction, stroke, cardiovascular mortality) comparable with that of patients with symptomatic coronary artery disease. It is imperative that we accurately and proactively diagnose PAD, especially in high-risk patients who appear asymptomatic for PAD. The high yield of positive PAD findings on DUSALE in diabetics age 50-69 asymptomatic for PAD and without prior diagnosis of PAD suggests a more sensitive screening method and more stringent criteria to initiate PAD screening may be warranted. Further study may aim to delineate the ideal age to start screening DUSALE in diabetic patients asymptomatic for PAD.

S7

Utilizing Doppler Ultrasound to Confirm Placement of Intraosseous Needles in Adult Embalmed Cadavers

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Introduction: Obtaining intravascular access on critically ill patients can be difficult and time-consuming. Use of the intraosseous (IO) route as a "non-collapsible vein" is an alternative vascular route when intravenous access is not available or fails. As of 2010, the American Heart Association recommends establishing IO access when intravenous (IV) route is not readily available, for patients of all ages. This central venous access enables drug and fluid delivery similar to that achieved by IV, as fluids and medications administered into the trabecular bone pass through veins connected to systemic venous circulation, IO placement is considered successful if the cannula has a stable position in the bone and allows for a 10 cc flush of fluid without resistance or extravasation. Utilizing Doppler ultrasound can provide additional confirmation for IO placement and it has been shown that ultrasonography can be utilized to confirm IO placement at the distal tibia on fresh frozen cadavers. However, the proximal tibia is a more common site of IO insertion.

Hypothesis: Ultrasonography can be utilized to confirm placement of IO in the proximal tibia, iliac crest and humeral head of adult embalmed cadavers.

Methods: A case-control trial was conducted. IOs were inserted at the proximal humeral head, the tubercle of the iliac crest, and at the proximal tibia of 2 adult embalmed cadavers bilaterally (n=12). IO placement was first confirmed by testing stability of cannula in the bone and the ability to flush 10 cc of water without resistance or extravasation. IO placement confirmation was then attempted utilizing color flow ultrasonography in the intraosseous space.

Results: Of 12 procedures performed, 11 were confirmed successful via the traditional methods of firm placement and ability to flush 10 cc fluid. Placement was confirmed utilizing color flow ultrasonography at one site.

Conclusion: While embalmed cadavers can be used as anatomically correct models for IO placement in living humans, the embalming process may compromise the sonographic window by displacing body fluid. IO placement is conducted as an urgent procedure in critically ill patients, when IV access is not available. Additional studies are needed to determine if ultrasonography is a suitable and time sensitive method to confirm IO placement in living humans.

♦S9

Examining the Doctor-Patient Relationship: Clinical Rotations and Health Care Delivery for LGBT Patients

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Introduction: Health care disparities related to lesbian, gay, bisexual, and transgender (LGBT) patients are of growing interest. LGBT patients face distinct health issues including disease risk, mental health, intimate partner violence, etc. Research suggests that many physicians are unprepared to holistically care for LGBT patients and that these patients received substandard care or were denied care due to their sexual orientation.

Hypothesis: The purpose of this study is to determine third- and fourth-year osteopathic medical students' ability to care for LGBT patients. We hypothesized that fourth-year students, as well as female students, would display a more holistic approach to their LGBT patients. We didn't anticipate differences between osteopathic medical schools.

Methods: Invitations were sent to all osteopathic medical schools to participate in a study aimed to determine LGBT acceptance and health care delivery. Students were asked to take an anonymous web-based survey. Consent was obtained when the participant accessed the survey. All scales were used with permission and have been used in multiple studies.

Results: When asked how often students treated self-reported LGBT patients differently than heterosexual patients, fourth-year students were more likely to provide substandard care to LGBT patients in comparison to their third-year counterparts (P=.019). In addition, male students reported not only treating their LGBT patients differently (P=.005), but also found treatment more challenging (P=.015), in comparison to their female counterparts. When taking a sexual history, students are instructed to ask patients, "Do you have sex with men, women, or both?" Third-year medical students were significantly less likely to ask this question compared to their fourth-year counterparts (P=.003). In addition, statistically significant differences existed between the 6 sampled osteopathic medical schools (P=.002).

Conclusion: It is evident that disparities exist in the way osteopathic medical students treat their self-identified LGBT patients. In addition, it appears that students are reluctant to ask their patients about both sexual behavior and orientation, which may lead to an increased risk of making heteronormative assumptions. These assumptions could be detrimental to the health care of LGBT patients and hinder the doctor-patient relationship. As such, it is evident that a more effective approach in how we train our osteopathic students to deal with LGBT health-related issues is necessary.

S12

Measuring Balance in Children With Cerebral Palsy Using Video Games

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Introduction: Video game use as a therapeutic tool in rehabilitation for children and adults has recently been gaining recognition as a motivating and appealing activity. This venue is especially appealing in the pediatric population and augments traditional treatment methods. The Wii Fit is a video game system that is controlled by a force plate activated under the user's feet while playing. The novel part of this study is that balance parameters collected by the experimentally modified Wii system were analyzed to characterize Gross Motor Function Classification System (GMFCS) levels for children with cerebral palsy.

Hypothesis: Our hypothesis was that GMFCS levels could be discriminated by the analysis of Wii Fit

♦Abstract that won first or second place in the 2013 SOMA Student Poster Competition.

information. We also attempted to explore the possibility of monitoring changes in balance following therapy using the same measurements.

Methods: The study targeted patients between the ages of 5 and 17 who had previously been diagnosed with cerebral palsy (CP). They were categorized by GMFCS as a broad classification of motor function. A group of CP patients classified at GMFCS levels I-III as well as a group of age-matched controls were asked to play video games for a period of 30-40 minutes. A timed up and go (TUG) and pediatric balance scale (PBS) assessment were also measured for more specific classification of each patient's mobility. Balance parameters that were measured included postural sway, postural stability, and velocity of center-of-pressure change.

Results: We found that these parameters differ with GMFCS classification and that we could also predict a patient's GMFCS level based on data obtained from playing the game. Analysis also showed that video game testing was more sensitive than TUG or PBS testing to changes in balance and motor function.

Conclusion: These results suggest that the Wii Fit can be used to diagnose functional mobility as well as accurately monitor outcomes in children undergoing therapy. Future uses of the technology and advantages over current mobility measures (TUG, PBS, and GMFCS) are described in our discussion.

S13

Can Digital Breast Tomosynthesis Provide Accurate Preoperative Tumor Size?

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Introduction: Within the scope of breast cancer, tumor size has proven to be an important prognostic factor. Until the advent of digital breast tomosynthesis (TOMO), magnetic resonance imaging (MRI) was considered to be the unequivocal gold standard. In this study we compared preoperative measured tumor size obtained from TOMO, MRI, and ultrasound (US) studies against pathologic size.

Hypothesis: TOMO will be more accurate in measuring tumor size than conventional MRI and US studies.

Methods: A retrospective review was conducted with IRB approval of patients who had TOMO, MRI, and US prior to surgical intervention. All patients had an image guided biopsy confirming diagnosis of carcinoma prior to surgery. Breast lesions were measured by an experienced radiologist and a medical student. In each imaging modality the maximum tumor measurement was used and rounded to the nearest millimeter. The MRI and US measurements were done at the time of the patient's appointment without physician knowledge that the result would be used in a study, however it is possible that US results may have influenced MRI or vice versa. The TOMO measurement was done between June – July 2013 with both the physician and medical student blinded of the previously calculated MRI and US sizes. Following measurement, the Pearson (r) correlation coefficient and χ^2 test were used to analyze the data.

Results: The study took place at Elizabeth Wende Breast Care, LLC in Rochester, NY. The subjects were all women who were pre-surgically diagnosed with breast cancer from February 12 – December 31, 2012. Subjects were excluded if they received neoadjuvant chemotherapy prior to surgery or if the TOMO and/or MRI did not demonstrate the suspected cancer. Thirty-four patient cases were included for MRI and TOMO comparisons and 26 for US. Statistical analysis was conducted using Pearson Correlation Coefficient between the imaging modality and the final surgical size. The MRI, US, and TOMO showed correlation at 61.25% (r=0.61254, P<.05), 56.46% (r=0.5646, P<.05), and 66.9686% (r=0.669686, P<.05), respectively. MRI tended to overestimate tumor size (55.88% of cases) while US and TOMO tended to underesti-

mate tumor size (57.69% of cases and 55.88% of cases, respectively).

Conclusion: Our results indicate that TOMO provides a more accurate tumor size assessment than MRI or US when compared to surgical size. Further research is necessary to confirm these results.

S15

Awareness of Hereditary Cancer in Osteopathic Physicians

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Introduction: Cancer genetic testing can aid cancer screening and prevention in high-risk patients. Studies demonstrate that physicians are more likely to order genetic testing due to patient inquiry rather than recommended guidelines. It is unclear to what extent osteopathic primary care physicians are aware of standards of care for hereditary cancer.

Hypothesis: Physicians will have decreased awareness of genetic testing and hereditary cancer guidelines. This can be best evidenced by responses to survey questions pertaining to current national guidelines in place.

Methods: From August to November 2012, a survey was administered to osteopathic physicians evaluating past training in genetics and knowledge regarding hereditary cancer.

Results: 140 osteopathic physicians (82.9% family practice or internal medicine) responded to the survey. Most physicians were aware that if a person is found to have a hereditary cancer mutation, something can be done to improve screening for cancer (n=121, 86.4%). For cancer syndromes affecting mostly women, most physicians falsely believed that maternal history is more important than paternal history (n=49, 34.5%). In the total study population, only 46.4% (n=65) of physicians correctly answered that genetic tests ordered for a given hereditary condition would not be the same regardless of the patient's ethnicity. Only a quarter of the physicians correctly identified that molecular tests other than sequencing must be used to detect gene deletions or re-arrangements (n=33, 23.6%). Compared to physicians who do not frequently refer patients for genetic services, physicians who do frequently refer were more likely to recognize that if a person is found to have hereditary cancer mutation, something can be done to improve screening for cancer (OR=3.51; 95% CI, 1.10, 11.19; $P<.05$).

Conclusion: Our data suggest that genetics training may be associated with awareness of general risk assessment for hereditary cancer. However, in other areas, a vast majority of physicians surveyed had knowledge deficiencies in regards to hereditary cancer, regardless of reported past genetics training. Adding to existing literature, results from this study reinforce the need for continuing medical education on hereditary cancer to be made easily available to all physicians.

S26

Coordination of Hand and Eye Movement in Individuals With Parkinson Disease

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Introduction: Parkinson disease (PD) is a progressive neurodegenerative disease affecting 1 million people in the United States. PD is caused by neuronal loss in the substantia nigra within the basal ganglia, the part of brain that regulates motor control. Common symptoms of PD are bradykinesia, rest tremor, rigidity, hypophonia, hyposmia, and micrographia. Micrographia (decreased handwriting size) is a sequela of PD reported in 75% of patients. The mechanisms of micrographia are not well understood and the symptoms are highly variable. Studies have shown that writing size increases when eyes are closed, suggesting that vision plays a role in micrographia. It is thought that movement (including handwriting) is executed according to plans and

cognitive representations of space in the brain. In this conception, the distorted handwriting of people with PD may be due to poor hand control or to mistakes in spatial planning which might be reflected in eye movements.

Hypothesis: Size and location errors in handwriting of participants with PD are related to problems with movement planning, rather than execution.

Methods: We measured simultaneous hand and eye movement during writing to determine whether people with PD foveate the spot they are going to write in as healthy people do, ie, whether hand and eye make the same errors, reflecting a common motor plan. In this IRB approved study, participants with micrographia were recruited from the NYIT College of Osteopathic Medicine Adele Smithers clinic. Participants reproduced print and cursive writing models in 3 sizes. Writing was captured on a computer monitor/writing tablet (WACOM) utilizing Adobe Illustrator and a mouse stylus. The eye movements were captured using a head mounted eye tracker (ISCAN).

Results: The accuracy (size and location) of the handwriting when reproducing the models was poorer in the people with PD than the controls. Participants with PD foveate the erroneous spot before they put their pen in that spot to begin writing.

Conclusion: The common hand and eye errors in participants with PD suggest that movement planning and spatial representations are negatively affected by impaired eye muscle control.

S27

Injury Profile of Mixed Marital Arts Competitors

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Introduction: Although previous studies on mixed martial arts (MMA) injuries to date are informative, they often rely on small sample sizes, exclude female fighters, and use injury data from self-report surveys of fighters instead of objective physician assessments. In addition, most of the studies on MMA injuries were conducted prior to the adoption of the Unified Rules of Mixed Martial Arts in 2009 which introduced changes related to referee training, gloves, moves, amateur and female fighters, and a host of other elements that could affect injury rates and/or injury types. Given these issues, up-to-date studies utilizing better methodological approaches are needed to help maximize the safety of MMA by informing fighters, trainers, promoters, physicians, and sanctioning/governing bodies.

Hypothesis: The objectives of the current study were 2-fold: (1) to provide a contemporary, detailed description of physician-diagnosed injuries incurred during male and female, professional and amateur MMA competitions; and (2) to examine predictors of injuries during MMA competitions.

Methods: Correlational and multivariate analyses were conducted on cross-sectional data to examine injuries sustained during 711 MMA bouts. One physician diagnosed any injuries occurring during the bouts which occurred at various sports venues in Kansas and Missouri. Participants were male and female, amateur and professional MMA competitors contributing to 1422 fight participations (fight participations=711 bouts × 2 fighters/bout).

Results: The overall injury rate was 8.5% of fight

participations (121 injuries/1422 fight participations) or 5.6% of rounds (121/2178 rounds). Injury rates were similar between men and women, but a greater percentage of the injuries caused an altered mental state in men. The risk of being injured was significantly greater for bouts held in Kansas, at the professional level, lasting more rounds, and ending in a KO/TKO. Fighters also were more likely to be referred to the emergency department if they participated in longer bouts ending in a KO/TKO.

Conclusion: The observed injury rate was lower than previously reported suggesting recent regulatory changes have made MMA a safer sport. Increased clinical awareness and additional research should be extended to head-related injuries in MMA especially those associated with KOs/TKOs.

S31

Efficacy of Osteopathic Manipulative Treatment on Pulmonary Function in Healthy Adult Male Subjects

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Introduction: Prior studies investigating the effects of osteopathic manipulative treatment (OMT) on pulmonary function have been equivocal. Our long-term goal is to design a tightly controlled experimental protocol by which basic science and clinical research can be combined to examine the efficacy of OMT on pulmonary function. This protocol was initiated in the present study which examined the efficacy of OMT on pulmonary function in healthy adult males, both acutely and at 24 hours.

Hypothesis: The treatment of somatic dysfunction with OMT will increase chest compliance, increase lung volumes, and improve pulmonary function.

Methods: Midwestern University Institutional Review Board approval was obtained (#2327). A tightly controlled healthy adult male population was recruited and randomly divided into a control group (n=10) or OMT group (n=15). Pulmonary function (lung volumes, forced vital capacity [FVC], forced expiratory volume in 1 second [FEV_1], breath-holding time, and chest excursion) was measured in both groups at 3 time points. Following baseline measures and structural diagnosis, OMT directed at somatic dysfunction of the cervical, thoracic, and lumbar spine, abdominal wall, diaphragm, ribs, and sacrum was performed (K.P.H.). The control group read quietly for ~20 minutes. After OMT or quiet reading, pulmonary function was reassessed within 10 minutes (acute) and remeasured at 24 hours.

Results: There were no statistical differences between the control and OMT groups at baseline. Additionally, there were no changes in pulmonary function in the control group at 24 hours. In the OMT group, upper thoracic excursion increased from 5.5 to 6.1 cm ($P=.07$); vital capacity increased from 5.26 to 5.40 L ($P=.06$); FVC increased from 5.00 to 5.14 L ($P=.03$); and breath-holding time increased from 83.8 to 93.5 seconds ($P=.004$) after 24 hours. Because of the increase in FVC, and lack of change in airway resistance, pulmonary function measured by the FEV_1/FVC ratio decreased from 79.8 to 77.5% ($P=.05$).

Conclusion: Our preliminary data suggest that OMT increases upper thoracic excursion and lung volumes in healthy adult males at 24 hours post-OMT. While the FEV_1/FVC ratio decreased, it was due to the increase in FVC. These data suggest OMT of somatic dysfunction in healthy subjects can increase thoracic compliance. Further studies will determine whether OMT can improve pulmonary function and quality of life in patients with pulmonary disease.

S34

Prevalence of Nasal Colonization of Methicillin-Resistant *Staphylococcus aureus* in Homeless and Economically Disadvantaged Populations in Kansas City

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Introduction: Methicillin-resistant *Staphylococcus aureus* (MRSA) is a virulent infectious agent with antibiotic resistances that make controlling proliferation a challenging aspect of public health.

Hypothesis: Due to limited access to health care and sanitation facilities, we hypothesized that the homeless and destitute are susceptible populations to infectious disease and colonization, and therefore have a higher carriage rate of MRSA than the general populous. With the added factor of frequent close proximity, those who frequent shelters become even more ideal hosts for proliferation of MRSA. Our goal was to test this hypothesis and to quantify the extent to which these populations are at greater risk. Findings from a similar 2009 study were consistent with our hypothesis.

Methods: With approval from our institutional review board, our study tested the anterior nares of 113 homeless and economically disadvantaged subjects at a Kansas City homeless shelter for MRSA colonization and a survey was administered to each subject. Because surface contact is believed to be a source of MRSA, multiple surfaces within the shelter were also sampled, with analog surfaces from our University serving as controls. All samples were cultured on tryptic soy agar plates as well as media selective for MRSA (HardyCHROM). All positive results were confirmed by Gram stain, catalase, and coagulase tests.

Results: Surprisingly, samples from multiple surfaces within the shelter yielded no MRSA positive results, nor did the surfaces from the University. A prevalence rate of 8% MRSA among the population of the shelter of was found (9 of 113 subjects). This represents more than 5 times the Centers for Disease Control and Prevention's reported rate (1.5%) for the general population, but only about 30% of the rate reported for homeless subjects in the 2009 study. Of 35 biopsychosocial criteria tested for correlation, only age and days per week of church attendance were found to be statistically correlated to MRSA carriage ($P=.029$ and $P=.005$, respectively).

Conclusion: Our results support the hypothesis that this population would have a relatively high MRSA carriage rate, but the difference in the rate from this study compared to previous studies is a curious finding. Expansion of this study, or initiation of a similar study with other risk and protective factors such as drug/alcohol use and diet, might offer further insight. The implications of this research could have far reaching effects in the fields of public health and infectious disease.

S44

Survey of Demographics, Injury Patterns, and Transition Periods in Minimalist Runners

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Introduction: Many runners switching to minimalist running shoes (MRS) do so hoping to prevent injury. Currently there is only anecdotal data on injury patterns in MRS, and no proven transition regimen

for switching. The goal of this study is to collect data on the status of running injuries in new minimalist runners, as well as the transition time allowed for switching shoe types. This information will allow physicians to provide evidence-based advice on the risks and benefits of changing to MRS, as well as transition times and exercises that reduce injuries.

Hypothesis: Typically, runners wearing traditional running shoes (TRS) heel strike on impact, unlike habituated minimalist runners who land mid or forefoot first. Forefoot striking in MRS may dampen initial impact forces, but significant force is still involved. This force may cause injury, particularly if the intrinsic foot muscles are insufficiently developed (eg, short transition periods). Kinematic differences in MRS and TRS runners may relate to different injury patterns.

Methods: The public, internet based survey opened in July of 2013 and will stay open for a minimum of 6 months. Advertisements were posted across Indiana, Ohio, Michigan, North Carolina, Virginia, and West Virginia. Questions addressed: (1) minimalist runner demographics; (2) the length of the transition period when switching from TRS to MRS; (3) details of overuse injuries in TRS; (4) details of overuse injury in MRS.

Results: The survey had 19 responses. Most respondents were 18-34 years old, ran $<$16 miles/week, had been running for $>$5 years, and allowed a transition period $\leq$4 weeks. Approximately half of the respondents had been wearing MRS $<$1 year. 4 had injuries before they switched to MRS. 2 runners reported improvement of their injuries while a third's injury worsened. 3 respondents developed injuries after switching to MRS, with 1 reporting severe hip and knee pain and a displaced fibula.

Conclusion: Many respondents reported running $>$5 years, so the switch to MRS may reflect discontent in TRS or curiosity with MRS. Nearly all subjects reported use of a transition period while switching from TRS to MRS. A larger sample size is needed to determine the effect of transition period length and assess injury patterns. In the coming months more advertisements will be placed and we expect the number of responses to increase for a more meaningful analysis.

S47

Kawasaki Disease: Do Early Diagnosis and Treatment Improve Outcome and Prevent Complications?

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Introduction: Kawasaki disease (KD) is an acute, self-limited vasculitis of unknown cause that has a striking predilection for the coronary arteries of infants and young children. Complications such as coronary artery aneurysms, depressed myocardial contractility and heart failure may develop. Clinical criteria have been established to assist physicians in diagnosing KD because there is no definitive diagnostic test. The classic diagnosis of KD is based on the presence of 5 or more days of fever and 4 or more of the 5 principal clinical features. Those features are (1) changes in the hands and feet (erythema, edema, peeling), (2) polymorphous exanthema, (3) bilateral bulbar conjunctival injection without exudate, (4) changes in the lips and oral cavity (erythema, strawberry tongue), and (5) cervical lymphadenopathy.

Hypothesis: The purpose of this study is to determine if early diagnosis and intravenous immunoglobulin (IVIG) treatment in patients with KD can prevent development of coronary artery disease (CAD) and its progression after development.

Methods: Retrospective chart review of 10 children admitted to Spartanburg Regional Medical Center with diagnosis of KD over 6 years period. IRB review was exempted for this study.

Results: Ten patients diagnosed with KD; 5 with CAD at presentation in the form of coronary dilatation or ectasia (Group 1) and 5 without CAD (Group 2). Average age of "Group 1" is 27.6$\pm$17.2 months

and of "Group 2" is 35.4±17.1 months. Length of hospital stay for Group 1 is 6.01±3.6 days and for Group 2 is 2.86±1.8 days. All children had changes in lips and oral cavity. Five children had cervical lymphadenopathy greater than 1.5 cm in diameter. All children had elevated CRP and 8 children had elevated ESR. One child had aseptic meningitis. The average durations of fever before IVIG given were 6.4±1.8 and 7.2±1.9 days in patients without and with CAD, respectively. No significant statistical differences between the 2 groups in age (P=.26), length of hospital stay (P=.08), and duration of fever before IVIG (P=.26). All 10 patients were treated with IVIG. At 1 year follow-up; none of the patients in Group 2 develop a coronary artery disease, and all patients in Group 2 showed complete resolution of their coronary artery disease.

Conclusion: Treatment with IVIG within the first 10 days of illness could either prevent the development of CAD or help resolution of the disease once started. Prompt diagnosis of KD is crucial for reducing the risk of coronary artery lesions and preventing the development of coronary artery aneurysm.

S48

Effects of 7-Technique Osteopathic Manipulative Protocol on Patients With COPD

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Introduction: There have been few studies that have measured the long-term effect of osteopathic manipulative treatment (OMT) on chronic obstructive pulmonary disease (COPD).

Hypothesis: This pilot study tested the hypothesis that an OMT intervention protocol used over a series of visits would be safe, feasible and would improve pulmonary function in clinically diagnosed COPD patients.

Methods: This randomized, single-blinded pilot study was completed over 18 months with 2 recruitment cycles including 25 participants older than 40 years. The first cycle consisted of 7 participants with 4 in the OMT group and 3 in the sham group. The second cycle consisted of 18 participants with 8 in the OMT group and 10 in the sham group. OMT consisted of 7 standardized techniques. The sham group received light touch protocol. Both protocols occurred over 4 visits. Objective measures obtained included pulmonary function testing (PFT) and a 6-minute walk test (6MWT). Subjective measures obtained were the Clinical COPD Questionnaire (CCQ) and St George's Respiratory Questionnaire (SGRQ).

Results: A difference was noted between sham and OMT groups forced expiratory flow (FEF) 25%-75%, across 4 visits. We did find a trend of improvement in both groups at baseline visit post-FEF compared to subsequent visits. Baseline (z=−.575, P=.572), visit 1 (z=−.767, P=.467), visit 2 (z=−.1.230, P=.235), visit 3 (z=−1.830, P=.072). However, when treatment and sham groups were collapsed and baseline posttest FEF was compared to visit 3 posttest FEF, a significant improvement was noted, (z=2.251, P=.024). The 6-minute walk test also demonstrated a significant difference when the groups were collapsed (z=−2.617, P=.009). There were no major adverse events during the duration of the study and the study protocol proved feasible to implement.

Conclusion: These pilot results demonstrate the possible benefit of OMT on certain pulmonary function parameters, specifically with improvements in FEF and physical exertion as demonstrated by the 6MWT in patients with COPD. Pilot results are promising and should be replicated with a larger sample size. The intervention was safe and well tolerated without need for design modifications.

Acknowledgments: This study received IRB and internal funding from KCUMB as a component of the KCUMB OMM fellowship.

S59

Phase One, Open Label, Single Arm Study to Demonstrate the Safety of the Antria Cell Preparation Process During Facial Fat Grafting Assisted With Autologous, Adipose-Derived Stromal Vascular Fraction

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Introduction: Facial lipoatrophy is diagnosed as the loss of adipose tissue in the face over time, which can result from autoimmune diseases as well as aging. Current treatments for facial lipoatrophy necessitate a more efficacious treatment option, as autologous facial fat grafting produce inconsistent results due to low graft survival and the use of dermal fillers can be an economically damaging and time constraining process. Antria cell preparation process and its special reagent Adipolyx may display a safe method of supplementing traditional lipografts with adipose-derived stromal vascular fractions (SVFs), which can be utilized in cosmetic or therapeutic applications. Imperative to the function of SVF is believed to be adipose-derived stem cells (ADSCs). ADSCs possess the ability to differentiate into various tissue types, inhibit inflammation, and stimulate angiogenesis. Additionally, the cellular population of SVF has been shown to secrete various growth factors that sustain the lipograft.

Hypothesis: The phase I study seeks to verify the safety of SVF-enhanced lipografts as prepared by Antria proprietary reagent and methodology within human subjects.

Methods: Under FDA regulatory compliance and IRB approval, 6 subjects who are already scheduled for liposuction and facial fat grafting procedure elect to have lipograft enriched with adipose-derived SVF isolated via Antria Cell Preparation Process. Safety of the process is analyzed with physical examinations, safety laboratory assessments, and long-term follow-ups of up to 36 months postoperative.

Results: Neither treatment-related adverse events or serious adverse events have been observed. In comparison of preoperative and postoperative laboratory safety tests, no significantly altered laboratory values in complete blood count, liver function test, basic metabolic profile, or urinalysis have been observed. Furthermore, sterility testing for bacteria and fungi during the Antria Cell Preparation Process has been negative. Although efficacy is not the focus of this study, injected SVFs were counted to have greater than 70% cell viability.

Conclusion: As an ongoing study, results will be updated as more data are observed from patient visits in the coming months, with the final decision on safety following FDA and IRB analysis. However, current data obtained in this study suggest the safety of the Antria Cell Preparation Process for facial fat grafting assisted with autologous, adipose-derived SVF.

Basic Science

S10

Degradation of P62/SQSTM1 in Group B Coxsackievirus–Infected Cells

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Introduction: Coxsackievirus B3 (CVB3) is a prevalent human pathogen that causes viral myocarditis which may progress to dilated cardiomyopathy and heart failure. It has been shown that replication of Coxsackievirus requires the function of the proteasome and autophagic machinery.

Hypothesis: In this study we show that p62 is degraded during Coxsackievirus infection.

Methods: HeLa cells were infected with CVB3 and treated with MG-132 to inhibit proteasome activity. The cells were then fixed or lysed to monitor

changes in the steady-state-level of p62.

Results: Western blot analysis on lysates from infected cells show a decrease in p62 protein and the appearance of a stable immunoreactive fragment. Mass spectrometry performed on p62 immunoprecipitates show viral proteins are associated with p62/SQSTM1. Immunofluorescent localization of p62 in infected cells fails to show colocalization of p62 with viral proteins shown to associate with it by mass spectrometry unless the proteasome is inhibited. Inhibiting p62 protein expression with siRNA increases viral propagation as measured by increases in viral proteins and released virions.

Conclusion: The data from this study demonstrate that p62/SQSTM1 is involved in inhibition of viral replication and targeted for degradation during infection of cells with Coxsackievirus. This suggests that p62/SQSTM1 can have anti-viral functions that may be expandable to other viral infections.

S14

Cellular and Axonal Diversity in a Model of Double Cortex Syndrome

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Introduction: BXD29 mice display subcortical band heterotopia (Sbh) and may therefore be a good model of Double Cortex Syndrome in humans. However, no study has yet to describe the axonal or cellular constituents of this malformation.

Hypothesis: We hypothesize that Sbh in BXD29 mice contain a diversity of neuron types, receive innervation from various subcortical regions, and may exhibit gliosis.

Methods: Adult BXD29 mice were perfused and brains sectioned for immunocytochemistry. Primary antibodies against neuronal-, glial-, and axonal-specific markers were used. Digital photomicrographs were captured using a light microscope. In vitro electrophysiological recordings from slices of juvenile BXD29 mice were used to identify synaptic connections on heterotopic neurons.

Results: GABAergic interneurons were identified in the Sbh as well as 3 glial cells including astrocytes, oligodendrocytes, and microglia. However, no gliosis was observed. Diverse axons were present in Sbh including catecholaminergic, serotonergic, and cholinergic axons. Intracellular recordings revealed the presence of postsynaptic potentials in all heterotopic cells.

Conclusion: Sbh in BXD29 mice contain diverse neuron, glial, and axonal types suggesting a similar diversity of cells and axons in heterotopia in humans. These data provide clues to how Sbh in humans result in epilepsy and cognitive disability.

♦S16

Voluntary Exercise Reduces Intestinal Content of *Lactobacillaceae* in a Model of Diet-Induced Obesity

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Introduction: The role of intestinal bacteria in the development of obesity has gained the attention of scientific and medical communities. Investigators are evaluating the effects of dietary intake on changes in the gut microbiota in efforts to understand the role of microbial balance in health and disease. The microbial family *Lactoabacillaceae* is an important group of bacteria found in both the human and mouse gut microbiota. While some species of *Lactoabacillaceae* are linked to weight loss, others are linked to obesity. The regulation of various species of *Lactobacillaceae* by voluntary exercise (Ex) as a means of controlling weight gain due to a high fat diet has not been evaluated. The purpose of this study is to examine the effects of a high fat diet on the relative levels of *Lactobacillaceae* species in sedentary mice and Ex mice.

Hypothesis: *Lactobacillaceae* is elevated in a high fat diet-induced obesity (DIO) mouse model and is reduced by Ex.

♦ Abstract that won first or second place in the 2013 SOMA Student Poster Competition.

Methods: 5-week-old, male C57Bl/6 littermates were distributed equally into 4 groups (n=6/group): low fat (10kcal% fat) sedentary (LF/Sed), low fat exercise (LF/Ex), high fat (60kcal% fat) sedentary (HF/Sed), and high fat exercise (HF/Ex). The bacterial 16S ribosomal RNA (rRNA) gene was extracted from fecal pellets collected at weeks 0, 6, and 12. Samples were sequenced using 16S ribosomal DNA to the taxonomic level of bacterial family. Initial and final body weights, Ex distance, epididymal fat pad weight, 24-hour food intake, and oral glucose tolerance were evaluated. The data were analyzed by a 2-way ANOVA and presented as mean + SE.

Results: Prior to starting the diet and Ex protocol, rRNA gene sequencing demonstrated no significant difference in *Lactobacillaceae* content between the groups (diet $P=.48$, Ex $P=.57$). At week 12, DNA sequencing demonstrated elevated levels of *Lactobacillaceae* in HF/Sed mice compared to all other groups. Ex significantly reduced *Lactobacillaceae* content in both LF and HF diet mice (HF/Sed 20.85?5.16; HF/Ex 0.35?0.31; LF/Sed 11.58?4.49; LF/Ex 6.55?3.32; $P<.05$)

Conclusion: The *Lactobacillaceae* family is downregulated by exercise, especially in HF-fed mice, but the effect of Ex and HF diet on specific species remains to be determined. *Lactobacillaceae* may be involved in exercise-regulation of body weight, but this will require further study.

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♦ Abstract that won first or second place in the 2013 SOMA Student Poster Competition.

♦S17

Role of Tight Junction Proteins in Mediating Oxidative Damage of Renal Epithelial Cells

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Introduction: Renal epithelial cells form continuous cell sheets that separate body fluid compartments. The circumferential tight junction (TJ) structure located at the apicolateral border of adjacent renal epithelial cells limits the movement of solutes and water between adjacent cells (paracellular permeability barrier). Renal ischema/reperfusion injury leads to a loss of the renal tubular paracellular permeability barrier with backleak of ultrafiltrate into the body. Hydrogen peroxide (H_2O_2) mediates partially ischemia/reperfusion induced renal injury. Previous studies have suggested roles for the TJ proteins occludin, zonula occludens 1 (ZO-1), and zonula occludens 2 (ZO-2) in mediating this damage but many questions remain. We investigated the role of TJ proteins in mediating the effect of H_2O_2 on renal paracellular permeability. Expression of specific TJ proteins was genetically manipulated in Madin Darby Canine Kidney (MDCK) cells, a distal tubule-like dog renal epithelial cell line. The effect of treatment with varying H_2O_2 concentrations on paracellular permeability was compared as a function of TJ protein content.

Hypothesis: The tight junction proteins, occludin, ZO-1, and ZO-2, are involved in mediating the H_2O_2-induced increase in renal epithelial cell paracellular permeability.

Methods: Serum-starved, postconfluent MDCK cells grown on permeable membrane filters were pretreated with varying concentrations of H_2O_2 for 1 hour. Movement of calcein (a fluorescent marker of paracellular permeability) across MDCK mono-

layers was measured and compared to standards of known calcein content.

Results: Calcein moved across control MDCK cell monolayers at a linear rate. Treatment with H2O2 increased paracellular calcein movement in a concentration-dependent manner. Occludin protein knockdown (siRNA treatment) increased the sensitivity of paracellular calcein movement across MDCK cells to H_2O_2. In contrast, occludin protein overexpression diminished the ability of H_2O_2 to increase paracellular calcein movement. Knockdown of ZO-1 protein expression increased sensitivity and knockdown of ZO-2 protein expression decreased sensitivity of MDCK cell paracellular permeability to H_2O_2.

Conclusion: These results indicate that occludin, ZO-1, and ZO-2 proteins differentially modulate the sensitivity of MDCK cells to the H_2O_2-induced increase in renal epithelial cell paracellular permeability.

S18

Sanguinarine-Mediated Sensitization of SiHa Cells to TRAIL for Cervical Cancer Therapy

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Introduction: Cervical cancer is the sixth most deadly cancer in the world and is primarily caused by the human papilloma virus (HPV), which transforms normal cervical cells into cancerous cells that are highly resistant to radiation and chemotherapy. Induction of apoptosis in the transformed cells is a key strategy in successfully treating HPV-induced cervical cancer. TRAIL (tumor necrosis factor related apoptosis-inducing ligand) has been shown to selectively induce apoptosis in cancer cells by binding to death receptors (DR4 and DR5) and activating the extrinsic pathways for apoptosis. However, certain cervical cancers, such as the cultured cell line SiHa, are remarkably resistant to TRAIL. In this study, we have explored the use of sanguinarine, an extract from the plant *Sanguinaria canadensis*, to sensitize SiHa cells to TRAIL. Sanguinarine has been shown to induce apoptosis in cancer cells by activating multiple cell death pathways, including the upregulation of DR5 via reactive oxygen species (ROS) in primary effusion lymphoma cells.

Hypothesis: Since sanguinarine can lead to an upregulation of DR5, we hypothesize that it can potentially sensitize SiHa cells to TRAIL and lead to apoptosis.

Methods: Cultured SiHa cells were exposed to sublethal doses of sanguinarine in combination with TRAIL. Cell viability was assessed using a tetrazolium-based colorimetric assay, and morphological changes were observed via microscopy. Annexin V/Propidium iodide (PI) staining of treated cells is being used to differentiate between apoptosis and necrosis, and apoptotic induction is being further investigated by caspase activation assays. DR5 expression on the cell surface is being analyzed by flow cytometry.

Results: Treatment of SiHa cells with a combination of sanguinarine and TRAIL led to a significant reduction in cell viability. Morphological changes indicated that the treated cells may have undergone programmed cell death. AnnexinV/PI staining and caspase activation assays will confirm the induction of apoptosis.

Conclusion: The observed synergistic effect of sanguinarine and TRAIL on SiHa cells is promising for the treatment of cervical and possibly other HPV-induced cancers. However, the precise molecular mechanisms behind the observed effect, including the upregulation of DR5 and the involvement of ROS, require further investigation. This knowledge will enable us to devise more effective treatments for those who suffer with this devastating disease.

S19

Thyroid Hormone Effect on Brain Vasculature

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Introduction: Thyroid hormones (THs) are essential for the function of diverse organ systems including the heart and brain. Hypothyroidism can often lead to clinical symptoms such as dementia, lethargy, hyporeflexia, and depression, demonstrating clear effects of low TH levels on brain function. In contrast, hyperthyroidism can result in hyperreflexia, anxiety, and irritability, demonstrating that both abnormally high or low levels of THs alter brain function. The precise mechanisms by which altered TH levels affect brain function is not fully understood

Hypothesis: We hypothesize that altered TH levels affect vessel architecture and angiogenesis of the neocortex and hippocampus.

Methods: Sprague-Dawley rats were thyroidectomized and then treated with thyroid hormone (T4) to establish euthyroid, hypothyroid, and hyperthyroid conditions. The brains of the rats were harvested, and coronal sections containing frontal lobe and hippocampus were immunostained. Antibodies against alpha smooth muscle actin was used for labeling arteries and arterioles. Immunostained sections were colabeled with isolectin B4 in order to visualize the general vasculature. Sections were also DAPI counterstained in order to identify neocortical lamina and hippocampus. Epifluorescence and confocal microscopy were used for analysis and photographic archival.

Results: Thyriodectomy produced significant decreases in T3 and T4 and an increase in thyroid stimulating hormone (TSH) in all rats. Following T4 administration, 3 groups of rats were established exhibiting hypothyroidism (low T4/high TSH) and hyperthyroidism (high T4/low TSH), as well as a euthyroid group. Altered TH levels were associated with changes in cardiovascular physiology indicating a systemic treatment effect. Altered TH levels were associated with changes in brain vasculature. Preliminary data suggest a reduction in small arterioles in the hypothyroid group.

Conclusion: These data demonstrate the effect of altered TH levels on brain vasculature in a rodent model. These data suggest clinically relevant alterations in brain vasculature occur in altered thyroid states.

S21

Anaplerotic Therapy for the Neurogenetic Pediatric Leukodystrophy: Canavan Disease

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Introduction: Canavan disease (CD) is a monogenic, autosomal recessive childhood neurodegenerative disorder caused by mutations in the aspartylacylase gene (ASPA). The lack of functional enzyme leads to an increase in the substrate molecule *N*-acetyl aspartate (NAA), which prevents normal myelination and results in spongiform degeneration of the brain. The natural history of untreated CD is irreversible brain damage and death within the first decade of life. ASPA catabolizes the acetylated amino acid derivative NAA into aspartate and free acetate. Loss of this function results from mutations in ASPA and leads to the accumulation of noncatabolized NAA: the major diagnostic feature of CD. A mouse model (nur7 mice contain a mutation in ASPA) has been constructed and provides a useful tool in studying the disease. If the nur7 brain was provided with an anaplerotic substrate before the peak of myelination, the augmentation of the Kreb's cycle intermediate may increase the acetyl groups available for fatty acid synthesis, resulting in

reduced oxidative stress. Triheptanoin is a triglyceride composed of 7-carbon fatty acids, which is undergoing Phase I/II testing for the treatment of defects in fatty acid oxidation and adult polyglucosan body disease. In vivo, triheptanoin is converted into ketone bodies and acetyl-CoA. Because acetyl-CoA lies at a complex intersection of lipid catabolism and lipid biosynthesis, triheptanoin may have beneficial effects on both Kreb's cycle output and myelin synthesis in CD. Using the nur7 mouse model, we tested the hypothesis that dietary supplementation of metabolic intermediates will rescue oligodendrocyte loss, dysmyelination, and motor deficits in CD.

Results: Our preliminary studies thus far have confirmed the ability of neonatal triheptanoin treatment to promote oligodendrocyte development, increase myelin markers, increase Kreb's cycle output, and reduce oxidative stress and vacuolation. Phenotypic recovery indicates a significant improvement in pathological indices in neonatal triheptanoin-treated animals. The successful completion of these studies will generate efficacy and preliminary safety data to support the development of a phase I/II study to assess benefit of triheptanoin in patients affected by CD.

S22

Spontaneous Activity of Pyramidal Neurons in Neocortical Layers 2/3 and 5 in the Normal and the Acallosal Brain

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Introduction: Human behavior arises from the intricate neuronal activity embedded in neocortical circuits. For this reason, any disturbances to the neocortical circuitry due to developmental malformations such as agenesis of the corpus callosum, injury, or other disease processes can render behavioral changes. Furthermore, it can manifest clinically as epilepsy and/or cognitive impairment. Thus advancing our knowledge of neocortical connectivity and activity provides a crucial route to developing new treatment strategies for diseases of neocortical origin. One way to understand neuronal activity is by using electrophysiological methods. For example, using a zero magnesium (Mg^{2+}) medium can induce synaptic activity since Mg^{2+} ions normally block *N*-methyl-D-aspartate receptors. In this study, we collected data demonstrating the activity of neocortical layer 2/3 and layer 5 pyramidal neurons of normal as well as acallosal mice under in vitro zero Mg^{2+} stimulation.

Hypothesis: We hypothesize that spontaneous activity in response to zero Mg^{2+} stimulation of layers 2/3 and 5 pyramidal neurons would differ within themselves and across both normal and acallosal groups.

Methods: C57BL/6J mice were used as the normal strain and BTBR mice were used as the acallosal strain. Neocortical slices were prepared from both groups of mice at postnatal day 14-21 using a vibratome. These slices were maintained in zero Mg^{2+} artificial cerebrospinal fluid (ACSF). Neocortical layer 2/3 and layer 5 pyramidal cells were located on these prepared slices, and whole-cell patch clamp recordings were performed.

Results: A subset of layer 2/3 and layer 5 pyramidal neurons of both groups of normal and acallosal mice were stimulated by zero Mg^{2+} ACSF, and these activities were characterized by vigorous burst spiking followed by quiescent periods. Preliminary analysis demonstrated differences in burst firing, the number of action potentials per burst, and the time between bursts between layers 2/3 and 5 pyramidal neurons of the normal as well as acallosal mice.

Conclusion: Pyramidal neurons in layer 2/3 and layer 5 respond differently to zero magnesium stimulation, which suggest differences in the synaptic connections formed within their respective lamina. In addition, these data reveal that the acallosal brain is also characterized by changes in neocortical circuitry.

S23

Effect of Tumor Necrosis Factor-α on Xanthine Dehydrogenase Expression and Cleavage in Adipocytes

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Introduction: Obesity is associated with elevated serum levels of uric acid (UA) and it has been proposed that UA may contribute to the development of metabolic syndrome. UA is a byproduct of purine catabolism and the final steps in its synthesis are catalyzed by xanthine dehydrogenase/xanthine oxidase (XDH/XO). This enzyme is initially expressed as XDH which transfers electrons to NAD, but is reversibly converted into XO which transfers electrons to oxygen and generates damaging radicals. XDH can also be irreversibly cleaved into XO. It has been suggested that irreversible conversion to the radical-producing form is stimulated by inflammation. The inflammatory cytokine TNF-α was shown to increase XDH/XO expression and UA production in epithelial cells. XDH/XO is required for murine adipocyte maturation in vitro and we have confirmed that it is expressed in murine and human white adipose tissue. Because obesity is associated with elevated adipose production of TNF-α, the effects of this cytokine on XDH may explain the impaired adipokine production and increased UA levels seen in obese patients. The goal of this study was to determine if exposure of adipocytes to TNF-α causes increased expression of XDH/XO and increased conversion to the XO form.

Hypothesis: Treatment of 3T3-L1 cells with TNF-α will lead to increased expression of XDH/XO as well as increased XO to XDH ratio. Treatment will also cause irreversible cleavage into the truncated XO form of the enzyme.

Methods: Differentiated 3T3-L1 adipocytes were treated with TNF-α or vehicle control and UA levels in the media were measured. XDH and XO activity were determined in cell lysates using a fluorescent assay that monitors conversion of pterin to isoxanthopterin in the presence of different electron acceptors. Expression level and cleavage were also investigated through Western blotting.

Results: No significant difference in XDH/XO activity or ratio was seen between treated and control cells. The cleaved form of the enzyme was not detected on Western blotting. There was no change in UA production when comparing treated and untreated cells.

Conclusion: TNF-α does not cause a significant increase in the expression of XDH/XO, conversion to XO, or UA production in murine adipocytes. Future experiments can investigate the effects of other inflammatory mediators and the mechanisms responsible for the differential regulation of XDH/XO activity in adipose and epithelial cells.

S24

Xanthine Dehydrogenase Is Highly Expressed in White Adipose Tissue

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Introduction: Several studies have demonstrated that serum uric acid (UA) is elevated in obese patients and is inversely correlated with levels of the insulin-sensitizing hormone adiponectin. UA synthesis is catalyzed by the enzyme xanthine dehydrogenase/xanthine oxidase (XDH/XO), which is highly expressed in the liver. This enzyme has 2 different catalytic mechanisms in which either NAD (XDH) or oxygen (XO) is used as an electron acceptor. Mechanisms responsible for regulating conversion of XDH to XO are not well understood but may affect oxidative damage to tissues since XO activity generates reactive oxygen species. In tissue culture experiments, XDH activity was shown to be important for maturation of adipocytes and we have demonstrated that XDH/XO is present in hu-

man and rat adipose tissue. However, its expression level in adipose tissue in comparison to other tissues has not characterized. The goal of this study was to compare expression of XDH/XO in white adipose tissue (WAT) to that of other tissues.

Hypothesis: XDH/XO will be highly expressed in WAT at a level comparable to that seen in the liver.

Methods: WAT, liver, kidney and spleen tissue were obtained from adult mice. Expression level was investigated using both Western blotting and a fluorescent assay monitoring XDH/XO activity in the presence of different electron acceptors.

Results: XDH/XO was highly expressed in WAT. Total XDH/XO enzymatic activity was over 20-fold greater in liver and WAT tissue than kidney and spleen. The ratio of XDH to XO activity in all tissues was highly variable between animals.

Conclusion: XDH/XO is highly expressed in WAT suggesting that adipose production of uric acid may contribute significantly to serum levels. This finding may partially explain the link between hyperuricemia and obesity. Additional studies are needed to investigate the factors controlling XDH to XO ratio.

S28

In Vitro Model System to Investigate Drug Resistance Mechanisms in Pancreatic Cancer Cells

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Introduction: With a 5-year survival rate of less than 6%, the diagnosis of pancreatic cancer is devastating news for any patient. Gemcitabine, the most commonly used chemotherapy drug, only improves survival by approximately 1.5 months. A major obstacle to the treatment of pancreatic cancer with gemcitabine is the development of drug resistance. To better understand the precise mechanisms by which patient tumor cells gain resistance to gemcitabine, a cell culture model system that more accurately reflects the development of drug resistance in vivo is required.

Hypothesis: Depending on the treatment regimen, the ability of cell culture model systems to simulate acquired drug resistance in patients undergoing gemcitabine treatment for pancreatic cancer varies considerably.

Methods: Cultured pancreatic adenocarcinoma BxPc3 cells were subjected to 2 different treatment regimens. The first method, termed the *constant dose method*, involves periodically treating separate cultures of BxPc3 cells with constant predetermined doses of gemcitabine below, at, or above the IC50 of the drug. The second treatment regimen, termed the *incremental dose method*, consists of treating BxPc3 cells with increasing doses of gemcitabine from 10 to 100 nanomolar.

Results: Cells that survived gemcitabine treatment by both methods showed enhanced resistance to gemcitabine, as evidenced by higher IC50s and slower growth as compared to the parental cell line. Morphological changes observed in the drug resistant cells indicate a likely epithelial-to-mesenchymal transition (EMT). Molecular mechanisms related to drug resistance are currently being assessed by investigating changes in gene and protein expression. Cell surface markers are also being assessed by flow cytometry to determine EMT and the possible presence of cancer stem cells in the resistant lines.

Conclusion: When using a cell culture model to study mechanisms of acquired resistance to gemcitabine in pancreatic cancer cells, it is important to identify a model system that best simulates the resistance observed in patients undergoing treatment. This work aims to identify the ideal dosing regimen for cultured cells in order to better understand the mechanisms of gemcitabine resistance in patients. This knowledge will help devise better strategies to overcome acquired drug resistance in pancreatic cancer cells as well as to improve patient outcomes.

S29

Amyotrophic Lateral Sclerosis Transgenic Mice With Altered Calcineurin (CaN) and Superoxide Dismutase (SOD1) Activities Showed Increased Zinc Activity Along Their Spinal Cord Segments

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Introduction: Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disease characterized by the selective loss of motor neurons. Although the molecular mechanisms of the onset of ALS are not well known, the presence of mutant (Cu/Zn) superoxide dismutase (SOD1) plaques, a decrease in calcineurin (CaN) enzyme activity, and the accumulation of cellular labile zinc (Zn) to toxic levels have all been observed along the spinal cord.

Hypothesis: These observations lead us to hypothesize that defective SOD1 and CaN interactions will lead to a labile zinc accumulation along the spinal cord of ALS subjects/patients in a region specific fashion.

Methods: We used G93A SOD1 transgenic mice as a model animal for ALS and utilized Western blot analysis, calcineurin cellular activity assay, SOD1 activity assay, and zinc analysis assay to test this hypothesis.

Results: We have found that the transgenic mice had an increase in SOD1 and a decrease in CaN enzyme activity as compared to the control mice, and that there were slight differences in the protein expression of these 2 proteins along the spinal cord sections in both the control and transgenic mice. The decrease in CaN activity was more pronounced in both the thoracic and lumbar regions; with statistical significance observed in the thoracic region (*t* test; $P=.008$). We also found an elevation of zinc activity in all regions of the spinal cords of the transgenic mice compared to those of the control. The most pronounced zinc elevation was observed in the lumbar region (<50% of control) which was statistically significant (*t* test; $P=.009$).

Conclusion: We conclude that mutant superoxide dismutase (SOD1) and calcineurin (CaN) do not interact efficiently and that this event leads to an elevation of zinc activity along the spinal cord in G93A mutant mice.

S30

Cadaveric Investigation Into the Innervation of the Long Head Triceps Brachii

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Introduction: The classic innervation to all 3 heads of the triceps brachii muscle is the radial nerve. Cases of axillary nerve injury have been associated with paralysis of the long head triceps (LHT) in addition to paralysis of the deltoid and teres minor muscles. A previous study of 20 cadaveric shoulders found that in 13 specimens the LHT was supplied by a branch of the axillary, not the radial nerve (Rezzouk et al). The LHT is an extensor of the arm and stabilizer of the glenohumoral joint. Understanding the correct nerve supply to LHT has significant osteopathic implications. Commonly used techniques in osteopathic medicine rely on intact neuromuscular circuitry. In tailoring the manipulation techniques for shoulder rehabilitation, it benefits the osteopathic physician to be aware that some of the patients may have this variation. When full arm extensor force is expected and is not obtained, for example, one must consider the LHT to have an axillary contribution. We studied the specific innervation pattern of the LHT with a focus on supply other than the classic radial.

Hypothesis: Differences in innervation of the LHT will direct the osteopathic physician toward spe-

cific diagnoses and treatment techniques.

Methods: 16 brachial plexuses in 8 embalmed cadavers were dissected through an anterior approach and an extensile dorsal approach (Hager et al) under 2.0× magnification. Photographs and nerve maps were created for 16 of the specimens. Distances from proximal LHT attachment to the point of neuromuscular insertion were measured with calipers.

Results: In 7 of the 16 shoulders dissected (44%), the LHT had exclusive supply by the radial, 9 of the 16 specimens (56%) presented with nerve patterns other than the classic, 6 of the 9 (66%) revealed dual innervation; axillary and radial, and 3 of the 9 (33%) demonstrated axillary supply only.

Conclusion: Anatomic sources teach that the radial nerve innervates LHT. In some clinical situations of axillary injury, unexpected triceps brachii dysfunction has been identified. This has led to investigations that revealed LHT innervation other than radial. Our investigation has confirmed previous findings of axillary contribution to LHT. Additionally, our study has revealed the presence of dual innervation of the LHT. The nerve supply to the LHT proves to be quite variable and complex carrying with it great relevance to current rehabilitation approaches to shoulder injury.

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S32

ATP Depletion by a Synthetic Protein: A Novel Strategy for Cancer Therapy

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Introduction: The use of chemotherapeutic agents that specifically target key metabolic processes in cancer cells is an important strategy for therapy. Cancer cells exhibit reduced mitochondrial activity and are known to largely depend on glycolysis for the generation of adenosine triphosphate (ATP). Although produced in relatively low amounts in cancerous cells, ATP is a vital energy carrier that is crucial for various biochemical reactions. Depletion of ATP using a novel, synthetic ATP-binding protein (DX) offers an unconventional but promising approach to interfere with the metabolism of cancer cells and compromise viability.

Hypothesis: DX, an artificial ATP-binding protein, will effectively chelate ATP and negatively impact the metabolism and viability of cancer cells thereby offering a new strategy for cancer therapy.

Methods: Cultured pancreatic adenocarcinoma BxPc3 cells were transfected with an expression vector containing DX (pZS::DX), whose expression was driven by a cytomegalovirus promoter. As a control for DX expression and cell transfection, BxPc3 cells were transfected with pZS::GFP (green fluorescent protein) and cultured under identical conditions. To assess the subcellular localization of DX, a construct expressing DX fused to GFP (pZS::GFP-DX) was similarly transfected and cultured in BxPc3 cells. The impact of DX on BxPc3 cell viability and morphology was assessed using a tetrazolium-based colorimetric cell viability assay and by both light and fluorescent microscopy.

Results: BxPc3 cells expressing DX experienced reduced cell viability and altered morphology compared to cells expressing GFP alone. These results suggest that ATP depletion, accomplished by DX, potentiate programmed cell death in BxPc3 cells. Cell death by apoptosis will be assessed by annexin V/propidium iodide staining of DX-transfected cells. In addition, fluorescence microscopy revealed that the DX-GFP fusion protein is primarily restricted to the cytoplasm of BxPc3 cells.

Conclusion: Our results indicate that the perceived depletion of ATP, mediated by an artificial ATP-binding protein, negatively affects the viability of pancreatic cancer cells. The reduction in available ATP pools, and the consequence of this on biochem-

ical pathways and cell viability requires further investigation. We suggest that synthetic proteins, such as DX, could be used to control and regulate specific targets in metabolic pathways and represents a new approach for cancer chemotherapy.

♦S33

Investigation of the Role of Carcinoma-Associated Fibroblasts in Tumor Angiogenesis

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Introduction: It is known that tumor growth is dependent on angiogenesis; however, tumor cells themselves cannot directly provide the support necessary for growth. It has become more evident that other cell types contribute to this process, namely tumor-associated fibroblasts and endothelial cells.

Hypothesis: We hypothesize that breast cancer enhances the formation of vascular networks via tumor-associated fibroblasts. It is our goal to elucidate the role of tumor-associated fibroblasts contribution to tumor angiogenesis.

Methods: Human dermal fibroblasts (HDFs), human umbilical vein endothelial cells (HUVECs), and MDA-MB-231 triple negative breast cancer cells were plated separately in cell culture flasks and expanded in their appropriate media conditions prior to culturing cell types together. Upon co-culturing of cells, we visualized formation of vascular networks by staining for endothelial cell marker CD31 and imaged using fluorescence microscopy. We also stained for fibronectin, an extracellular matrix protein produced by fibroblasts. Quantitative PCR was used to assess expression of pro-angiogenic factors after co-culture treatments.

Results: After co-culturing HUVECs with breast cancer cells, no vascular networks were formed. However, in the presence of fibroblasts significant vascular networks were present. Breast cancer cells, therefore, do not directly support angiogenesis but rather indirectly by activation of tumor-associated fibroblasts. Without tumor-associated fibroblasts, endothelial cells lack the support necessary to form vascular networks. Next, we looked at production of pro-angiogenic factors by tumor-associated fibroblasts. Fibroblasts significantly increased expression of fibronectin in the presence of breast cancer cells conditioned media. Furthermore, we quantitatively assessed these data and found a 3-fold increase in VEGF expression and nearly 2-fold increase in fibronectin. Thus, we concluded that breast cancer cells enhance production of pro-angiogenic factors by tumor-associated fibroblasts. Lastly, we assessed the effect of breast cancer cells on the formation of vascular networks. We co-cultured fibroblasts and endothelial cells only and also fibroblasts and endothelial cells in breast cancer conditioned media. Compared to the control, we found that breast cancer cells significantly enhance the formation of vascular networks.

Conclusion: We conclude that breast cancer does enhance angiogenesis in vitro via tumor-associated fibroblasts. Future studies will include using 3D models to more accurately recapitulate the tumor environment and to identify factors secreted by breast cancer cells that activate fibroblasts.

S35

Extrachromosomal Circular DNA in Parkinson Disease

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Introduction: Parkinson disease (PD) is the most prevalent age-linked neurodegenerative movement disorder worldwide with well-established pathology but poorly defined etiology and pathogenesis. Findings on self-mobilizing genomic DNA in our laboratory uses an approach which focuses on the identification of disease-specific extrachromo-

♦ Abstract that won first or second place in the 2013 SOMA Student Poster Competition.

somal circular DNA (eccDNA) patterns. Highly repetitive genomic patterns, such as the large tandem repeats encoding ribosomal DNA, are prone to eccDNA formation—especially in older organisms. Insufficient protection can therefore lead to genetic mosaicism, as well as partial aneuploidy, which could be the cause for degenerative diseases, including PD.

Hypothesis: We hypothesize that the pathogenesis of PD involves comprehensive disease-specific eccDNA patterns in affected human brain areas, which can be analyzed with microarray technology.

Methods: Nuclear and cytoplasmic eccDNA were isolated from cortical brain samples of 12 advanced-stage PD patients with high Lewy pathology and 12 matching controls (Mayo Clinic, Phoenix, Arizona) using established protocols. Nuclear and cytoplasmic eccDNA from PD and control samples were differentially labeled using distinct fluors and subsequently hybridized onto a customized oligonucleotide microarray (designed with Agilent eArray Web Application, https://earray.chem.agilent.com/earray/) containing many thousands of oligonucleotide elements of known genomic map location targeted towards exonic regions of genes associated with, or involved in pathways contributing towards Parkinson disease pathogenesis. The intensities of the fluors was detected at each spot by laser using the Agilent G2565CA Microarray Scanner and, after appropriate background correction, the total fluorescent intensity and the ratio of the fluors was calculated using Agilent Feature Extraction (FE) Software v10.1 and deposited into an Excel database for further statistical analysis.

Results: Our microarray data suggest that eccDNA formation is more active in healthy controls than in PD specimen. PD samples revealed a few distinct genomic "eccDNA hotspots," which were less prevalent in control samples.

Conclusion: Preliminary data analysis supports the hypothesis that PD involves disease-specific eccDNA patterns that can be analyzed with microarray technology. Whether these patterns are part of the molecular pathology of PD or contribute to its pathogenesis is now a matter for further investigation.

S36

NF-kB, Hero or Villain?

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Introduction: Cardiomyocyte injury is a complication that can occur with reperfusion therapy after a myocardial infarction (MI). The pathophysiology of ischemia-reperfusion (IR) injury is complex, however, and involves pro-apoptotic, anti-apoptotic, and necrotic pathways, ultimately resulting in cardiomyocyte death. The transcription factor nuclear factor kB (NFkB) has been implicated in the regulation of cardiomyoctyte inflammation, death, and survival. As expected, NFkB has emerged as a key biochemical target of IR injury. However, its precise role is a matter of intense debate. Recent studies have demonstrated that NFkB is cardioprotective during acute hypoxia and reperfusion, yet cardiotoxic during chronic hypoxia and reperfusion. Therefore, further delineating the role of NF-kB in IR injury is critical prior to investigating its therapeutic intervention for an MI.

Hypothesis: Inhibiting NFkB during reperfusion will increase IR-induced cell death by enhancing apoptosis of cardiomyocytes.

Methods: Murine HL-1 cardiomyocytes underwent 2 hours of simulated ischemia followed by 1 or 3 hours of simulated reperfusion in the presence of the NFkB inhibitors, QNZ, BAY-11-7082 (BAY), or vehicle control. Their effect on cell apoptosis and necrosis was assessed by measuring caspase 3 activity, or annexin V/propidium iodide (PI) staining by flow cytometry.

Results: Unexpectedly, both QNZ and BAY decreased IR-induced apoptosis, as evidenced by a significant reduction in IR-induced caspase 3 activity

(for both) and annexin V staining (for QNZ). However, this did not lead to cardioprotection, because both inhibitors increased IR-induced cell necrosis, as evidenced by a significant increase in IR-induced annexin V/PI staining.

Conclusion: NFkB has a multitude of downstream targets that can affect various cell survival pathways making its role in IR-injury very complex. Here we demonstrate that NFkB is instrumental in preventing IR-induced necrosis, but can contribute to IR-induced apoptosis. Hence, it appears to have a dual role in IR-injury, being both cardioprotective and cardiotoxic. This suggests that NFkB inhibitors may not be good therapeutic options for an MI.

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S37

Potential Alzheimer Disease Treatment Drugs That Modulate the Calpain-Mediated ER Stress/Autophagy Pathway in *Caenorhabditis elegans*

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Introduction: Alzheimer disease (AD) leads to dementia that shows deficits in cognitive functions due to pathological aggregations of β-amyloid (Aβ) and tau proteins. Aβ is processed from an amyloid precursor protein (APP) and when these proteins are not removed, Aβ aggregates begin to develop. A mechanism to remove such toxic proteins involves pathways for ER stress response and autophagy. The processes are regulated in part by calcium channels and the cysteine protease, calpain.

Hypothesis: The aim of the present study is to analyze the role of the calpain-mediated ER stress/autophagy pathway by observing the effects of Aβ toxicity on phenotypic parameters seen in the nematode, *Caenorhabditis elegans*. The hypothesis of this project is that there is a phenotypic difference between AD strain and wild-type *C elegans*.

Methods: Standard phenotypic analysis was used to test for reproduction, morphology, locomotion, and behavioral abnormalities in the AD transgenic strain and wild-type *C elegans*. An automated imaging analysis was performed using Multi-Worm Tracker (MWT) to compare and assess for motor activities during different stages of their life cycle.

Results: Phenotypic analysis indicates that the AD strain shows a toxicity of Aβ in hatchability. Morphological abnormalities were not observed. Automated imaging analysis showed that AD-induced *C elegans* logged a slower average speed than the wild-type worms. The results are consistent with the observation that the AD patients with dementia tend to show deficits in physical activities, including frequent falls. The phenotype and speed characterization may be useful to assess suppressor activities of the drugs.

Conclusion: In this study, the Aβ-induced deficits were observed in the *C elegans* model of AD. The buildup of Aβ resulted in less hatchability and slower average speed, suggesting that overexpression of Aβ in neurons indeed causes protein toxicity. Thus, the focus of this ongoing study is whether or not inducing the autophagy pathway can clear up Aβ-toxicity seen in the AD strain. Future experiments aim to shed light on the relationship between AD drugs and potential Aβ clearance via the proposed calpain-mediated autophagy pathway. This study will enhance future treatments by showing the effectiveness of current FDA-approved AD treatment interventions that stimulate autophagy and alleviate the Aβ buildup seen in AD patients.

S38

Development of a Rapid Flow Cytometric Assay to Quantitate Human Astrovirus Particles

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Introduction: Viral pathogens are believed to cause up to 80% of all infectious gastroenteritis cases worldwide, yet many of these agents are difficult to study. One such virus, human astrovirus, is a common but understudied cause of childhood diarrhea and vomiting, and very little is known about astrovirus pathogenesis or replication. Astroviruses have a unique replication step: capsid protein requires cleavage by trypsin for full activation. In the absence of trypsin, new astrovirus particles are un-infectious, meaning that a single replication cycle occurs in vitro and no plaques are formed. Since plaque-forming assays are the traditional method used to quantitate viruses, astroviruses have been quantified using a variety of other methods of variable efficacy, including ELISA, PCR, and immunofluorescence. Considering that a rapid and accurate method was lacking, we sought to develop an improved assay to quantify infectious astrovirus particles.

Hypothesis: We hypothesized that, because of the unique astrovirus replication strategy, flow cytometry could be effectively used to rapidly quantify infectious astrovirus from in vitro samples.

Methods: Human gastrointestinal CaCo-2 cells were infected with trypsin-activated human astrovirus-1, fixed and stained with an anti–astrovirus-capsid antibody to detect viral capsid protein. After staining with anti-mouse-488 cells were then analyzed by flow cytometry. To validate flow cytometry data, cells were similarly stained with anti-capsid antibody for immunofluorescence, costained with DAPI to stain nuclei, and visualized by fluorescent microscopy.

Results: Peak expression of astrovirus capsid protein, as monitored by both flow cytometry and immunofluorescence, was seen at 24 hours postinfection. No increase in the percentage of infected cells was seen at 48 hours postinfection, supporting the notion of the unique single-cycle replication strategy of astrovirus. Overall, calculated viral titers from flow cytometry data were nearly identical to immunofluorescence data, validating this method.

Conclusions: Our data demonstrate that flow cytometry is readily applicable for quantifying infectious astrovirus, and is superior to immunofluorescence in speed as well as accuracy, since there is no user bias during cell counting. These improvements in methodologies will facilitate our ability to study the pathogenic mechanisms employed by these viral agents.

S40

Block of the Cardiac Potassium Channel HERG by Extracellular Divalent Cations and Hydrogen

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Introduction: The human ether a-go-go related gene (HERG) encodes a cardiac potassium channel that is important in the repolarization of the action potential. A reduction in the number of HERG channels has been implicated in long QT syndrome, which in some cases can degenerate into the lethal arrhythmia Torsades de Pointes. Many patients present with abnormal serum electrolyte levels due to a variety of conditions including gastrointestinal dysfunction, renal and endocrine disorders, diuretic use, alcoholism, and aging. Changes in extracellular divalent cations and extracellular pH have been shown to reduce HERG channel function by a variety of mechanisms.

Hypothesis: The hypothesis of this project is that extracellular H^+ and extracellular cations block the pore of the HERG channel by acting at the same or closely related binding site.

Methods: Experiments were performed using 2-electrode voltage clamping of Xenopus oocytes expressing either wild-type HERG, WT ELK (ether-a-go-go-like K^+ channel) or the HERG mutants S631A, or G628CS631C. S631 is thought to be located in the outer pore of the HERG channel. cRNA was injected into enzymatically defolliculated oocytes and currents recorded 1-5 days after injection.
Results: Changing extracellular potassium from 0 mM to 20 mM resulted in a greater decrease in WT HERG current due to an increase in either extracellular hydrogen, calcium, magnesium, cobalt, or manganese. There was no difference in block of the HERG mutant S631A by calcium compared to WT HERG, whereas there was less block of the HERG double mutant G628CS631C by calcium compared to WT HERG. The related potassium channel, ELK, showed significantly less block by calcium compared to WT HERG.
Conclusion: Although the mechanism by which extracellular divalence and pH reduce current through HERG channels is not clear, one plausible explanation is pore block. The dependence of block on the permeant ion (potassium) for all extracellular cations tested, points to the possibility of a single extracellular binding site located near the outer pore of the HERG channel. The lack of block seen with the closely related potassium channel ELK suggests that this extracellular blocking site may be unique to HERG. This study has implications for an increased risk of cardiac arrhythmias in patients with hypokalemia.

S41

Neural Circuitry of Thermosensation and Its Circadian Regulation in *Drosophila*

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Introduction: Temperature sensation and circadian regulation are necessary for animals to adapt to changing environments. In order to maintain essential functions such as proper development, metabolism, and the sleep-wake cycle, animals must have mechanisms to maintain homeostasis. Previous research has established the importance of transient receptor potential (TRP) channels in thermosensation, but the neural circuitry of thermosensation and temperature preference behavior is unknown. Our experiments focused on studying the internal anterior cell (AC) neurons due to their anatomical position with peripheral thermosensory neurons. The AC neurons, which express the TRPA1 channel, are responsible for warmth detection and the regulation of temperature preference behavior. The PYX channel, found in the *Drosophila* antennae, was examined due to its known involvement in thermotolerance. In addition to its thermosensory role, the AC neuron also projects onto circadian clock cells in the *Drosophila* brain. Similar to the necessity of adapting to different temperatures, animals utilize the circadian clock to adapt to changing day-night cycles. Homologous to the circadian-regulated body temperature rhythms (BTR) in mammals, ectotherms have temperature preference rhythms (TPR) that enable them to choose different preferred temperatures as the day progresses.
Hypothesis: If TRP and PYX channels expressed in *Drosophila* neurons are involved in thermosensation, then they may also be involved in circadian regulation of TPR.
Methods: A Ca^{2+}-indicator was utilized in staining the AC neuron. TPR assays were performed on an

18-32°C aluminum gradient for 30 minutes, and the average preferred temperatures were calculated.

Results: Peaks in fluorescence were noted at both ~25°C via TRPA1 and ~27°C via PYX. When comparing the TPR of TrpA1-dsRNA (TrpA1 knockdown) to wild-type control flies, an abnormal temperature change was noted during the dawn time zone in the TrpA1-dsRNA flies.

Conclusion: The staining suggests that AC neurons utilize both internal TRPA1 as well as PYX for thermosensation. The experimentation therefore demonstrated the integration of TRPA1 and PYX in warmth detection. The results of the TPR assays indicate that TRPA1 in the AC neuron may influence TPR in *Drosophila*. Our research will facilitate a better understanding of the mechanisms of sleep disorders, determining ideal environmental temperatures for neonatal neurological development, and investigating a connection between BTR and the sleep-wake cycle.

S42

Investigation of the Role of Transforming Growth Factor β in Satellite Activation and Differentiation in Vitro

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Introduction: Adult skeletal muscle can regenerate physiological function after injury to a limited degree. This process in vivo is known to involve inflammatory cells, fibroblasts, and satellite cells. The niche of satellite cells that differentiate into new myoblasts in response to injury is the key to understanding how to optimize muscular repair. TGFβ is released during muscular damage by neutrophils, but the effect on satellite cells is not well understood. Previous studies on the contribution of TGFβ to repair have suggested that it does not have a favorable role on muscle fibers in vivo.

Hypothesis: Our hypothesis is that TGFβ inhibits differentiation of satellite cells into mature myofibers, but does not have a major effect on their proliferation.

Methods: Individual muscle fibers were harvested from tibialis anterior of 3 month old BalbC mice. Isolated myofibers were cultured on glass cover slips coated with Matrigel in 24 well culture plates for 6 days in a proliferation medium, followed by 6 days in differentiation medium. TGFβ-1 was added to differentiation media at 3 concentrations. Cultures were fixed at 12 days and stained with Toluidine blue or immunostained for myoD and myogenin. Coverslips were mounted on slides, viewed under brightfield, and images acquired using a digital camera. Cells were classified according to morphological criteria as either early (myoblasts and early myofibers) or late (single nucleus myofibers and multinucleated myofiber) and the number of cells in each classification was expressed as a percentage of the total number of cells. At least 4 fields per group (control, 3 TGFβ concentrations) for a total of at least 100 cells were evaluated. Significant differences were determined using a 2-way fixed model ANOVA.

Results: Exposure of the cultures to TGFβ resulted in an increased percentage of early muscle cells types and a decreased percentage of late muscle cell types. Increased dosage of TGFβ was correlated with an increased effect. Significant differences ($P<.05$) were observed between control cultures and all TGFβ groups; additionally significant differences were observed among all TGFβ groups.

Conclusion: The addition of TGFβ to muscle precursor cells in vitro resulted in an increased number of myoblasts and early muscle fibers indicating a role for TGFβ in a maintaining muscle precursor cells in an undifferentiated state.

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S43

Astrocyte ALDH1L1 and GFAP Expression in the Brainstems of Young and Aged Mice

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Introduction: Astrocytes, once thought to be mere supportive cells, play a dominant role in aging and associated neurodegeneration, as well as in injury and neuroinflammation. Previous studies have shown astrocyte numbers to be reduced in the hippocampus of aged rodents, a region responsible for memory. Dysmorphic astrocytes have been viewed in several regions of the cerebral cortex of aged mice, and there are indications that theses astrocytes may no longer be neuroprotective but may be neurotoxic. The brainstem region, specifically the pons and midbrain region, was chosen for investigation due to its involvement with critical functions such as swallowing, vision, hearing, motor control, and the sleep/wake cycle—functions that deteriorate with normal aging. Two proteins were examined: GFAP, the traditional marker for astrocytes, and ALDH1L1, recently identified in cortical astrocytes. Evidence suggests that GFAP may only label a subpopulation of astrocytes and is expressed in other CNS cell types. ALDH1L1 has been proposed as a more specific astrocyte marker. However, its distribution in the brainstem has not yet been examined.

Hypothesis: We propose that a difference in astrocyte number as detected by ALDH1L1 and GFAP would be observed in the brainstems between young and aged mice.

Methods: Total protein was extracted from the midbrain-pons region of 3-month-old mice using standard protocols. Proteins were separated by SDS PAGE and transferred to nitrocellulose membranes for western blot analysis. Membranes were probed with the following antibodies: anti-GFAP (Encor Biotechnology Inc), anti-ALDH1L1 (Neuromab) and monoclonal G3PDH (Millipore). Band intensities were analyzed using Kodak Molecular Imaging software; GFAP and ALDH1L1 values were normalized to G3PDH to control between group variability.

Results: There was a trend ($P = .0596$) toward a significantly increased expression of GFAP compared to ALDH1L1 in the midbrain-pons from old animals, but no significant difference was observed in young animals. No significant differences were observed in ALDH1L1 or GFAP expression between old and young midbrain-pons.

Conclusion: The lack of any significant change between young and aged in the expression of either ALDH1L1 or GFAP suggests that astrocytes may not have a role in aging in the mouse brainstem. ALDH1H1 was expressed in the midbrain-pons region of both young and aged mice, but the results of this study do not support its use as a more sensitive marker than GFAP.

S46

Insulin Does Not Reduce Susceptibility to Ischemia-induced Ventricular Fibrillation in Isolated Rat Hearts

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Introduction: Acute GIK (glucose, insulin, potassium) therapy following an episode of cardiac ischemia has been shown to lead to fewer arrhythmias and decreased damage from ischemia-reperfusion injury. In recent years, there has been a renewed interest in the mechanisms of this protection in the search for safe antiarrhythmic drugs. While the administration of potassium has been demonstrated to reduce the prevalence of arrhythmias during episodes of cardiac ischemia, the effect of insulin has not been thoroughly investigated. While insulin can increase glycolytic flux, it can also prevent glycogen breakdown, potentially 2 antagonizing effects

on myocardial ATP supply during ischemia. This is of relevance since ATP depletion is proposed to be the source of the electrophysiological disturbances in myocardial ischemia that create a substrate for arrhythmias. In the present research, we examined whether administration of high or low concentrations of insulin prior to and during regional ischemia in isolated rat hearts reduced susceptibility to ischemia-induced ventricular fibrillation (VF).

Hypothesis: It was hypothesized that insulin would protect against VF by increasing glycolytic ATP generation during ischemia.

Methods: Isolated rat hearts were perfused in the Langendorff mode at 37°C with modified Krebs solution containing vehicle, 0.1 U/L insulin, or 10 U/L insulin (n=12/group). After 20 minutes, regional ischemia was induced by occlusion of the left main coronary artery and maintained for 30 minutes. The incidence of VF during a 30 minute period of myocardial ischemia was determined from the ECG. An intraventricular balloon was used to record left ventricular developed pressure (LVDP).

Results: At the onset of ischemia, hearts perfused with the high dose insulin had greater mean LVDP than controls, indicating an increased contractility in the presence of insulin. However, neither high nor low dose insulin supplementation reduced the incidence of VF compared to control (VF incidences were 75%, 83%, 83% in controls, low and high dose insulin, respectively). Similarly, insulin did not delay the occurrence of VF, with mean onset times of 863±64, 846±74, and 1021±97 seconds (P=NS) in controls, low and high dose insulin, respectively.

Conclusion: Insulin did not reduce susceptibility to VF in isolated rat hearts. This suggests that the reduction in arrhythmias observed clinically with GIK therapy is unrelated to the presence of insulin.

S49

Development of a Rapid Flow Cytometry Assay to Examine Cell Adherence of the Gastrointestinal Pathogen *Plesiomonas shigelloides*

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Introduction: *Plesiomonas shigelloides* are Gram negative, rod shaped bacteria that can cause gastroenteritis as well as various extraintestinal infections, and are of particular concern in immune compromised individuals. Although some potential virulence factors of *P shigelloides* have been recognized, mechanisms of pathogenesis by this organism are largely uncharacterized to date. The overall goal of the laboratory is to identify and characterize virulence factors of *P shigelloides*. One important virulence mechanism used by most gastrointestinal bacterial pathogens allows adherence to the intestinal lumen. *P shigelloides* is known to adhere and invade human cells, but the mechanism is not well understood. The goal of this project is to develop a rapid assay to test adherence of *P shigelloides* to human cells.

Hypothesis: We hypothesize that the adherence mechanisms of *P shigelloides* can be studied using a flow cytometry-based adherence assay.

Methods: The human gastrointestinal cell line, Caco-2 (ATCC), was infected for various times with green fluorescent labeled–*P shigelloides* bacterial cells (BacLight green; Invitrogen). Cultures were then analyzed using flow cytometry to determine the degree of bacterial adherence. This flow cytometry adherence assay was also performed on various pathogenic bacteria including *Staphylococcus epidermidis*, *Listeria monocytogenes*, *Serratia marcescens*, *Escherichia coli*, and *Aeromonas hydrophila* (ATCC). We further tested this flow cytometry assay

using other gastrointestinal cell lines (HT-29 and T84) in addition to HeLa cells in order to compare the adherence characteristics of other pathogens with those of *P shigelloides*.

Results: Each bacterial strain stained successfully with the BacLight Green stain and demonstrated various kinetics of adherence to all cell lines tested. The use of flow cytometry demonstrated rapid, sensitive, and consistent *P shigelloides* adherence to various cell lines and adherence was similar to other known gastrointestinal pathogens.

Conclusion: The protocol developed from this project detected consistent *P shigelloides* adherence to multiple human cell lines. This successfully optimized flow cytometry-based adherence assay to be implemented to investigate cell adherence and other virulence factors of *P shigelloides*.

S50

Effects of Lipopolysaccharide on the Calcium Pump in BV-2 Microglial Cells

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Introduction: Microglia are the major immune cells of the central nervous system (CNS). Stimulation of microglial cells leads to activation of pro-inflammatory pathways, producing cytokines and reactive oxygen species. The resultant oxidative stress can damage critical proteins. The plasma membrane calcium-ATPase (PMCA) is a Ca^{2+} pump that maintains Ca^{2+} homeostasis, critical for cell survival. We have previously shown that PMCA is very sensitive to oxidative stress. The goal of this study was to determine the effects of LPS on PMCA in microglial cells. Loss of PMCA function would cause Ca^{2+} overload and subsequent cell death thus exacerbating the neurotoxic milieu in the CNS. Our studies are pertinent to the pathogenesis of diseases such as Alzheimer and Parkinson.

Hypothesis: We hypothesize that increasing concentrations of LPS in BV-2 cells will inhibit PMCA activity.

Methods: BV-2 cells were cultured using DMEM and 10% fetal bovine serum. The cells were stimulated with LPS at the following range of concentrations: 1 pg/mL to 1 µg/mL. Total protein in cell lysate was measured by bicinchoninic acid assay. PMCA activity was assessed by measuring inorganic phosphate released upon Ca^{2+}-dependent ATP hydrolysis by the Malachite Green method. PMCA protein levels were measured by immunoblots using PMCA primary antibodies and HRP-conjugated secondary antibodies.

Results: Exposure of BV-2 cells to LPS caused morphological changes indicative of toxicity at concentrations 100 pg/mL and above. Cells appeared to be rounded off. Measurement of PMCA activity showed ~40% increase at 1 pg/mL compared to control. Further increase in LPS caused a dose-dependent decline in activity. At 100 ng/mL LPS there was ~50% reduction in PMCA activity (n=3). Immunoblot analysis indicated an increase in PMCA protein levels at all LPS concentrations. The greatest increase in protein levels (~40%) was observed at 100 pg/mL, after which the effect plateaued off (n=5). Currently, we are measuring PMCA mRNA levels to determine if the increase is via transcription. We are also monitoring the effects of LPS on intracellular Ca^{2+} levels.

Conclusion: Our results indicate that LPS has a biphasic effect on PMCA activity. Low doses stimulate activity presumably to counteract LPS-mediated increase in intracellular Ca^{2+} whereas higher doses are inhibitory, possibly due to oxidative inactivation of PMCA. In contrast, PMCA protein levels increased to compensate for the loss of activity.

S51

Novel Drug to Inhibit Podoplanin Mediated Tumor Cell Migration

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Introduction: Oral cancer will kill an estimated 8000 people this year in the United States, and many more in other countries. Oral cancer can affect the salivary glands, tongue, gums, and lymph nodes. Unfortunately, current therapies are inadequately effective to treat oral cancer, and surgery is often required. However, surgical removal of oral cancer tissue can lead to severe disfigurement of the face, head, and neck. Patients can suffer long term effects of surgery including eating and speech problems. Over 90% of oral cancers are caused by oral squamous cell carcinoma (OSCC). We are developing reagents to specifically target OSCC cells to more effectively prevent and treat oral cancer. Most malignant OSCC cells express robust levels of the podoplanin (PDPN) transmembrane receptor protein. PDPN is a functionally relevant biomarker and potential chemotherapeutic target for oral cancer. For example, about 100% of postoperative patients with tumors that express low levels of PDPN remain cancer free for 5 years, while less than 40% of patients with tumors expressing high levels of PDPN remain cancer free for 5 years. PDPN interacts with members of the cytoskeletal complex to promote tumor cell invasion and metastasis. We have found that Maackia amurensis seed lectin (MASL) can target PDPN to inhibit tumor cell growth and migration. However, the dynamics of how MASL works has not been elucidated.

Hypothesis: We hypothesize that MASL is internalized into cells after binding to PDPN.

Methods: We utilized live cell imaging and fluorescent microscopy to examine trafficking of fluorescently labeled MASL into human OSCC cells.

Results: We report that MASL localizes to the cell membrane, and is subsequently internalized into the cytoplasm in pharmacologically relevant time periods. In addition, tumor cells treated with MASL show a decrease in migration compared to nontreated cells.

Conclusion: These results indicate that MASL associates with PDPN and enters the cytoplasm to suppress tumor cell motility. These studies provide insight into mechanisms of action by which MASL may be used as a targeted therapy to prevent and treat oral cancer.

S52

Hormonal Influence on Hyperostosis Frontalis Interna Based on Organ Histopathology

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Introduction: Hyperostosis frontalis interna (HFI) is characterized by lumpy growths of bone on the inner surface of the frontal bone that form in poorly organized layers that histologically and macroscopically differ from other neurocranial thickenings like Paget disease. It is extremely common in postmenopausal women (80%) and rare in men. The etiology behind these overgrowths, however, is unknown and uncommonly studied, though the demographic distribution would suggest a hormone-mediated origin. Though medical records are not accessible for the cadaver population of medical schools because of privacy laws, the opportunity to partially interpret medical history from histopathology can allow a limited opportunity to formulate an etiology for HFI. Unlike archaeological specimens in which HFI

is most commonly observed, cadavers retain the soft tissues that can be sampled for histopathology. And unlike living patients in which broad sampling of tissues would be too invasive, cadavers offer much broader access to tissues that one would never sample in the living, even in biopsy.

Hypothesis: The study was conducted to verify our theory that estradiol, a hormone found in both men and women, is linked to the formation of HFI.

Methods: Cadavers from the anatomy laboratory of New York Institute of Technology College of Osteopathic Medicine were examined for the presence of HFI. Samples of their livers, gonads, and pituitaries were collected as well and microscopically examined for the presence of abnormalities, particularly of estrogenic origin.

Results: The population of cadavers with HFI was significant (68.9%). Of these cadavers, a significantly greater amount were females (74.2%). 83.3% of males with HFI also had testicular atrophy and decreased Leydig cells, indicating decreased estradiol. Bile stasis was present in 86.4% of cadavers without HFI, indicating a lack of cholestasis present in those with HFI. One cadaver with HFI also had a liver sample that presented with a metastasis of endocrinological origin.

Conclusion: HFI does seem to be linked to a decrease in a base level of estradiol.

S53

ATP Depletion in Breast Cancer Cells: A New Approach to Cancer Therapy

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Introduction: The use of chemotherapeutic agents that target key metabolic processes in cancer cells is an important strategy for therapy. As a result of reduced mitochondrial activity, adenine triphosphate (ATP) is produced mainly by glycolysis and lactic acid fermentation in the cytosol of cancer cells, a phenomenon known as the Warburg effect. Even with reduced production, ATP is still a vital energy carrier that is crucial for various biochemical reactions in cancerous cells. Thus, interfering with the production or availability of ATP offers a new approach to cancer therapy. To assess this idea, a synthetic ATP-binding protein, DX, which binds ATP by a mechanism of protein-mediated ligand sequestration, was tested as a novel cancer therapy.

Hypothesis: Reduced ATP availability, due to the expression of DX in breast cancer cells, will negatively affect cellular metabolism and viability.

Methods: Cultured mammary gland/breast adenocarcinoma MDA-MB 231 cells were transfected with an expression vector containing DX (pZS::DX), whose expression was driven by the cytomegalovirus promoter. As a control for cell transfection and DX expression, MDA-MB 231 cells were transfected with pZS::GFP (green fluorescent protein) and cultured under identical conditions. To determine the subcellular localization of DX, a construct expressing DX fused to GFP (pZS::GFP-DX) was similarly transfected and cultured in MDA-MB 231 cells. The impact of DX protein expression on MDA-MB 231 cell viability and morphology was assessed using a tetrazolium-based colorimetric cell viability assay and by both light and fluorescent microscopy.

Results: MDA-MB 231cells expressing DX experienced reduced cell viability and altered morphology compared to cells expressing GFP alone. These results suggest that ATP depletion, accomplished by DX, potentiate cell death in MDA-MB 231 cells. Fluorescence microscopy revealed that the DX-GFP fusion protein is primarily restricted to the cytoplasm of MDA-MB 231 cells.

Conclusion: Our results indicate that reduced intracellular ATP levels, mediated by a synthetic ATP-binding protein, negatively affects the viability of breast cancer cells. The reduction in available ATP, and the consequence of this on biochemical pathways and cell viability requires further investigation. We suggest that artificial proteins, such as DX, could be used to control and regulate specific

targets in metabolic pathways and represents a new approach for cancer chemotherapy.

S54

Appalachian Misconceptions About the Relationships Between Health and Health Behaviors

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Introduction: Appalachia ranks among the worst in overall health and disease prevention behaviors. Previous studies have shown that Appalachian adults' health perception is incongruent with their actual health status.

Hypothesis: Our hypothesis was to show that rural Appalachian adults' perception of health is directly correlated with their participation in disease prevention behaviors.

Methods: Rural Appalachian adults (n=437) were surveyed regarding their perceived health and their disease prevention behaviors. Disease prevention behaviors were defined as habits that have been shown as preventive against disease or to be consistent with a healthy lifestyle. Healthy disease prevention behaviors included: moderate physical activity (≥91 min/wk), vigorous physical activity (≥46 min/wk), sugar drink intake (≤1/day), smoking (non-smoker), alcohol intake (≤1 drink/day), blood pressure (≤120/80), and fast food intake (≤1 time/wk). Participants were divided into groups based on self-reported levels of overall health (healthy=health rating ≥5 on a 0-10 scale), healthy body weight (healthy=yes), and blood pressure (healthy=not high). Jaccard Binary and Russel and Rao Dichotomy Coefficients were used to determine associations between health perception and disease prevention behaviors. A *t* test was used to determine differences in the number of disease prevention behaviors between groups.

Results: People who reported being healthy also reported having a healthy body weight (r=0.555), a healthy sugar drink intake (r=0.552), a healthy alcohol intake (r=0.742), a healthy fast food intake (r=0.481), and not smoking (r=0.704). The average number of disease prevention behaviors exhibited by those who considered themselves healthy was significantly higher than those who didn't consider themselves healthy (Good Health Perception: 2.841±1.123, Poor Health Perception: 2.192±1.079; P=.000).

Conclusions: These data suggest that behaviors such as smoking and drinking are regarded by Appalachians as important for one's overall health while other behaviors such as physical activity and maintaining a low blood pressure are not. This could explain why Appalachians perceive themselves as healthy when they actually are unhealthy. These data show potential for bettering the health of Appalachians through education programs focused on behaviors such as physical activity and blood pressure. These data also challenge the misconception that Appalachians do not care about their health.

S55

Salmonella Typhimurium Induced Gastroenteritis: Does Epithelial Cell Heat Shock Protein 70 Have a Protective Role?

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Introduction: *Salmonella* Typhimurium (*Salmonella*) is an enteric pathogen that affects the gastrointestinal health of individuals globally. *Salmonella* causes gastroenteritis by adhering to and invading the lining epithelial cells of the gastrointestinal tract (GI). While *Salmonella* infection is typically treated with antibiotics, there is a need to explore and exploit the innate immune response to minimize the production of antibiotic-resistant bacteria. Heat shock protein 70 (Hsp70), a protein normally

expressed under stressed conditions, may offer protection as an innate host defense mechanism against *Salmonella* infection.

Hypothesis: We tested the hypothesis that Hsp70 would protect against *Salmonella*-induced gastroenteritis using a murine model of infection.

Methods: Three mouse lines were used in this study: C57BL/6 wild type mice (WT), Hsp70 transgenic mice (TG) and in house wild type TG littermates (IWT). Each mouse was pretreated with streptomycin (20 mg) 24 hours prior to oral gavage with 106-108 colony forming units (CFUs) of *Salmonella*. *Salmonella* invasion of Peyer patches (PP), mesenteric lymph nodes (MLN), spleen, and blood were measured. Cecal changes were characterized.

Results: WT/IWT mice who underwent a 48 hour infection showed a dose dependent *Salmonella*-induced decrease in cecal weight and length ($P=.008$, $P<.0001$). However, TG mice demonstrated less of a decrease in the cecum weight compared to the WT/IWT mice ($P=.002$). A time dependent change in cecal weight and length was observed at 24 and 48 hours in TG/IWT ($P<.05$, $P<.05$). *Salmonella* detection in PP at 24 and 48 hours was significantly less in the TG compared to the IWT ($P=.012$, $P=.009$). *Salmonella* infection of MLN and spleen was comparable in all groups ($P=.355$, $P=.229$).

Conclusion: Cecal changes in size and weight are hallmarks of *Salmonella* infection. Heavier cecal weights detected in TG mice suggests less of a *Salmonella* infection when compared to WT/IWT. Reduced *Salmonella* infection in the PP supports Hsp70 mediated protection against invasion. These findings suggest a role for innate production of Hsp70 within the GI as a means to minimize *Salmonella* infection, the mechanism of which warrants exploration.

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S56

Thyroid Hormone Replacement Therapy May Reduce Atrial Fibrillation/Flutter Inducibility in a Rat Model of Myocardial Infarction/Heart Failure

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Introduction: Heart failure (HF) is associated with increased atrial fibrillation (AF) risk. Accumulating evidence suggests the presence of low myocardial T3 in various cardiac diseases and this may contribute to HF development. There is also evidence that thyroid hormone (TH) replacement therapy can improve left ventricular function in HF. However, hyperthyroidism may lead to increased atrial arrhythmogenesis and possible overdosing is a common fear. Recent data from our group clearly demonstrated that hypothyroidism also leads to increased AF inducibility.

Hypothesis: Thyroid hormone replacement therapy in heart failure may reduce, rather than increase atrial fibrillation risk.

Methods: Myocardial infarction (MI) was produced in rats by ligation of the left anterior descending coronary artery. Rats with large MI (≥40% of left ventricular circumference by echocardiography) were randomized into L-thyroxine (T4, n=10) and placebo (n=11) groups 2 weeks after surgery. Rats received 3.3 mg T4 (in 60-day release form) or placebo pellets for 2 months. Echocardiography, in vivo cardiac electrophysiology and AF inducibility test (with transvenous cardiac catheter approach) were performed at the end of the study.

Results: Compared with placebo, T4 treatment decreased left ventricular internal diameters as well as left atrial diameter. T4 treatment showed a tendency of reduced atrial effective refractory period (37±4 ms vs 32±7 ms, $P=.067$) and atrial tachyarrhyth-

mia inducibility. AF/Flutter was inducible in 8/11 rats in placebo vs 3/10 rats in T4 group (P=.086).

Conclusion: Our preliminary data indicate that TH replacement therapy in HF may reduce atrial arrhythmia inducibility in a rat MI/HF model. This is in contrast to the common concern of increased atrial arrhythmia propensity. Thus, our results may have important clinical implications in applying TH replacement therapy in HF.

♦S58

Multidisciplinary Approach to Characterizing Cardiac Function in Aging BALB/c Mice

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Introduction: Aging is a complex process that affects the body from the molecular to gross level. Before using BALB/c mice as a study model, it is important to identify baseline processes of aging to differentiate the pathologic from the physiologic. Studies involving myocardial infarction generally use younger animals, and pathological changes that occur with aging might affect outcomes. Therefore, this study aims to understand the physiologic changes aging induces on cardiac function as part of an ongoing study of the aging process in BALB/c mice.

Hypothesis: Older BALB/c mice will exhibit decreased ejection fraction (EF), fractional shortening (FS), and heart weight to body weight ratio (HW/BW) and increased posterior wall thickening (PWT) and left ventricular mass (LVM) when compared with younger BALB/c mice, with males having proportionally higher values than females.

Methods: Old (13-16 months) and young (2-4 months) male and female mice were studied. Cardiac function was assessed by echocardiography. Mice were anesthetized with 60 mg/kg pentobarbital and heart rate and oxygen saturation were monitored. A 15-6L linear ultrasound transducer was used with a SONOS 5500 Ultrasound machine. A parasternal short axis view of the left ventricle was identified in 2-D mode and measured using M-mode. Measurements were taken during diastole and systole and used to assess left ventricular function. Cardiac remodeling was determined by evaluating the collagen content of the heart from young, old, and an older group of mice (17-20 months) by Mason-Trichrome staining.

Results: Old males exhibited greater LVM than young males (0.17±0.01 g vs 0.12±0.01 g, P<.02) and old females (0.17±0.01 g vs 0.11±0.01 g, P<.01). Old males exhibited greater HW/BW than old females (5.88±0.14 mg/kg vs 5.18±0.13 mg/kg, P<.01). Young females exhibited greater HW/BW than old females (7.52±.87 mg/kg vs 5.18±.13 mg/kg, P<.02). PWT is greater in young females (66.81±11.04%) than young males (33.01±7.97%, P=.05) and old females (34.8±7.81%, P=.05). Preliminary data suggest that there may be an increase in the collagen content of the hearts from young to old mice.

Conclusion: Old males exhibited greater LVM than young males and old females and greater HW/BW than old females. Young females exhibited greater HW/BW than old females. PWT was greater in young females than young males and old females.

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♦ Abstract that won first or second place in the 2013 SOMA Student Poster Competition.

S61

Selective Targeting the EP2 and EP4 Signaling Pathways May Provide a Strategy for Chemotherapy of COX-2-Positive Colon Cancers

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Introduction: Poor prognosis in various human carcinomas correlates with the extent of prostaglandin E2 (PGE2) production. Experimental and clinical evidence shows that cyclooxygenase-2 (COX-2) activity and increased levels of PGE2 can contribute colorectal tumorigenesis. These findings provide the rationale for the use of COX-2 inhibitors for chemotherapy. However, therapeutic utility of COX-2 inhibitors is limited due to the side effects. However, selective inhibition of PGE2 effects via pharmacologic targeting of PGE2 receptor(s) may augment anti-cancer chemotherapies. PGE2 signaling through EP2 and EP4 receptors stimulate tumor growth by suppressing apoptosis. Thus, antagonists of the EP receptors may represent an alternative therapeutic approach to cancer treatment.

Hypothesis: We hypothesized that targeting E2 and EP4 receptors with their selective antagonists may potentiate induction of the intrinsic and extrinsic apoptosis in tumor cells.

Methods: To test our experimental hypothesis we used COX-2-positive HCA-7 human carcinoma cells which have been established from primary human colorectal adenocarcinoma. When cells were analyzed in our laboratory, HCA-7 cells strongly expressed COX-2 protein and secreted significant amounts of PGE2. The extrinsic apoptosis was induced by treating HCA-7 cells with tumor necrosis factor (TNF) whereas the intrinsic apoptotic pathway was activated by an exposure to ultraviolet light (UV). Induction of apoptosis in carcinoma cells was assessed by using a CellTiter 96 AQ Assay and Proteome Profiler Human Apoptosis Array.

Results: Our data show a strong suppression of apoptosis-inducing potential of TNF (extrinsic pathway) in HCA-7 cells treated with Butaprost, a selective agonist for the EP2 receptors. Specifically, decreased protein levels of pro-apoptotic Bad, Bax, pro-caspase 3, cleaved caspases 3, and SMAC/Diablo were detected in TNF/Butaprost-treated HCA-7 cells as compare to that in cells treated with TNF only. However, neither EP2 nor EP4 antagonists significantly affected TNF-induced apoptosis in tumor cells. In contrast, EP2 and EP4 antagonists were equally effective in rendering the resistance to UV-induced apoptosis which were further elaborated by Proteome Profiler Human Apoptosis Array. Of importance, EP2 and EP4 antagonists showed the capacity to reduce levels of pro-apoptotic pro-caspase 3, cleaved caspases 3, and cytochrome c and to increase amounts of anti-apoptotic protein survivin and enzyme catalase.

Conclusion: Taken together, our findings suggest that selective targeting the EP2 or EP4 signaling pathways may provide a strategy for the chemoprevention/chemotherapy of COX-2 colon cancers.

Health Policy

S25

Socioeconomic Disparities of Paraplegics With Spinal Cord Injuries Secondary to Gunshots in Metropolitan Detroit

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Introduction: Paraplegics secondary to gunshot spinal cord injuries (SCIs) have major unrecognized health care challenges. This study sought to

assess socioeconomic challenges for paraplegics that developed pressure ulcers secondary to gunshot wounds and the implications of those challenges for the rehabilitation of these individuals and the health care system.

Hypothesis: The standardization of proper supportive care for patients with SCI secondary to gunshot wound can positively influence their self-efficacy and overall health outlook, as well as relieve long term cost of care.

Methods: A survey was conducted from July 2010 through April 2012 among patients between the ages of 18-89. All patients were gunshot wound victims with previously acquired SCIs and pressure ulcers. We identified patients that met inclusion criteria from a daily pressure ulcer report of all admitted patients with pressure ulcers. The collected information was entered into a secured database for data abstraction and analysis

Results: Among 28 patients that met inclusion criteria, 43% of the patients had chronic pressure ulcers, 50% of those with chronic pressure ulcers had superimposed infection. 71% of all respondents were receiving supplemental security income (SSI) and 100% of those with infected ulcers were receiving SSI. Only 11% of the individuals surveyed remained employed after their diagnosis of SCI. This number dropped from 64% employment before injury. 79% of patients reported their physical and mental health as fair or poor and 52% of all patients reported worsening physical health in the past year. In contrast, 83% of those who received free physical therapy equipment reported good physical health status.

Conclusion: Paraplegics with pressure ulcers and SPI secondary to gunshots face socioeconomic adversity, which influences health outcomes as well as overall costs of rehabilitation.

Medical Education

S20

Global Health Education in Haiti: Student Knowledge and Education

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Introduction: Interest in global health, particularly in Haiti, has been growing rapidly among individuals who are training in the field of medicine. It is unclear what proportion of osteopathic medical students are interested in traveling to Haiti to provide short or long term medical service, and to what extent students have the proper training to provide care in Haiti.

Hypothesis: Students with an interest to travel to Haiti may possess more knowledge regarding medical issues afflicting Haiti.

Methods: We conducted a cross-sectional survey of students from the New York Institute of Technology College of Osteopathic Medicine. The survey contained demographic questions, questions about willingness to practice medicine internationally, and 16 knowledge questions. Data were analyzed using all students and stratified by year in school. Trend tests were conducted to see if student knowledge about medical issues specific to Haiti increased with their year in school. Using unconditional logistic regression models, age-adjusted odds ratios and their 95% confidence intervals (CIs) comparing responses for students willing to provide medical care in Haiti to those who were not willing.

Results: For most knowledge-based items related to cholera, dengue, malaria, and HIV, there was a significant trend ($P<.001$) for students to become

more knowledgeable as they progressed in their education. However, some there were some areas of knowledge that remained low throughout all 4 years of schooling. For instance only 31.9% (n=22) of fourth-year students knew that Malaria in Haiti is considered to be susceptible to chloroquine. Those who desired to provide medical care in Haiti were more knowledgeable about some issues than those who did not wish to provide medical care in Haiti. After controlling for year in school, those students willing to travel to Haiti were twice as likely as those who were not to know that Dengue has been documented in both native Haitians and visitors to Haiti (OR=2.05; 95% CI, 1.26, 3.32; *P*=.004).

Conclusion: There are some areas of knowledge that did not change with training, and in other areas, knowledge improved with training (year of medical school). Students who travel as a part of school early in the school process need additional training, while students traveling later in the process have acquired more knowledge and may be better equipped. Students with a specific interest in traveling to Haiti seem more aware of issues. Targeted training should be made available to interested students.

S39

Preliminary Findings From an Asynchronous IPE Activity: A Qualitative Study of Health Professions Students' Interprofessional Education Experience in a Virtual Environment

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Introduction: Interprofessional Education (IPE) is being increasingly implemented in graduate health degree programs worldwide. Integration of IPE into curricula, and early interaction between health professions, offers an opportunity for students to understand how they can use their colleagues in complementary ways to enhance patient outcomes.

Hypothesis: The purpose of this research project was to examine the use of a case-based, asynchronous, virtual IPE learning activity on students' self-assessment of their own learning outcomes. Our study tested the hypothesis that a virtual learning environment can be used to effectively create a valuable IPE experience.

Methods: Participants (N=314) were health professions students from 8 clinical and nonclinical graduate programs at Des Moines University, who were randomly assigned to an interdisciplinary team. This qualitative project used narrative reflection papers as the method to obtain data for analysis. These data were coded for major themes and sub-themes.

Results: Preliminary findings indicate that the participants were able to identify key knowledge and affective domain learning outcomes which corresponded to desired IPE core competencies.

Conclusion: Conclusions support the use of a virtual learning environment and patient case study as an innovative and effective IPE teaching method to enhance learning outcomes.

S45

Impact of Interprofessional Health Fairs on Students' Willingness to Work Together on Interprofessional Projects: Implication for Future Practice

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Introduction: With increasing focus on interprofessional education, there has been an emphasis in health professions education to integrate interprofessional education throughout the curriculum. Interprofessional education is difficult given the many logistical barriers involved in coordinating the learning of several professions together. A rural-

based health fair serving a large diverse population brought together students from 9 health professions for a 2-day health fair where students worked side by side. The interprofessional health fair is an ideal opportunity to measure the impact of underserved health fairs on students' willingness to work on interprofessional projects and future teams.

Hypothesis: Various health profession students' participation in a rural health fair will create statistically significant changes in the readiness for interprofessional learning scale (RIPLS) demonstrating an increased level of willingness to work on interprofessional projects and an interprofessional team.

Methods: Students volunteering at the health fair were given a RIPLS pretest to observe his or her position on interprofessional projects and learning. Following the fair, students were given a posttest to see changes in their score. The 18 question survey is analyzed by 3 subscales: (1) team work and collaboration, (2) professional identity, and (3) roles and responsibilities. Research has indicated that these 3 domains are key to interprofessional collaboration, education, and planning. Qualitative data were collected as to students' attitude and knowledge of interprofessionalism. Data were examined to measure the willingness of students to work on interprofessional projects and in a health care team. The questions were on a scale of 1 to 7 with 1 being strongly disagree and 7 being strongly agree. Scores were tested for significance using the *t* test for each question then combined into subcategories and tested again. The study was done across 2 years. The 2 years were compared to observe reproducibility and any factors that may have changed the outcomes.

Results: The results showed statistically significant changes in 3 different aspects of the study.

1. Different health profession
2. Subcategories
3. Year to year

Conclusion: All aspects of the survey showed significant changes demonstrating the importance of interprofessional health fairs in encouraging future health professionals' willingness to work on interprofessional projects and in interprofessional teams. Students showed increased willingness to work in a team and understood the impact it may have on patient care. The participants better understood professional identity and their role in a greater capacity. With promising trends in all aspects of the study the importance of early interactions with other health care professions in interprofessional projects is emphasized.