UNIVERSITY of MARYLAND
SCHOOL OF MEDICINE

38th Annual

# Medical Student Research Day

Hosted by
Office of Student Research, Dean's Office
Alpha Omega Alpha Honor Society

Thursday, September 17, 2015
University of Maryland School of Medicine
Baltimore, MD 21201

# Abstract Booklet

# ABSTRACTS

## Oral Presentation Abstracts

**O.01**

CLINICAL CHARACTERISTICS OF PEDIATRIC PATIENTS WITH CARBON MONOXIDE TOXICITY. Taylor Douglas*, Angela Comer[1], Jon Mark Hirshon[2], Robert Rosenthal[3], and Kinjal Sethuraman[3], [1]Department of Epidemiology and Public Health and [3]Division of Hyperbaric Medicine, [2]Department of Emergency Medicine, University of Maryland School of Medicine, Baltimore, MD.

Symptoms vary among pediatric patients suffering similar exposures to carbon monoxide (CO), complicating the decision to treat mild to moderate CO toxicity with hyperbaric oxygen therapy (HBOT). The goals of this retrospective review were to describe the clinical presentations of pediatric patients exposed to CO and treated with HBOT. The study is based on data from patients 25% only for patients who were unresponsive or had smoke inhalation/burns. There is little published literature describing CO poisoning in pediatric patients. Our observations can be used for further study of the relationship between serum COHb level and initial presentation and outcome in pediatric patients.

This research was supported by the EMRA Research Grant.

**O.02**

WHOLE-EXOME SEQUENCING AND COPY-NUMBER VARIATION ANALYSIS OF 20 NEUROFIBROMATOSIS TYPE 2-ASSOCIATED SPINAL AND INTRACRANIAL MENINGIOMAS. Ramita Dewan*, Alexander Pemov[1], Ashok Asthagiri[2], and Douglas Stewart[1], [1] Clinical Genetics Branch, National Caner Institute, National Institutes of Health, Bethesda, MD and [2]Department of Neurosurgery, University of Virginia, Charlotte, VA.

Neurofibromatosis type 2 (NF2) is an inheritable autosomal dominant tumor predisposition disorder (incidence 1:33,000), caused by a germline mutation in one of two copies of the tumor suppressor *NF2*. Although the hallmark of NF2 is bilateral vestibular schwannomas, individuals with NF2 are prone to developing multiple benign central and peripheral nervous system tumors, including schwannomas, meningiomas, and ependymomas. Spinal and cranial meningiomas affect about half of all NF2 patients, and since surgical resection is the standard of treatment, most patients face substantial morbidity and a reduced life expectancy. The two-hit mechanism of somatic inactivation of the second copy of *NF2* initiates meningioma formation, but little is known about what other genes or pathways are involved in NF2 meningioma tumorigenesis. In this study, we investigated the mutation burden and genomic architecture of twenty tumor specimens, ten cranial and ten spinal from seven NF2 patients. Whole exome sequencing using the Illumina HiSeq 2500 platform and Illumina HumanOmniExpress SNP-array analysis of the tumor and germline DNA samples revealed that somatic inactivation of *NF2* is the most frequent and only recurrent genetic event in NF2-associated meningiomas. It occurs mostly by large LOH events, such as deletion of entire chromosome 22 or portions of 22q containing the *NF2* gene. Large LOH events elsewhere on the genome, especially chromosome 1, could represent a common path of tumor progression toward a more aggressive/advanced stage. We identified 65 somatic mutations, of which 17 were potentially damaging. Compared to the prevalence of chromosome 22 deletion events, somatic single nucleotide substitutions and small indels are relatively rare in these tumors, and understanding the role of these types of mutations in NF2-associated meningioma tumorigenesis may provide further insight into phenotypic variability of tumor presentation and treatment response.

This research was supported by the Intramural Research Program of the National Institute of Neurologic Disorders and Stroke, National Cancer Institute and National Human Genome Research Institute at the National Institutes of Health, as well as by the 2015 Carolyn L. Kuckein Student Research Fellowship and ABTA 2015 Medical Student Summer Fellowship.

**O.03**

OF EARS AND TEETH - AN UNEXPECTED CONNECTION. Graham Trent*, Maggie Matern, Lorna Silipino, and Ronna Hertzano, Department of Otorhinolaryngology - Head and Neck Surgery, University of Maryland School of Medicine, Baltimore, MD.

The *Cello* mouse possesses a mutated *Ikzf2* gene, which encodes for the Helios transcription factor. In the mouse inner ear, Helios is expressed exclusively in the outer hair cell nuclei. *Cello* mice are deaf. An RNA-Seq gene expression analysis of ears from wild type and mutant *Cello* mice identified the dental enamel genes *Enam*, *Amelx* and *Ambn* as downregulated in the *Cello* mutant mice. This study sought to validate the RNA-Seq results, characterize the expression levels of *Ikzf2* (Helios), *Enam*, *Amelx*, and *Ambn* in the teeth of *Cello* mutant mice and their wild type littermate controls, and to evaluate *Cello* mutant mice for abnormal dental enamel. To validate the RNA-Seq results, RNA was extracted from wild type and mutant inner ears and mandibles and gene expression was quantified using real time RT-PCR. To determine whether the *Ikzf2* mutation affects the thickness of the dental enamel, mandibles were extracted from wild type and mutant mice and processed to ultimately obtain sections which were stained with H&E. Dental enamel thickness was evaluated using captured images of H&E stained sagittal mandible sections. Preliminary evaluation of sectioned tissues suggests that the *Cello* mouse possesses a thinner enamel layer than its wild type counterpart. Preliminary analysis of comparative threshold qPCR data quantifying expression levels of *Enam*, *Amelx*, and *Ambn* in mandibular samples does not reach the threshold of significance. These findings suggest *Cello* may serve as an animal model for Heimler syndrome, a condition in which patients present with dental enamel hypoplasia and sensorineural hearing loss, for which there is no currently identified causative gene.

This research was supported in part by the Proposed Research Initiated by Students and Mentors (PRISM) Program, University of Maryland School of Medicine Office of Student Research.

**O.04**

UNDERSTANDING THE GENETIC BASIS OF VERY HIGH HDL THROUGH NOVEL GENETIC ASSOCIATIONS. Connor Oates*, Michael Miller, and Jeff Rhyne, Division of Cardiovascular Medicine, Department of Medicine, University of Maryland School of Medicine, Baltimore, MD.

Coronary heart disease (CHD) is the leading cause of death worldwide. Yet, while epidemiological studies have consistently demonstrated an inverse association between CHD and high-density lipoprotein cholesterol (HDL-C), there is a lack of understanding regarding the genetic basis of familial hyperalphalipoproteinemia (FHA), a phenotype characterized by very high HDL-C and longevity. Though the heritability of HDL-C is estimated to be up to 80%, the genes commonly identified with HDL-C metabolism have been shown to account for less than 10% of HDL-C variance. To identify novel genes that influence HDL-C variance, but have escaped identification by traditional methods, we chose to utilize a model of genetic investigation incorporating family studies as well as population based studies. First, we identified nonsynonymous SNPs (nsSNPs) in 94 genes of interest within 4 unrelated pedigrees with FHA and no mutations in known candidate genes. We then identified 52 individuals with high HDL-C >/= 80 mg/dl from 1,479 subjects in Cardiovascular Health Study (CHS), Jackson Heart Study (JHS), Multi-Ethnic Study of Atherosclerosis (MESA) and Framingham Heart Study (FHS) in which to investigate our 94 genes

of interest for polymorphisms. After excluding nsSNPs within these high HDL individuals that were shared with individuals with HDL-C

This research was supported in part by the Proposed Research Initiated by Students and Mentors (PRISM) Program, University of Maryland School of Medicine Office of Student Research.

**O.05**

X-RAY CRYSTAL STRUCTURE DETERMINATION OF THE N-TERMINAL IGV-LIKE DOMAIN OF CEACAM16. David Sayre*, Eric Sundberg, Daniel Bonsor, and Michael Loukeris, Department of Microbiology and Immunology, University of Maryland School of Medicine, Baltimore, MD.

Carcinoembryonic antigen related cell adhesion molecules (CEACAMs) are a family of primarily membrane bound proteins which play a crucial role in intercellular adhesion and cellular signaling. The function and ligand specificity of each CEACAM is in part dictated by the structure of its variable IgV-like domains. CEACAM16 is a unique member of the family because it contains no apparent membrane attachment and has a variable domain at both its C-terminus and N-terminus ends. CEACAM16 is found exclusively in the tectorial membrane of the inner ear and is involved in hearing sensitivity at high and low frequencies. Alteration in the structure of CEACAM16, such as the missense mutation present in DFNA4 hearing impairment, disrupts CEACAM16's interaction with α-tectorin and β-tectorin. This disturbance reduces membrane elasticity which is essential for normal mammalian hearing. In this study, we have expanded upon earlier efforts to crystallize and determine the structure for other members of the CEACAM family. Structure determination of the variable domains of CEACAM16 allows for further characterization of its structural motifs and how these may contribute to its importance in tectorial membrane elasticity.

This research was supported in part by the Proposed Research Initiated by Students and Mentors (PRISM) Program, University of Maryland School of Medicine Office of Student Research.

**O.06**

CELLULAR SENESCENCE ALTERS THE MITOCHONDRIA-ASSOCIATED MICRORNA PROFILE OF WI-38 CELLS. Jackline Joy Lasola*, Ji Heon Noh, and Myriam Gorospe, National Institute on Aging, National Institutes of Health, Bethesda, MD.

Mitochondria are involved in many metabolic processes with a primary function being to convert energy from nutrients into ATP through oxidative phosphorylation (OX-PHOS) whereas mitochondrial dysfunction has been implicated in aging and various disease states, including cancer. Although human mitochondrial DNA (mtDNA) contains 13 genes encoding components of the OX-PHOS system, 22 tRNAs, and two rRNAs, a large proportion of mitochondrial proteins necessary for maintaining mitochondrial structure and function are encoded by the nuclear genome, synthesized in the cytoplasm, and imported into mitochondria. In addition, several long noncoding RNAs (lncRNAs) transcribed in the nucleus also play key roles in regulating mitochondrial gene expression. Previous work in the lab identified GRSF1 in mitochondria as essential for translocation of the nuclear-encoded RMRP (RNA component of mitochondrial RNA processing endoribonuclease) to the mitochondria where it functions as the RNA component of the mitochondrial RNA processing endoribonuclease (RNase MRP) necessary for mitochondrial DNA replication and RNA processing. I hypothesized that given the role of GRSF1 in the translocation of RMRP, GRSF1 may also be responsible for mitochondrial import of a particular subset of mitochondria-associated microRNA (miRNA) that also function to fine-tune mtDNA gene expression. To investigate the role of GRSF1 in miRNA mitochondrial-import and how this changes as cells reach advanced age, young and senescent WI-38 cells were fractionated into cytoplasmic and mitochondrial components. Protein was extracted from each subcellular fraction to

confirm successful isolation of mitochondria and RNA was extracted to screen for the expression of known mitochondria-associated miRNAs in the young and senescent WI-38 cells. Reverse transcriptase and quantitative polymerase chain reaction (RT-qPCR) demonstrated that cellular senescence led to alterations in the expression profile of specific miRNAs in the cytosolic and mitochondrial fractions. These alterations in miRNA localization during cellular senescence may hint at a possible mechanism for mitochondrial dysfunction seen in aging and cancer.

**O.07**

IMMUNOMODULATION OF POST-NAION M1 UPREGULATION WHEN TREATING WITH IL4, TGFB, AND GLATIRAMER ACETATE (COPAXONE) IN A RODENT MODEL. Sara Francomacaro*, Zara Mehrabyan, and Steven Bernstein, Department of Ophthalmology and Visual Sciences, University of Maryland School of Medicine, Baltimore, MD.

Nonarteritic anterior ischemic optic neuropathy (NAION) results from an ischemic lesion of the anterior optic nerve, leading to vision loss. NAION is the leading cause of vision loss in people over 55 and there are currently no treatment options. It is understood that vision loss in NAION is accompanied by edema and inflammation of the optic nerve head. Cellular inflammation is a balance between neurodegeneration (M1 classical activation pathway) and neuroprotection (M2 alternative activation pathway), which can be adjusted through immunomodulation. It has been shown that IL4 + TGFβ cytokine treatment is effective in immunomodulation, inducing M2 activation. Copaxone, a treatment for multiple sclerosis, has also been shown to upregulate M2. Our goal is to determine if immunomodulation, through IL4, TGFβ and Copaxone, is a feasible NAION treatment option, utilizing a rodent model of NAION (rNAION). On Day 1, rNAION was induced in one eye of each animal, which also received an intraventricular injection of IL4 and TGFβ or control (saline). Experimental animals also received daily high dose Copaxone. We verified stroke severity on Day 3 using optical coherence tomography (OCT). We collected experimental tissue (optic nerve lamina), and positive control tissue (spleen) on Day 3 and Day 7 and evaluated macrophage markers to determine relative expression of M1 and M2. Spleen tissue showed that treatment successfully upregulated M2 (markers Arg1 and PPARγ) and down-regulated M1 (marker iNos), verifying the immunomodulation capability of our treatment. In the lamina of the optic nerve, Arg1 was induced in macrophages following treatment, showing an upregulation of M2 compared to saline treated controls. iNos upregulation over saline control was also noted post-treatment, however this was localized to the astrocyte component of the nerve. Thus our data showed that IL4, TGFβ and Copaxone induced iNos in astrocytes, while also inducing Arg1 in macrophages at 3 and 7 days. Evaluating protein expression following NAION induction, suggests that there is potential to immunomodulate the inflammatory response in the optic nerve.

This research was supported in part by the Proposed Research Initiated by Students and Mentors (PRISM) Program, University of Maryland School of Medicine Office of Student Research, by the Bernstein Lab at UMB, and by RO1-EY015304 from the NIH.

**O.08**

BCL-2 INHIBITORS AND ARTEMISININS COOPERATE AGAINST LEUKEMIAS. Kalyani Kumar*, Jennifer Fox[1], Xiaochun Chen, and Curt Civin, Department of Pediatrics, University of Maryland School of Medicine, Baltimore, MD.

Artemisinins and their semisynthetic derivatives are potent, low toxicity, inexpensive antimalarials. Two artemisinin derivatives, Artesunate (AS) and ART-838 have demonstrated antileukemic activity in both in vitro and in vivo studies. In laboratory studies of acute myeloid leukemia (AML) treatment, the Civin lab recently found strong synergistic antileukemic activity in vitro between either AS or ART-838 and BCL-2 inhibitors. The targeted BCL-2 inhibitor ABT-199

is undergoing Phase I and Phase II clinical trials for several blood cancers and was recently granted breakthrough therapy designation by the FDA. The purpose of this study was to determine the cellular and molecular mechanism(s) of the observed cooperativity between ABT-199 and AS/ART-838 in AML. Combination of either AS or ART-838 with ABT-199 synergistically inhibited cell growth in the MOLM14 AML cell line, in a dose-dependent manner. These drug combinations invoked additive to synergistic effects on apoptosis, which is the mechanism of action of ABT-199. Moreover, as compared to the individual drugs, combination of either AS or ART-838 with ABT-199 significantly increased mitochondrial reactive oxygen species; ROS is involved in artemisinin-mediated leukemia cell killing.

This research was supported in part by the Proposed Research Initiated by Students and Mentors (PRISM) Program, University of Maryland School of Medicine Office of Student Research and by the Civin Lab.

**O.09**

DEVELOPMENTAL REGULATION OF THE OLFACTORY BULB-LATERAL ENTORHINAL CORTEX AXIS IN MICE. Allison Arai* and Sandra Jurado, Department of Pharmacology, University of Maryland School of Medicine, Baltimore, MD.

Early detection of Alzheimer's disease (AD) is a critical factor in combating this devastating disease. Developing biomarkers to detect early-stage AD would allow preventative treatments of increased efficacy to ameliorate early symptoms of neurodegeneration. Olfactory dysfunction precedes memory loss in AD but also in normal aging. To investigate olfactory dysfunction as a biomarker for AD, the decline in olfaction related to normal aging must be distinguished from pathological processes associated with AD. In addition to olfactory deficits, neuropathology of the entorhinal cortex has been observed early in AD. While current research demonstrates the importance of the entorhinal cortex-hippocampal circuit to learning and memory, the function of the reciprocal connectivity between the lateral entorhinal cortex (LEC) and the olfactory bulb (OB) remains unexplored. We hypothesized that in development mice will exhibit a malfunction of the OB-LEC axis. Specifically, we explored the possibility that OB-LEC malfunction in older mice may be due to a reduction in the number of neurons within this axis. To test this hypothesis, we performed in vivo stereotaxic injections in three age groups of mice (P60) of retrograde fluorescent latex beads into the OB and piriform cortex, two of the primary regions involved in olfaction. Imaging experiments confirm the existence of the OB-LEC axis. However, our preliminary results show an increase in the number of OB-LEC cells as age increases in contrast to our working hypothesis. In the future, we plan to confirm these findings using viral-dependent transynaptic labeling using pseudotyped rabies virus. This novel tool for transynaptic labeling will allow us to explore two alternative hypothesis. One hypothesis is that physical degradation in the OB-LEC axis may only become apparent in older mice (e.g. greater than one year old). A second possibility is that changes in synaptic strength may underlie OB-LEC function impairments. Future experiments will include extended time points and functional assays such as electrophysiology to explore the cellular underpinnings of the aging of the OB-LEC axis.

This research was supported by the National Institute on Aging of the National Institutes of Health under award number R01AG049937. This content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. This research was also supported by the University of Maryland, Baltimore School of Medicine Medical Scientist Training Program (MSTP).

**O.10**

EMERGENCY CARE ASSESSMENT TOOL FOR HEALTH FACILITIES. Crystal Bae*, Emilie Calvello[1], and Lee Wallis[2], [1]Department of Emergency Medicine, University of Maryland School of Medicine, Baltimore, MD and [2]Division of Emergency Medicine, Department of Surgery, University of Cape Town School of Medicine, Cape Town, South Africa.

To date, health facilities in Sub-Saharan Africa have not had an objective measurement tool for evaluating comprehensive emergency service provision. One major obstacle is the lack of consensus on a standardized evaluation framework, applicable across a variety of resource settings. The African Federation for Emergency Medicine (AFEM) has developed an assessment tool, specifically for low and middle income countries, via consensus process that assesses provision of key medical interventions. These interventions are referred to as essential emergency signal functions for the five sentinel conditions that occur prior to death: respiratory failure, shock, altered mental status, severe pain/trauma, and dangerous fever. A signal function represents the culmination of knowledge of interventions, supplies, and infrastructure capable for the management of an emergent condition.

This study intends to use the Emergency Care Assessment Tool (ECAT), proposed at the African Federation for Emergency Medicine Consensus Conference 2013, in a variety of settings to allow for the necessary refinement and context modification prior to more expansive roll out throughout the region. To enhance effectiveness, ECAT was administered in multiple different regions and facility levels with different health care workers. Four countries were chosen, Cameroon, Uganda, Egypt, and Botswana, to represent West, East, North, and Southern Africa.

This research was supported by Royal College of Emergency Medicine (UK).

**O.11**

RETROSPECTIVE REVIEW OF ROUTINE REPEAT CRANIAL CT FOR PATIENTS WITH MILD TBI. Claire Rosen*, Molly Deane, and Deborah Stein, Department of Surgery, University of Maryland School of Medicine, Baltimore, MD.

Routine repeat cranial computed tomography (RHCT) is the current standard of care for the 1.7 million Americans each year suffering from traumatic brain injury (TBI). Of those affected, 75% suffer only mild TBI, but are subject to the harmful radiation and increased costs of RHCT, despite mixed evidence as to its necessity. This preliminary analysis is part of a larger retrospective chart review that investigates what components of mild TBI require zero, six, and 24-hour RHCT, compared to clinical presentation and original diagnostic CT alone, with future goals to develop protocol for when RHCT is necessary. This analysis included 50 patients with mild TBI from December 2014-January 2015 at the R Adams Cowley Shock Trauma Center (STC) at the University of Maryland Medical Center (UMMC). Patients who met further inclusion criteria (n = 39) were then defined as needing no intervention (n = 20), medical intervention (n = 12), or surgical intervention (n = 7) and compared using paired T-tests, stratified by injury classification on original diagnostic CT, change in Glasgow coma score (GCS) over the course of RHCT, demographics, and medical history. Patients requiring surgical intervention were found to have greater change in GCS score over the course of RHCT, larger subdural hematoma injuries, and more pronounced midline shift, but no significant difference in demographics, medical history, vital signs, or subarachnoid hemorrhage. This study may help us to minimize patients' exposure to harmful radiation and to decrease healthcare costs, an issue of paramount importance in the changing healthcare system and current economy.

This research was supported in part by the Proposed Research Initiated by Students and Mentors (PRISM) Program, University of Maryland School of Medicine Office of Student Research.

**O.12**

CHARACTERIZING PERI-ICTAL MOOD CHANGES IN PATIENTS WITH PSYCHOGENIC NONEPILEPTIC SEIZURES. Serena Yin*, Scott Thompson[1], and Jennifer Hopp[2], [1]Department of Physiology and [2]Department of Neurology, University of Maryland School of Medicine, Baltimore, MD.

Patients with psychogenic non-epileptic seizures (PNES) have episodes of apparent alteration of awareness and changes in behavior that resemble epileptic seizures but do not concur with abnormal brain activity on an EEG. PNES is classified as a conversion disorder, in which psychological distress manifests as a physical symptom. Generally, patients with PNES have been reported to have greater rates of trauma and abuse in their lifetimes. This study seeks to characterize peri-ictal mood changes in patients following a seizure event. We postulate that because patients suffering from PNES may have seizures as a way to cope with stress, they will have decreased depression and anxiety in the various time intervals following a seizure. We enrolled patients in the Epilepsy Monitoring Unit (EMU) at the University of Maryland Medical Center. Mood scores were assessed at baseline admission to the EMU and at specified time points (1-4 hours, 12 hours, 24 hours, 2 weeks) after a seizure, using the Beck Depression Inventory-II (BDI-II), the Montgomery Asberg Depression Rating Scale (MADRS), and the Beck Anxiety Inventories (BAI). Higher scores indicate greater severity of anxiety and depressive symptoms. For the 10 patients in the study who presented with PNES, there was an overall decrease in depression and anxiety scores following a seizure. The BDI-II and MADRS showed a decrease in depression scores compared to baseline after 1-4 hours (-1.1, -3.3), 12 hours (-3.1, -6.3), and 24 hours (-1.8, -5.2), but the average BDI-II score increased after two weeks (+1.6). Average anxiety scores on the BAI decreased at 1-4 hours (-3.6), 12 hours (-6.9), 24 hours (-5), and 2 weeks (-1.3). While our current sample size is small, the preliminary data suggests that PNES patients achieve some degree of mood improvement and anxiety reduction through their seizures. This supports the notion that PNES is linked to patients' maladaptive coping and may inform useful behavioral targets for stress management and treatment of seizures.

This research was supported in part by the Proposed Research Initiated by Students and Mentors (PRISM) Program, University of Maryland School of Medicine Office of Student Research.

**O.13**

IN-VITRO EVALUATION OF BREAST PROSTHETIC IRRIGATION SOLUTION EFFECT ON BIOFILM. Sarah Chang*, Karan Chopra, Devinder Singh, and Yvonne Rasko, Division of Plastic Surgery, Department of Surgery, University of Maryland School of Medicine, Baltimore, MD.

Although many plastic surgeons have adopted the practice of breast-pocket or implant irrigation to minimize the risk of capsular contracture and biofilm formation following breast augmentation, there is no consensus on which irrigant solution is most effective. After the FDA discouraged the use of Betadine due to cytotoxic effects, a study concluded that Triple Antibiotic solution (TAB) was the most effective alternative to Betadine breast irrigants. Our study seeks to further evaluate the role of TAB on biofilm formation by directly observing the effects of soaking breast implants in irrigant solutions. We designed an in vitro model to mimic "in theater" breast augmentation implant preparation in which the breast implant is immersed in an irrigant solution prior to insertion through a skin incision. Implants were first immersed in one of the five selected irrigant solutions (normal saline, povidone-iodine, triple antibiotic, Prontosan and Clorpactin), followed by a suspension of S. aureus bacteria. Biofilm formation was allowed to occur and bacterial content was subsequently analyzed using serial dilution and plating, fluorescent microscopy, and electron microscopy. We conducted a total of 9 trials for this study. After immersion in the five selected irrigant solutions, the average final biofilm content on the implants was calculated (Normal Saline: 388,500.00 CFU; Betadine: 22,281.11 CFU; Prontosan: 98,884,78 CFU; Triple Antibiotic: 136,479.56 CFU;

Clorpactin: 158,708.25 CFU). Scanning electron microscopy also demonstrated significant reduction in bacterial growth after implant irrigation. Although past studies indicate the use of Triple Antibiotic, we observed that Prontosan, a solution that contains a gentle surfactant and a powerful antimicrobial agent may actually be the most efficacious in reducing bacterial growth and biofilm formation on breast implants.

**O.14**

EFFECTS OF IN VIVO INJURY ON THE NEUROMUSCULAR JUNCTION IN HEALTHY AND DYSTROPHIC MUSCLES. Gloribel Le*, Stephen J.P. Pratt[1], Ana P. Valencia[1], Sameer B. Shah[2], and Richard M. Lovering[1], [1]Department of Orthopaedics, University of Maryland School of Medicine, Baltimore, MD and [2]Department of Orthopaedics, University of California San Diego School of Medicine, San Diego, CA.

The most common and severe form of muscular dystrophy is Duchenne muscular dystrophy (DMD), a disorder caused by the absence of dystrophin, a structural protein found on the cytoplasmic surface of the sarcolemma of striated muscle fibers. The MDX mouse also lacks dystrophin and has been widely used as an animal model of DMD. Considerable attention has been dedicated to studying myofiber damage and muscle plasticity, but there is little information to determine if damage from contraction-induced injury occurs at or near the nerve terminal axon. The purpose of this work was to compare the NMJ morphology & function of healthy (wild type, WT) and dystrophic (MDX) murine muscles after injury induced by lengthening contractions. We studied changes in NMJs after injury induced with an established in vivo animal injury model. Neuromuscular transmission, electromyography (EMG), and NMJ morphology were assessed in WT and MDX muscle with or without injury. Injury resulted in a significant loss of maximal torque in WT (39 ± 6 %) and MDX (76 ± 8 %) quadriceps, but significant changes in NMJ morphology, neuromuscular transmission, and EMG data were found only in MDX following injury. Compared with WT mice, motor endplates of MDX mice demonstrated less continuous morphology, more disperse acetylcholine receptor (AChR) aggregates, increased branching and increased number of individual AChR clusters, an effect that was exacerbated following injury. Neuromuscular transmission failure increased and the EMG measures decreased after injury in MDX mice only. NMJ occupancy, defined as the ratio of the footprint occupied by presynaptic vesicles versus that of the underlying motor endplate (i.e., geometric coupling between presynaptic and postsynaptic morphology) was altered in MDX mice, even without injury. The data show that eccentric contraction-induced injury causes morphological and functional changes to the NMJs in MDX skeletal muscle, which may play a role in excitation-contraction coupling failure and the progression of the dystrophic process.

This research was supported by the National Institutes of Health (1R01AR059179) to RML by the University of Maryland School of Medicine Office of Student Research and supported in part by the Proposed Research Initiated by Students and Mentors (PRISM) Program, University of Maryland School of Medicine Office of Student Research.

**O.15**

EFFECT OF EXTERNAL FIXATION ON TERRIBLE TRIAD OF THE ELBOW OUTCOMES. Andrew Fischer*, Karan Dua, and Joshua Abzug, Department of Orthopaedics, University of Maryland School of Medicine, Baltimore, MD.

The 'terrible triad' is a devastating orthopedic injury of the upper extremity. It involves fractures of the radial head and coronoid process of the ulna with concomitant posterior elbow dislocation. Because the injury occurs secondary to severe trauma at the elbow, the majority of cases require open reduction and internal fixation (ORIF). Patients experience a high rate of post-operative

complications including contracture of the elbow, chronic elbow instability, heterotopic ossification, and nonunion at fracture sites. The high complication rate and poor prognosis associated with the injury has led to different management strategies. The use of an external fixation device in addition to ORIF has been hypothesized to prevent the recurrence of elbow instability. A retrospective study was conducted at University of Maryland Shock Trauma to assess if the use of an external fixation device placed with ORIF can lead to better outcomes. Our research team hypothesized that the use of external fixation in patients with terrible triad injuries reduces the occurrence of re-dislocation and other complications, particularly in poly-trauma patients, while having no impact on clinical outcome measures like range of motion, rehabilitation time, and time to recovery. Patients who sustained a terrible triad injury from 2000-2015 were retrospectively reviewed to understand what aspects of their injury and surgical care led to more favorable outcomes. The use of external fixation completely eliminated re-dislocations and lowered the rate of reoperation from 20% to 7.69%. Furthermore, no significant difference was seen in flexion, extension, pronation, or supination during the first four follow-ups (~30 weeks). In the poly-trauma subgroup and in patients over 60 years old, no patients that received external fixation required subsequent surgeries. Findings from the current analysis suggest the utility of liberal external fixation use, particularly in poly-trauma and older patients, in the treatment of the terrible triad injury of the elbow.

This research was supported in part by the Proposed Research Initiated by Students and Mentors (PRISM) Program, University of Maryland School of Medicine Office of Student Research.

**O.16**

EFFECTS OF REVASCULARIZATION ON MICROVASCULAR PERFUSION AND PHYSICAL FUNCTION IN PATIENTS WITH PERIPHERAL ARTERY DISEASE. Michael Lu*, Odessa Addison, and Steven Prior, Division of Gerontology and Geriatric Medicine, Department of Medicine, University of Maryland School of Medicine, Baltimore, MD.

Current treatment strategies for patients with advanced peripheral artery disease (PAD) focus on surgical revascularization of the affected limbs and treatment of vascular risk factors. While revascularization addresses macrovascular muscle perfusion, its potential to enhance microvascular perfusion to restore mobility and physical function in patients with PAD is less well known. Our hypothesis is that calf muscle microvascular perfusion and physical function are reduced in PAD patients compared to normal controls, and that revascularization in PAD patients will increase microvascular perfusion to improve physical function. To test this hypothesis, we are using contrast-enhanced ultrasound (CEU) to measure basal and exercise-induced calf muscle perfusion and are assessing mobility function in 10 PAD patients, before and after revascularization, and in 10 healthy controls. Compared to normative data, mobility function is markedly lower in PAD patients. Six-minute walk distance (1,064.5 ± 73.1 ft) is ~50% lower than normal; MPPT score (29.0 ± 2.8) is ~20% lower than normal; and usual-pace gait speed (1.04 ± 0.1 m/s) is ~20% slower than normal. Preliminary muscle perfusion data show that the exercise-induced peak perfusion is lower in PAD patients compared with healthy controls [19.9 ± 4.2 vs. 27.5 ± 11.7 video intensity (Vi), respectively]. Likewise, time-to-peak perfusion during exercise was longer in PAD patients compared with controls (34.9 ± 9.9 vs. 18.2 ± 8.3 sec, respectively). These perfusion characteristics do not appear to significantly improve in PAD patients after revascularization, as peak perfusion was 17.7 ± 3.8 Vi and time-to-peak perfusion was 29.1 ± 12.4 sec after stenting. Our results suggest that the low microvascular perfusion in PAD patients likely contributes to reduced physical function in PAD patients because diffusion of oxygen and metabolites is limited. In addition, revascularization alone does not appear to significantly increase microvascular perfusion in PAD patients. These data suggest the need for additional interventions to improve microvascular perfusion and physical function in patients with advanced PAD.

This research was supported by the Summer Program in Obesity, Diabetes and Nutrition Research Training under NIH award number T35DK095737, the University of Maryland Pepper Center (P30-G028747), and the Baltimore VA GRECC.

**O.17**

TRAUMATIC PEDIATRIC PATELLA DISLOCATION UTILITIES ACQUISITION AND DECISION ANALYSIS. Conan So*, Benedict Nwachukwu[1], William Schairer[1], Daniel Green[2], and Emily Dodwell[2], [2]Division of Pediatric, [1]Department of Orthopaedics, Hospital for Special Surgery, New York, NY.

Primary traumatic patella dislocation is one of the most common lower extremity injuries in adolescents. Patients can be managed conservatively or surgically, but it remains unclear which treatment strategy is optimal. Although costs of surgery are significantly higher, recent evidence suggests that surgery has lower rates of repeat dislocations. A cost-decision analysis can be useful to compare the higher surgical costs with the improved clinical outcomes. The purpose of this study was to: 1) perform a comparative systematic review to determine if there is a significant difference in the rate of repeat dislocation and clinical outcome between conservative management and surgery for first time patella dislocation in adolescents; 2) establish utility scores in our patient population for health states associated with traumatic patella dislocation and 3) evaluate the cost effectiveness of these treatment options using a 10-year Markov model. A systematic review of the MEDLINE database was performed: 11 studies with 627 knees met the inclusion criteria. Chi square analysis, independent t-tests and weighted mean pooled cohort statistics were performed. Conservative management (470 knees) was associated with a 31% rate of recurrent dislocation whereas surgery (157 knees) had a 22% recurrence rate ($p=0.04$). Surgical treatment conferred a clinically important, statistically significant improvement in quality of life and sporting benefit based on established thresholds for minimal detectable change. We collected utility scores for health states from our patient population for inputs to the Markov model. Transition probabilities were identified through our systematic review. The principal outcome measure of our model was the incremental cost-effectiveness ratio (ICER). Our Markov model demonstrated that delayed and immediate surgery are cost effective treatments (ICER of $11,150 and $75,150 respectively), with immediate surgery having the maximal quality adjusted life year gain (7.1). Based on initial evidence, surgery may be preferred as a first-line treatment for active adolescents since it reduces the risk of recurrence and maximizes functional outcome.

This research was supported by the 2015 Hospital for Special Surgery Medical Student Summer Research Fellowship.

**O.18**

AUTOLOGOUS OSTEOCHONDRAL TRANSPLANTATION FOR OSTEOCHONDRAL LESIONS OF THE TALUS: DOES PREVIOUS BONE MARROW STIMULATION AFFECT CLINICAL OUTCOME? Keir Ross*, Andrew Ross[1], Ethan Fraser[2], Timothy Deyer[3], and John Kennedy[2], [1]Touro College of Osteopathic Medicine, [2]Division of Foot and Ankle, Department of Orthopaedics, Hospital for Special Surgery, and [3]East River Imaging, New York, NY.

Osteochondral lesions of the talus have been increasingly recognized, however, there is a paucity of evidence regarding the optimal treatment paradigm. While microfracture is often the index operative intervention, the effect of failed microfracture on subsequent revisions, including autologous osteochondral transplantation (AOT), has not been reported. The purpose of this study was to determine if patient reported functional outcomes and magnetic resonance imaging (MRI) were significantly different between patients receiving primary AOT and patients receiving secondary AOT following failed microfracture. Patient reported outcomes were evaluated using the

Foot and Ankle Outcome Score (FAOS). Superficial and deep tissues at the repaired defect, as well as adjacent normal cartilage, were analyzed using quantitative T2 mapping MRI. The Magnetic Resonance Observation of Cartilage Repair Tissue (MOCART) score allowed for morphological evaluation of repair tissue. A group of 77 patients was retrospectively analyzed. Twenty-three patients received primary AOT and 54 received secondary AOT following failed microfracture. Patient characteristics between groups were similar with regard to age, gender, lesion size, and follow-up. Mean post-operative FAOS was 10 points higher in the primary AOT group ($p = 0.01$). Regression analysis showed that secondary AOT patients preoperative to postoperative change in FAOS was 9 points lower than in primary AOT patients after adjustment for age, preoperative FAOS and lesion size ($p = 0.04$). Mean MOCART score, superficial T2 and deep T2 values, and difference between normal and repair cartilage T2 values were all slightly higher in the primary AOT group, but these differences were not significant. Lesion size was negatively correlated MOCART scores ($r=-0.2$, $p=0.04$) and positively correlated with difference in T2 values between repair and adjacent normal cartilage in the superficial layer ($r=0.3$, $p = 0.045$). Primary AOT demonstrates better functional outcomes compared to secondary AOT in patients with similar characteristics and lesion size. No significant differences in T2 mapping relaxation times and MOCART scores were identified.

**O.19**

LIVER BIOENGINEERING: NEONATAL RECELLULARIZATION OF AN ADULT RAT LIVER SCAFFOLD. Stephen Klepfer*, Carlos Rivera-Pratts*, Wessam Hassanein, Mehmet Uluer, Dawn Parsell, and John LaMattina, Department of Surgery, Unveristy of Maryland School of Medicine, Baltimore, MD.

This experiment aims to demonstrate the viability of using Wistar rat neonatal liver cells to recellularize an adult rat liver scaffold and produce a functional liver. This lab previously developed a protocol for decellularization using Sodium Dodecyl Sulfate over a 24 hour period, controls showed a minimal amount of DNA via DNA Quantification. Native and recellularized livers are examined using Immunohistochemistry (IHC) stains for Collagen IV to ensure the scaffold is present as well as Vascular Endothelial Growth Factor (VEGF) to ensure the hepatocytes have encouraged the regrowth of the vasculature of the liver. The cell lines are given 5 days to grow in an ex vivo perfusion system prior to testing. On day five, samples are taken for DNA quantification while the remainder of the liver is sectioned, stained, and analyzed. The concentrations and origins of cells will be varied. Titration trials run based on the age of the neonatal pups when their livers were harvested did not show a significant difference, DNA Quantification results have not shown a substantial difference between samples based on age. IHC stains for Collagen IV and VEGF as well as DAPI stains are pending. Currently, only preliminary results are available for full liver recellularization as we refine procedures. The results of this experiment could have the potential to guide larger scale research, one day leading to the growth of human livers for transplantation.

This research was supported in part by the Proposed Research Initiated by Students and Mentors (PRISM) Program, University of Maryland School of Medicine Office of Student Research.

**O.20**

CAN THE PERIOPERATIVE SURGICAL HOME RESCUE TRAUMA SURVIVORS? A PILOT STUDY OF PATIENT'S NEEDS FOLLOWING TRAUMATIC INJURY. Elena Grill*, Daniel Slack*, DANIEL SLACK, ERIN HALL[1], FRANCES GRISSOM[2], Maureen McCunn[3], [1]Department of Surgery and [3]Department of Anesthesiology, University of Maryland School of Medicine and [2] Trauma Survivor Network, University of Maryland School of Nursing, Baltimore, MD.

Many trauma survivors leave the hospital with on-going physical and mental health concerns. Despite the fact that fifty percent of trauma survivors exhibit symptoms of post-traumatic stress disorder (PTSD), only ten percent of patients who complain of cognitive deficits receive treatment. The concept of the Perioperative Surgical Home (PSH) is intended to optimize patient care pre-operatively, manage post-operative care, and facilitate hand-off to the primary care provider upon discharge. In light of these early PSH studies, we sought to characterize the unmet needs of the discharged trauma patient in the hopes that this pilot data could further guide efforts to provide coordinated 'optimal care' for patients in a trauma-focused PSH model and illuminate how to better serve this population. Eighteen survivors of physical trauma and 17 of their social support network were interviewed by 2 trained medical students May-September 2015. Ninety-four percent of survivors were victims of nonviolent trauma and that 6 percent were victims of violent crimes. The unmet needs that emerged from these interviews centered on the need for psychiatric and financial support in the face of coming to terms with what was commonly referred to as the "new normal." All subjects reported that psychological support resources were not offered upon discharge and 60% of these subjects reported currently needing psychiatric support (with 3 of these 21 subjects reporting a past history of suicidal ideations or suicide attempts). Of the three subjects who expressed suicidal ideations, all are survivors and two were in possession of multiple firearms during their suicidal period. Our data suggest a disconnect between an initial success of the trauma patient as an inpatient cleared for discharge and a failure to address and treat the longer-term medical and social needs of the trauma outpatient that significantly limit their quality of life. The possible transition of anesthesiologists into a role of managing surgical patients from their perioperative evaluation through post-discharge follow-up, could be the missing link between the modern trauma patient and the resources they so desire.

This research was supported by the Foundation of Anethesia Education and Research and by the Proposed Research Initiated by Students and Mentors (PRISM) Program, University of Maryland School of Medicine Office of Student Research.

**O.21**

THE RATES OF PARENTAL STRESS IN A PEDIATRIC OPHTHALMOLOGY POPULATION. Clare DeLaurentis*, Osamah Saeedi[1], Sachin Kalarn[1], Lorraine Tran[2], and Roni Levin[1], [1]Department of Ophthalmology and Visual Sciences and [2]Department of Psychiatry, University of Maryland School of Medicine, Baltimore, MD.

Rates of parental stress have recently been gaining more attention in association with childhood illness. Despite the growing interest in identifying and measuring parental stress within pediatric disease populations, little is known about the impact of pediatric ophthalmic conditions on parental stress levels. With these conditions, parents often play an important role in intervention, including administration of eye drops and enforcing the wearing of glasses or an eye patch. This study aims to determine the rates of parental stress in a pediatric ophthalmology population as compared to the general population. Eighty-nine children (53 males and 36 females) with ocular diagnoses were included in the study. The parents of these children (76 mothers and 13 fathers) were administered the Parental Stress Index Short Form (PSI-4 SF) to assess levels of parental stress. The population consists of parents with a mean age of 32.73 $\pm$ 7.69. 85.4% of the parents are female and 70.8% are African American. Data analysis revealed a mean Total Stress score of 0.4182 $\pm$ 0.2443 ($42^{th}$ percentile), a mean Parental Distress (PD) score of 0.4697 $\pm$ 0.2366 ($47^{th}$ percentile), a mean Parent-Child Dysfunctional Interaction (P-CDI) score of 0.4210 $\pm$ 0.2451 ($42^{th}$ percentile), and a mean Difficult Child (DC) score of 0.4072 $\pm$ 0.2608 ($40^{th}$ percentile). Comparative means by independent T-test demonstrated significant difference in stress scores for marital status, parent depression/anxiety, and education level. Total stress scores and DC scores of parents were

significantly higher in non-married parents than married parents ($p<0.05$). PD scores of parents with self-reported depression/anxiety were significantly higher than those without such diagnosis and Total Score and PD scores of parents with a HS degree or less were higher compared to those with higher levels of education ($p<0.05$). This study suggests that there is no significant difference in parental stress between the pediatric ophthalmology population and the general population. Future work will assess the rates of parental stress associated with specific pediatric ophthalmology diagnoses and interventions.

This research was supported in part by the Proposed Research Initiated by Students and Mentors (PRISM) Program, University of Maryland School of Medicine Office of Student Research.

**O.22**

DEVELOPMENT OF NOVEL PREDICTIVE ALGORITHMS FOR RETINOPATHY OF PREMATURITY (ROP). Nisha Donthi*, Osamah Saeedi[1], Janet Alexander[2], and Sachin Kalarn[3], Department of Ophthalmology and Visual Sciences, University of Maryland School of Medicine, Baltimore, MD.

Retinopathy of Prematurity (ROP) is a leading cause of childhood blindness in the world. ROP is caused by the aberrant development of immature retinal blood vessels in premature infants. Increased vessel tortuosity and vessel diameter are cardinal features of this disease, and impaired blood flow is involved in its pathogenesis. Premature infants are at the highest risk for developing severe ROP with a high risk of vision loss. However, ROP is highly preventable. Tools which enable early screening at a low cost and can be used without specialized ophthalmologists are necessary for early treatment of patients with severe ROP and in preventing long term complications. This need is even more pronounced in regions which are under resourced. We are working with Vasoptic Medical Inc. to develop a handheld retinal imager (XyCAM-) with novel predictive software algorithms for early detection of ROP. We aim to develop a completely automated software for the XyCAM- which will be able to quantify the previously stated cardinal features of ROP (tortuosity, vessel diameter). This is a retrospective review of infants screened for high grade ROP and controls. In this study we obtained fundus images from premature infants born at or before a gestational age of 30 weeks. Images are obtained using the RetCam3 (Clarity Medical Systems, Inc.). In order to validate the Vasoptic Suite software we are comparing its efficacy against three different measures. These measures include manual segmentation, existing software such as Automated Retinal Image Analyzer (ARIA) and Computer Aided Image Analysis of the Retina (CAIAR), and finally expert ophthalmologists' assessment of the same images. Our preliminary results include data derived from 20 fundus images of 13 males and 7 females. Thirteen images which are Stage 2 or lower are classified as controls and 7 images which are either Stage 3, Plus Disease, Pre-plus Disease are classified as ROP cases. The mean gestational age of these patients is 27 weeks (SD +/- 2). This research is ongoing.

This research was supported in part by the Proposed Research Initiated by Students and Mentors (PRISM) Program, University of Maryland School of Medicine Office of Student Research and the Little Giraffe Foundation.

**O.23**

DYNAMIC MODELING OF PHYSICIAN EYE GAZE TO UNDERSTAND THE EFFECTS OF ELECTRONIC HEALTH RECORDS ON PATIENT SATISFACTION IN AN OPHTHALMOLOGY PRACTICE. Hannah Kleiman* and Osamah Saeedi, Department of Ophthalmology and Visual Sciences, University of Maryland School of Medicine, Baltimore, MD.

The aim of this study was to examine physician behaviors and eye-gaze patterns during doctor-patient interactions in an ophthalmology practice that uses Electronic Health Records (EHR), and to

determine if there is a relationship between the amount of time a physician gazes at the computer and patient satisfaction. The increasing use of EHR systems in recent years has changed the way healthcare is delivered, and has thus raised concerns about physician efficiency and patient satisfaction. This topic is particularly interesting for ophthalmology practices, which see high volumes of patients and traditionally document with hand-drawn diagrams that are not always accommodated by EHR. For this study, 60 patient visits with 6 ophthalmologists were video recorded over a 2 month period. Videos were separately coded for the behaviors Doctor-Gaze-Computer, Doctor-Gaze-Patient, Doctor-Gaze-Chart, Doctor-Gaze-Other, Doctor-Examining-Patient, and Doctor-Talking. Patients also filled out a 10 question satisfaction survey with answers on a 1-5 scale from "strongly disagree" to "strongly agree." Data was analyzed using SPSS Statistical Suite software. 46% of patients were male and 54% of patients were female. 68% of patients were African American and 32% of patients were White. The average age of patients was 58.98 ± 15.66 years. While with a patient, doctors spent an average of 36.88% ± 16.79% of their time gazing at the computer, and an average 27.33% ± 17.96% of their time gazing at the patient. They spent 8.37% ± 9.75% gazing at the chart, 11.87% ± 4.25% gazing at other people or objects, 16.27% ± 8.04% examining the patient, and 56.98% ± 15.26% talking. 10/10 questions on the patient satisfaction survey had an average rating >4 ("agree"), with the lowest rated one having an average of 4.04. The data collected did not show any significant difference in patient satisfaction ratings for physicians spending more or less time gazing at the computer or patient. This, in conjunction with the high variability in physician behavior, led us to conclude that the time an ophthalmologist spends gazing at the computer or at the patient has no effect on patient satisfaction.

**O.24**

ANTERIOR SEGMENT ULTRASOUND BIOMICROSCOPY IMAGE MEASUREMENTS USING IMAGE J SOFTWARE: INTRA-OBSERVER REPEATABILITY AND INTER-OBSERVER AGREEMENT. Azam Qureshi*, Haoxing Chen, Mona Kaleem, Osamah Saeedi, and Janet Alexander, Department of Ophthalmology and Visual Sciences, Unveristy of Maryland School of Medicine, Baltimore, MD.

Ultrasound biomicroscopy is commonly used by ophthalmologists to evaluate anatomical arrangement within the anterior segment of the eye to study pathological mechanisms, disease course, and treatment responsiveness in many ocular diseases including cataracts and glaucoma. This preliminary work describes a standardized protocol for measuring parameters on anterior segment ultrasound biomicroscopy images using Image J software while proposing use of the trabecular-iris angle apex as a peripheral landmark reference point for established angle-related measures previously dependent upon the scleral spur, which has been shown to be difficult to reliably identify. Furthermore, by utilizing pre-placed markers set by a single observer for the subset of angle-related measures, variability associated with each measurement was isolated from any variability from landmark identification itself. 20 images from 20 eyes of 10 patients were analyzed by 4 observers of varying experience levels and statistical analysis was carried out to determine intra-observer repeatability and inter-observer agreement for all angle-related and non-angle-related measures. Results showed good intra-observer repeatability for all measurements (CV range: 0.60 – 27.44%) and good inter-observer agreement for angle opening distance (500 microns), trabecular-iris angle, trabecular-ciliary process distance, anterior chamber depth, theta 2 and 3, pupil size, sulcus-sulcus distance, ciliary body integrated density, and iris-lens contact distance (ICC range 0.82 – 1.00). There was less agreement between observers for central and paracentral corneal thicknesses, iris thicknesses 1, 2, and 3, theta 4 and 5, iris-ciliary process distance, ciliary body-iris contact distance, and ciliary body length, thickness, and area (ICC range: 0.22 – 0.72). The growing variability for angle-related measurements less directly dependent upon peripheral landmark identification

supports use of a more reliably determined landmark to minimize measurement variation. This study provides an assessment of reliability for many anterior ocular measurements applicable to past and future ultrasound biomicroscopy image studies.

This research was supported by the Knights Templar Eye Foundation.

## Poster Presentation Abstracts

**P.01**

SYNTHETIC NANOPARTICLES THAT MIMIC LIPOPROTEINS AND APOPTOTIC CELLS. Joshua Olexa* and Andrei Maiseyeu[1], [1]Division of Cardiovascular Medicine, Department of Medicine, University of Maryland School of Medicine, Baltimore, MD.

Natural endogenous nanoparticles such as lipoproteins that are composed of multiple proteins and lipid species are robust transporters of cholesterol in cells that regulate lipid homeostasis. Lipoproteins are taken up by cells through receptor-mediated endocytosis or non-receptor mediated macropinocytosis. Mimicking the uptake of lipoproteins via synthetic nanoparticles that are similar in size to endogenous lipoproteins offers a "theranostic" approach for targeting cells with lipid imbalance. Thus, theranostic nanoparticles bearing signaling lipids with therapeutic and diagnostic properties (i.e. "theranostic") represent powerful tools to elucidate pathways in atherosclerosis, where excessive lipid accumulation is a hallmark of the disease. ATP Binding Casette Protein A1 (ABCA1) is a protein involved in the efflux of cholesterol out of cells and is inducibly expressed in macrophages in the presence of cAMP. It is hypothesized that acid sphingomyelinase (aSMase) serves to release free cholesterol, thereby allowing ABCA1 to transport free cholesterol to the membrane for uptake into HDL. In this study, designer nanoparticles were synthesized, and their applications for studying reverse cholesterol efflux were explored. RAW 264.7 macrophages were transfected with various transfection agents or electroporation using GFP-expressing plasmid for optimization of transfection efficiency. siRNA targeted at aSMAse (siSMPD1) was then used to transfect the cells. A small library of theranostic nanoparticles was synthesized and tested in various settings with the aim to optimize labeling efficiency, stability, and biological response. These nanoparticles were then used in cholesterol efflux assays and ABCA1 mRNA expression studies to determine the role of aSMAse in cholesterol transport. Results show no significant difference between efflux of siSMPD1 cells and negative control but do show significantly lower ABCA1 expression in siSMPD1 group. Absence of aSMase in RAW cells leads to a significant decrease in ABCA1 expression, possibly through loss of degradation of cholesterol-sphingomyelin adducts which would likely in turn inhibit LXR signaling, ABCA1's nuclear receptor.

**P.02**

EVALUATING THE ROLE OF BK CHANNEL IN BLOOD PRESSURE REGULATION USING A SMOOTH MUSCLE DELETION OF BK (*SM22-CRE; KCNMA1*$^{FL/FL}$). Zulqarnain Khan* and Andrea Meredith[1], [1]Department of Physiology, University of Maryland School of Medicine, Baltimore, MD.

Over 70 million US adults have high blood pressure (HBP), a precursor for cardiovascular disease (leading cause of death in Baltimore City). Previous studies demonstrated that large conductance, $Ca^{2+}$ activated $K^+$ channels (BK) play a role in regulating BP (Sausbier et al., 2005). However, those studies utilized mice with a global genetic deletion of the BK channel (*Kcnma1*$^{-/-}$), which altered endocrine profiles (i.e. hyperaldosteronism). In order to eliminate such variables, we utilized a novel mouse line in which BK has been genetically deleted in only smooth muscle (*SM22-Cre; Kcnma1*$^{fl/fl}$) to determine whether BK in VSM has a pronounced role in regulating BP. We predicted that *SM22-Cre(+); Kcnma1*$^{fl/fl}$ mice would exhibit higher BP and increased vascular tone compared to mice used in previous studies. Initially, we used non-invasive tail cuff measurements to quantify pulse and systolic blood pressure (SBP) of control and *SM22-Cre; Kcnma1*$^{fl/fl}$ mice. Contrary to our prediction, there were no significant differences in pulse (*WT*: 688.0 ± 34.5 bpm, *SM22-Cre(-)*: 630.4 ± 25.3 bpm, *SM22-Cre(+)*: 601.9 ± 64.3 bpm) or SBP (*WT*: 104.8 ± 12.2 mmHg, *SM22-Cre(-)*: 105.6 ± 10.8 mmHg, *SM22-Cre(+)*: 118.9 ± 8.4 mmHg) between genotypes. Next, we used isometric

tension recordings to measure the response of isolated thoracic aorta (TA) strips to 5 μM phenylephrine (PE). Unexpectedly, the *SM22-Cre(+)* strips (9.83 ± 0.10 mN) did not exhibit increased PE responses compared to *SM22-Cre(-)* strips (9.85 ± 0.07 mN). To determine whether expression of BK differed between *SM22-Cre(+)* and *SM22-Cre(-)* TA, all strips were treated with 10 μM paxilline (PAX, an inhibitor of BK) and PE responses were recorded. As expected, there was no post-PAX increase in PE response for *SM22-Cre(+)* strips (9.78 ± 0.05 mN); paradoxically, the *SM22-Cre(-)* strips also did not show an increased response (9.63 ± 0.11 mN). Our data suggest that *SM22-Cre(+)* mice do not have the predicted SBP elevation possibly due to the presence of renal mechanisms for BP regulation (i.e. RAAS) and that BK may not have a prominent regulatory role in TA function; future studies may seek to investigate cerebral or mesenteric arteries.

This research was supported in part by the Proposed Research Initiated by Students and Mentors (PRISM) Program, University of Maryland School of Medicine Office of Student Research.

**P.03**

BIG DATA: TESTING THE EFFECT OF USING DOMAIN INFORMATION TO CHARACTERIZE DISEASE-ASSOCIATED SNPS IN THE PREDICTION OF CORONARY ARTERY DISEASE. Matthew Lotz* and Michael Grasso, Department of Medicine, University of Maryland School of Medicine, Baltimore, MD.

Coronary artery disease (CAD) is the most common cause of death globally. It is a complex, polygenic disease that is influenced by a vast array of genetic and environmental factors. Currently, clinicians rely on clinical risk factors to judge risk of CAD in pre-symptomatic patients. Genetic information offers potential improvement in disease prediction of pre-symptomatic individuals but has failed to yield any meaningful improvement in prediction to date. So far, CAD-related single nucleotide polymorphisms (SNPs) have been used in predictive algorithms without data to characterize their importance. In this study, we use SNP domain data (e.g., odds ratio, gene closest to SNP, etc.) to differentiate CAD-related SNPs. To do this, we use machine learning, which is a powerful computational tool to test the effectiveness of risk factor data in predicting disease outcomes. We predicted that the incorporation of SNP domain information to CAD-related SNPs and clinical risk factors would improve CAD prediction when using a Support Vector Machine (SVM). To test our hypothesis, we used data from the 5,888 participants of the CHS CARe study to build targeted datasets of 10 clinical risk factors and 21 CAD-related SNPs for each patient. We also used dbSNP to collect 12 domain attributes to characterize each SNP. Combinations of these data (i.e., clinical; clinical and genomic; or clinical, genomic and domain) were used to train and test SVMs using 10-fold cross validation. We evaluated the accuracy of each predictive model using the average Area under the Receiver Operating Characteristic curve (AROC). When trained with clinical risk data, the model provided an improvement over random chance with an AROC of 0.5682. When genomic data was added to the clinical data during training, the model improved slightly (AROC = 0.5955). However, when domain information was added to the clinical and genomic data, the model showed no improvement.

This research was supported in part by the Proposed Research Initiated by Students and Mentors (PRISM) Program, University of Maryland School of Medicine Office of Student Research.

**P.04**

OUTCOMES OF NEWBORN SCREENING FOR CRITICAL CONGENITAL HEART DISEASE (CCHD) AT UNIVERSITY OF MARYLAND CHILDREN'S HOSPITAL. Elena Donald*, Maura Heffernan[1], and Natalie Davis[2], [2]Division of Neonatology, Department of Pediatrics, [1]University of Maryland School of Medicine, Baltimore, MD.

Critical congenital heart disease (CCHD) refers to heart lesions requiring surgical intervention within the first year of life. In Maryland, 2.3 of every 1000 newborns have CCHD, and delayed diagnosis increases morbidity and mortality. In 2010 the American Heart Association recommended universal pulse oximetry screening for CCHD in all newborns, but little data exists to determine if this screening is identifying these infants. Recent studies of oximetry screening detected no infants with CCHD, which the authors related to effective prenatal echocardiography screening in their population. The University of Maryland Medical Center (UMMC) has a large population of mothers who receive little to no prenatal care due to social and financial issues. We hypothesized that pulse oximetry screening would have a higher sensitivity for identifying infants with CCHD in a resource-poor setting. We performed a retrospective record review of infants born in 2013 at UMMC who spent time in the newborn nursery. We collected the primary outcome of oximetry result and results of any subsequent medical evaluations at UMMC (emergency visits or admissions). Our study cohort consisted of 1276 eligible infants with available documentation. Prenatal care was limited in 19%, and 1.6% received no prenatal care. None of the subjects who failed the oximetry screen (n=10) had congenital heart disease. 95% of the cohort received pulse oximetry screening only, 0.6% receiving only an ECHO, and 4.8% received both oximetry and an ECHO. ECHOs were performed in 68 subjects for prenatal concerns (40%) and postnatal clinical concerns (57%). Only one subject received an ECHO for a failed CCHD screen. One subject who passed an oximetry screen was found to have been diagnosed with mild aortic coarctation and mild hypoplastic pulmonary artery at one month of age. We found no associated clinical or demographic risk factors that may increase a newborn's likelihood of failing the CCHD test. Despite 21% of mothers that received limited, late or no prenatal care, the pulse oximetry screen has a low sensitivity for diagnosing newborns with CCHD at UMMC, which calls into question the utility of the CCHD screen.

This research was supported in part by the Proposed Research Initiated by Students and Mentors (PRISM) Program, University of Maryland School of Medicine Office of Student Research.

**P.05**

TREATMENT OF FOCAL AORTIC DISEASE BY TEVAR: HIGH SUCCESS, LOW MORBIDITY AND MORTALITY.

Solomon Hayon*, Michael Huffner*, Donald Harris[1], Solomon Hayon[2], Michael Huffner[2], and Robert Crawford[3], [1]Department of Surgery and [3]Division of Vascular, Department of Surgery, [2]Unveristy of Maryland School of Medicine, Baltimore, MD.

Thoracic endovascular aortic repair (TEVAR) is an established treatment strategy for patients with thoracic aortic dissection, aneurysm, or traumatic pseudoaneurysm. However, its use is poorly studied for the treatment of less common aortic pathologies, such as penetrating aortic ulcer (PAU), intramural hematoma (IMH), and pseudoaneurysms (PSA). Together, these may be considered as focal aortic lesions, and the purpose of this study was to review the use of TEVAR in the treatment of patients with these lesions. This was a retrospective analysis of a 10-year TEVAR series at a high-volume aortic referral center; patients with traumatic aortic injury were excluded. The study group was patients undergoing endovascular repair of focal aortic disease (PAU, IMH, or PSA), while patients with non-focal disease (dissection or non-traumatic aneurysm) served as controls for comparison. The primary outcome was inpatient mortality, and secondary outcomes were neurologic complications, duration of mechanical ventilation, and hospital length of stay. TEVAR was performed in 135 patients with 100% technical success. 50 patients had focal aortic disease, 48 were treated for dissection, and 37 were treated for aneurysm. Both groups had similar demographics and comorbidities, but those with focal disease were more likely to be symptomatic or have AAS. The most common symptoms among both groups were chest pain or back pain (overall 42% and 18%, respectively). Patients with focal disease had similar rates of postoperative neurologic deficits as the control group (4% vs. 13%, P=0.13), but had a trend toward shorter duration of mechanical

ventilation. Overall mortality was 6%, but was significantly lower for patients with focal aortic lesions (0% vs 9%, P=0.03). Focal aortic lesions are often symptomatic, and patients usually present with AAS. Despite this emergent nature, TEVAR is a highly effective treatment and is associated with similar perioperative morbidity and lower mortality than patients treated for dissection or rupture. These findings suggest focal aortic disease can be treated by elective TEVAR with an acceptable risk profile prior to onset of AAS.

**P.06**

MODULATING LUNG INJURY WITH STEM CELLS. Michael Rouse*, Mandheer Wadhwa, Pablo Sanchez, Si Pham, and Bartley Griffith, Department of Surgery, University of Maryland School of Medicine, Baltimore, MD.

Systemic Inflammatory Response Syndrome (SIRS) is a serious complication for patients who have experienced significant trauma. Acute Respiratory Distress Syndrome (ARDS) is the number one mortality cause in patients with SIRS after trauma. ARDS is a condition characterized by inflammation and decreased gas exchange capability. While the specific mechanism of SIRS/ARDS remains unknown, one hypothesis suggests that native molecules present inside cells are released into circulation after tissue injury. Once spilled out, these cell products, known as damage-associated molecular patterns (DAMPs), trigger a response by activating the immune system. Clinically, this response is indistinguishable to the one generated by pathogen-associated molecular patterns (PAMPs) in severe bacterial infections. The objective of this experiment was to establish a rodent model of SIRS/ARDS through acute lung injury caused by histones and to evaluate the therapeutic potential of Amnion-derived Cellular Cytokine Solution (ACCS). Histones are proteins that DNA winds around to form chromatin and are one example of DAMPs. ACCS is the conditioned medium of Amnion-derived Multi-potent Progenitor cells and contains wound healing, anti-apoptotic, and growth factors such as TIMP 1 and 2, annexin 2 and 5, angiogenin, and VEGF. Fourteen female Lewis rats were divided into three groups: DAMPs (injury), 500 uL ACCS before DAMPs (study group), and 1,000 uL ACCS before DAMPs (study group). Outcomes were evaluated by a Kaplan-Meier survival curve and lung injury score (hemorrhage). These parameters were used to quantify the extent of lung injury and modulatory effects of ACCS. From our preliminary data, we conclude that ACCS represents a potential novel therapy for the treatment of ARDS triggered by SIRS.

This research was supported in part by the Proposed Research Initiated by Students and Mentors (PRISM) Program, University of Maryland School of Medicine Office of Student Research and the American Association for Thoracic Surgery's Summer Intern Scholarship.

**P.07**

RESOLUTION OF DONOR NON-ALCOHOLIC FATTY LIVER DISEASE FOLLOWING LIVER TRANSPLANTATION. Andrew Posner* and John LaMattina, Department of Surgery, University of Maryland School of Medicine, Baltimore, MD.

Non-alcoholic steatohepatitis/fatty liver disease (NAFLD) is becoming increasing prevalent worldwide, in parallel with metabolic syndrome and the obesity epidemic. NAFLD is expected to become the leading indication for liver transplantation (LT), while also affecting the quality and quantity of donor livers available for LT. In response to the liver donor shortage, transplant centers have begun utilizing grafts with increasing levels of macrosteatosis (MaS) and microsteatosis (MiS), which historically have been contraindications for use in LT. The objective of this study is to characterize the resolution of high donor liver steatosis following LT. A sample of 29 matched liver transplant donors and recipients were identified. Donors received liver biopsies displaying either MaS or MiS - 15%, while recipients received postoperative liver biopsies for cause. Paired-samples t-

tests were conducted to compare percent MaS, MiS, and total steatosis (MaS+MiS) in donor biopsies and recipient postoperative biopsies. The mean donor percent MaS and MiS were 15.6 (range 0-60) and 41.3 (range 7.5-97.5), respectively. There was a significant difference in percent MaS in donor biopsies (M=15.6, SD=15.9) and in recipient postoperative biopsies (M=0.86, SD=4.56), $p < 0.001$. There was also a significant difference in percent MiS in donor biopsies (M=41.3, SD=24.4) and in recipient postoperative liver biopsies (M=1.8, SD=8.82), $p < 0.001$. Finally, there was a significant difference in the total steatosis in donor biopsies (M=54.8, SD=24.48) and in recipient postoperative liver biopsies (M=1.8, SD=8.82), $p < 0.001$. The mean number of days postoperatively that recipient biopsies demonstrated resolution of MaS and MiS was 116 (range 4-384). Full resolution of MaS and MiS was observed in all but two recipients, who only had biopsies 3 and 14 days postoperatively. There is statically significant evidence that high degrees of MaS, MiS, and total steatosis in donor livers resolve in recipients following LT. The phenomenon of resolution of donor NAFLD following LT has not been previously reported. Insight into the mechanisms responsible could lead to therapeutic targets for treating NAFLD.

**P.08**

THE EFFICACY OF HM-CHITOSAN IN THE IN VIVO RAT EPISTAXIS MODEL.
Saikrishna Gourishetti*, Mayur Narayan[1], Kalpesh Vakharia[2], Ronna Hertzano[2], and Lorna Silipino[2], [1]Department of Surgery and [2]Department of Otorhinolaryngology - Head and Neck Surgery, University of Maryland School of Medicine, Baltimore, MD.

Epistaxis is the most frequent Otorhinolaryngology emergency. In this case-control study, the *in vivo* hemostatic efficacy of two different modalities of hydrophobically-modified chitosan, hm-chitosan, (liquid and gauze) were tested as potential treatments for anterior epistaxis in a rat model. Wistar-Hannover rats were randomized into 4 groups: no treatment, gauze without hm-chitosan, hm-chitosan gauze and hm-chitosan liquid. After achieving a fully anticoagulated state with heparin IV bolus (640 units/Kg), an incision was made in the anterior nasal septum mucosa to induce unilateral anterior epistaxis. After the onset of bleeding, the amount of total blood loss and the time to hemostasis were collected. Due to the high variability in the *in vivo* rat model, rats were excluded based on the following four recurring criteria: inadequate IV heparin delivery, no bleeding following successful IV heparin delivery, unintended intra-operative awareness resulting in interruption of the procedure or death from asphyxiation. The number of total rats tested and excluded for each respective group were: no treatment 11 (8), hm-chitosan liquid 5 (0), gauze without hm-chitosan 5 (1) and hm-chitosan gauze 7 (3). After the exclusions, the averages for total blood loss were as follows: no treatment 0.80 g, hm-chitosan liquid 0.25 g, gauze without hm-chitosan 1.25 g and hm-chitosan gauze 0.47 g. There was a significant decrease in total blood loss when hm-chitosan gauze was used ($p = 0.0009$). The averages for the time to 30 second hemostatic stabilization were as follows: no treatment 214.7 s, hm-chitosan liquid 157.4 s, gauze without hm-chitosan 207.8 s and hm-chitosan gauze 68.3 s. There was a significant decrease in the time to hemostatic stabilization when hm-chitosan gauze was used ($p = 0.017$). As evidenced by the high variability in these data, our *in vivo* rat model was sub-optimal secondary to exclusion of multiple rats. The data suggest that hm-chitosan may reduce blood loss and time to reach hemostatic stabilization; however, further studies are needed on a different *in vivo* model to draw final conclusions on the efficacy of hm-chitosan in treating anterior epistaxis.

This research is supported in part by the Department of Trauma Surgery, University of Maryland School of Medicine, Baltimore, MD, the Department of Otorhinolaryngology – Head and Neck Surgery, University of Maryland School of Medicine, Baltimore, MD, and the Proposed Research Initiated by Students and Mentors (PRISM) Program, University of Maryland School of Medicine Office of Student Research.

**P.09**

WHEN ARE STATIC/MOVING TWO POINT DISCRIMINATION AND SEMMES-WEINSTEIN MONOFILAMENT TESTS RELIABLE IN CHILDREN?. Tim Lancaster*, Karan Dua, and Joshua Abzug , Department of Orthopaedics, University of Maryland School of Medicine, Baltimore, MD.

Objective sensory testing is a critical component of the physical examination, especially when lacerations occur. This is especially true in children, as they may be unable to communicate that numbness is present. The purpose of this study was to determine at what age objective sensory tests can be reliably performed on the hand. Uninjured patients aged 2-17 years were enrolled in the study. Monofilament and static/moving two-point discrimination tests were performed bilaterally assessing the median, ulnar, and radial nerves. Three trials were performed for each test in each nerve distribution and the child was considered to be able to perform the test if they answered correctly all three times. Statistical analysis was performed using univariable linear regression and Welch's t-test. 256 hands were tested utilizing monofilaments and 236 hands utilizing the two-point discrimination tests. The ulnar and median nerve distributions are more sensitive than the radial nerve during monofilament testing ($p<1x10-9$). For both static and moving two-point discrimination, children display the best discrimination ability in the median nerve distribution, followed by the ulnar nerve, and then the radial nerve ($p <1x10-14$). For all nerve distributions, children can better discriminate moving points compared to static points ($p <0.0001$). Hand dominance did not affect monofilament or two-point discrimination scores. All children 5 and older in our cohort were capable of performing the monofilament test, while 83% of 4 year olds and only 14% of 3 year olds were capable. The percentage of 5 year olds capable of testing is significantly greater than the percentage of 3 and 4 year olds combined ($p = 0.002$). For the two-point discrimination tests, all children 7 and older were able to at least partially complete the test, compared to 88% of 6 year olds and 65% of 5 year olds. The percentage of 7 year olds capable of partially completing testing is significantly greater than the percentage of 5 and 6 year olds combined ($p = 0.003$). Thus, objective testing of sensation can be reliably performed in children of appropriate age, with decreasing reliability in younger children.

This research was supported in part by the Proposed Research Initiated by Students and Mentors (PRISM) Program, University of Maryland School of Medicine Office of Student Research.

**P.10**

SELECTIN BLOCKADE USING RHPSGL-1 ON HUMAN NEUTROPHIL ADHESION TO GALTKO.HCD46 PORCINE ENDOTHELIAL CELLS IN THE CONTEXT OF XENOTRANSPLANTATION. Nancy Ye*, Beth French[1], Agnes Azimzadeh[2], and Richard Pierson[2], [1]Department of Microbiology and Immunology and [2]Department of Surgery, University of Maryland School of Medicine, Baltimore, MD.

As the gap widens between the number of patients waiting for an organ and the available supply of suitable donors, increasing attention is being directed towards alternative solutions, such as xenotransplantation, the transplantation of tissues from one species to another. While many advances have been made with xenografts, specifically from genetically modified porcine donors, in terms of limiting hyperacute rejection and diminishing the effects of complement activation, there is still a lack of understanding surrounding the dysregulated coagulation and inflammatory pathways that ultimately cause xenograft failure. Selectins are carbohydrate-binding molecules expressed on endothelial cells, platelets, and leukocytes. They are highly conserved between species and play crucial roles in inflammatory responses as well as blood coagulation and thrombosis. When stimulated, endothelial cells will immediately release P-selectins, and, after approximately 4 hours, E-selectins to the cell surface. With flow cytometry, we confirmed that when GalTKO.hCD46 porcine

aortic endothelial cells (PAECs) are exposed to human TNF (25 ng/mL), this leads to the upregulation of P/E selectins; we also showed that when PAECS are exposed to human thrombin (20 μg/mL), histamine (100 nM), and plasma (10% and 100%), this also leads to the upregulation of selectins. We begin to see expression of selectins after one hour, and higher levels of expression after 2 hours. The selectins bind to P-selectin glycoprotein ligand-1 (PSGL-1), which is expressed on all neutrophils, and they mediate the first step of leukocyte recruitment into the tissue. Using the BioFlux ex vivo microfluidic flow chamber perfusion system, we demonstrated that selectin blockade using recombinant human PSGL-1 led to decreased neutrophil adhesion to TNF-activated PAECs by approximately 30% (n=1). Investigating the role of selectins may bring light to the mechanisms of xenogeneic neutrophil adhesion and lead to new therapeutic strategies to limit inflammation and extend xenograft survival time.

This research was supported in part by the Proposed Research Initiated by Students and Mentors (PRISM) Program, University of Maryland School of Medicine Office of Student Research.

**P.11**

SMALL-FRAGMENT PLATE FIXATION OF HUMERAL SHAFT FRACTURES. Giuliana Rotunno*, Robert O'Toole, Marcus Sciadini, and Andrew Eglseder, Division of Traumatology, Department of Orthopaedics, University of Maryland School of Medicine, Baltimore, MD.

Humeral shaft fractures have traditionally been treated surgically with large-fragment (4.5mm) plates. Orthopaedic traumatologists at our institution often prefer treatment with small-fragment (3.5mm) plates. Our hypothesis was that fractures treated with a 3.5mm plate would have an unacceptable complication rate in comparison to patients treated with 4.5mm plates, particularly in the group allowed full weight bearing on the humerus. A retrospective chart and radiographic review was performed of all humeral shaft fractures OTA 1.12A-C treated with open reduction and internal fixation at a level I urban trauma center from January 2003 to June 2014. We excluded patients with peri-articular extensions (n=169) and patients with inadequate follow-up (n=93). Patients were managed with immediate weight bearing as tolerated without bracing except in cases such as ipsilateral upper extremity fracture preventing weight bearing or radial nerve palsy. Plate thickness was based upon surgeon preference. Our study group consisted of 191 fractures that were further subdivided into four groups: (1) 3.5-mm plate with immediate weight bearing (n= 96), (2) 3.5-mm plate without immediate weight bearing (n=41), (3) 4.5-mm plate with immediate weight bearing (n=29), and (4) 4.5-mm plate without immediate weight bearing (n=9). Two-sided fisher exact was used for the analysis. Consistent with prior studies, we had a low overall non-union rate in our study group (n=191, nonunion = 8.3%, 95% CI: 4.4% – 12.3%). The non-union rate was similar in the 3.5mm and the 4.5mm group overall (8.7% non-union vs. 7.3%, p = 1.00) as well as within the subgroups that did and did not have immediate weight bearing (3.5mm: 9.38% non-union vs. 4.5mm: 3.45%, p = 0.46 and 3.5mm: 9.76% non-union vs. 4.5mm: 22.2%, p = 0.59). Our data contradict our hypothesis. Humeral shaft fractures treated with 3.5mm plates appear to have a comparable non-union rate to controls treated with 4.5mm plates. This study is limited by lack of randomization and potential selection bias as 27% of the patients were treated with 4.5mm plates.

**P.12**

PREVALENCE OF DEPRESSION AND PTSD FOLLOWING ACUTE ORTHOPAEDIC TRAUMA. Stefano Muscatelli*, Hayley Spurr[1], and Gerard Slobogean[2], [1]Royal College of Surgeons in Ireland School of Medicine, Dublin, Ireland and [2]Department of Orthopaedics, University of Maryland School of Medicine, Baltimore, MD.

Depression and post-traumatic stress disorder (PTSD) in patients following acute orthopaedic trauma have been shown to impact recovery, compromise patient reported health outcomes,

increase pain, and decrease physical function. To identify the magnitude of this problem, we sought to determine the prevalence of PTSD and depression in adult patients following acute orthopaedic trauma. We performed a systematic review in accordance with guidelines from the Cochrane Collaboration. We identified 5,589 potentially relevant studies using electronic searches of Medline, Embase, PsycINFO and Cochrane Central. Studies were included if they reported the prevalence of depression or PTSD in patients who experienced acute orthopaedic trauma to the appendicular skeleton or pelvis. Two reviewers independently performed all eligibility screening and data abstraction. A random effects model was used to quantitatively pool the prevalence data from the included studies. Twenty-seven studies with a total sample size of 7,109 patients were included. The pooled prevalence of depression or PTSD was found to be 33.7% (95%CI, 26.7-41.4%). Female gender and multiple-injury trauma were associated with increased prevalence of PTSD or depression. Following orthopaedic trauma, one-third of patients suffer from PTSD or depression. This suggests that many patients will have decreased quality of life following their injury in both physical and mental health domains. In order to maximize patient recovery, combined strategies that address mental health and physical rehabilitation should be investigated.

**P.13**

EFFICACY OF PAIN CONTROL IN POST-RENAL TRANSPLANT PATIENTS USING TRANSABDOMINAL PLANE NERVE BLOCK WITH BUPIVICAINE/LIPOSOMAL BUPIVICAINE MIXTURE. Neal Desai*, Jonathan Danquah*, Neal Desai, and Paul Bigeleisen, Department of Anesthesiology, University of Maryland School of Medicine, Baltimore, MD.

It is well known that transverse abdominal plane nerve blocks are effective in reducing post-operative opiate requirements, as well as severity of pain following abdominal surgery. However, its efficacy as an appropriate analgesic technique for patients undergoing renal transplantation remains unclear. Research has also studied the use of a form of local anesthetic that is encapsulated within a liposomal carrier molecule designed to increase its time at the site of action and has shown that it is a useful option for prolonged reduction of postsurgical pain with significant reduction in opioid consumption. This study consists of patients greater than 17 years of age who are invited to enroll when they are entered into the transplant registry or upon arrival to the hospital for their kidney transplant. All enrolled patients are placed in Group 1 and receive a TAP block at the beginning of surgery consisting of a solution of 10 mL of 0.5% bupivacaine and 20 mL of liposomal bupivacaine (266 mg). The plane between the internal oblique and transverse abdominis muscles was visualized on ultrasound and the solution was injected into the fascial plane between the 2 muscles. Patients in this group also receieve a PCA pump containing 0.2 mg/mL of hydromorphone post-operatively. Group 2 consists of eligible patients who received only the PCA pump post-operatively. Data for this group was retrospectively collected on patients who underwent surgery between May and July of 2015. Outcomes include total post-operative opioid consumption throughout the remaining hospitalization. Our preliminary results show that patients who receive a TAP block have a decrease in total opioid consumption in comparison to non-treatment groups. The treatment group required an average of only 6.3 mg of opioid during their hospitalization versus 18.08 mg in the non-treatment patients.

**P.14**

THE ROLE OF HEPATIC KISSPEPTIN AND ESTROGEN RECEPTOR IN REGULATING METABOLIC AND REPRODUCTIVE ACTIVITY. Nuval Cherian*, Prerana Chatty[1], Shuiqing Qui[2], and Andrew Wolfe[2], [1]Department of Biology, Cornell University School of Undergraduate, Ithaca, NY and [2]Department of Pediatrics, Johns Hopkins University School of Medicine, Baltimore, MD.

Recently, kisspeptin has been shown to have a more widespread physiological role than previously thought. Kisspeptin receptor is found on a wide variety of metabolically and reproductively active tissues suggesting a signaling role in these axes. Kisspeptin has well established effects in the regulation of reproductive function by its action on the GnRH neurons of the hypothalamus. Recent studies have shown that kisspeptin attenuates glucose-stimulate insulin secretion from the pancreas. This study explores how liver estrogen receptor α (ESR1), may regulate metabolic and reproductive function of lean female mice by regulating Kiss1 expression. We used CRE/LoxP technology to selectively knockout Esr1 in the liver of ovariectomized female mice implanted with an estrogen pellet. Changes in gene expression were measured using qPCR with Gapdh mRNA levels as a control. Metabolic function of the mice was tested using insulin and glucose tolerance tests. Reproductive function was gauged by measuring LH and FSH hormone levels from a terminal blood sample using a Luminex assay. We found that our knockout method significantly lowered Esr1 expression in the liver but not in other tissues. We also found a strong negative correlation between Esr1 expression and Kiss1 expression ($p=.021$, $n=17$). For the metabolic tests, we found that Esr1 knockout mice had significantly higher insulin sensitivity ($p=.026$, $n=16$) compared to control. However, glucose tolerance was not significantly different than control ($p=.35$, $n=15$) suggesting that insulin secretion is higher in Esr1 knockout mice. Esr1 knockout mice had higher levels of both LH and FSH, though the results were not statistically significant ($p=.109$, $P=.097$, $n=15$). The data suggest crosstalk between the metabolic and reproductive endocrine axes mediated by ESR1 and hepatic kisspeptin.

**P.15**

CAREGIVER-ADOLESCENT PHYSIOLOGICAL SYNCHRONY AMONG YOUTH WHO VARY IN PRENATAL DRUG EXPOSURE. Hallie Green*, Stacy Buckingham-Howes, and Maureen Black, Division of Growth and Nutrition, Department of Pediatrics, University of Maryland School of Medicine, Baltimore, MD.

Prenatal drug exposure (PDE) acts as an early life stressor that may negatively impact the development of the hypothalamic-pituitary-adrenal (HPA) axis and caregiver-child physiological synchronization. PDE causes the fetal brain to be exposed to excessive cortisol, which may lead to down-regulation of the HPA axis and emotion and attention problems throughout life. In addition to altering HPA axis development, PDE may also decrease caregiver-child cortisol synchrony. Synchrony in infancy is critical for proper development and is associated with social competence and emotion regulation through adolescence. This study examines whether caregiver-child physiological synchrony, measured by cortisol, varies by PDE. The sample of 105 adolescents(mean age 15.48 years, 47.6% male, 98.3% African American) and their caregivers were recruited from a longitudinal study of PDE (cocaine and/or heroin) and non-exposed (NE) children (n= 59, 46) from the same urban, low-income community. In a laboratory evaluation, each dyad member completed two mild stressor tasks. Saliva samples, later assayed for cortisol, were collected before and after the tasks. Three latent cortisol variables (resting cortisol, cortisol reactivity, and cortisol recovery) were created using a latent change score within the latent curve framework. Using multiple-group structural equation modeling, we tested whether caregiver-adolescent cortisol synchrony varied as a function of PDE. Results suggest caregiver-child cortisol reactivity synchrony was significantly weaker in the PDE vs. the NE group, with no group differences in resting or recovery synchrony. PDE as a stressor during fetal development combined with PDE associated childhood environmental stressors may disrupt caregiver-child cortisol reactivity synchrony.

This study was supported by the National Institute on Drug Abuse (R01-DA07432, R01-DA021059 and 1F32DA036274-01).

**P.16**

IMPACT OF CHANGES IN URINE CULTURE ORDERING PRACTICES ON ANTIMICROBIAL UTILIZATION IN INTENSIVE CARE UNITS AT AN ACADEMIC MEDICAL CENTER. Greer Waldrop*, Surbhi Leekha[1], Mohamed Sarg[2], Mona Beier[1], and Emily Heil[2], [1]Department of Epidemiology and Public Health, University of Maryland School of Medicine, and [2]Department of Pharmacology, University of Maryland School of Pharmacy, Baltimore, MD.

The objective of this study is to assess antimicrobial utilization before and after a practice change in urine culture ordering in adult intensive care units (ICUs) whereby urine cultures would only be performed in the presence of pyuria. The design is a quasi-experimental study. The setting is at a 816-bed academic medical center. Participants consists of patients admitted to any adult ICU. Aggregate data for all adult ICUs were obtained for population-level antimicrobial use (days of therapy (DOT)), number of urine cultures performed, and bacteriuria, all measured per 1000 patient-days before (January-December 2012) and after the intervention (January-December 2013), and compared using interrupted time series negative binomial regression. Randomly selected patient charts from the population of adult ICU patients with orders for urine culture in the presence of indwelling or recently removed urinary catheters were reviewed for demographic, clinical, and antimicrobial use characteristics, and compared before and after the intervention. Comparing post- to pre-intervention periods, there were statistically significant reductions in aggregate monthly rates of urine cultures performed and detected bacteriuria but not DOT. At the patient level, compared to the pre-intervention group (n=250), the post-intervention group (n=250) had fewer patients newly started on antibiotics based on urine culture results (23% vs. 41%), but no difference in the mean DOT. A change in urine culture ordering practice was associated with decrease in proportion of patients newly started on antibiotics based on urine culture results but not in duration of antimicrobial use in adult ICUs. Other drivers of antimicrobial use need to be evaluated by antimicrobial stewardship teams in ICU patients.

**P.17**

THE PRESENCE AND ROLE OF EXOSOMES IN YOUNG WOMEN'S BREAST CANCER. Jing Xiang*, Kimberly Jordan, and Virginia Borges, Division of Medical Oncology, Department of Medicine, University of Colorado School of Medicine, Baltimore, MD.

Exosomes, 40-200 nm particles derived from multi-vesicular bodies or from the plasma membrane, have been previously shown to impact cancer metastasis. This study examined the presence and role of exosomes in young women's breast cancer, the leading cancer diagnosis for women under 45 and accounting for approximately 25,000 annual cases. Exosomes were collected via size exclusion chromatography using a Sepharose CL-2B column from the conditioned media of human breast cancer cell lines MDA231 and MCF10DCIS.com, the plasma of human healthy donors and young women's breast cancer patients, and the serum and plasma of healthy and tumor bearing rodents. This method was able to clearly separate the sample's exosome content from the protein content. Total exosome concentration and mean and mode particle size were determined by nanoparticle tracking analysis (NTA) to be within the known physiological range. Electron microscopy images were taken and confirmed the morphology and size of human and rodent exosomes. Exosome presence was further established with a western blot for all three species' protein content, which displayed the presence of marker proteins CD9, CD63, and HSP70. This was further corrobrated with mass spectrometry for a pooled healthy rat sample's protein content, which detected the presence of CD9 and HSP70. Finally, the effects of human exosomes on breast cancer cell proliferation were assessed with a growth and motility assay, which showed that the more invasive MDA231 exosomes increased the proliferation and motility of both MDA231 and MCF10DCIS.com cells while the less invasive MCD10DCIS.com exosomes increased the

proliferation and motility of only the MCF10DCIS.com cells. In conclusion, size exclusion chromatography successfully isolated exosomes from the human cell line media, human donor and patient plasma, and rodent plasma and serums. Compared to ultracentrifugation, this method reduced contaminating serum proteins in the exosome samples and enabled the detection of exosome proteins. The in vitro tumor assays suggest exosomes produced by aggressive tumor cells can potentially influence neighboring cells and the tumor microenvironment.

This research was supported by the University of Colorado Cancer Center Cancer Research Summer Fellowship, the United States Department of Defense (W81XWH-13-1-0078), and the Grohne Family Foundation.

**P.18**

THE EFFECT OF MATERNAL MALARIA ON FETAL HUMORAL IMMUNE PRIMING. Kristen Brao*, Sarah Boudova[1], and Miriam Laufer[2], [1]Department of Microbiology and Immunology and [2]Department of Pediatrics, University of Maryland School of Medicine, Baltimore, MD.

Malaria during pregnancy can significantly impact the health of both mother and child, including altering the infant's susceptibility to malaria through *in utero* priming. Fetal malaria exposure, via maternal peripheral blood infection or placental malaria infection, can elicit an immune response in the neonate. Although prior studies have generally focused on the priming of the cellular immune response, a humoral response can also be generated. In order to investigate the relationship between maternal infection status and fetal anti-malaria antibody development, I planned to test cord blood samples from infants born to mothers who participated in a clinical trial in Malawi for IgM anti-malarial antibodies. Detailed maternal and placental data have been collected as part of the clinical to document infections. Because IgM antibodies do not cross the placenta, their presence would be indicative of a fetal immune response. As placental malaria could disrupt the maternal-fetal barrier and increase the chance of transfer of infected maternal blood cells or antigens, I hypothesized that infants born to mothers with placental malaria are more likely to develop anti-malarial antibodies compared to either infants born to mothers with peripheral malaria or infants born to uninfected mothers. As the first step in the project, I developed an ELISA to detect malaria-specific IgM antibodies. In future studies, we will examine the impact of the fetal immune response on the risk of acquiring malaria infections during infancy. Gaining a better understanding of the relationship between maternal infection and fetal immune priming will enable the development of better antenatal interventions to improve the health of both mothers and children.

This research was supported by Maryland MD/PhD T32 Training Grant.

**P.19**

DIFFERENTIAL EXPRESSION OF GENES INVOLVED IN WOUND HEALING BY NEONATAL AND ADULT DERMAL FIBROBLASTS. Leila Bahmani Kazerooni* and Sripriya Sundararajan, [1]Division of Neonatology, Department of Pediatrics, University of Maryland School of Medicine, Baltimore, MD.

Wound healing is a complex process and often results in excessive deposition of fibrous tissues that results in a scar. Besides loss of function, scarring of tissues has an enormous burden on families with both social and financial implications. Scarring is a gradual age-dependent process that matures with advancing age as demonstrated by fetal wounds that heal with minimal to no scar in-contrast to older adults who heal wounds with abundant scar formation. Understanding the biological complexity behind the mechanism of scar can offer therapeutic benefit aimed at minimizing organ damage, and thereof preserve organ function. Our study aimed to study the functional differences in gene expression between neonatal and adult dermal fibroblasts with and without transforming growth factor β, a naturally occurring growth factor responsible for

extracellular matrix generation and remodeling in the wound healing process. Complementary DNA from harvested adult and neonatal dermal fibroblasts were used to study the gene expression of various factors that are involved in wound healing process, including Collagen 1A1 and 1A2, Collagen 3A1, IL4 receptor, and TGFβ receptors by RTqPCR. Future directions include assessing the intracellular signaling mechanism behind the differential responses between adult and neonatal fibroblasts using western blot analyses.

**P.20**

THE ROLE OF POLYCYSTIN-PAR3/APKC INTERACTION IN ESTABLISHING ENDOTHELIAL CELL POLARITY. Katelyn Kalutkiewicz*, Patricia Outeda, and Terry Watnick, Division of Nephrology, Department of Medicine, University of Maryland School of Medicine, Baltimore, MD.

Autosomal dominant polycystic kidney disease (ADPKD) is the most common inherited renal disease and is caused by mutations in two genes, *PKD1* (protein: polycystin-1) and *PKD2* (protein: polycystin-2). Polycystin-1 (PC1) and Polycystin-2 (PC2) work together at the cell membrane to initiate calcium-based signaling pathways. Deletion of either gene results in a failure of endothelial cells to establish polarity and undergo directional migration, which in turn lead to defects in branching of lymphatic vessels. Here we investigate whether PC1 promotes polarity through the Par3/aPKC pathway, as demonstrated in fibroblasts. Using co-immunoprecipitation in both WT and *Pkd1* depleted endothelial cells, we observed in preliminary data that Par3 interacts with full-length (FL) PC1. Consistent with this finding, pull-down of PC1 reveals Par3-100, an isoform previously shown to interact with PC1 in fibroblasts. Interestingly, Par3 does not interact with PC2, suggesting a function for PC1 that is independent of PC2. Knock-down of PC1 expression also suggests that levels of FL-PC1 are more stable than cleavage forms. Together, our data suggest a generalizable role for PC1 as it likely forms a pro-polarity complex with Par3 and aPKC in endothelial cells, thus enabling directional migration and proper development of lymphatic vessels within the kidney.

**P.21**

CRITICAL CONGENITAL HEART DISEASE SCREENING VS. INFANT CAR SEAT CHALLENGES FOR DETECTING INFANTS AT RISK FOR DESATURATION EVENTS IN THE NURSERY. Maura Heffernan*, Elena Donald[1], and Natalie Davis[2], [2]Division of Neonatology, [1]Department of Pediatrics, University of Maryland School of Medicine, Baltimore, MD.

Premature and low birth weight infants are at increased risk of respiratory distress syndrome, apnea of prematurity, and cardiac anomalies, leading to significant issues with hypoxemia including impaired development and cognitive performance. Therefore, early detection of hypoxia in neonates prior to discharge and early intervention is critical. The Infant Car Seat Challenge (ICSC) and Critical Congenital Heart Disease (CCHD) screen are two tests commonly performed to detect infants at risk for adverse cardiopulmonary events. CCHD screening involves performing pre- and post-ductal pulse oximetry on all infants. ICSCs are periods of observation to monitor for apnea, bradycardia, and desaturations while in a car safety-seat position. Little evidence exists to determine the utility of ICSCs in identifying infants at risk for adverse cardiopulmonary outcomes. We hypothesize that selective ICSCs will be less sensitive than universal CCHD screening for detecting infants at risk for desaturation events at the time of hospital discharge. We performed a retrospective medical record review of neonates born in 2013 at University of Maryland Medical Center who qualified for both the ICSC and CCHD screens. We reviewed the primary outcomes of CCHD result and ICSC result as well as clinical and demographic risk factors for failure of each. On preliminary analysis of 445

subjects, 54 underwent both screening tests. None failed the CCHD screen but 9.3% failed the ICSC. In fact, there were no CCHD failures in the cohort. ICSC failure rate was 6.7% in those with adequate prenatal care (PNC), 14% in those with limited PNC, and 50% in those with no PNC. There were no significant differences between those who passed vs. failed the ICSC based on birth gestational age, weight, apgar scores, gender, race, respiratory support requirements, or pre- or post-ductal saturations on the CCHD screen. None of those who failed had an ECHO vs. 12% of those who passed. In conclusion, we did not find an association between CCHD and ICSC failure, indicating that performing CCHD screens alone in this population may miss infants at risk of adverse respiratory events.

This research was supported in part by the Proposed Research Initiated by Students and Mentors (PRISM) Program, University of Maryland School of Medicine Office of Student Research.

**P.22**

IRON STATUS AND HOUSEHOLD WEALTH: A CROSS-SECTIONAL STUDY ON INFANT DEVELOPMENT IN RURAL INDIA. Jennifer Reid*, Nicholas Tilton, and Maureen Black, Division of Growth and Nutrition, Department of Pediatrics, University of Maryland School of Medicine, Baltimore, MD.

Over 200 million children under 5 years old fail to reach their developmental potential in low and middle income countries (LMIC), in part due to poor nutrition. One quarter of the global population is affected by anemia, with roughly half caused by iron deficiency. Anemia is most concentrated in preschool aged children (0 to 5 years old). With no internationally agreed upon iron marker, this paper aims to identify the iron measure most closely associated with the Mullen Scales of Early Learning (MSEL) development using baseline data on 513 infants enrolled in Project Grow Smart, a community-based randomized controlled trial of micronutrient fortification in rural India. Using the identified iron measure, this paper investigates whether relations between iron status and child development vary by household wealth. Pearson correlation analysis revealed soluble transferrin receptor (sTfR) and sTfR-ferritin index were nearly equally correlated with gross motor and receptive language; neither was correlated with fine motor, visual reception, or expressive language. In a linear regression analysis that included household wealth, sTfR-ferritin index was negatively associated with gross motor ($\beta$= -0.14, p = .02) and receptive language ($\beta$ = -0.10, p = .04) development. These relations did not vary by household wealth. These findings suggest that: 1) infants with low iron status are at risk for low gross motor and receptive language development and 2) interventions to promote infants' gross motor and receptive language development should consider their nutritional (iron) status.

This research was supported by The Summer Program in Obesity, Diabetes and Nutrition Research Training under NIH award number T35DK095737 and by grants from The Micronutrient Initiative, Ottawa, Canada and The Mathile Institute for the Advancement of Human Nutrition, Dayton, Ohio.

**P.23**

SINGLE NEURON DEEP BRAIN IMAGING IN THE HORIZONTAL DIAGONAL BAND OF BROCA. Jacob Danoff* and Adam Puche, Department of Anatomy and Neurobiology, University of Maryland School of Medicine, Baltimore, MD.

The Horizontal Diagonal Band of Broca (HDB) is a basal forebrain nucleus that sends GABAergic/cholinergic projections to the main olfactory bulb (MOB) and the hippocampal CA1 region. Through phase-locking to respiration, these projections are hypothesized to modulate the processing of olfactory information within the MOB. However, the complexity of different neural

types within the structure has made the involvement of specific neural classes in these functions elusive. In order to characterize the cholinergic neuronal population in vivo, the structure was stereotactically infected with the GCAMP6S virus in ChATcre transgenic mice. This construct is a genetically coded calcium sensor which in this line of mice is only expressed in the cholinergic neurons of the HDB. Combining this approach with the new technique of deep brain imaging through a gradient index (GRIN) lens will enable imaging of specific neural populations deep within the in vivo brain. Our results will help elucidate how olfactory and respiratory pathways function and provide insight into how the brain modulates olfaction.

This research was supported in part by the Proposed Research Initiated by Students and Mentors (PRISM) Program, University of Maryland School of Medicine Office of Student Research.

**P.24**

MMP9 AND ACTIVATED MACROPHAGES ARE INCREASED IN THE BRAIN 30 DAYS AFTER POLYTRAUMA. Sarah Doran*, Philip Chan[1], Julie Proctor[2], Adam Puche[3], and Gary Fiskum[2], [1]Department of Medicine, Tufts University School of Medicine, Boston, MA and [2]Department of Anesthesiology and [3]Department of Anatomy and Neurobiology, University of Maryland School of Medicine, Baltimore, MD.

Many civilian and warfighter TBI victims experience additional injuries, including those that result in hemorrhagic shock (HS). Hemorrhage, with attendant hypotension and reduced delivery of oxygen to the brain, places the TBI victim at significant risk for exacerbation of the primary brain injury. Thus, use of inspired or ventilatory O2 might overcome reduced O2 delivery and improve neurologic outcome. However, both preclinical and clinical studies suggest that hyperoxic resuscitation following moderate TBI and other forms of acute brain injury can worsen outcome, based on excessive production of reactive oxygen species and oxidative modifications to macromolecules. Excessive oxidative stress causes the blood brain barrier to breakdown permitting leukocytes to migrate into the brain and secrete pro-inflammatory cytokines, exacerbating brain damage. Using a rodent model of polytrauma, our lab is investigating the extent of secondary inflammation brain damage 30 days after injury. ED1 is a known marker for activated macrophages and MMP9 is known to play a role in early blood brain barrier breakdown and later in neovascularization and neural plasticity. I hypothesized that due to increased oxidative stress, mice treated in a hyperoxic environment would have more MMP9 positive ED1 positive cells. Using fluorescent immunohistochemistry with a double-labelling technique and an optical fractionator program to count colablled cells, we found that MMP9 positive ED1 cells were significantly more abundant in the cortex of polytrauma animals than in sham animals. Yet, we found no difference between hyperoxic and normoxic treated animals, indicating that at 30 days after injury MMP9 and activated macrophage activity is the same between oxygen treatment groups.

This research was supported by the US Air Force.

**P.25**

CORRELATING PERI-ICTAL MOOD SCORES TO HIPPOCAMPAL VOLUME IN PATIENTS WITH EPILEPSY. Kathryn Grimes*, Maureen Cassady[1], Serena Yin[1], Scott Thompson[2], and Jennifer Hopp[1], [1]Department of Neurology and [2]Department of Physiology, University of Maryland School of Medicine, Baltimore, MD.

Depression is one of the most common comorbidities to coincide with epilepsy, making it clinically significant for epilepsy treatment and of high concern to patients. While the association of depression and epilepsy has been studied extensively, little has been done to assess mood changes in the hours to days surrounding a seizure, in the peri-ictal period. Because Electroconvulsive Therapy (ECT) treats depression by inducing a seizure, we expect that mood may improve following an

epileptic seizure. In temporal lobe epilepsy (TLE), the most common type of focal onset epilepsy, seizures often originate from the hippocampus, an area of the brain critical for mood regulation. As such, we hypothesize that following a seizure, patients with TLE will have a greater improvement in mood than patients with generalized onset epilepsy. In addition, we are aiming to see whether there are any structural differences in the hippocampus in patients with TLE, such as hippocampal volume loss, that correlate with their mood scores. We hypothesize that patients with TLE and hippocampal volume loss will have higher baseline depressed mood and have smaller improvements in mood after seizure. We recruited patients admitted to the Epilepsy Monitoring Unit for video EEG monitoring, and administered 3 well-established mood questionnaires upon enrollment and at four specified time points after a seizure. Seizure type was classified by EEG analysis as focal or generalized. We then analyzed clinically acquired MRI scans using an automatic segmentation computer program called Freesurfer to measure hippocampal volumes. 59 patients have been enrolled in the study so far. Patients with TLE have greater baseline depressive mood and show greater improvement at the 4 hour time point following a seizure compared to patients with generalized onset epilepsy. The hippocampal volumes of 8 patients (4 with TLE) were measured. TLE patients with smaller hippocampal volumes displayed lower baseline depressive mood with less of an improvement in mood after seizures compared to those with larger volumes. Further analysis with additional patients of varying epilepsy types may yield more conclusive evidence.

This research was supported in part by the Proposed Research Initiated by Students and Mentors (PRISM) Program, University of Maryland School of Medicine Office of Student Research.

**P.26**

SIRT1 AS A POTENTIAL MARKER OF DISEASE ACTIVITY AND RESPONSE TO TREATMENT WITH GLATIRAMER ACETATE IN MULTIPLE SCLEROSIS. Daniel Hewes*, Adam Kruszewski, Alexandru Tatomir, and Horea Rus, Department of Neurology, University of Maryland School of Medicine, Baltimore, MD.

SIRT1 is a member of the histone deacetylase (HDAC) class III family of proteins and is an NAD-dependent histone and protein deacetylase. SIRT1 can induce chromatin silencing through histones deacetylation and can modulate cell survival by regulating transcriptional activities. We have previously shown that SIRT1 mRNA expression was significantly lower in the peripheral blood mononuclear cells (PBMCs) of multiple sclerosis (MS) patients during relapses than in the PBMCs of stable patients. We have now investigated SIRT1 as a possible biomarker as a predictor of relapse as well as responsiveness to glatiramer acetate (GA) treatment in relapsing-remitting MS (RRMS) patients. Over the course of 2 years, a cohort of 15 GA-treated RRMS patients were clinically monitored using the Expanded Disability Status Scale (EDSS), and blood samples were collected at 0, 3, 6, and 12 months. Target gene mRNA expression was measured in patients' isolated PBMCs by real-time quantitative PCR and protein expression by western blotting. During relapses MS patients had a decreased expression of SIRT1 mRNA ($P<0.003$) and protein when compared to stable MS patients. Non-responders to GA treatment were defined as patients who exhibited at least two relapse events following initiation of GA treatment. Responders to GA treatment had significantly higher SIRT1 mRNA ($p=0.01$) as compared to non-responders. Additionally, SIRT1 protein levels decreased in non-responders over time, but the SIRT1 protein levels were unchanged in responders. Receiver operating characteristic (ROC) analysis was used to assess the predictive power of SIRT1 as a putative biomarker. The predictive values of relapse for SIRT1 mRNA was 72% ($p<0.02$). The predictive values of responsiveness to GA treatment were 70% ($p=0.04$) for SIRT1 mRNA. Our data suggest that SIRT1 could serve as a potential biomarker in order to predict a MS relapse and evaluate a patients' responsiveness to GA therapy.

This research was supported in part by the Proposed Research Initiated by Students and Mentors (PRISM) Program, University of Maryland School of Medicine Office of Student Research and by the Foundation of the Consortium of Multiple Sclerosis Centers' MS Workforce of the Future program.

**P.27**

KINEMATIC AND KINETIC OUTCOMES OF ROBOT ASSISTED NEUROREHABILITATION IN CHRONIC MODERATE-TO-SEVERE HEMIPARETIC STROKE. Tahreem Iqbal*, Susan S. Conroy[1], Anindo Roy[2], and Christopher T. Bever[3], [1]VA Maryland Health Care System, [2]Division of Robotics Neurorehabilitation, [3]Department of Neurology, University of Maryland School of Medicine, Baltimore, MD.

Robotic rehabilitation therapy for persons with moderate-to-severe arm function impairment has been shown to improve arm kinematic and kinetic measures of impairment following stroke but functional improvements have been limited. Preliminary data suggested that adding conventional therapy, which we have called transition to task therapy, to robotic rehabilitation, may improve functional outcomes. The current trial is a randomized, single-blind study to confirm those results. We performed a secondary outcome analysis comparing the effects of planar robot therapy alone (RT) or in combination with transition to task therapy (TTT) on kinematic and kinetic measures of arm function. Forty-one moderate-to-severe chronic stroke patients (Mean Fugl Meyer 21.47±1.36, range 8.33-37) were randomized to either RT (n=19, Mean FM 22.47±2.03, range 8.33-37.33) or TTT (n=22, Mean FM 20.61±1.86, range 10.67-37.33). A blinded examiner evaluated functional (based on FM scores), kinematic, and kinetic outcomes at 12 weeks of training and at 24 weeks for retention. Treatment responders were defined as changes in FM scores of 4.25 or more and response rates were compared using the Chi Square test. Kinematic and kinetic outcomes were evaluated with student t-tests for two independent means, using a significance level of p-0.05. The response rates for RT and TTT at 12 weeks were 21% and 45% (p = 0.10, Chi) while at 24 weeks were 22% and 24%. Between groups comparisons of RT and TTT were not significant for the kinematic and kinetic parameters at p-0.05. Longitudinal analysis showed significant improvements at p-0.05 for both groups in smoothness (i.e. speed metric) and accuracy (i.e. reach error and path error metrics) at both 12 and 24 weeks, but not for the speed parameters. Furthermore, there were significant RT group improvements in shoulder abduction and flexion at p-0.05. The response rate was greater in the TTT than RT groups but the difference was not statistically significant. Significant between groups differences were not seen in any of the kinematic or kinetic outcome measures either but significant within group longitudinal improvements were seen in smoothness and accuracy.

This research was supported by American Academy of Neurology (AAN) and the VA Department of Research and Development VA Merit Award B6935R (PI Christopher Bever).

**P.28**

ANATOMIC SPECIALIZATION OF MICROGLIA ALONG ADULT NEURONAL MIGRATORY PATHWAYS IN THE OLFACTORY BULB. Brittany Schuh* and Adam Puche, Department of Anatomy and Neurobiology, University of Maryland School of Medicine, Baltimore, MD.

Microglia play an active role in monitoring the local environment and clearing cellular debris via highly motile ramified processes. One of the hallmarks of microglia processes is that they rarely respect boundaries between neuronal structures, but instead ramify across regional and white matter boundaries. These innate immune cells may also be involved in the regeneration of neuronal circuits, potentially attacking transplanted stem cells. The major neurogenic process active in adult is the

adult subventricular zone (SVZ) in which neuroblasts are generated, migrate along the rostral migratory stream (RMS), and integrate into the olfactory bulb. This migratory pathway is a unique environment guided by tightly associated astrocytic structures. We hypothesized that this protected pathway may exclude microglial processes. To assess this we performed Immunohistochemistry for microglia in a line of mice expressing green fluorescent protein in neuroblasts and interneuron populations. Using the GFP labeling as a guide to RMS boundaries we compared microglial process organization in the RMS and in the adjacent neuropil of the olfactory bulb. Initial observation indicates that microglial processes preferentially oriented parallel or perpendicular to the rostral migratory stream, with comparatively few processes penetrating into or across the streams of neuroblasts. In contrast, microglia in adjacent neuropil regions ramified processes in all directions irrespective of the local tissue architecture. These observations suggest that microglia contact to migratory neuroblasts is limited. We hypothesize that this may serve to 'protect' immature neuroblasts from recognition by the mature phagocytic microglia of the brain and conjecture that protection of stem cells from microglia during transplant may improve overall survival/integration rates.

**P.29**

EPILEPTIC SEIZURES PRODUCE A TRANSIENT IMPROVEMENT IN MOOD IN EPILEPTIC PATIENTS WITH DEPRESSION. Katherine Turlington*, Maureen Cassady*, Mary Richert[1], Jennifer Hopp[2], and Scott Thompson[3], [2]Department of Neurology and [3]Department of Physiology, [1]University of Maryland School of Medicine, Baltimore, MD.

There is a well-documented comorbidity between clinical depression and epilepsy, as well as an overlap in brain regions that regulate mood and the anatomical locations of seizure foci. However, it is not known whether there are immediate post-ictal effects of epileptic seizures on mood and how long any such changes persist. Electroconvulsive Therapy (ECT), a treatment for severe depression, is thought to induce convulsive activity comparable to the electrical activity of seizures, leading us to ask whether patients with epileptic seizures (ES) would experience changes in mood after seizures. We therefore tested the hypothesis that epileptic patients with depressive symptoms will experience a greater improvement in mood in the postictal period compared to those with non-epileptic seizures (NES), because epileptic seizure activity is similar to the activity induced in the brain during ECT. We also hypothesized that patients with focal seizures would be more likely to experience post-ictal improvements in mood. Subjects were enrolled (n=79) from the Epilepsy Monitoring Unit at the University of Maryland Medical Center and completed Beck Depression Inventory-II (BDI-II), Beck Anxiety Inventories (BAI), and the Montgomery Asberg Depression Rating Scale (MADRS). These scales were completed prior to seizures and post-ictally within a 1-4 hour interval, at 12 hours, 24 hours and 2 weeks.

We found that epileptic patients showed a sustained improvement in mood over 24 hrs post-ically. In contrast, NES patients experienced more variable post-ictal mood changes. Our data also showed that epileptic patients with focal seizures displayed a trend toward greater mood improvements than ES patients with generalized seizures. Statistical analysis will be used to measure the significance of these results. In conclusion, patients with ES and NES have similar levels of depressive symptoms before seizures but ES patients appear to have a more sustained short-term improvement in mood after seizures. Continuing enrollment of subjects is underway to confirm these results and further this hypothesis.

**P.30**

SCA2 PRESENTING AS A FOCAL DYSTONIA. Heather Wied* and Stephen Reich, Department of Neurology, University of Maryland School of Medicine, Baltimore, MD.

SCA2 is due to an expansion of CAG repeats in the ataxin-2 gene on chromosome 12q24. Patients typically present in adulthood with gait and limb ataxia, slow saccades and neuropathy. Extrapyramidal signs are not uncommon including Parkinsonism, which may be responsive to levodopa; dystonia has been observed in at least 14% of patients (van Gaalen J, et al. Mov Disord 2011) but is usually not the presenting sign. When SCA2 begins with a Movement Disorder with little or no ataxia, the diagnosis may not be considered. At age 41y an African American woman noticed difficulty manipulating a pencil with her right hand. On examination there was dystonic writer's cramp of the right hand as well as mild dystonia with other tasks. There was slight dysmetria of both upper limbs and mild difficulty tandem walking but neither of these findings was symptomatic. An MRI demonstrated cerebellar and brainstem atrophy. Her mother was reported to have a progressive gait disorder and her maternal grandmother was similarly affected; two of three siblings were affected as well as maternal uncles and cousins. A total of ten individuals were reported as symptomatic in a three-generation pedigree (Fig). It was subsequently learned that her mother presented with a cerebellar syndrome and was found to have SCA2 (37 CAG repeats); as her disease progressed, she was observed to have a rest tremor and mild cervical dystonia. Our patient's cerebellar signs have been minimally progressive during follow-up of 8 years, in contrast to the dystonia which has worsened to the extent that she can barely use the right hand due to flexion of the thumb and fingers which exacerbates during attempted use. She did not improve with botulinum toxin or levodopa but has had some improvement with trihexyphenidyl. This case demonstrates that SCA2 may present as a focal dystonia with minimal cerebellar signs and that throughout the course, the dystonia may remain the predominant symptom.

**P.31**

NUCLEUS ACCUMBENS MITOCHONDRIAL DYNAMICS IN DRUG ABUSE AND DEPRESSION. Jeremy Winer*, Mary Kay Lobo, Ramesh Chandra, and Chase Francis, Department of Anatomy and Neurobiology, University of Maryland School of Medicine, Baltimore, MD.

The nucleus accumbens (NAc) is bilateral structure in the basal forebrain and has an important role in the reward pathway, vital to the processing of reward, pleasure, motivation and reinforcement. As such, the NAc is involved with many psychiatric disorders, including addiction and depression. 95% of the NAc is composed of two types of medium spiny neurons (MSNs), which are differentiated by their enrichment of dopamine D1 vs. D2 receptors. Previous work shows these neurons have opposing effects, with activity in the D1-MSNs associated with a positive reward and affect, while D2-MSN activity is associated with a negative reward and affect. Due to these opposite effects, it is plausible that these MSNs may have differential energetic usage in different psychiatric states. For instance, D1-MSNs have been shown to be more active in addiction models, while D2-MSNs are expected to be more active in depression models. To investigate the differential activity levels and subsequent energy usages we have begun to examine genes important for mitochondria biogenesis and function in the two MSN subtypes. Using a Ribotag methodology, we were able to isolate mRNA from the two MSN subtypes in mice that underwent chronic social defeat stress (CSDS), a model with strong face validity for depression, and after repeated cocaine exposure. We observed that mRNA for mitochondrial biogenesis and function molecules are altered in MSN subtypes after cocaine exposure, while a few of these mRNAs are altered after CSDS. In parallel we have examined these molecules in postmortem NAc from individuals with major depressive disorder (MDD) or cocaine dependency. We find many of these mRNAs are reduced in NAc of individuals with MDD but increased in NAc in cocaine dependent individuals. Finally, to determine if the changes in mitochondrial related genes lead to altered mitochondrial biogenesis we

are using cre-inducible mouse lines and an adeno-associated virus to examine mitochondrial number and density. Collectively our studies will provide new information into the molecular mechanisms underlying mitochondrial dynamics in selective neuronal subtypes in depression and drug abuse.

This research was supported in part by the Proposed Research Initiated by Students and Mentors (PRISM) Program, University of Maryland School of Medicine Office of Student Research and supported by NIH grants R01MH106500 and R01DA038613.

**P.32**

RAPID ANTIDEPRESSANT ACTION OF AN ALPHA5-SELECTIVE BENZODIAZEPINE PARTIAL INVERSE AGONIST: RESTORATION OF EXCITATORY SYNAPTIC STRENGTH. Jackie Zhang*, Jonathan Fischell[1], and Scott Thompson[2], [1]Department of Medicine and [2]Department of Physiology, University of Maryland School of Medicine, Baltimore, MD.

Major depression is characterized by persistent feelings of low mood and loss of interest in rewarding events and stimuli. Selective serotonin reuptake inhibitors (SSRIs) are the conventional treatment for patients with major depressive disorder, but are unfortunately effective in only half of patients and take several weeks to relieve symptoms. Other compounds rapidly reduce depressive symptoms, but have significant negative side effects. Based on how these compounds work to reverse symptoms of depression, we predict that alpha5-selective partial inverse agonists at the benzodiazepine site of GABAA receptors would also produce similar effects, but with minimal side effects. The Thompson lab has previously tested two compounds that act on this site and achieved promising results in rodents subjected to chronic stress. These compounds are not suitable for clinical trials however. Here, we examined an alpha5-selective partial inverse agonist developed by Pfizer, called CP-457,920, which is FDA approved for clinical trials. We used well-established stress- and antidepressant-sensitive behaviors (sucrose preference and social interaction tests) to assay alterations in depression-like symptoms, specifically hedonic behavior, before and after an acute administration of CP-457,920. We also used standard electrophysiological procedures to examine the stress-sensitive excitatory synapses between temporoammonic (TA) afferents and the distal dendrites of CA1 pyramidal cells in brain slices from stressed rats that did or did not receive the drug. We completed treatment and analysis for seven rats, and are in the process of beginning another cohort of rodents on our protocol. We predict that CP-457,920 will produce significant relief of anhedonia in our behavioral tests and produce a rapid reversal of stress-induced synaptic changes within 24hrs of a single systemic injection, indicating a significant reduction of depressive symptoms.

This research was supported in part by the Proposed Research Initiated by Students and Mentors (PRISM) Program, University of Maryland School of Medicine Office of Student Research.

**P.33**

MORPHOLOGICAL AND FUNCTIONAL CHANGES IN RETINAL INTERNEURON POPULATIONS IN A HUNTINGTON'S DISEASE RAT MODEL. Vivian Shi*, Steven Bernstein, and Mary Johnson, Department of Ophthalmology and Visual Sciences, University of Maryland School of Medicine, Baltimore, MD.

Huntington's Disease (HD) patients have been recently shown to display unusual visual deficits hypothesized to be due to retinal changes in early and later disease stages; however, the pathophysiology behind these symptoms is poorly understood. Since HD selectively affects interneurons in the CNS, we aimed to evaluate whether HD also compromises retinal interneuron function, specifically horizontal and/or amacrine cell populations. Using a novel electrophysiological test recently presented by our lab, we observed a distinctive alteration in HTN rat model ERG and OP profiles suggesting horizontal cell dysfunction. In order to determine if the functional loss

correlates with structural loss, we used IHC to investigate horizontal cell morphology. We have found that affected cells do not selectively express mutant Huntingtin (mHtt) protein accumulation, compared with other retinal cell types in the same layers. However, our data suggests that there may be dendritic tree loss within the horizontal cell layer in the INL, consistent with other affected tissues in the CNS. Previous reports suggest morphological changes such as axonal pruning and dendritic loss occur in HD affected brains. This structural loss would provide an explanation for the functional alterations seen in the ERG data. Data provided by our study will confirm the use of this valuable diagnostic tool in HD analysis and as a potential biomarker for effective treatment.

This research was supported in part by the Proposed Research Initiated by Students and Mentors (PRISM) Program, University of Maryland School of Medicine Office of Student Research and by NIH grant EY105304 to SLB.