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Abstract Booklet

ABSTRACTS

Oral Presentation Abstracts

O.01

EARLY MICROCHIMERISM AFTER FACE TRANSPLANTATION DETECTED BY QUANTITATIVE REAL-TIME POLYMERASE CHAIN REACTION OF INSERTION/DELETION POLYMORPHISMS. Benjamin Schultz*, Eduardo Rodriguez[1], Rolf Barth[2], and Jhade Woodall[3], [1]Department of Plastic and Reconstructive Surgery, New York University School of Medicine, New York, NY and [2]Division of Transplantation, [3]Department of Surgery, University of Maryland School of Medicine, Baltimore, MD.

Transplantation of vascularized composite allografts (VCA) containing vascularized bone marrow (VBM) has been shown in a nonhuman primate model to be associated with improved graft survival and evidence of macrochimerism. Sustainable chimerism has not been reported in any clinical VCA recipients. We investigated the presence of chimerism in our clinical full-face VCA with upper and lower jaw VBM components using established techniques of flow cytometry and short tandem repeat analysis without detecting any evidence of macrochimerism. We subsequently analyzed post-operative whole blood samples from our face transplant recipient using an assay (AlleleSEQR) that screens and quantifies DNA by real time quantitative polymerase chain reaction (rtPCR) utilizing insertion/deletion (InDel) polymorphisms as genetic markers sensitive to 0.001% [10]. Samples were taken from post-operative days (POD) 3 to 335. On POD 3 the recipient demonstrated 0.05% microchimerism that subsequently decreased to 0.000%. These results in a full face transplant with VBM demonstrated no macrochimerism and only transient microchimerism at early time points. Peripheral blood chimerism is an unlikely mechanism for any immunologic benefit of clinical VCA with standard immunosuppression.

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O.02

TRANSVERSE INFRA-CLAVICULAR THORACOACROMIAL (TIC TAC): A NEW APPROACH TO A RARELY USED RECIPIENT IN MICROSURGICAL BREAST RECONSTRUCTION. Vasilios Mavrophilipos*, Karan Chopra, Jeffrey Zapora, Luther Hamilton Holton III, and Devinder Singh, Division of Plastic Surgery, Department of Surgery, University of Maryland School of Medicine, Baltimore, MD.

The internal mammary and thoracodorsal vessels, commonly used recipients for microvascular breast reconstruction, are sometimes unavailable or compromised. This study demonstrates that a transverse infraclavicular (TIC) incision can provide ideal exposure to quickly and reliably perform the anastomosis of a free flap to the thoracoacromial (TAC) vessels for breast reconstruction. A cadaver torso was used to demonstrate the feasibility of harvesting and delivering the thoracoacromial vessels through a transverse infraclavicular incision. We also report a bilateral MS-TRAM to TIC TAC vessels for delayed breast reconstruction in a non-irradiated 47 year old patient with a history of tissue expanders explanted for infection. Review of the literature revealed five descriptions of the thoracoacromial vessels used in breast reconstruction: two cases as a primary recipient, two cases for supercharging, and one case for a free latissimus flap. The cadaver dissection demonstrated an average pedicle length of 5.25 cm and diameter of 3.75 mm for the artery and vein combined. In the cadaver dissection, the pedicle was prepared in 10 minutes on one side and in 13 minutes on the other side. In the case reported, the pedicle was isolated and delivered through an infraclavicular incision in 16 minutes on one side and in 12 minutes on the other side.

Based on our review of the literature, a transverse infraclavicular approach to the thoracoacromial vessels has never been described. Our cadaver dissection and clinical case show that this approach is feasible for microvascular breast reconstruction.

O.03

COMPARISON OF OPEN CARDIAC MASSAGE VERSUS CLOSED CHEST COMPRESSIONS IN TRAUMA USING END-TIDAL CARBON DIOXIDE MONITORING AS A MARKER FOR RESUSCITATION. Luke Chang*, Brandon Bonds, Matthew Bradley, and Deborah Stein, Department of Surgery, University of Maryland School of Medicine, Baltimore, MD.

Mortality following traumatic cardiac arrest is extremely high despite all medical interventions available. While closed chest compression (CCC) is the initial therapy following cardiac arrest, left anterolateral thoracotomy with open chest cardiac massage (OCCM) has been reported to be hemodynamically superior. However, most of these studies have been performed in animal models or in non-traumatic cardiac arrest patients. This project investigated the effects of OCCM compared to CCC utilizing end-tidal carbon dioxide (EtCO2) as a marker of resuscitation after traumatic cardiac arrest. This prospective observational study included patients who presented in extremis to a Level I Trauma Center. Continuous vital signs were collected for each patient, as well as EtCO2 measurements corresponding to periods of CCC and OCCM. Seventeen patients were enrolled over a 5-month period. Patients were predominantly male (88.2%) aged 41.6±21.5 years, who generally arrived with CCC in progress (82.4%). Ten patients received CCC-only while 7 patients received OCCM after a brief period of CCC. At presentation to the trauma center, there was no statistically significant difference between the initial EtCO2 values of the two groups respectively (12.0±15.2 vs. 3.6±2.9, p=0.17). This suggests that the degree of hemodynamic compromise was similar in the two groups, though the observed difference in EtCO2 may be clinically significant. Additionally, resuscitative efforts did not yield statistically significant differences in the final, peak, and average EtCO2 values of the CCC-only group compared to those of the OCCM group (13.9±9.1 vs. 10.1±9.2, p=0.42; 26.2±14.8 vs. 23.3±13.2, p=0.68; 13.5±9.0 vs. 9.0±3.2, p=0.23 respectively). Return of spontaneous circulation (ROSC) was far more prevalent in those who received CCC only compared to patients who received OCCM (50.0% vs. 14.3%, p=0.32). Hospital mortality was near universal in both groups, with 90% mortality in the CCC-only group and 100% mortality in the OCCM group. Preliminary findings suggest that while OCCM may be necessary for emergent surgical repair of a thoracic injury, it does not offer any resuscitative benefits over CCC.

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

INVESTIGATING THE ROLE OF PKD1 HOMOLOGS IN DROSOPHILA FERTILITY. Steven Chan*, Weizhe Li, Stacey Bridges, and Terry Watnick, Division of Nephrology, Department of Medicine, University of Maryland School of Medicine, Baltimore, MD.

Autosomal Dominant Polycystic Kidney Disease (ADPKD) is a renal disease that contributes significantly to the prevalence of end-stage renal disease. Though a devastating and progressive disease, little is known about the genes and proteins involved. Currently, 2 families of genes have been identified that have been linked to the majority of cases- PKD1 and PKD2. Previous research in animal models has shown PKD homologs to be involved in cilia movement and male fertility. However, individual knockouts of Drosophila PKD1 genes CG30048 and Pry have not demonstrated an impact on fly fertility. In this project, we aim to characterize the fertility of CG30048 Pry double knockout to assess if the genes affect fertility in a combinatorial fashion. Our results of n=44 mutant single cross fertility tests show that the double knockout does not affect fly

fertility. We hypothesize that a triple KO of the 3 known Drosophila PKD1 homologs (CG30048, Pry, along with CG42685) will show a reduced fertility. By characterizing the effects of mutant PKD1 genes, we hope to elucidate the mode of action and an understanding of PKD1 mutant effects. As many Drosophila studies have led to information that has helped human clinical research, we have high hopes that any results can yield new information on treating human ADPKD.

O.05

THE ROLE OF PC1 CLEAVAGE AT ITS GPS DOMAIN IN THE DEVELOPMENT OF BLOOD AND LYMPHATIC VESSELS. Kathleen McAvoy*, Patricia Outeda, Feng Qian, and Terry Watnick, Division of Nephrology, Department of Medicine, University of Maryland School of Medicine, Baltimore, MD.

Autosomal dominant polycystic kidney disease is the most common form of inherited kidney disease and results after mutations in *PKD1* (polycystin-1, PC1) or *PKD2* (polycystin-2, PC2). Murine embryos lacking both alleles of either gene die at mid-gestation (E14.5) with a variety of phenotypes including focal hemorrhage, polyhydramnios and edema. Lethality is attributed to defective angiogenesis in the placental labyrinth layer, but the functional role of polycystins in the vasculature remains unknown. PC1 contains an extracellular ectodomain with a GPS domain (G protein-coupled receptor proteolytic site). It has been shown that PC1 undergoes cleavage at the GPS domain, resulting in a peptide with an N-terminal fragment and a C-terminal fragment that remain tethered noncovalently. The role of cleaved and uncleaved PC1 in the vasculature is unknown. Interestingly, cleavage of PC1 has been found to be necessary for proper formation of tubular epithelium in kidneys, pancreas, and liver during postnatal maturation, but not essential for embryonic development. Since embryos harboring a mutation in the GPS domain (*Pkd1*$^{v/v}$) can survive gestation without edematous phenotypes, we hypothesized that cleavage of PC1 is not necessary for proper embryonic development of blood vessels and lymphatic capillaries. Using immunohistochemistry directed at isolectin β4, we found that *Pkd1*$^{v/v}$ placentas had comparable blood vessel number and complexity to wild type placentas (E14.5), while knockout mice had significantly fewer vessels. Immunofluorescence targeting Lyve1 and Endomucin showed similar results for dorsal lymphatic capillaries. Our results suggest that uncleaved PC1 is fully sufficient for proper vascular and lymphatic development.

O.06

CHARACTERIZATION OF GFR AND PATIENT-REPORTED OUTCOMES IN PATIENTS WITH AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE (ADPKD). Anna Pham*, Stephen Seliger[1], Thomas Dowling[2], Charalett Diggs[1], and Terry Watnick[1], [1]Division of Nephrology, Department of Medicine, University of Maryland School of Medicine and [2]Department of Pharmacology and Experimental Therapeutics, University of Maryland School of Pharmacy, Baltimore, MD.

ADPKD, the most common genetic renal disease, is characterized by enlargement of renal and hepatic cysts, increasing kidney size, and progressive renal failure. Accurate estimation of renal filtration function defined by glomerular filtration rate (GFR) is important for tracking disease progression. However, traditional creatinine-based estimates of GFR (eGFR) may be inaccurate in ADPKD due to enhanced tubular secretion of creatinine. Furthermore, accurate measurement of patient patient-reported outcomes (PRO) such as pain and sleep disturbance (related to progressive cyst enlargement) is an important aspect of quantifying disease severity and the potential response to novel treatments. As part of an NIH-funded observational cohort study, we measured gold-standard GFR, total kidney volume (TKV), and collected PRO in adults with ADPKD not on dialysis. We determined the bias, precision, accuracy, and sensitivity/specificity of widely-used creatinine-based

estimating equations for GFR (MDRD and CKD-Epi equations). We further examined patient-reported anxiety, fatigue, pain interference, physical function, depression, and sleep disturbance with the NIH-sponsored PROMIS instruments. Among N=49 patients (age=44.1, 67% female, GFR=77.7±38.7), both estimating equations under-estimated true GFR, though the CKD-Epi equation was less biased (-5.0 vs. -11.7 cc/min/1.73m^2) and more precise (18.34 vs. 18.52) than the MDRD equation. Greater TKV was correlated with lower estimated and measured GFR. Surprisingly, patient-reported fatigue, pain interference, depression, and sleep disturbance in our PKD patients were either equivalent to or better than the general population; PROs were not significantly worse among those with prior urological complications of PKD. Greater physical function was correlated to younger age (r=-0.5), greater Hb (r=0.3), and higher measured GFR (r=0.3). However, none of the 6 PROs were related to kidney size. It still needs to be determined which marker, or combination of markers, best estimates GFR. New approaches to quantifying PRO are needed in ADPKD, as standard measures are insensitive to disease status and severity.

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O.07

Abstract Retracted

O.08

"IS CT SLIC ENOUGH?" PARSING THE DIAGNOSTIC UTILITY OF CT AND MRI USING THE THE SUBAXIAL CERVICAL SPINE INJURY CLASSIFICATION (SLIC) SYSTEM. Daniel Mascarenhas*, David Dreizin, and Uttam Bodanapally, Division of Trauma and Emergency Radiology, Department of Diagnostic Radiology and Nuclear Medicine, University of Maryland School of Medicine, Baltimore, MD.

The Subaxial Injury Classification (SLIC) is a 3-axis scoring system for determining need for surgery (bony morphology, discoligamentous complex (DLC), and neurology), relying on CT, MR and neurologic exam. The superiority of SLIC to older schemes was shown by Vaccaro et al in a study with 11 pts. DLC was the least reliable axis due to variability at MR. No large blinded retrospective study has assessed performance of CT+MR or the utility of CT only vs CT+MR in triage. Patients included if: admission CT+MR within 48 hrs; both performed prior to surgery; follow up available for non-surg cases; and neurology score could be determined from a documented exam. 202 consecutive cases (139 case; 63 controls) from 2010-13 were reviewed separately by 2 blinded trauma imagers. Readers gave SLIC score (<4-nonsurg; 4-indeterminate; >4-surgical) based on neurology and CT only. To minimize recall, after 4 wks scoring was repeated with CT+MR. Sens, spec, AUC, and agreement (*K*) for both sessions was determined. Using cutoff of 4 (to include all possible surgical candidates) SLIC with CT+MR had sens of 94%, spec 72, AUC 0.88, and *K*=0.51. SLIC with CT only had sens 86%, spec 77, AUC 0.88, and *K*=0.71. Omitting DLC from SLIC resulted in sens 80%, spec 85, AUC 0.90, and *K*=0.83. While MR dictates surgical approach, our results suggest SLIC can be used to accurately and reliably triage for surgery with CT only. "CT SLIC" performed similarly to CT+MR in terms of AUC, but with substantially improved *K*. AUCs for CT+MR were similar between the 2 readers, with higher sens obtained at the expense of spec and vice versa, resulting in lower *K*. Our data are in line with c-spine clearance studies showing MR to be sensitive but variable, but this has not been shown for triage in cases with injuries. In practice, DLC and bony morphology are closely tied and a change in one affects the other. As MR reveals abnormalities of uncertain significance, we conclude this reduces reliability without adding to performance. A modified SLIC with DLC omitted produced a borderline-

excellent test based off ROC. Future studies should evaluate the effect on outcome, decreased time to therapy, and cost.

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O.09

IN VIVO TRACKING OF MESENCHYMAL PROGENITOR CELL SURVIVAL AND PROLIFERATION IN MURINE POSTEROLATERAL INTERTRANSVERSE LUMBAR SPINAL FUSION. Ioan Lina*, Timothy Witham, and Christina Holmes, Division of Spine, Department of Neurosurgery, Johns Hopkins University School of Medicine, Baltimore, MD.

While spinal fusion surgery has advanced over the past decade, a great deal is unknown regarding the underlying mechanisms which contribute to spinal fusion failure or pseudoarthrosis. Clinically, bone marrow cells (BMCs) in the form of aspirate have been used with grafting materials to augment fusion. Future use of stem-cell based therapies is contingent on better understanding cellular properties within the fusion space. Here we propose a novel murine model for the *in vivo* monitoring of implanted transgenic luciferase-expressing bone marrow cells following spinal fusion. The objectives of this study were to: 1) Develop a murine model of lumbar spinal fusion for the *in vivo* tracking of mesenchymal progenitor cells. 2) Assess transient cell viability using luciferase expressing syngeneic BMCs. Forty FVB/NJ mice underwent posterolateral intertransverse process lumbar spinal fusion surgery and were divided equally into 4 groups: syngeneic iliac crest bone graft alone, Vitoss® bone-matrix alone, bone matrix with syngeneic-only BMCs or matrix with syngeneic BMCs isolated from transgenic luciferase-expressing mice. BMCs were isolated from the long bones of syngeneic FVB mice such that 2.5×10^6 cells were used per side. Bioluminescence imaging was performed at day 1, 7, 14, 28 and 42. Micro-CT imaging was subsequently performed at 4 and 6 weeks to assess fusion status at which point the animals were euthanized. Bioluminescent imaging data of mice transplanted with syngeneic luciferase expressing BMCs demonstrated quantifiable cellular viability as early as 24 hours following surgery. Animals imaged at increasing time points correlated with increased bioluminescence signal. Micro-CT data confirmed the location of grafting material and bridging of osseous tissue. We have demonstrated a novel murine model which enables non-invasive *in vivo* monitoring of implanted transgenic luciferase expressing bone marrow cells following spinal fusion surgery. Future applications of this model will include the assessment of additional therapeutics for improving spinal fusion in translational research studies.

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O.10

MAGNETIC NANOBEADS FOR TARGETED DELIVERY OF HUMAN STEM CELLS IN REGENERATIVE MEDICINE. Emily Shea Kowalski*, Michal Zalzman[1], and Lorna Silipino[2], [1]Department of Biochemistry and Molecular Biology and [2]Department of Otorhinolaryngology - Head and Neck Surgery, University of Maryland School of Medicine, Baltimore, MD.

Mesenchymal stem cells (MSCs) are adult stem cells, which can be propagated in tissue culture after being harvest from living donors. Thus, MSCs hold the potential to form autologous tissue grafts. MSCs receive intense focus for their promise in regenerative therapies in numerous diseases, including diabetes, chronic renal failure and Alzheimer's disease. Our lab develops novel methods of enhancing the differentiation and replication potential of adult mesenchymal stem cells. By discovering new methods of overcoming the aging process MSCs undergo, we hope to expand these cells and make them more useful for stem cell therapies. Clinical application of MSCs will demand we find ways of mobilizing them to our tissues of interest. Magnetically targeting cells could enable us to deliver a significant number of cells to key areas of specific organs. Our goal was to develop a

method of mobilizing tonsil derived mesenchymal stem cells (T-MSCs) in tissue culture using nanobeads. Additionally, we sought to demonstrate that the T-MSCs remain viable and that this process does not alter their differentiation potential. Our results reveal visible intracellular nanobead inclusions in T-MSCs as early as 24 hours after treatment with each size nanobead (100nm, 300nm and 500nm). Cells counts substantiate viable cells and little toxicity associated with any size nanobead. We further show that T-MSCs with intracellular nanobead inclusions mobilize against a magnet. Mobilized T-MSCs proliferate again in cell culture with no signs of toxicity from treatment with the magnet. When cultured in appropriate media conditions, we demonstrate that mobilized T-MSCs can differentiate into adipocytes, neurospheres, chondroblasts and osteoblasts. The inclusion of nanobeads into T-MSCs and successful mobilization and differentiation of these cells reveals a potential system for targeting T-MSCs to a particular tissue site for regeneration, suggesting this technique may be useful for medical cell therapies.

O.11

KINEMATIC ANALYSIS OF ARM REACHING MOVEMENTS IN DIVERSE NEUROLOGIC POPULATIONS. Christine Kang*, Susan Conroy[1], Anindo Roy[2], and Christopher Bever[2], [1]Department of Physical Therapy and Rehabilitation Science and [2]Department of Neurology, University of Maryland School of Medicine, Baltimore, MD.

Rehabilitation robots provide interactive task-specific practice and precise measurement of patient performance. In contrast to clinical measures, robot-derived outcomes are more precise; less vulnerable to ceiling/flooring effects and more robust to inter- and intra-rater variability. Robotic measures of arm (shoulder-elbow) kinematics have been used to characterize motor recovery in patients with movement disorders after stroke and Parkinson's disease (PD), and have been shown to be reliable disease-specific diagnostic biomarkers. In this preliminary study, our objective was to compare robotic measures of point-to-point reaching movements across neurological disease. Subjects with clinically defined movement disorders resulting from multiple sclerosis (MS, n=4), PD (n=3), Huntington's disease (n=1), and cerebellar ataxia (ATX, n=2) performed unassisted, visually-evoked center out movements (14 cm to a 12 o'clock target) using a planar robot. Measures of movement quality (speed, smoothness) and excursion (distance to target, path length) were computed. Two-tail paired t-tests were computed to assess differences in performance metrics across groups at significance level α=.05. Our findings were: a) Reaching speed (relative time to 1st peak in speed profile; higher values reflect slower speeds, and vice versa) was lower in subjects with MS (0.6±0.1%) compared to those with ATX (0.3±0.1%, p=.07); and b) Movement smoothness (mean arrest period ratio i.e., time duration for which movement is below 10% peak speed; higher values reflect less smooth movements, and vice versa) was higher in those with PD (12.5±4%) compared to those with ATX (31±8%, p=.07). There are no statistically significant differences in any other metrics across groups. While our sample size precludes generalizability of these findings, it does lay a computational framework for analysis of arm reaching movements in diverse neurologic populations. Future work will investigate validity of these trends in larger disease-specific cohorts and also compare robotic outcomes to clinical scales.

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O.12

L-655,708 INDUCED ELECTROPHYSIOLOGICAL CHANGES IN THE HIPPOCAMPUS AND NUCLEUS ACCUMBENS OF THE RAT BRAIN. Natalie Hesselgrave* and Scott Thompson, Department of Physiology, University of Maryland School of Medicine, Baltimore, MD.

Depression is a debilitating disease that affects more than 20% of the population and is associated with poor health and increased risk of suicide. Current first line antidepressants, selective serotonin reuptake inhibitors (SSRIs), have a 3-8 week latency for clinical improvement and remission of symptoms is reported in less than 50% of patients. Ketamine, an antagonist of NMDA-type glutamate receptors has rapid antidepressant effects, but is addictive and induces psychotomimetic hallucinations. Ketamine probably works by relieving inhibition and promoting neural excitability. My lab has shown that a subtype selective negative allosteric modulator of GABA receptors called L-655,708 has antidepressant effects in rodent models of depression with minimal anxiolytic side effects. I hypothesized that L-655,708 may also enhance neural excitability by decreasing inhibitory influence of GABARs, thereby increasing synchronous activity between the hippocampus and nucleus accumbens, two brain regions implicated in stress-induced animal models of depression . To elucidate the in vivo electrophysiological effects of L-655,708, electrodes were chronically implanted in these two brain regions in rat. Signals were recorded in the awake implanted rat following intraperitoneal administration of saline vehicle and L-655,708. The animals were sacrificed and histological sections prepared to verify electrode placement. Signal analysis demonstrated decreased power but increased synchronous activity in the ventral hippocampus and nucleus accumbens in response to L-655,708. The increased synchronicity may underlie the anti-depressant effects of L-655,708 and support the role of GABARs in pathology and treatment of depression.

O.13

THE AUDIOLOGICAL AND HISTOLOGICAL CONSEQUENCES OF NOISE TRAUMA IN B6/CBAF1/J MICE. Virginia Drake* and Ronna Hertzano, Department of Otorhinolaryngology - Head and Neck Surgery, University of Maryland School of Medicine, Baltimore, MD.

Noise-induced hearing loss (NIHL) is permanent and affects five percent of the population worldwide. Since there are no effective treatments for NIHL, identifying the critical molecular pathways within the cochlea and examining what precisely underlies cell survival or cell death following noise trauma is very important. The susceptibility to noise trauma in mice is strain and age-specific. CBA/CaJ mice are commonly used to study the consequences of noise trauma as they have low hearing thresholds and are not prone to age related hearing loss. Transgenic mice, such as RiboTag mice, allow for cell type-specific gene expression analysis. They are available only in the C57BL/6 background, a strain that is especially prone to age-related hearing loss. However, mice that are generated as a cross between CBA/CaJ mice and C57BL/6 mice are likely to both allow for cell type-specific gene expression analysis and serve as an effective model to study noise induced hearing loss. Our primary objective is to define the noise exposures in B6/CBAF1/J mice that will result in temporary and permanent thresholds shifts. Our secondary objective is to assess inter-ear variability in threshold shifts as a result of the noise exposure, sex differences and to quantify hair cell loss. Groups of eight six-week old B6/CBAF1/J were exposed to 90, 100 or 105 dB SPL noise for two hours at least 2 days after having their baseline hearing thresholds measured by auditory brainstem responses (ABR) and outer hair cell function measured by distortion product otoacoustic emissions (DPOAE). ABR and DPOAE measurements were then repeated at 24h, as well as 8 days and 30 days post exposure followed by histological analyses. Using these data, we will analyze to what extent hearing thresholds return to baseline, the symmetry of hearing loss between left and right cochleae, and the variability within each cohort of mice. As well, we will correlate the functional and histological data to evaluate how frequency-specific threshold shifts correspond with patterns of hair cell loss within the cochlea.

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O.14

COMPARATIVE EFFECTS OF 3 CLINICALLY RELEVANT TREATMENTS IN SPINAL CORD INJURY. Hillary Hosier* and J. Marc Simard, Department of Neurosurgery, University of Maryland School of Medicine, Baltimore, MD.

Preclinical studies have identified three treatments that are especially promising for reducing acute lesion expansion following traumatic spinal cord injury (SCI): riluzole, hypothermia and glibenclamide. Each has demonstrated efficacy in multiple studies with independent replication, but there is no way to compare them in terms of efficacy or safety, since different models were used, different laboratories were involved, and different outcomes were evaluated. Here, using a model of lower cervical hemicord contusion, we compared safety and efficacy measures for the three treatments, administered beginning 4 hours after trauma. Treatment-associated mortality was 30% (3/10), 30% (3/10), 12.5% (1/8) and 0% (0/7), in control, riluzole, hypothermia and glibenclamide groups, respectively. For survivors, all three treatments showed overall favorable efficacy compared to controls. On Basso, Beattie and Bresnahan scores, hypothermia- and glibenclamide-treated animals were largely indistinguishable throughout the study, whereas riluzole-treated rats underperformed for the first 2 weeks; during the last 4 weeks, scores for the three treatments were indistinguishable, and significantly different than controls. However, on tests of complex motor function (inclined plane, grip strength and beam balance), hypothermia and glibenclamide treatments showed small albeit statistically significant advantages over riluzole. Lesion volumes at 6 weeks are currently being determined. After trauma, rats in the glibenclamide group rapidly regained a normal trajectory of weight gain that differed markedly and significantly from that in all other groups. Overall, in terms of safety and efficacy, hypothermia and glibenclamide were superior to riluzole.

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O.15

EFFECTS OF ROUTINE PATIENT CARE AND EXTERNAL STIMULI ON INTRACRANIAL PRESSURE LEVELS OF PATIENTS WITH SEVERE TRAUMATIC BRAIN INJURY. Anish Gonchigar*, Brandon Bonds[1], Peter Hu[2], and Deborah Stein[1], [1]Department of Surgery and [2]Department of Anesthesiology, University of Maryland School of Medicine, Baltimore, MD.

The care of patients with traumatic brain injury (TBI) centers on prevention of secondary injury by management of intracranial pressure (ICP) and avoidance of intracranial hypertension (ICH). Generally accepted basic methods to lower ICP include manipulating the head of bed (HOB) angle and limiting external stimuli. However, critically injured patients are routinely subjected to numerous external stimuli from both family interactions and basic clinical care. The purpose of this study was to measure the effects of these interventions and stimuli on ICP, as well as the duration of any effect. Patients (n = 13) with severe TBI (motor Glasgow Coma Scale (GCS) <5) were observed for 4 hour periods by a site observer on hospital days 1 and 3. Stimuli were recorded and later matched with high resolution vital signs data (every 6 seconds) for corresponding ICP levels. Mean ICP levels one minute post-stimuli, as well as average levels during the stimuli, were computed and compared to the one minute average ICP prior to the stimuli. Results show that family interactions had no effect on ICP (Change during stimuli (Δ during) = 0.1 mmHg $\pm$ 0.9, p = 0.48) nor did basic nursing care (Δ during = 0.03 mmHg $\pm$ 1.5, p = 0.88). Only raising the head of bed angle consistently caused a prolonged decrease in ICP (Δ post-stimuli = -3.5 mmHg $\pm$ 3.1, p = 0.01). Statistically significant elevations in ICP were observed when lowering a patient's head of bed (Δ during = 4.9

mmHg ± 5.9, p = 0.0005), whereas repositioning the patient (Δ during = 2.5 mmHg ± 4.1, p = 0.34) and airway suctioning (Δ during = 2.7mmHg ± 3.7, p = 0.10) showed potentially clinically significant changes. While the lasting effects of these stimuli on ICP levels were minimal, 41.7% (20/48) resulted in short periods (<3 minutes) of ICH (mean peak ICP 33.4 mmHg ± 10.8) and were routinely performed repeatedly throughout the day. Further work is needed to define the cumulative effects these short bursts of ICH may have on patient outcomes. Protocols directing the care of patients with severe TBI may need to be adjusted to balance the necessity of these interventions with the effects shown on ICP levels.

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O.16

THE DOMINANT NEGATIVE EFFECT OF PC1 MUTANTS G593R AND G209R. Justin Cohen*, Elias Blancon, and Iris Lindberg, Department of Anatomy and Neurobiology, University of Maryland School of Medicine, Baltimore, MD.

PC1 is a prohormone convertase, encoded by the PCSK1 gene, which cleaves various proneuropeptides and prohormones into their bioactive forms, including proinsulin, proglucagon, and proopiomelanocortin. It has been found that mutations in PC1 can result in various metabolic disorders. A study with a sample size of 6000 was performed and it was found that mutations causing partial PCSK1 deficiency increased the risk of obesity 8.7 fold. PC1 mutations G593R and G209R are two mutations identified and upon analysis it was determined that these mutant PC1s are retained in the endoplasmic reticulum instead of traversing the secretory pathway. Prior to this study, an enzymatic assay was performed on cells that were co-transfected with WT PC1 and 3 different mutant PC1s: G593R, G209R, and N309K. N309K is a complete loss of function mutation but unlike the other two mutants, it traverses the secretory pathway. The assay displayed a substantial decrease in enzymatic activity within cells transfected with G209R and G593R as compared to N309K. In this study, we set out to determine what the underlying etiology of this dominant negative effect was. Using immunofluorescence and co-localization analysis, it was displayed that the dominant negative effect was not due to aggregation between the mutant PC1 and the wild-type PC1 or aggregation with the pro-hormone. It was found that these cells were experiencing ER stress, which triggered the unfolded protein response, resulting in an overall decrease in protein expression.

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O.17

EVALUATING THE ROLE OF ACTIN BUNDLING PROTEIN FASCIN IN AROMATASE INHIBITOR RESISTANT BREAST CANCER CELLS. Richa Kalsi*, Angela Brodie, and Amanda Scheh, Department of Pharmacology and Experimental Therapeutics, University of Maryland School of Medicine, Baltimore, MD.

Aromatase inhibitor (AI) therapy with drugs like Letrozole, Anastrozole, and Exemestane is the first line treatment for post-menopausal women with estrogen receptor positive (ER+ve) breast cancer. AIs safely and reliably decrease the amount of available estrogen that feeds tumor growth, and thus are an effective treatment for ER+ve disease. The actin-bundling protein fascin has been shown to be a key mediator of enhanced migration and metastasis in numerous different cancer types. A recent proteomics study using a systems biology approach which compared Letrozole-resistant (LTLTCa) cells to their parental MCF7ca cells (ER+ve, letrozole sensitive) found fascin to be overexpressed in LTLTCa cells. This upregulation was confirmed in both LTLTCa and exemestane resistant (ExR) cells by Western blot. LTLTCa and ExR cells were then treated with

fascin siRNA to knockdown fascin expression, which was confirmed by qRT-PCR. Fascin knockdown was found to decrease proliferation and cell number in the resistant cells compared to the scramble control (fascin positive). Further analysis of fascin knockdown cells by Western blot showed both downregulation of proliferative factors and reduction in anti-apoptotic factors. Additionally, fascin knockdown decreased migration of LTLTca cells through a Boyden Chamber compared to scramble-treated cells, but had no discernible effect on mammosphere formation. The effect of fascin siRNA on existing mammospheres is being explored to determine whether fascin knockdown can eliminate cancer stem cells in LTLTCa. In addition to its effects on proliferation and migration, fascin has also been shown in previous studies to be activated by the TGF-beta-Smad signaling pathway in MDA-MB-231 (triple negative breast cancer cells). Inhibition of the TGF-beta pathway using the TGF-beta inhibitor LY2157299 has been investigated, showing apparent induction of fascin expression in these cells. This reveals that unlike in other cell types, fascin expression does not have as concrete an expression profile and may actually be at the center of very complex regulation and multiple feedback loops in AI resistant cells.

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O.18

WHAT IS THE IMPACT OF RADIOTHERAPY ON CARDIAC FUNCTION IN PATIENTS RECEIVING TARGETED HER2 BASED SYSTEMIC THERAPY? Daphna Katz*, Katherine Tkaczuk[1], Kaitlin Baron[2], Kruti Patel[3], and Steven Feigenberg[3], [1]Division of Hematology-Oncology, [2]Department of Medicine and [3]Department of Radiation Oncology, University of Maryland School of Medicine, Baltimore, MD.

Adjuvant Trastuzumab therapy dramatically improves survival in human epidermal growth factor receptor 2 (HER2) positive breast cancer patients but increases the risk of acute cardiac toxicity. Radiation therapy (RT) also improves treatment outcomes but can produce long-term cardiac complications. Changes in cardiac function due to concomitant administration of Trastuzumab and RT have previously been examined in only a few series. This is a retrospective analysis of 37 patients with stage I – III HER2 positive breast cancer treated with Trastuzumab at the University of Maryland Medical Center between January 2000 and June 2011. The primary endpoint was defined as heart failure (HF), meaning a ≥16% decrease in left ventricular ejection fraction (LVEF) from baseline, or a ≥10% decrease in LVEF from baseline if dropped below 50%. Changes in LVEF were measured using MUGA at 3, 6, 9, and 12 months following initiation of Trastuzumab. In order to determine if the dose of radiation to the heart contributed to significant changes in cardiac function, tumor laterality and internal mammary lymph node (IMN) radiation were tested. The incidence of HF among the entire group of patients who were treated with Trastuzumab with or without concurrent RT was 24.3% (9/37). Of these HF cases, 55.6% (5/9) were reversible. The use of radiation was not found to significantly increase the risk of HF. There was no difference in the incidence of HF by tumor laterality or by the use of IMN radiation. Additional risk factors such as age, race, and co-morbidities did not cause an increased risk of HF, however 89% of patients who developed HF were being treated with Anthracyclines. Based on these results, radiation does not increase the incidence of HF among the majority of patients receiving HER2 based systemic therapy. Increased radiation doses to the heart with left-sided radiation and/or targeting of the IMN chain was not associated with an increased risk for HF. Future studies are needed to confirm these findings, investigate the effects of Anthracyclines, and determine whether there is a need to lower doses to the heart using more sophisticated radiation techniques.

Supported in part by the Summer Fellowship in Radiation Oncology and the Office of Student Research, University of Maryland School of Medicine.

O.19

VEGF AND SDF-1 AS PREDICTORS OF WOUND HEALING. James Van Meerbeke* and Stephen Thom, Department of Emergency Medicine, University of Maryland School of Medicine, Baltimore, MD.

Diabetes has become one of the most prevalent health concerns in the United States. One common complication of diabetes is diabetic foot ulcers (DFUs) which are expensive to treat and often result in poor patient outcomes including digit or limb amputations when severe. Currently, it is difficult to predict which DFUs are likely to heal and which are likely to become refractory and need adjunctive therapies. DFU healing occurs due to the concurrent processes of angiogenesis and vasculogenesis, and our laboratory is currently studying the role of stem/progenitor cells (SPCs) in this process. During ischemia, SPCs are mobilized from the bone marrow and home to hypoxic areas through a series of molecular signals that includes vascular endothelial growth factor (VEGF) and stromal cell-derived factor 1 (SDF-1). Previous preliminary data suggest that numbers and intracellular content of regulatory proteins in SPCs may predict wound healing, but one remaining question is how the presence/levels of proteins such as VEGF and SDF-1 in wound margin tissue may also correlate with healing rates. Both VEGF and SDF-1 have been documented to play a role in wound healing in animal models but have not been investigated in DFU tissue from human patients. Preliminary data using immunofluorescence and confocal microscopy indicate that DFU wound margin tissue stains positive for both VEGF and SDF-1 and that these markers co-localize with SPC-specific and endothelial cell-specific proteins. Quantifying these data will allow us to correlate healing rates of DFUs with levels of VEGF and SDF-1. Combined with information regarding the levels and intracellular content of circulating SPCs, these data could be used to develop laboratory tests to objectively determine whether a DFU is likely to heal or likely to need adjunctive therapy. Earlier addition of adjunctive therapies in patients with refractory DFUs could save the healthcare system money and more importantly improve patient outcomes.

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O.20

CALCIUM SIGNALING IN ARTERIOLES AND SMALL ARTERIES OF CONSCIOUS OPTICAL BIOSENSOR MICE. Scarlett Hao*, Seth Fairfax, Joseph Mauban, Mark Rizzo, Jin Zhang, and W. Gil Wier, Department of Physiology, University of Maryland School of Medicine, Baltimore, MD.

Two-photon fluorescence microscopy and conscious, restrained optical biosensor mice were used to study smooth Ca2+ signaling in ear arterioles. Conscious mice were used in order to preserve normal mean arterial blood pressure (MAP) and sympathetic nerve activity (SNA). ExMLCK mice, which express a genetically-encoded smooth muscle-specific FRET-based Ca2+ indicator, were equipped with blood pressure telemetry and immobilized for imaging. MAP was 101±4 mmHg in conscious restrained mice, similar to the freely mobile state (107±3 mmHg). Oscillatory vasomotion or irregular contractions were observed in most arterioles (71%), with the greatest oscillatory frequency observed at 0.25 s-1. In a typical arteriole with an average diameter of ~35 μm, oscillatory vasomotion of a 5-6 μm magnitude was accompanied by nearly uniform [Ca2+] oscillations from ~ 0.1 to 0.5 μM, with maximum [Ca2+] occurring during the rapid decrease in diameter. Very rapid, spatially uniform 'Ca2+ flashes' were also observed but not asynchronous

propagating Ca2+ waves. In contrast, vasomotion dynamic Ca2+ signals were rarely observed in ear arterioles of anesthetized exMLCK biosensor mice. Hexamethonium (30 μg/g BW, i.p.) caused a fall in MAP to 74±4mmHg, arteriolar vasodilation, and abolition of vasomotion and synchronous Ca2+ transients. MAP and HR were normal during high-resolution Ca2+ imaging of conscious, restrained mice. SNA induced continuous vasomotion and irregular vasoconstrictions via spatially uniform Ca2+ signaling within the arterial wall. Importantly, these results represent the first measurements of [Ca2+] dynamics in vascular smooth muscle cells during unaltered physiological conditions.

O.21

PARENTAL OPINION ON WHOLES GENOME SEQUENCING AS A DIAGNOSTIC TOOL IN THE UMMC NICU. Jenna Maggin*, Linda Jenna[1], and Dina El-Metwally[2], [1]Department of Biochemistry and Molecular Biology and [2]Department of Pediatrics, University of Maryland School of Medicine, Baltimore, MD.

Neonates in the Intensive Care Unit with undiagnosed genetic disorders cause a major strain on both parents and care givers. With the current standard of care, parents could wait months until a diagnosis (if any) is given. Meanwhile, the family may be suffering while their child undergoes many diagnostic procedures, creating an even greater emotional burden. Whole-genome sequencing (WGS) allows geneticists to look at a patient's entire genetic sequence and better identify known and rare mutations, or even discover novel mutations. WGS is a relatively recent procedure, and current testing takes approximately 3-4 months to give results. A new rapid WGS method is being developed that will shorten the diagnostic process to approximately one week, allowing the parents and medical staff to make more informed decisions about prognosis and management. Parental opinion regarding WGS and the importance of having a genetic diagnosis is a necessary element that needs to be considered before incorporating new genetic tests into clinical practice. We designed a survey to gauge parental perception and opinion on the usage of rapid WGS as a diagnostic tool in the UMMC Neonatal Intensive Care Unit. Our preliminary results clearly indicate that the vast majority of parents would prefer to receive a genetic diagnosis for their child as soon as possible, regardless of outcome. In addition, we discovered that 100% of participants thus far believe that having a genetic diagnosis for their child as early as possible will help the medical team determine the best course of treatment. It was also interesting to note that 78% of parents polled wanted information about adult-onset diseases as well. When we reach our target goal, we hope that we continue to see these positive trends and be able to offer rapid WGS to patients in the near future.

Supported by ACMG Summer Scholars Fellowship.

O.22

ELUCIDATING THE UV-INDUCED TLR4/MYD88-DEPENDENT APOPTOTIC SIGNALING PATHWAY. Kerry Heitmiller*, Rita Fishelevich[1], Erin Harberts[2], and Gaspari Anthony[1], [1]Department of Dermatology, and [2]Department of Microbiology & Immunology, University of Maryland School of Medicine, Baltimore, MD.

MyD88 and TLR4 are important proteins involved in ultraviolet radiation (UVR)-induced immunosuppression and UVR-induced apoptosis. Immunosuppression and apoptosis have been shown to be important processes that promote skin carcinogenesis. Our experiment aimed to elucidate the unique UVR-induced TLR4/MyD88-dependent apoptotic cell death pathway. MyD88 knockout (KO) cell line, peritoneal macrophages (PM) from MyD88 KO mice, and THP1 human monocytes were transfected with AU1-epitope tagged plasmid containing MyD88. The transfected cells and the untransfected cells were irradiated with 10 mJ/cm^2 UVB. Immunoprecepitation followed by Western Blot identified FADD (Fas-associated protein with death domain) as the molecule being recruited by and forming a complex with MyD88 after UVR. Therefore, we

concluded that UVR induces FADD recruitment to the TLR4/MyD88 signaling complex (myddosome), which then activates downstream molecules involved in the apoptotic cell death pathway. Our results prompted us to explore the effect of the protein NleB1, a FADD blocker, on apoptotic cell death. We transfected plasmids containing NleB1 or mutant nleb1 into p388 cell line and exposed the cells to various doses of UVB radiation. After UVR, DNA laddering suggested less apoptosis in the NleB1 transfectants compared to the mutant nleb1 transfectants and the non-transfectants. However, immunofluorescence with cleaved caspase 3 did not show a significant difference in cell behavior. Ongoing experiments are examining cell death pathways in these transfectants.

O.23

A NOVEL LARGE ANIMAL MODEL OF ACUTE RESPIRATORY DISTRESS SYNDROME INDUCED BY SEVERE TRAUMA. Diana Pratt*, Pablo Sanchez, and Bartley Griffith, Division of Cardiac Surgery, Department of Surgery, University of Maryland School of Medicine, Baltimore, MD.

Trauma is a major cause of morbidity and mortality worldwide. Patients who survive often remain critically ill. One life-threatening post-traumatic complication is Systemic Inflammatory Response Syndrome (SIRS), which is characterized by shock and multi-organ failure. The lung is the organ that most often fails after trauma, resulting in SIRS induced Acute Respiratory Distress Syndrome (ARDS). The molecular mechanism underlying the development of SIRS induced ARDS and the similarity between post-traumatic and septic SIRS are poorly understood. It was recently shown that mitochondrial products released to circulation after trauma activate the immune system through mechanisms similar to those used by microbes, generating a sepsis-like state. We aimed to develop a large animal model of trauma-induced SIRS resulting in ARDS. 5 pigs (30-40kg) received an intravenous (IV) dose of disrupted mitochondrial products (DAMPS) produced from liver tissue and were followed up for 6 hours under general anesthesia. These animals were compared to a control group (anesthesia only) and a well-established model of sepsis induced ARDS by lipopolysaccharide (LPS) IV administration. The animals that received DAMPS developed tachycardia (204$\pm$12.3 bpm) compared to the control (100$\pm$12.7 bpm) and the LPS (178$\pm$18 bpm). There was also a significant increase in temperature in both the DAMPS (41.2$\pm$1.2) and LPS group (41.6$\pm$0.5) compared to the control group (37.8$\pm$0.5). Lung oxygenation capacity (PO_2/FiO_2) showed a significant decrease in the DAMPS (187$\pm$39) and LPS groups (176$\pm$49) compared to the control group (494$\pm$45). Furthermore, histological lung injury scores were significantly higher in DAMPS group (64.63) when compared to controls (13.53), but not the LPS group (53.60). Lung injury in the DAMPS and LPS groups was associated with increased neutrophils and correlated with increased expression of MMP8 in lung tissue. Our data demonstrates that the injection of mitochondrial products leads to SIRS and ARDS, which are clinically indistinguishable from sepsis. This new large animal model paves the way for the development of clinically translatable therapies for post-traumatic SIRS induced ARDS.

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O.24

RGC-32 AS A POTENTIAL MARKER OF RELAPSES AND RESPONSE TO TREATMENT WITH GLATIRAMER ACETATE IN MULTIPLE SCLEROSIS. Adam Kruszewski*, Cosmin Tegla, Cornelia Cudrici, and Horea Rus, Department of Neurology, University of Maryland School of Medicine, Baltimore, MD.

Relapsing-Remitting Multiple Sclerosis (RRMS) is a prototype for central nervous system autoimmune demyelinating disease. RRMS is a progressive neurological disease characterized by unpredictable bouts of sensory, motor, visual, and/or cognitive loss (relapses) followed by months to years of remission. Due to the heterogeneous nature of RRMS, it is extremely difficult to predict patient prognosis and response to treatment. Currently there is critical need for the development of reliable biomarkers to aid clinicians in the management of RRMS patients. Previously we have shown that the Response Gene to Complement (RGC)-32 is expressed by CD3+ as well as CD4+ T cells in peripheral blood and in brain tissue from RRMS patients. We have also found that RGC-32 mRNA expression is significantly lower in patients with relapses compared to those in remission and healthy controls. Presently, for the first time we longitudinally investigated the role of RGC-32 as a possible biomarker of relapse and predictor of response to glatiramer acetate (GA) treatment in RRMS patients. Over the course of 2 years, a cohort of 15 GA-treated RRMS patients was clinically monitored using the Expanded Disability Status Scale and blood samples were collected. RGC-32 mRNA expression was measured in patients' isolated peripheral blood mononuclear cells using real-time quantitative PCR. As expected, patients in remission exhibited high levels of RGC-32 expression while those in clinical relapse exhibited low levels of RGC-32 expression. Over time, 6 responders to GA treatment showed persistently high levels of RGC-32 expression, 4 non-responders showed persistently low levels, and 5 partial-responders showed high and low levels during periods of remission and relapse, respectively. Of note, a drop in RGC-32 mRNA expression was correlated with the detection of new active brain lesions via MRI in patients who otherwise appeared clinically stable. The data suggest that RGC-32 expression could serve as a potential biomarker for the prediction of MS relapse and the evaluation of patient response to GA therapy. Such information could help guide treatment decisions and improve MS patient outcomes.

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O.25

DISADVANTAGE, TRAUMA AND EMOTION REGULATION IN CHILDREN: THE ROLE OF FAMILIES IN MODERATING PHYSIOLOGICAL STRESS RESPONSES. Alice Zhang* and Laurel Kiser, Department of Psychiatry, University of Maryland School of Medicine, Baltimore, MD.

Disadvantage can expose individuals to chronically stressful and traumatic environments. Children growing up in disadvantaged environments are at an increased risk for self-regulatory behavior problems, emotion dysregulation and psychophysiological distress. Respiratory sinus arrhythmia (RSA) provides one measure of emotional regulation and stress. In a pilot study, we measured the RSA responses in both children with post-traumatic stress disorder (PTSD) and their caregivers. The goals of this study were to: 1) examine the ability of families to moderate RSA responses in children with PTSD, and 2) provide preliminary evidence for using RSA as a measure of affect reactivity within a family-based setting. This study was conducted with the Strengthening Family Coping Resources (SFCR) project, a family-centered intervention which promotes the resilience and coping of children with trauma and stress-related disorders. Four children and their caregivers participated in this study. Participants completed two rounds of an emotion induction task. Task 1 was completed individually whereas task 2 was completed with their family member. RSA responses were measured using a three-lead ECG. The caregivers' baseline RSA decreased from 5.437 in the individual task to 5.110 in the joint task, while the children's baseline RSA increased from 5.871 to 6.613. The caregivers experienced RSA withdrawal when performing the

emotion induction task individually but demonstrated RSA augmentation when they were with their child. Conversely, the child experienced RSA augmentation in the individual task but demonstrated RSA withdrawal in the joint task. This study presents preliminary evidence suggesting RSA responses of traumatized children are modified in the presence of their caregiver. Furthermore, given both children and caregivers experienced changes in RSA responses in the joint task, it is suggested that RSA be used as a measure of affect reactivity for a family-based intervention. Future studies with larger sample sizes and rigorous statistical analyses should be conducted to reinforce the findings of this pilot study.

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O.26

EXERCISE, METABOLIC FLEXIBILITY, AND ENDOTHELIAL PROGENITOR CELL MOBILIZATION IN OLDER, INSULIN RESISTANT ADULTS. Andrew Lutz*, Steven Prior, and Andrew Goldberg, Division of Gerontology and Geriatric Medicine, Department of Medicine, University of Maryland School of Medicine, Baltimore, MD.

Reduced skeletal muscle capillarization may contribute to the metabolic and physical declines in function in patients with insulin resistance through decreased delivery of oxygen, insulin, and glucose. This reduction in capillarization is likely mediated in part through decreased circulating endothelial progenitor cell (EPC) number, as EPCs are involved in angiogenesis and maintenance of the vasculature in skeletal muscle. In this project, we analyzed the effect of an acute bout of submaximal exercise on EPC mobilization and the metabolic response to a bout of exercise (metabolic flexibility, defined as the ability to shift from fat to carbohydrate utilization with increasing exercise intensity) in older adults with insulin resistance and normal glucose tolerance. Subjects exercised for 30 minutes at 60% of their maximal aerobic capacity (VO2max); metabolic flexibility was measured as the change in respiratory exchange ratio during exercise, and EPCs were enumerated by flow cytometry in blood samples drawn before and after exercise. Our preliminary analyses show that both metabolic flexibility and EPC mobilization were lower in insulin resistant adults comparted to normal controls, and that the degree of metabolic flexibility was directly related to the degree of EPC mobilization. This suggests that metabolic inflexibility could contribute to reduced EPC mobilization in insulin resistant older adults. We are also analyzing the effect of 6-month aerobic exercise training to potentially improve EPC mobilization and metabolic flexibility in these older subjects. Subject are undergoing thrice-weekly exercise (45 min at 70% VO2max)and will repeat submaximal exercise testing after exercise training. We hypothesize that aerobic exercise training will improve metabolic flexibility and EPC mobilization, and that these improvements may relate to clinically relevant measures of insulin resistance (oral glucose tolerance) and vascular function (endothelial vasoreactivity). Such findings would identify novel mechanisms by which aerobic exercise improves cardiometabolic function in older adults.

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O.27

INDIVIDUAL CHROMOSOMAL TELOMERE LENGTH IN HEALTHY AMISH SENIORS: THE ROLE OF TELOMERE BIOLOGY IN HUMAN AGEING. Justin Donlan* and Ying Zou, Division of Clinical Cytogenetics Laboratory, Department of Pathology, University of Maryland School of Medicine, Baltimore, MD.

Telomeres are the end structures of mammalian chromosomes which contain repetitive DNA sequences and DNA binding proteins. It is well accepted that telomeres function to hide the ends of the chromosomes from being recognized as double strand breaks and prevent them from end-end

fusion. Telomere shortening occurs with cell divisions due to a combination of incomplete replication, end processing events and oxidative damage. Abnormal telomere attrition has been associated with numerous human diseases including cancers, cardiovascular disease (CVD), hypertension, diabetes and end-stage renal disease as well as premature aging syndromes, such as Werner's syndrome, Hutchinson-Gilford Progeria, and Dyskeratosis congenital (DKC). An interesting phenomenon called telomere position effect (TPE) has been described in *Drosophila*, *S. cerevisiae*, *S. pombe*, mice and humans. TPE results in the silencing of genes positioned next to telomeres, and its efficiency varies with telomere length. Since abnormal telomere attrition is associated with human diseases, this raises the probability that TPE might be involved in different types of functions in human cells and may contribute to the development of human diseases. However, one central question in telomere biology remains unanswered: What is a normal telomere pattern in healthy longevity individuals without human diseases, as well as how do telomeres regulate the expression of subtelomere genes? We hypothesize that specific telomere end(s) are much longer/shorter than other telomere ends in healthy longevity individuals and these longer/shorter telomere ends lead to differentially expressed and post-translational modification of histones and/or DNA modification of this region correlated with the expression of their subtelomere genes. To test these hypotheses, we will use Quantitative Fluorescence *In-Situ* Hybridization (Q-FISH) to determine whether there exists a pattern of specific telomere ends being lengthened/shortened in a cohort of 5 long lived Amish and their younger offspring. This study will provide additional insights into telomere biology and may lead to an improved understanding of human ageing and human diseases.

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O.28

DISPARITIES IN PRESCRIBING BIOLOGIC DMARDS IN OLDER PATIENTS WITH RHEUMATOID ARTHRITIS. Christopher Morrow*, Amit Golding, and Marc Hochberg, Division of Rheumatology, Department of Medicine, University of Maryland School of Medicine, Baltimore, MD.

Effective use of biologic disease-modifying antirheumatic drugs (DMARDs) in patients with Rheumatoid Arthritis (RA) is essential to controlling disease activity and reducing morbidity and mortality associated with the disease. Some data suggest that older patients with RA may be less likely than younger patients to receive appropriate biologic therapy in a timely fashion. Addressing this disparity is important given the growing and potentially vulnerable nature of the older RA population. A retrospective analysis of medical charts was performed on a total of 335 subjects with RA who were recruited based on having active DMARD prescriptions with the Maryland Veteran Affairs Arthritis Clinic between 2010 and 2014. Biologic DMARD use and disease activity in older (≥65 years of age) and younger patients were tracked to identify patterns in prescribing practices and clinical outcomes. Within the study sample, 56% of patients were classified as older. 30% of younger and 19% of older patients were on biologic DMARDs during the study period. Overall, older age was associated with a decreased use of biologics compared to the younger population ($p = 0.02$). However, for the 12% of patients who began a biologic during the study period, there was no difference in the proportion of younger versus older patients. In this study older age was associated with less use of biologics, representing a disparity in the treatment of older patients with RA. Initiation of biologic therapy during the study period, however, was not biased based on age. These results suggest that challenges to the equitable treatment of older RA patients persist, but recent prescribing practices may be improving. Prospective studies are needed to confirm these associations in order to better define prescribing practices in older patients with RA.

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O.29

PREGNANT WOMEN'S KNOWLEDGE AND ATTITUDES REGARDING ELECTRONIC CIGARETTES. Brooke Farquhar*, Mishka Terplan[1], Margaret S. Chisolm[2], and Katrina Mark[3], [1]Department of Obstetrics, Gynecology and Reproductive Sciences, Behavioral Health Systems Baltimore, [2]Department of Psychiatry, Johns Hopkins University School of Medicine, and [3]Department of Obstetrics, Gynecology and Reproductive Sciences, University of Maryland School of Medicine, Baltimore, MD.

Electronic cigarettes are a relatively recent phenomenon, serving dual roles as an alternative vehicle for nicotine-delivery and a smoking-cessation tool. The purpose of this survey was to determine pregnant women's knowledge and attitudes regarding electronic cigarettes. A voluntary, anonymous survey was distributed to pregnant women presenting to a University-based outpatient OBGYN clinic in Baltimore City. After survey completion, participants received information about smoking cessation and electronic cigarettes. Data were analyzed using chi squared analysis, fisher's exact, and ANOVA. STATA was used for analysis. Of 316 women surveyed, 42 (13%) reported having ever used electronic cigarettes. The most common reasons given for use were the perception of less harm than traditional cigarettes (74% of electronic cigarette users) and more help with smoking cessation (72% of users). Ever users were slightly older (27.3 vs 25.4 years, $p=0.007$) and more likely to be current smokers (43% vs. 14%, $p<0.001$) compared to women who had never used electronic cigarettes. Knowledge of the harms of smoking was similar between the two groups. Overall only 57% of all respondents believed that electronic cigarettes contain nicotine, 61% that electronic cigarettes can be addictive, and 43% that electronic cigarettes are less harmful to a fetus than traditional cigarettes. Misconceptions about electronic cigarettes are common among pregnant women, posing risks for both maternal and child health. Screening and education regarding electronic cigarettes should be included in prenatal care. Future research might consider examining pregnancy outcomes among women using electronic cigarettes.

O.30

CAN VIEWS OF THE PROXIMAL FEMUR BE RELIABLY USED TO PREDICT MALROTATION AFTER FEMORAL NAILING? Andrew Dubina*, Michael Rozak, and Robert O'Toole, Department of Orthopaedics, University of Maryland School of Medicine, Baltimore, MD.

Malrotation after intramedullary nailing of femoral shaft fractures has been reported to occur in 15-40% of cases. A commonly used technique to evaluate rotation is to compare the amount of lesser trochanter that is visualized on standard anterior-posterior (AP) hip film vs. the amount on the contralateral, uninjured side. Our hypothesis is that this technique will be able to reliably detect clinically important differences in malrotation. Twenty matched cadaveric femur pairs ($n=40$) were obtained and mounted on a custom jig. C-arm fluoroscopic images were taken of the proximal femur at 10-degree increments of internal and external rotation. The width of lesser trochanter visualized was measured using PACS clinical software and normalized to the maximum size observed to provide a percentage of trochanter observed for each image. The relationship between percentage of the lesser trochanter observed and angle of femoral rotation was analyzed. Rotation of the proximal femur demonstrates a consistent, linear relationship to the lesser trochanter visualized ($r2 = 0.87$), indicating that for each 10% deviation in lesser trochanteric size corresponds to approximately 8 degrees of femoral rotation. The maximal size of the lesser trochanter was seen at an average external rotation of 34 degrees, when the intertrochanteric ridge begins to be visualized superior to the lesser trochanter. There was little variation in values between the left and right of

each pair (paired t-test $p>0.1$) with the exception of one pair ($p=0.02$), demonstrating that the contralateral hip is an excellent indicator of rotation. Our data demonstrate that the relationship between angular rotation of the femur and the size of the lesser trochanter is both highly linear ($r2 = 0.87$) and is quite sensitive to rotation. Previous authors have argued that clinically significant malrotation is thought to be 15-30 degrees, which corresponds to an easily measured change of 20 to 40% in size of the lesser trochanter. Clinicians can estimate the amount of malrotation using the relationship that roughly 8 degrees of malrotation exists for every 10% difference in normalized size of the lesser trochanters.

Poster Presentation Abstracts

P.01

CORRELATING ANTI-CD40 AND ANTI-CD154 TROUGH LEVELS WITH CARDIAC ALLOGRAFT OUTCOMES IN CYNOMOLGU MACAQUES. Anthony Kronfli*, Agnes Azimzadeh, and Richard Pierson, Division of Cardiac Surgery, Department of Surgery, University of Maryland School of Medicine, Baltimore, MD.

A topic of intensive research is how to induce and maintain allograft acceptance by suppressing pathogenic T-cell-driven immune injury while preserving regulatory T cell function. T cell immune response involves antigen presenting cell (APC) and T cell interactions, causing T cell activation via two-way costimulation. Both CD40/CD154 and CD28/B7 binding between APCs and T cells provide (separate) pathways for T cell activation. The Pierson/Azimzadeh Laboratory focuses on selective blockade of these key signals involved in immune responses with the long term goal of developing longer lasting immunosuppressive treatments for transplant patients. In this study, we obtained trough "therapeutic" antibody levels of 2C10R4 (anti-CD40) using an ELISA protocol developed over the course of the summer. This was done in cynomolgus macaques who had received a cardiac allograft and 2C10R4 treatment. The serum concentration of 2C10R4 was calculated using a standard created with the purified antibody. Serum samples were taken weekly for six weeks, and then weekly/every other week until the graft was explanted or failed. By precisely defining these trough levels at various time points, we showed that 2C10R4 serum levels were reaching therapeutic levels (estimated at 100 mg/ml) for a period of 12 to 13 weeks after transplantation, and that this concentration was sufficient to prevent graft rejection during that time period. Graft rejection occurred around week 13 in three macaques, and was associated with trough levels below 100 mg/ml. In subsequent experiments, we hope to test the effect of simultaneous CD40/CD154 and CD28/B7 blockade, and to correlate treatment levels with graft outcome (cardiac allograft vasculopathy), survival length of animals and histologic evaluation.

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P.02

EVALUATION OF PLATELET AND NEUTROPHIL ACTIVATION IN A XENOGENIC LUNG PERFUSION MODEL. Aakash Shah*, Agnes Azimzadeh, and Richard Pierson, Division of Cardiac Surgery, Department of Surgery, University of Maryland School of Medicine, Baltimore, MD.

Xenotransplantation, using pig organs, is a promising solution to the shortage of human donor organs. The use of genetically modified pigs that lack galactosyltransferase and express human complement regulatory proteins has significantly increased xenograft survival. However these xenografts, particularly lungs, still get injured, and recent work points to mechanisms involving neutrophil and platelet activation, which we evaluated in a xenogenic lung-human blood perfusion model. After explantation, the pig lungs are perfused ex vivo with blood from human donors via the pulmonary arteries. The blood drains from the pulmonary veins and is run back through the circuit. Samples of the blood perfusate collected at various time points during the lung perfusion were analyzed by flow cytometry. The activation of CD11b leads to the activation and adhesion of neutrophils, as well as providing a site for interaction with platelets. Therefore, we studied the activation of CD11b by measuring both its level of expression (mean fluorescence intensity), and the proportion of neutrophils expressing a neo-epitope formed on activated CD11b (CD11b ACT). Fixed whole blood was analyzed for CD41 (platelet marker), and CD62P (P-selectin, expressed by

activated platelets). P-selectin is a cell adhesion molecule that promotes platelet aggregation through platelet-fibrin and platelet-platelet binding. Finally, antibodies against human and pig leukocyte markers and CD41 were used to identify and quantify human-pig leukocyte chimerism and leukocyte-platelet conjugates over time during perfusion. Neutrophil expression and activation was significantly increased upon beginning perfusion. In addition neutrophil-platelet conjugates were observed before the start of perfusion. Human leukocytes disappear, and pig cells appear in the perfusate as the perfusion begins. As the perfusion of pig lungs begin, platelet count decreases and the % of remaining platelets that are activated increases. The evaluation of these neutrophil-platelet conjugates may provide further insight into mechanisms of xenograft injury and act as a possible target of treatment in the future.

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P.03

PROGNOSTIC VALUE OF CARDIAC TROPONIN I FOLLOWING SEVERE TRAUMATIC BRAIN INJURY. Stephen Cai*, Deborah Stein, and Brandon Bonds, Department of Surgery, University of Maryland School of Medicine, Baltimore, MD.

Recent studies reported elevated cardiac troponin I (cTnI) was frequently observed following severe traumatic brain injury (sTBI) and was associated with worse outcomes. Exact relationship and clinical applicability of cTnI following sTBI is not well understood. To determine the association between cTnI elevation and risk of mortality, isolated sTBI (brain Abbreviated Injury Scale score ≥ 3 and other bodily regions ≤ 2) patients with cTnI measurements within 24hrs of admission admitted from 2007 to 2014 were reviewed. Four cTnI strata were predefined as undetectable (< 0.06 ng/mL) and detectable tertiles (0.06-0.1 ng/mL, 0.1-0.25 ng/mL, and > 0.25 ng/mL). Kaplan-Meier survival analysis and Cox proportional hazard model were applied. Stratification analysis was performed by age (≤ 65y or > 65y) and admission Glasgow Coma Scale (aGCS) score (mild 13-15, moderate 9-12, and severe 3-8). In a total of 2711 patients, elevated cTnI was found in 502 (18.5%) patients. Five-day survival rate was significantly lower in the patients with detectable cTnI compared to those with undetectable cTnI (72.26% vs 88.77%, $p < 0.0001$). Risk of mortality increased with increasing cTnI levels in a dose-dependent manner (p-trend < 0.0001). Patient in the highest cTnI strata reported 1.55-fold (95% CI: 1.18-2.04, p-trend = 0.0002) higher hazard ratio (HR), or risk of mortality, compared with patients of undetectable cTnI when age, injury type, and injury severity were adjusted. Further stratification underscored the positive association between cTnI levels and risk of mortality, particularly in patients ≤ 65y (HR: 3.10, 95% CI: 2.09-4.59, p-trend < 0.0001) or with severe aGCS (HR: 1.57, 95% CI: 1.16-2.14, p-trend = 0.0006). Similar association was not observed in patients > 65y or with mild or moderate aGCS. Current findings suggest elevated cTnI is an independent predictor of mortality following sTBI and is associated with higher risk of mortality via a positive, non-linear dose-dependent relationship. This association is predominately seen in patients ≤ 65y or with severe aGCS. Elevated cTnI may not be a sensitive predictor of mortality in patients > 65y or with mild or moderate aGCS.

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P.04

THE INTERACTIVE EFFECTS OF AGE AND COMORBIDITIES ON PHYSICAL FUNCTION IN THE ELDERLY. My-Linh Nguyen*, Steven Prior, and Jacob Blumenthal, Division of Gerontology and Geriatric Medicine, Department of Medicine, University of Maryland School of Medicine, Baltimore, MD.

Functional decline due to sarcopenia, the loss of muscle mass, has been observed in aging populations. Past studies have used exercise testing to examine functional decline in patients with individual co-morbidities, such as dementia. However, little work has been done to compare functional decline amongst patients with different co-morbidities or examine potential interactions. Similarly, previous work in even highly-trained athletes who continue to train has demonstrated declines in function. Geriatric patients often cope with multiple co-morbidities at once, so an understanding of the relative impact(s) of individual co-morbidities, as well as their interactions (both with each other as well as primary "aging" effects) will have significant implications. The purpose of this investigation was to compare function, across a range of ages, in patients with common disorders (including diabetes, stroke, and dementia), as well as normal, "healthy" individuals. Patients enrolled in existing studies focused on diabetes, stroke and dementia underwent a number of physical performance tests -- Short Physical Performance Battery (SPPB), six-minute walk, timed up-and-go, as well as assessments of handgrip strength and gait speed. Groups of patients were compared using t-tests, and linear regression analyses was used to examine trends over time between the groups. Data from 136 individuals revealed both lower SPPB scores and gait speeds (compared to "normal aging" counterparts) in patients with dementia, stroke, and stroke with diabetes. However, this was not true for patients having diabetes alone. Furthermore, a history of stroke was associated with lower physical function at any age, while the presence of diabetes or dementia was associated with accelerated functional decline. These trends indicate that though there may be primary "aging" effects on physical function, comorbidities are largely responsible for changing the trajectory of functional decline.

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P.05

PRELIMINARY ASSESSMENT OF THE MOTOR ACTIVITY LOG-28 IN PATIENTS WITH CHRONIC STROKE. Alexandra Simpson*, Christopher Bever, Jr.[1], and Susan Conroy[2], [1]Department of Neurology and [2]Department of Physical Therapy and Rehabilitation Science, University of Maryland School of Medicine, Baltimore, MD.

Improvements in arm impairment following stroke are evaluated by self-report or clinical measures detecting motor impairment or function. The Motor Activity Log-28 (MAL-28) is a stroke specific semi-structured self-report questionnaire that uses two scales to measure use and quality of arm movement in daily activities outside the clinical setting. Previous studies of a modified MAL demonstrated the validity of the Amount of Use (AOU) and Quality of Movement (QOM) scales, but only the QOM scale was reliable. Our objective was to assess if the MAL-28 is a suitable measure to examine the relationship between arm impairment and use in stroke participants enrolled in an arm rehabilitation study. Specifically, we aimed to 1) determine whether the MAL-28 is a trustworthy self-report measure for characterizing arm use, and 2) assess sensitivity of the MAL-28 to detect change in impairment over the course of the study. Clinical and self-report data were analyzed at baseline, post therapy, and follow up. The clinical outcome measures analyzed were the Fugl-Meyer UE Motor Performance Test (F-M) and the Wolf Motor Function Test (WMFT). Self-report outcome measures were the MAL-28 and the Stroke Impact Scale (SIS). Participants were

stratified based on severity of impairment. Correlation analyses were conducted in the less impaired group (n=9) because they exhibited greater improvement and fewer floor effects. Baseline MAL-28 AOU and QOM scales significantly correlated with established scales (F-M, WMFT, SIS hand domain) at baseline. Baseline F-M scores had a Spearman correlation coefficient (ϱ) of 0.6889 ($p<0.0132$) and 0.7276 ($p<0.0073$) when compared to baseline AOU and QOM scores, respectively. Changes in AOU scores were sensitive to changes in the SIS physical domain scores ($\varrho=0.7342$, $p<0.0243$). Changes in QOM scores were sensitive to changes in WMFT Functional Ability scores ($\varrho=0.6245$, $p<0.0722$). The MAL-28 appears to be an acceptable self-report measure for our less impaired stroke participants to relate the extent of arm use in a nonclinical setting to observable changes in impairment and function detected by the evaluator in a clinical setting.

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P.06

GLAUCOMA MEDICATION ADHERENCE IN VETERANS OVER A 10 YEAR PERIOD.

Elyse McGlumphy* and Osamah Saeedi, Division of Glaucoma, Department of Ophthalmology and Visual Sciences, University of Maryland School of Medicine, Baltimore, MD.

We aim to characterize the association between adherence to glaucoma medication and progression of visual fields in patients at the Baltimore Veteran Affairs hospital. Here we present preliminary data on medication adherence and the impact of medical comorbidities in treatment compliance. Patients who were treated at the Baltimore Veterans Affairs Hospital in the Eye Clinic with a diagnosis of glaucoma, ≥3 Humphrey Visual Field examinations, and have been prescribed topical glaucoma therapy within 1/1/2002-12/31/2011. Chart review was performed using the Computerized Patient Record System. Mean possession ratio (MPR) was used to assess medication adherence and was calculated using total days of medication possessed by the patient divided by total days needed. A total of 200 patients were included in the study with a mean MPR of 1.13±0.39, median 1.11. The study population was 99% male, with 59.5% African American, 33.5% Caucasian, 6.5% other or unknown. No statistical significance was observed in average MPR between African American and Caucasians ($p= 0.09$). The most prevalent medical comorbidity was hypertension (0.83), followed by hyperlipidemia(0.63), diabetes(0.44), arthritis(0.29), substance abuse(0.235), mood disorders(0.17), obesity(0.155), hearing loss(0.15), dementia(0.115), and OSA(0.09). Using a paired t-test analysis, no significant difference in mean MPR was identified between subgroups. This study aimed to investigate glaucoma medication adherence in 200 patients at the Baltimore Veteran Affairs Hospital. The mean MPR in our study (1.1) is higher than those reported in similar studies across the US. Despite the reported association between African American race and decreased adherence to glaucoma medication, this was not reflected in our data. Furthermore, we did not find any predictors of decreased adherence to medications across the specified medical and psychological comorbidities. These findings may be due to our method of patient selection which required the completion of 3 visual field tests and may present an inherent bias towards greater compliance. We will use this data to investigate the role of adherence in visual field progression.

Supported by the American Glaucoma Society.

P.07

SCHIZOPHRENIA AND HIGH RISK OF SMOKING: UNDERSTANDING A NEUROBIOLOGICAL LINK THROUGH FUNCTIONAL MAGNETIC RESONANCE IMAGING. Sarah Aronson* and L. Elliot Hong, Division of Maryland Psychiatric Research Center, Department of Psychiatry, University of Maryland School of Medicine, Catonsville, MD.

Patients with schizophrenia (SZ) are at a 3-fold higher risk for nicotine addiction compared with the general population. The cause for this increased risk is unknown. Nicotine addiction is a complex behavior that includes a failure of behavioral inhibition for stopping smoking despite intention to quit. Past fMRI studies have suggested that nicotine addiction is associated with abnormal brain circuits that regulate inhibitory behaviors. Additionally, patients with SZ have been shown to have brain circuit abnormalities when performing inhibitory tasks during fMRI. We hypothesize that the high risk of smoking in SZ may be due to a significant impact of SZ on the inhibitory brain circuit, rendering patients with SZ more vulnerable to developing nicotine addiction and/or less able to successfully quit smoking. We collected fMRI data during a Go/NoGo inhibitory task in 118 age-matched participants divided into four groups: 19 SZ smokers, 28 SZ nonsmokers, 33 normal control (NC) smokers, and 38 NC nonsmokers. Data were collected in an ongoing study using a 3T Siemens Trio scanner with a 32 channel headcoil. Data were processed using AFNI, E-prime and SPSS. SZ patients had less brain activation in the midbrain during successful inhibitions (corrected $p<0.05$), and less activation in the left inferior frontal gyrus during failed inhibitions (corrected $p<0.05$), than NC. Smokers had higher activation in the left insula/claustrum (corrected $p<0.05$) during failed inhibitions than non-smokers. There was an interaction effect in the right posterior cingulate cortex during failed inhibitions (corrected $p<0.05$), and post-hoc tests showed that similarly increased activations in SZ nonsmokers and NC smokers compared with NC nonsmokers, suggesting some overlapping circuits. The results demonstrate that smoking and SZ affect only partially overlapped behavioral inhibition circuitry. It is important to continue to study the role of inhibitory brain circuitry in SZ and co-occurring nicotine addiction to better treat the condition and further our understanding of the neurobiology of schizophrenia.

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P.08

PSYCHOSOCIAL PREDICTORS OF HEALTHY AND UNHEALTHY INTERPREGNANCY INTERVALS. Ruth Young*, Wendy Lane[1], Bronwyn Mayden[2], Renee Fox[3], and Stacey Stephens[4], [1]Division of Preventive Medicine and [3]Division of Pediatrics, Department of Epidemiology and Public Health, University of Maryland School of Medicine, and [2]Department of Social Work, University of Maryland School of Social Work, and [4] Department of Social work, Morgan State University School of Social Work, Baltimore, MD.

Both short (<18 months) and long (>59 months) interpregnancy intervals (IPIs) have been shown to significantly increase the risk of adverse maternal and fetal outcomes, including low birth weight, preterm delivery, and maternal anemia potentially due to folate depletion and/or postpartum stress. This study was part of the B'more for Healthy Babies – Upton/Druid Heights (BHB-U/DH) program, a city-wide initiative intended to improve the health of at-risk pregnant women and their newborns through media messages, community outreach and place-based initiatives. This study examines the influence of psychosocial factors, including anxiety, depression, social support, maternal substance abuse, and intimate partner violence (IPV) on IPI. Participants of the study included women enrolled in BHB-U/DH who had at least one prior birth. Each completed baseline, postpartum, and follow-up forms with pregnancy, medical and psychosocial history questions. IPV, alcohol/substance abuse, anxiety and depression were assessed using validated screening questions. Social support was examined by asking participants about current support from family and friends,

and the availability of help with their baby. Associations between IPI (short vs. healthy vs. Long) and the independent variables were assessed using chi square analysis and ANOVA. Multivariable multinomial logistic regression models were developed to examine association between IPI and the independent variables controlling for the other independent variables and potential confounders, including maternal age, education, housing security, and smoking. Participants with current IPV were more likely to have a short IPI (OR = 13.1; 95% CI = 1.07 – 158.9; P = 0.04) than a healthy IPI and women with family social support were more likely to have a healthy IPI (OR = 5.88, 95% CI = 1.02 – 31.25, P = 0.05) than a short IPI. Thus, IPV increased the likelihood of having an unhealthy IPI among these already high-risk women and family social support increased the likelihood of having a healthy IPI. Additional efforts to address IPV and to enhance family social support may lead to improved pregnancy outcomes.

P.09

EVALUATING PERI-ICTAL MOOD CHANGES IN PATIENTS IN AN EPILEPSY MONITORING UNIT. Mary Richert*, Jennifer Hopp[1], and Scott Thompson[2], [1]Department of Neurology and [2]Department of Physiology, University of Maryland School of Medicine, Baltimore, MD.

Mood disorders, such as depression and anxiety, are common in patients with epilepsy. Although much work has been done characterizing the occurrence of co-morbidities, how seizure activity influences mood peri-ictally is still not well understood. A better understanding of changes in depressive symptoms relative to different types of ictal events may yield unique insight to the pathophysiology of epilepsy and depression. Here, we examine peri-ictal mood changes by observing patients in the inpatient Epilepsy Monitoring Unit (EMU) at the University of Maryland Medical Center. We used well-established questionnaires, Beck Depression Inventory-II (BDI-II®), Beck Anxiety Inventories (BAI), and the Montgomery Asberg Depression Rating Scale, to determine mood scores before and after seizure activity. We hypothesized that there would be greater changes in mood post-ictally for epileptic patients with depressive-like symptoms compared with non-epileptic patients with depressive-like symptoms. During this pilot study, we enrolled 14 individuals, 7 of whom had seizure events. There were 3 individuals that experienced epileptic seizures, and 4 individuals which had non-epileptic, psychogenic seizure events. Of the epileptic patients, two showed short-lived improvements from baseline mood scores. Additionally, two of the non-epileptic patients also showed improvements from baseline mood scores several hours after events. While this data subset is small and results are inconclusive at this point, we hope to expand the study with more participants to further explore mood changes post-ictally for epileptic patients. We aim to determine if there is a correlation between seizure type, seizure localization and the resulting influence on mood.

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P.10

INTERPLAY OF HEALTH LOCUS OF CONTROL, HIV-RELATED CONSPIRACY BELIEFS, AND GENERAL DISTRUST AMONG HIV-POSITIVE ADULTS IN BALTIMORE. Jamie Nichols*, Seth Himelhoch[1], and Melanie Bennett[2], [1]Division of Psychiatric Services Research and [2]Division of Psychology, Department of Psychiatry, University of Maryland School of Medicine, Baltimore, MD.

Antiretroviral therapy (ART) is a critical component of care for HIV-positive individuals, yet many who are prescribed ART do not use it or use it incorrectly. This study utilized data from an

ongoing trial of a brief intervention to assist individuals with HIV to begin taking ART (final n=50, n for this study=14). We examined the interplay of three factors related to the decision to take ART: HIV-related conspiracy beliefs, general distrust of others, and health locus of control (HLOC; the degree to which individuals attribute their health to their own actions or to external factors). Our objective was to examine relationships among these variables to determine whether they, in combination, would be useful in identifying individuals at highest risk for nonuse/noncompliance with ART. Overall, 14 participants were assessed. All were African American adults (71.4% over the age of 40), 85.7% were female, and 85.7% were unemployed. The most frequently endorsed HIV conspiracy beliefs were: "The U.S. government was involved in starting the HIV problem" (57.1% agreed/felt neutral) and "There is a cure for HIV but only certain people have access" (57.1% agreed/felt neutral). Descriptive data on HLOC shows that individuals attribute their health to a range of factors, both internal and external. Results of correlational analyses showed: (1) distrust total score was positively correlated with HLOC Chance ($r = .528$, $p = .026$), (2) HLOC Chance was positively correlated with HLOC Doctors ($r = .488$, $p = .038$), and (3) HLOC Internal was related to HLOC Doctors ($r = .459$, $p = .050$). There were no significant relationships with HIV conspiracy beliefs and any other variables. These results suggest that many people with HIV hold conspiracy beliefs, but that these beliefs are not related to their health LOC or their distrust of others. Those high in distrust may be more likely to think that their health outcomes are due to chance factors. Limitations include the small sample size and cross-sectional design. Future research should examine links between these variables, actual ART use, use of other HIV treatment services, and coping strategies.

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P.11

A SMARTPHONE INTERVENTION TO IMPROVE ADHERENCE TO ANTIPSYCHOTIC MEDICATIONS. Elizabeth Record* and Julie Kreyenbuhl, Division of Psychiatric Services Research, Department of Psychiatry, University of Maryland School of Medicine, Baltimore, MD.

Approximately 60% of individuals with schizophrenia do not take their antipsychotic medications as prescribed. Nonadherence to antipsychotic medications is associated with numerous adverse outcomes, including exacerbation of psychotic symptoms, increased emergency room use, and increased healthcare costs. MedActive is an interactive healthcare application that seeks to improve antipsychotic adherence among individuals with schizophrenia. This smartphone application facilitates the active involvement of patients with schizophrenia in managing their antipsychotic medication regimen and of psychiatrists in monitoring their patients' responses to treatment. MedActive sends personalized medication reminders to patients to take their antipsychotic medication as prescribed, and surveys them about the presence of any positive psychotic symptoms or side effects. This information is relayed to patients' psychiatrists in real time through a secure, online Clinician Interface. Using an iterative user-centered design approach, the aim of this study was to conduct a short-term open trial to determine the preliminary acceptability and feasibility of the application and Clinician Interface. Seven patients used the application for an average period of 2 weeks, during which time 6 psychiatrists monitored their patients' adherence, symptom, and side effect information on the Clinician Interface. The application was determined to be both feasible and acceptable to patient participants, as participants responded to 80% of all medication reminders and EMAs, and responded positively to an evaluation of their use of the application. Psychiatrists were interested in viewing the information provided by the Clinician Interface and were willing to log onto the Interface, but cited practical barriers to regularly accessing

the Interface. A smartphone application designed to increase medication adherence among individuals with schizophrenia is both feasible and acceptable to patients and psychiatrists alike.

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P.12

EFFECT OF PEAR1 GENOTYPE ON SOLUBLE P-SELECTIN LEVELS AFTER ASPIRIN THERAPY. Molly Bloom*, Alan Shuldiner[1], Joshua Lewis[1], and Adam Fisch[2], [1]Division of Endocrinology, Diabetes, and Nutrition, [2]Department of Medicine, University of Maryland School of Medicine, Baltimore, MD.

Heart disease is the leading cause of death for both men and women in the US, with coronary artery disease (CAD) accounting for the majority of heart-related mortality. Aspirin is widely used for the prevention of CAD, but studies have shown significant variability in patients' responses to the drug. Recently, in the Amish Pharmacogenomics of Anti-Platelet Intervention (PAPI) study our group identified an association between a common variant, rs12041331, in the platelet endothelial aggregation receptor 1 (PEAR1) gene and significantly lower levels of on-aspirin collagen-induced platelet aggregation. Another factor known to play a role in platelet aggregation is the cell adhesion molecule P-selectin. Like PEAR1, it is expressed on megakaryocytes and platelets, and based on its function in platelet aggregation we hypothesized that the PEAR1 rs12041331 minor allele will be associated with lower soluble P-selectin (sP-selectin) levels. For this project, I used a commercially available ELISA assay (R&D Systems, Minneapolis, MN) to measure sP-selectin in serum from 261 PAPI participants who were receiving aspirin treatment. Next, I determined the effect of rs12041331 on on-aspirin serum sP-selectin levels using the Mixed Model program for Analysis of Pedigree (MMAP, Baltimore, MD), in which I created a multivariable linear regression model adjusting for age, sex, and relatedness. Our findings from the association analysis were not significant ($P = 0.615$). Possible explanations for these results could be that PEAR1 is not involved in sP-selectin levels at all or that we are not sufficiently powered to detect the low effect size of this variant. In our future studies, we will measure serum from additional PAPI individuals to increase our statistical power as well as our ability to detect this potentially low-effect variant. These studies will aid in understanding a key variant affecting aspirin response, leading to a more effective individualized antiplatelet therapy and ultimately reducing the risk of recurrent cardiovascular events.

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P.13

PHARMACOGENETICS IN THE HOSPITAL SETTING: IMPLEMENTATION CHALLENGES AND OPPORTUNITIES. Chelsea Goodier* and Alan Shuldiner, Division of Endocrinology, Diabetes and Nutrition, Department of Medicine, University of Maryland School of Medicine, Baltimore, MD.

Since the completion of the Human Genome Project in April 2003, we have seen an expansion in knowledge surrounding the human genome and its integral role in health and disease. Of particular importance, through the use of candidate gene studies and other techniques, a number of gene-disease variants have been identified that influence patients' individual response to particular drugs. This pharmacogenomics information is extremely valuable to both clinicians and their patients. Testing a patient for a specific gene-disease variant, and then being able to tailor the pharmaceutical approach to treating that patient, allows clinicians to move from a "one size fits all" treatment approach to that of personalized medicine for treatment and prevention of disease.

However, the implementation of pharmacogenetic testing in the health care system has been met with some resistance. One of the barriers to implementation is "the inexperience of many clinicians with interpretation and acting on pharmacogenetic information" [3]. The mission of the Translational Pharmacogenetics Program (TPP) is to overcome this barrier as well as others to implement "evidence-based pharmacogenetic tests in diverse health-care settings" [3]. In order to assess clinicians' perceptions of pharmacogenetic testing, and its role in their clinical decision making, clinicians were asked to participate in an anonymous 18 question survey. The goal of this survey was to glean the clinician's current understanding of pharmacogenetics, and determine what role it plays in their drug prescription and dosing decisions. The results of this study were positive overall, indicating that the barriers to implementation have been sufficiently addressed, and full implementation of genetic testing in the hospital setting is the logical progression.

P.14

RACIAL DIFFERENCES IN INFANT TELOMERE LENGTH AND THE MODERATION OF EXPOSURE TO INTERPERSONAL VIOLENCE. Margaret Woodbury*, Kyle Esteves[1], Katherine Theall[2], and Stacy Drury[1], [1]Department of Psychiatry, Tulane University School of Medicine and [2]Department of Global Community Health and Behavioral Sciences, Tulane University School of Public Health and Tropical Medicine, New Orleans, LA.

Despite an increasing focus on the identification and elimination of the root causes of health disparities, differences across the life course for Black women and children continue to exist. A recent biomarker associated with racial differences in adults, related to negative health trajectories, and likely reflective of underlying biological mechanisms, is telomere length (TL). This study aims to examine the impact of race and maternal exposure to interpersonal violence (IPV) on infant TL. Demographic data from 37 Black and 17 White mothers, ages 18-41, were collected from maternal report and medical record abstraction. Maternal exposure to IPV was determined from maternal report. Infant DNA was extracted from newborn bloodspot cards. Telomere length was determined using monochromic multiplex qPCR (MMQPCR) and reported as the ratio of single copy gene to telomere repeat (T/S). Multivariate linear regression was performed to analyze the contributions of race and maternal exposure to IPV on TL. Black infants had significantly longer TL when accounting for gestational age, infant birth weight, infant sex, maternal age, and maternal education (β=*0.29, p=0.0207*). There was a trending relationship between IPV prior to pregnancy and shorter infant TL (β=*-0.28, p=0.0948*) across both racial groups. Black mothers who experienced IPV prior to pregnancy had infants with significantly shorter TL (*M=1.46, SD=0.10*) at birth when compared to children of non-exposed mothers (*M=1.84, SD=0.34*). This study suggests that racial differences in infant TL exist and that there may be an association between maternal life course stress and infant TL, a biological indicator of aging and potentially a biomarker of cumulative stress across the lifespan.

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P.15

THE IMPACT OF ENTEROPATHOGENIC E. COLI TYPE III SECRETION SYSTEM EFFECTORS ON RNASE-L ACTIVITY. Jackline Joy Lasola*, Heather Ezelle, and Bret Hassel, Department of Microbiology and Immunology, University of Maryland School of Medicine, Baltimore, MD.

Enteropathogenic *E. coli* (EPEC) is a human pathogen that causes diarrhea and is responsible for significant morbidity among infants in developing countries. Following adhesion to intestinal epithelia, EPEC utilizes a type III secretion system (T3SS) that functions as a bacterial "syringe" to inject effectors into host cells to modulate immune response and promote GI permeability. Previous work established that EPEC inhibits the activity of an innate immune mediator, ribonuclease L (RNase-L). RNase-L is a positive regulator of IFNβ anti-inflammatory activity and negatively regulates the pro-inflammatory cytokine TNFα. Thus EPEC-mediated inhibition of RNase-L was postulated to promote an inflammatory response leading to GI permeability and pathogenesis. The T3SS component NleD was identified as the putative effector responsible for down-regulating IFNβ induction it was not known if this involved upstream inactivation of RNase-L. We hypothesized that the NleD protease directly cleaves and inhibits RNase-L resulting in diminished IFNβ induction and increased TNFα induction. To test this we used HeLa cells that ectopically express an epitope-tagged RNase-L to enhance detection of its regulation and putative cleavage by NleD. To first validate in HeLa cells the EPEC-mediated inhibition of RNase-L reported in intestinal epithelial cells (IECs), RT-qPCR was used to determine expression of IFNβ and TNFα following infection of HeLa cells with wild type and NleD-deficient EPEC. Our results indicated that infection of HeLa cells with NleD-deficient EPEC recapitulated the RNase-L-dependent regulation of TNFα following infection seen in IECs. This finding suggests that NleD inhibits RNase-L-mediated regulation of TNFα, however further work is required to assess its direct effect on RNase-L activity and IFNβ induction. These data suggest that RNase-L is a key regulator of IFNβ and TNFα production and is inhibited as an EPEC host evasion mechanism. The HeLa system described provides a tractable model for dissecting the molecular pathways involved in T3SS-dependent modulation of RNase-L activity with the potential to identify drug targets to reduce EPEC-associated morbidity.

P.16

UTILITY OF ROUTINE HEMOCCULT TESTING IN PREDICTION OF NECROTIZING ENTEROCOLITIS IN PREMATURE NEONATES. Aimee Pickering*, Rachel White*, and Natalie Davis, Division of Neonatology, Department of Pediatrics, University of Maryland School of Medicine, Baltimore, MD.

Necrotizing enterocolitis (NEC) is a disease process seen most commonly in premature infants and is characterized by inflammation and death of intestinal tissue. If left untreated, NEC can lead to weakening and perforation of the intestinal wall, infection, and even death. Of the 7-14% of very low birth weight (VLBW) neonates who will develop NEC, 20-40% die of the disease. The high mortality and morbidity of NEC results in part from clinicians' limited ability to detect the onset of the disease and to diagnose it in its early stages. Hemoccult testing, which detects occult blood in stool, is routinely performed in an attempts to identify infants at risk of developing NEC. Despite the regularity with which hemoccult testing is used, few studies have explored the utility of the test. In order to address this, we performed a retrospective medical record review of VLBW (<1.5kg) infants admitted to the Neonatal Intensive Care Unit (NICU) at the University of Maryland Children's Hospital in 2013. The medical record of each eligible subject was reviewed in order to determine the occurrence of Stage II and/or III NEC (based on modified Bell's Criteria) and the results of all occult blood stool tests performed. We then constructed a 2x2 table comparing occult blood stool test results vs. diagnosis of Stage II or Stage III NEC. We calculated the sensitivity, specificity, positive predictive value, and negative predictive value of positive hemoccult testing in relation to Stage II or III NEC diagnosis. Of the 89 neonates included in the study, a total of 5

subjects were diagnosed with Stage II or Stage III NEC. None of these subjects had a positive hemoccult test result during the 7 days prior to their diagnosis. The occult blood stool test was found to have a sensitivity of 0% and a specificity of 39%. Its positive predictive value was 0% and its negative predictive values was 15%. Our data does not support the practice of routine hemoccult testing in the VLBW neonate population since this test was poorly predictive of NEC and since the high rate of false positives may cause a patient's course of care to be inappropriately changed.

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

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LYMPHOCYTES ADOPTIVELY TRANSFERRED INTO CHRONICALLY STRESSED RAG2-/- MICE CONFER RAPID ANTIDEPRESSANT EFFECTS. Mitra Haeri* and Miles Herkenham, Department of Neuroscience, National Institute of Mental Health, Bethesda, MD.

Rag 2-/- mice, which have no adaptive immune system, were used to show the effect of adaptive immunity on stress-induced depressive-like states. By placing these mice under chronic restraint stress, then performing an adoptive transfer of T-lymphocytes from unstressed UBC-GFP mice, we have shown the beneficial effects of adaptive immunity in recovery from stress-induced depressive-like phenotypes. We have also seen an amplification of these effects when transferring the lymphocytes from chronically stressed UBC-GFP mice. Additionally, we have examined the effect of chronic restraint stress on neurogenesis in the hippocampus.

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NEUROMUSCULAR JUNCTION LOCATION AND SARCOLEMMAL MECHANICS ARE ALTERED IN DYSTROPHIC MUSCLE. Kathleen Twomey*, Stephen J.P. Pratt[1], Karla P. Garcia-Pelagio[2], and Richard M. Lovering[1], [1]Department of Orthopaedics and [2]Department of Physiology, University of Maryland School of Medicine, Baltimore, MD.

Duchenne muscular dystrophy (DMD) is characterized clinically by severe, progressive loss of skeletal muscle. The disease is caused by the lack of dystrophin, a large muscle membrane-associated protein localized to the inner face of the sarcolemma. Muscle weakness and a susceptibility to muscle injury are both hallmarks of DMD, as well as an increase in the presence of malformed muscle fibers. Studies have shown that malformed myofibers (MMs) contribute to a decrease in muscle specific force and an increase in susceptibility to contraction-induced injury. In fact, the age-dependent increase in MMs has been suggested to account for the age-dependent increase in muscle damage and muscle weakness. The aim of this study is to provide further insight into the structure and function of MMs from *mdx* mice (murine model for DMD). We hypothesized that both neuromuscular junction (NMJ) location and sarcolemmal mechanics would be altered in MMs compared to myofibers with normal morphology or those from healthy (wild type, WT) muscle. Single muscle fibers were isolated from the flexor digitorum brevis muscles of WT and *mdx* mice, plated, and labeled with an NMJ specific fluorescent stain (α-Bungarotoxin, BTX). NMJ location was then quantified. Multiple types of MMs were observed including birfurcated, split, process, poly split, double bifurcated, and trifurcated (42.9, 25.7, 27.1, 1.4, 1.4, 1.4 % of abnormal fibers, respectively). Only one NMJ per myofiber was observed in both WT and *mdx*, however there was variability in the location of the NMJ. WT fibers showed the least amount of variability with the majority of NMJs centrally located and the greatest amount of variability was seen in MMs, including positions on the trunk or branch. Data collection from the mechanical studies is ongoing. Preliminary results suggest an altered NMJ location in *mdx* fibers with altered morphology, which may affect contractile function and susceptibility to injury. Data from the mechanical studies will provide more about these interesting changes in a subset of *mdx* myofibers.

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EXPRESSION AND FUNCTIONS OF BITTER TASTE RECEPTORS IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE. Wei Qi* and Kathryn Robinett, Division of Pulmonary and Critical Care Medicine, Department of Medicine, University of Maryland School of Medicine, Baltimore, MD.

Chronic obstructive pulmonary disease (COPD) causes airway obstruction characterized by bronchoconstriction. B-agonists, the only class of bronchodilators, have side effects like tachycardia and tremors and interactions with β-blockers. These all pose problems in treating the aging population, creating a need for new classes of bronchodilators. Bitter taste receptors (BTRs) are G-protein coupled receptors (GPCRs) on human airway smooth muscle (HASM). They mediate bronchodilation through a novel calcium dependent mechanism. As with some GPCRs, BTRs are potentially subject to regulation by inflammation, such as in COPD. Our study compares the expression and function of BTRs in HASM from subjects with and without COPD. To show the bronchodilatory effects of BTR agonists, normal human bronchi were mounted on a myograph, contracted then treated with isoproterenol or BTR agonists. Similarly, *ex vivo* mouse tracheas were contracted and treated with the BTR agonist chloroquine and isoproterenol. To characterize the effects of COPD on BTR expression, quantitative real-time polymerase chain reaction (RT-PCR) was performed on HASM from normal and COPD subjects, using commercially available primers to the 3 dominant BTRs. Lastly, the function of BTRs was measured by intracellular calcium release in HASM from subjects with and without COPD using a Fluo4AM assay. BTR agonists were more effective in stimulating airway relaxation in maximally contracted human bronchi, and they relaxed tracheal rings in an additive manner with β-agonists. Quantitative RT-PCR of TAS2R-10, -14, and -31, showed increased mRNA levels in HASM cells of COPD compared to normal subjects ($n = 3$ from each group). Interestingly, bitter tastants stimulated intracellular calcium release to a greater degree in HASM cells of normal as compared to COPD subjects. This study suggests that COPD may alter the expression of BTRs or their function in HASM cells.

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SELF-EFFICACY IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE. Mahoussi Aholoukpe*, Raymond Cross, and Guruprasad Jambaulikar, Division of Gastroenterology and Hepatology, Department of Medicine, University of Maryland School of Medicine, University of Maryland School of Medicine,, Baltimore, MD.

Self-efficacy is an important construct in chronic disease management. Little is known about the association between clinical factors and self-efficacy and the impact of self-efficacy on outcomes in patients with inflammatory bowel disease (IBD). Our aim was to assess the association between demographic and clinical variables and self-efficacy in patients with IBD and to evaluate the correlation between self-efficacy and disease activity and quality of life. Patients with IBD from the University of Maryland Baltimore, University of Pittsburgh Medical Center and Vanderbilt University Medical Center were recruited as part of an ongoing randomized, controlled trial whose specific aim is to assess the effectiveness of a candidate intervention, **TELE**medicine for patients with **I**nflammatory **B**owel **D**isease (**TELE-IBD**) over a one year period. Information on demographics and clinical history, disease activity, quality of life, health care utilization, patient

knowledge, social constraint are collected. The general self-efficacy scale was used to measure general sense of perceived self-efficacy. Complete baseline data from 77 out of 213 enrolled participants was available for analysis. 69% percent of participants had Crohn's disease and 31% had ulcerative or indeterminate colitis. 57% were women and 58% were non-smokers. 71% had commercial health insurance. Among the participants with CD, 47% had inflammatory disease while 53% had obstructing or perforating disease and 40% had perianal involvement. 57% had extra-intestinal manifestations of disease. The mean SES score of the participants was 32.4+/-4.1. We did not find an association between demographic or clinical factors and low self-efficacy scores. We plan to examine the association between additional factors such as disease duration, times since last flare, patient knowledge, and medication exposure and self-efficacy as well as to construct a logistic regression model to adjust for multiple variables. We also plan to include more participants in future analyses. Lastly, we will examine the association between self-efficacy and disease activity and quality of life.

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P.21

LOCUS OF CONTROL IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE. Joy Lee* and Raymond Cross, Division of Gastroenterology and Hepatology, Department of Medicine, University of Maryland School of Medicine, Baltimore, MD.

Inflammatory bowel disease (IBD) involves chronic digestive tract inflammation and consists of ulcerative colitis (UC) and Crohn's disease (CD). Patients experience symptoms such as abdominal pain, diarrhea, and rectal bleeding. In this study, we analyze locus of control (LOC) in an IBD population. LOC, a psychosocial variable, evaluates the extent to which one believes internal or external factors determine outcomes. We aim to discover which demographic/clinical factors are associated with LOC; and to discover if there is a relationship between LOC and disease activity and quality of life (QoL). We used data from IBD patients from University of Maryland, University of Pittsburgh, and Vanderbilt University through an ongoing TELE-IBD study, which investigates if telemedicine is efficacious for IBD patients. Subjects are randomized to 3 groups: standard care, TELE-IBD weekly, and TELE-IBD biweekly. Subjects from TELE-IBD arms reply to texts about symptoms/side effects; and receive medication prompts and educational tips. Patient responses generate action plans and alerts. Subjects complete visits at baseline, 6, and 12 months. We obtain demographic/clinical information. Additional data are collected on disease activity, QoL, and psychosocial status. Rotter's LOC is used to measure LOC. Scale ranges from 0-23; higher LOC scores represent external LOC. Baseline data are available for 77/213 subjects. 71% have CD; 29% have UC/indeterminate colitis. Mean age is 39+/-12 years; disease duration is 12+/-10 years. 41% of CD patients had perianal involvement; 57% had extraintestinal manifestations. Mean LOC score is 9.7+/-3.6. Chi square tests were completed to find associations between demographic/clinical variables and LOC scores. None is associated with the LOC score. Our results are preliminary. We will examine associations between: disease duration/activity, time since last flare. We will also use logistic regression to adjust for covariates. It is possible that we are not powered to identify small-moderate determinants of LOC. Future analyses will include a higher sample size. Lastly, associations between external LOC and disease activity and QoL will be examined.

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PRENATAL DRUG EXPOSURE, CORTISOL STRESS REACTIVITY AND ADOLESCENT PROBLEM BEHAVIORS AND WEIGHT STATUS. Dayna Mazza*, Maureen Black, and Stacy Buckingham-Howes, Division of Growth and Nutrition, Department of Pediatrics, University of Maryland School of Medicine, Baltimore, MD.

Toxic stress, such as prenatal drug exposure (PDE), can alter the Hypothalamic-Pituitary-Adrenal (HPA) axis, resulting in dysregulated stress reactivity, with long-term problems in child development. Although results are mixed, some adolescents with PDE are more likely to engage in problem behaviors and have a higher BMI than non-exposed (NE) adolescents. Little is known about the mechanisms underlying these associations. We hypothesize that among the NE group, typical stress reactivity is associated with few problem behaviors and low BMI while no such associations are expected in the PDE group. The study was conducted among adolescents (M=14.17 years, SD=1.17; range = 11.93-16.64) who varied in PDE exposure (PDE n=76; NE n=61). Adolescents were 50% male and 99% African American. Measured height, weight, cortisol (stress reactivity), caregiver reported problem behaviors, and youth report/urine samples for drug use were collected. Overall, 45.3% were overweight/obese (BMI for age $\geq$ 85th percentile) with no differences in PDE status. The NE group was significantly more likely to react to a mild stressor than the PDE group (26% vs. 12%; x^2=4.49, p=.03). The PDE group was more likely to experiment with tobacco/alcohol (25% vs. 10%; x^2=4.76, p<.05). Within each exposure group, we used linear/logistic regression to examine the association between stress reactivity, problem behaviors, and weight. The NE group with typical stress reactivity engaged in fewer problem behaviors (any drug use: aOR=0.49, CI: 0.25-0.94, p<.05; aggression: b=-4.99, p<.05) than adolescents with atypical stress reactivity with no identifiable pattern in the PDE group. There was no association between stress reactivity and weight status in the NE group (B=-.156, p=>.05); however, there was a marginal association between lower stress reactivity and higher BMI (B=-.871, p=.08). These results suggest disruption of the HPA axis in adolescents who are PDE, which blunts stress reactivity and interferes with expected associations between stress reactivity and adolescent problem behaviors and BMI. Future research might examine the associations at earlier time points to further understand causality.

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PHOSPHODIESTERASE9A REGULATES NATRIURETIC PEPTIDE-STIMULATED CGMP AND CARDIAC HYPERTROPHY. Xueying Hu*, Dong Ik Lee, and David Kass, Department of Cardiology, Johns Hopkins University School of Medicine, Baltimore, MD.

Cyclic guanosine monophosphate (cGMP), a second messenger molecule that transduces both nitric oxide (NO) and natriuretic peptide (NP) stimulated signaling, and its effector protein kinase G (PKG) are acting as a brake system in the heart physiology. Many studies have revealed that the drugs that enhance cGMP synthesis or block its degradation by specific phosphodiesterases (PDE) protect against a broad range of cardiac diseases. We have previously reported that PDE5A inhibition by sildenafil blunts maladaptive hypertrophy and remodeling. PDE5A inhibitors enhance cGMP, and while commonly used to treat erectile dysfunction they have recently become a focus for treating heart disease. However, PDE5A regulates NO-generated cGMP that is often depressed in heart disease. By contrast, the PDEs that regulate the NP-coupled cGMP pool remain uncertain. Using a trans-aortic constriction (TAC) mouse model, we test the hypotheses that cardiac myocytes

express PDE9A, and that the specific inhibition of PDE9A alters pressure-induced hypertrophy in the heart. We show cGMP-selective PDE9A is expressed and functional in cardiomyocytes, where it regulates NP-stimulated cGMP, but not NO-stimulated cGMP. Furthermore, we show that inhibition of PDE9A with PF-9613 or its specific siRNA regulate attenuated phenylephrine-induced pathological hypertrophic marker gene in RNCM and adult mouse myocytes. This shows that PDE9A's effects on myocytes depends upon up-regulation of cGMP and its activation is important in hypertrophy. In in vivo mouse model, PDE9A knockout mice ($PDE9A^{-/-}$) subjected to sustained pressure-stress display better heart function with less hypertrophy and fibrosis that was accompanied by the increased cGMP level compared to control. In addition, pre-established hypertrophy and dysfunction in control animals is reversed by chronic PDE9A inhibition. These data show that PDE9A targets NP-generated cGMP to regulate the pathological function of heart disease. By targeting different sub-cellular cGMP pools than PDE5A, we propose that there are non-redundant therapeutic opportunities for clinical inhibitors of PDE5A and PDE9A which could treat common forms of heart disease.

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VISUALIZING THE STRUCTURE OF HYBRID BIOMATERIALS INVOLVING POLYPROPYLENE FUMARATE (PPF) USING QUANTUM DOTS. Michael Lee* and John Fisher, Department of Bioengineering, University of Maryland School of College Park, College Park, MD.

The current gold standard for cardiovascular devices is glutaraldehyde fixed pericardial tissue, which has a maximum average lifespan of 10 years due to calcification and degradation. One possible resolution to this issue is to reinforce unfixed tissue with a synthetic polymer that provides initial structural support and encourages natural re-cellularization of the tissue. Ongoing studies in our lab suggest that polypropylene fumarate coupled to unfixed tissue leads to lower calcification rates and provides structural support both in vitro and in vivo. Now, we wish to use a unique three-dimensional printing process to control the exact shape and dimensions of the polypropylene fumarate on our tissue, which requires more spatial coupling specificity. In order to do this, we must have an idea how the polypropylene fumarate and tissue interact when coupled, which has proven difficult in the past due to a lack of an effective histological technique for visualizing polymers such as polypropylene fumarate. Quantum dots are a relatively new fluorescent molecule that can be made with many different outer layers, allowing them to dissolve in and bind to a large array of substances. Another advantage of quantum dots is their ability to maintain a strong fluorescent signal in most environments, such as in the relatively intense ultraviolet light required to crosslink liquid polypropylene fumarate into a solid polymer. We hypothesized that by using quantum dots coated in hydrocarbon, we would be able to suspend them in the organic polypropylene fumarate liquid and have them stay embedded in the crosslinked solid polypropylene fumarate. This allowed us to visualize the polypropylene fumarate/tissue interface and begin to answer questions such as whether the polypropylene fumarate moves deep into the tissue or stays along the surface to better understand how polypropylene fumarate binds to the tissue so we can manipulate the binding process using our three-dimensional printer.

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SITE-SPECIFIC TARGETING PLATELET-RICH PLASMA VIA SUPERPARAMAGNETIC NANOPARTICLES. Tara Talaie*, Richard Lovering[1], Stephen Pratt[1], Su Xu[2], Paul Yarowsky[3], [1]Department of Orthopaedics, University of Maryland School of Medicine, [2]Department of Diagnostic Radiology and Nuclear Medicine, and [3]Department of Pharmacology, University of Maryland School of Medicine, Baltimore, MD.

Platelet-rich plasma (PRP) contains a concentration of platelets up to eight times the concentration of platelets found in whole blood. Unlike using isolated growth factors, an appealing benefit of PRP is that it contains growth factors in physiological proportions. Through the aggregation of PRP to a desired site, growth factors can enrich the target area and will prevent premature loss of the platelets at the site of injection. The aim of this study is to target PRP to a site of muscle injury in vivo by exploiting the magnetic properties of NPs with the use of external magnets. PRP was obtained using a commercial system (~1 x 10^{11}). The platelets were cultured with fluorescent iron oxide-based superparamagnetic nanoparticles (NPs). Uptake of the NPs by platelets was confirmed by immunofluorescence and electron microscopy, and *in vitro* experiments were performed to confirm responsiveness to magnetization. For in vivo experiments, a muscle injury was induced in the tibialis anterior muscle (TA) muscle in Sprague-Dawley rats (N = 3) and the TA was injected with platelets containing NPs (50 μL), visualized by both *in vivo* magnetic resonance imaging (MRI) and fluorescence microscopy (after tissue harvesting). We secured a magnet over the injected TA for three days. The control group (N = 3) did not receive any injections nor an external magnet. Maximal dorsi-flexor torque was measured before and after injury and at Day 3 time points. In vivo MR imagining showed retention of the PRP in rats that had a magnet placed over the TA. The early data on contractile function shows a trend toward hastened recovery from injury. Although the application of NPs to track cell migration using MRI is still relatively new, the ability to use NPs to non-invasively track the location of PRP will provide novel and useful information. Muscle strains are one of the most common complaints treated by physicians in addition to comprising a majority of all sports-related injuries. Thus PRP with NPs could provide a minimally invasive, cost effective and low risk method to decrease recovery time in muscle injuries.

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OPTIMIZATION OF NANOPARTICLES FOR EFFECTIVE DRUG TRANSPORT IN THE TREATMENT OF GLIOBLASTOMA. Philip Smith*, Graeme Woodworth, and Anthony Kim, Department of Neurosurgery, University of Maryland School of Medicine, Baltimore, MD.

Glioblastoma Multiforme (GBM) is among the most difficult forms of cancer to treat due to its invasive nature and diffuse presentation. In many cases, the tumor core can be completely resected surgically, yielding clean post-operative MRI images, but individual GBM cells can migrate far from the original tumor and embed in healthy brain tissue. These diffuse outgrowths are difficult to treat and result in GBM having a very poor survival prognosis. Several major obstacles exist in delivering therapeutics to these invading tumor cells. First, diffusion through the dense brain extracellular matrix (ECM) is very difficult due to the tight mesh spacing. Additionally, therapeutics have a high propensity to adhere to matrix proteins. Finally, clearance of the foreign objects from the internal microenvironment, both in the brain and in the body at large, is common and inhibits therapeutic effectiveness. Prior art in the field of neurological drug delivery suggests that by packaging drugs in specifically designed nanoparticles, obstacles to delivery through the ECM of the brain can be overcome. However, these particles must be both small enough to fit through pores in the ECM and bioinert (hydrophilic and neutrally-charged) to avoid adhesive interactions with ECM components, so that they may pass effectively through the ECM to the target. Previous studies have demonstrated that polyethylene glycol (PEG) surface coatings of nanoparticles shield both charged and hydrophobic segments of the particle itself that can be prone to adhere to the ECM. This project focuses on optimizing such particles using several methods, such as multiple particle-tracking in matrigel and in vivo diffusion and clearance studies. From these studies, a tradeoff is apparent

between the major parameters of size and bioinertness. As more PEG is added, the beads become more bioinert, but also greater in size, limiting their ability to pass through pores in the ECM. This tradeoff suggests an optimum coating size to allow the particles to effectively reach the target.

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THE ROLE OF SRC FAMILY KINASES IN THE THERAPEUTIC TARGETING OF CD99 IN ACUTE MYELOID LEUKEMIA. Yue Li*, Stephen Chung, and Christopher Park, Human Oncology and Pathogenesis Program, Memorial Sloan Kettering Cancer Center, New York, NY.

Although most adult patients suffering from acute myeloid leukemia (AML) will respond to chemotherapies targeted to the cancer, few will be completely cured. This is because relapse is both common and fatal. Leukemias such as AML are initiated and sustained by leukemic stem cells (LSCs) that possess both self-renewing and proliferative capabilities. Like other stem cells, LSCs are also relatively quiescent and therefore resistant to chemotherapies targeted at proliferating cells. Consequently, LSCs likely contributes to the reservoir of minimal residual disease (MRD) leading to relapse after initial treatment. In this way LSCs represent both the key and obstacle to the development of efficacious therapies against leukemia. The Park lab has recently discovered a transmembrane glycoprotein, CD99 that is preferentially expressed in LSCs compared to normal hematopoietic stem cells (HSCs). Of several commercially available anti-CD99 monoclonal antibodies (mAb), H036-1.1 was found to induce cytotoxicity in AML cells. Here, I show that H036-1.1 activates the apoptotic program in AML cells, and that the mechanism of activation involves Src family kinases. Additionally, AML cell lines that are resistant to the cytotoxic effects of H036-1.1 were found to have lower overall Src activation upon treatment with H036-1.1 compared to "sensitive" cell lines. In doing so, I also validated phospho flow as a novel assay for analyzing Src activation and protein level in both cell lines and primary cells. Together, these data suggest that Src activation by anti-CD99 antibodies or other modalities represents a promising mechanism for targeting LSCs in the treatment of AML.

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IDENTIFICATION OF A NOVEL T CELL RECEPTOR FOR GENE THERAPY OF HPV-ASSOCIATED MALIGNANCIES. Lindsey Draper*, Tracy E. Campbell, Steven A. Rosenberg, and Christian S. Hinrichs, Tumor Immunology Section, Department of Surgery, National Cancer Institute, Bethesda, MD.

Metastatic or recurrent/refractory human papillomavirus (HPV)-associated cancers, including cervical, oropharyngeal, anal, vulvar, vaginal, and penile malignancies, are incurable and difficult to palliate, and better therapies are needed. T cell receptor (TCR) and chimeric antigen receptor (CAR) gene therapies are emerging adoptive cell therapy (ACT) technologies that have demonstrated durable and complete tumor regressions in patients with metastatic melanoma and B cell malignancies. However, successful targeting of epithelial cancers with such therapies has not been demonstrated, and the identification of novel tumor-specific target antigens not expressed on important normal tissues has limited the expansion of the field. HPV encodes two potentially ideal targets for therapy, the E6 and E7 oncoproteins, as they are viral antigens constitutively expressed by malignant cells and absent from healthy human tissue. We have identified a high-affinity HPV16 E6-specific, HLA-A*02-restricted TCR (E629-38 TCR) from the tumor infiltrating lymphocytes (TIL) of a patient with a complete and on-going disease-free interval 18 months after resection of her only site of disease. T cells exhibiting recognition of an HPV16 E6+, HLA-A*02+ cell line were isolated based on CD137 up-regulation, a marker of T cell activation. The dominant TCR alpha and beta chain clonotypes were determined by 5' rapid amplification of cDNA ends (5'RACE), and the sequences were cloned into an MSGV1 retroviral vector for subsequent experiments. T cells

transduced with the E629-38 TCR have demonstrated specific recognition of HPV16+ tumor cell lines, and TCR deep sequencing has confirmed an increased prevalence of the E629-38 TCR within the tumor relative to the patient's pre-surgery peripheral blood mononuclear cells (PBMC). This work has, for the first time, demonstrated the ability of T cells to specifically lyse un-manipulated HPV+ tumor cell lines, and has laid the foundation for a novel TCR gene therapy clinical trial to treat patients with advanced HPV+ malignancies. Additionally, these findings may serve as a prototype for the expansion of TCR gene therapies to treat other epithelial cancers.

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THE EFFECTS OF LEFT VENTRICULAR ASSIST DEVICES ON CARDIOPROTECTIVE B-ARRESTIN-MEDIATED SIGNAL TRANSDUCTION IN A LARGE ANIMAL HEART FAILURE MODEL. Isa Mohammed*, Progyaparamita Saha, Pablo Sanchez, Bartley Griffith, and Keshava Rajagopal, Division of Cardiac Surgery, Department of Surgery, University of Maryland School of Medicine, Baltimore, MD.

According to the WHO, ischemic heart disease is the leading cause of death in the developed world. It is estimated that approximately ¼ of all patients who suffer myocardial infarctions (MI) develop progression to heart failure (HF). While pharmacologic therapies for post-MI HF provide some survival benefits, mortality continues to be high. In the subset of post-MI HF patients with severe HF, either mechanical circulatory support via left ventricular assist device (LVAD), or orthotopic heart transplantation (OHT), demonstrate substantially superior survival in comparison to medical therapies alone. However, OHT is severely restricted by donor organ supply limitation. Consequently, LVAD support is now used in the majority of patients with end-stage HF. LVADs reduce pathologic LV remodeling by reducing mechanical load-induced signals, but in doing so may inhibit cardioprotective compensatory responses. In order to develop effective combined therapies, the physiological alterations in mechanical loading resulting from LVAD action need to be understood in the context of the effects of medical therapies on native cardiomyocytes. This project aims to elucidate the downstream signaling following LVAD implantation using Western Blots and Co-Immunoprecipitation. 16 Adult Dorsett hybrid sheep were used in this study: 4 sham sheep, 6 MI sheep, and 6 MI sheep with an implanted microaxial LVAD. Animals were maintained for 12 weeks and then their myocardial tissue was analyzed. Results indicate that the MI+LVAD group had significantly increased β-arrestin levels and decreased ubiquitinated β-arrestin levels, which is consistent with decreased β-arrestin-mediated signaling. β-arrestin levels are inversely proportional to β-arrestin-mediated signaling, since ubiquitinated β-arrestin is the active form. Cardioprotective effectors p-ERK and, significantly, p-Akt and EGF-R bound to β-arrestin are also lower in the MI+LVAD group, all of which suggests that the LVAD inhibits the cardioprotective β-arrestin-mediated signaling. Thus this data supports the pursuit of combined medical therapies in order to supplement LVAD therapy and its shortcomings.

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PREOPERATIVE ASPIRIN AND ACUTE LUNG INJURY AFTER AORTIC VALVE REPLACEMENT SURGERY. Woderyelesh Kassa*and Micheal Mazzeffi, Department of Anesthesiology, University of Maryland School of Medicine, Baltimore, MD.

Acute respiratory distress syndrome (ARDS) is an uncommon, but life threatening complication of cardiac surgery occurring in as many as 20% of patients and carrying an 80% mortality rate. We hypothesized that pre-operative aspirin use was associated with a reduced risk of ARDS and

improved oxygenation indices after aortic valve replacement surgery. We retrospectively reviewed 375 patients who had aortic valve replacement surgery, from July 1st 2008 to June 30th 2013. The primary outcome variable was development of ARDS and the secondary outcome variable was the lowest oxygenation index or P/F ratio during the first 72 hours after surgery. The outcome variables were compared between those who received aspirin within 5 days of surgery and those who did not. 22 patients in the cohort developed ARDS (5.9%) according to the Berlin definition, and 9 were on pre-operative aspirin (40.9%). Most patients who developed ARDS were septic or had pneumonia. There was no difference in the incidence of ARDS between the two groups ($p=0.52$); however in subgroup analyses ASA appeared to improve the oxygenation index (P/F ratio) in patients who received a moderate amount of FFP transfusion (5-6 units) ($p=0.015$). ASA did not reduce the incidence of ARDS in patients having aortic valve replacement surgery; however, it did improve the oxygenation index (P/F ratio) in patients receiving a moderate amount of FFP transfusion. Future prospective studies should evaluate aspirin's effect in surgical patients receiving FFP.

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IDENTIFICATION OF NOVEL VARIANTS RESPONSIBLE FOR EXCEPTIONALLY HIGH HDL-C. Darya Malinina*, Jeff Rhyne, and Michael Miller, Division of Cardiology, Department of Medicine, University of Maryland School of Medicine, Baltimore, MD.

Many past studies have shown that high HDL-C is protective against coronary heart disease (CHD), while low HDL-C is associated with premature CHD. Although the molecular cause of low HDL has been elucidated (due to mutations in APOA1, LCAT, or ABCA1) the mutations that underlie exceptionally elevated HDL-C have not been as thoroughly studied, except for the ones in the CETP, LIPG, LIPC, and more recently the GALNT2 gene. Previously in our lab, DNA samples from families of exceptionally high HDL-C levels have been collected (over 100 mg/dl), and mutations that are already known to be implicated in high HDL have been ruled out, which has led us to believe that the high HDL-C is likely the result of novel single-gene mutations. In order to identify these novel mutations, exome sequencing was completed on 9 members with exceptionally high HDL-C (highest being 201 mg/dl), and GWAS studies were used as a starting point to target genes implicated in lipoprotein metabolism. After rare variants were identified, we consulted the dbGaP database, (containing information on over 1000 individuals) to see if these rare variants were present in any of the individuals in the database and their corresponding HDL-C phenotype. We recently discovered that 2 novel mutations at the 11q23 locus containing the ZNF259/APOA5/APOA4/APOC3/APOA1 gene cluster, particularly in ZNF259 (R226Q) and APOA4 (E185K) could explain the exceptionally high HDL-C in one particular family. This particular gene cluster is known to be linked to triglycerides, but it may also implicated in lipoprotein metabolism. No individual in dbGaP had either of the variants so it could not provide us with any additional information regarding the HDL-C phenotype. Further functional studies are necessary to elucidate the impact of these mutations but we believe it will lead to a greater understanding of the protective properties of HDL-C.

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THE USE OF CARDIAC PET TO PREDICT MYOCARDIAL ELECTROPHYSIOLOGY TISSUE PROPERTIES. Nathan Maassel*, Mark Smith[1], Timm Dickfeld[2], and Vasken Dilsizian[1],

[1]Department of Diagnostic Radiology and Nuclear Medicine and [2]Division of Cardiology, Department of Medicine, University of Maryland School of Medicine, Baltimore, MD.

The purpose of this study was to investigate the use of point-by-point analysis of electrophysiology (EP) voltage and positron emission tomography (PET) uptake to predict EP derived myocardial tissue categories in ischemic patients undergoing left ventricular tachycardia (VT) ablation procedures. The study population was 18 males with an average age of 67, who had both F18-fluorodeoxyglucose (FDG) and Rb-82 PET studies. Polar plots were generated from 3D PET images and loaded into a multimodality analysis program, along with EP voltage data. PET and EP data sets were registered and matched values were output. Mean PET uptake for EP tissue classifications were computed where <0.5mV is defined as scar, 0.5-1.5mV is defined as border zone, and >1.5mV is defined as normal tissue. Receiver operator characteristic (ROC) curves were generated for prediction of scar and abnormal tissue from FDG and Rb PET amplitudes. FDG and Rb PET means for EP tissue categories were significantly different ($p<0.001$). ROC curves for abnormal and scar tissue prediction for Rb and FDG had areas under the curve (AUCs) between 0.70-0.74, with AUC (Rb) > AUC (FDG) ($p<0.001$).

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A PROSPECTIVE RANDOMIZED TRIAL OF TRICUSPID ANNULOPLASTY FOR MODERATE TRICUSPID REGURGITATION IN PATIENTS UNDERGOING MITRAL VALVE OPERATION. Eddy Zandee van Rilland*, James Gammie, and Faisal Cheema, Division of Cardiac Surgery, Department of Surgery, University of Maryland School of Medicine, Baltimore, MD.

Tricuspid regurgitation (TR) is a valvular heart disease that results in the reverse flow of blood from the left ventricle back into the left atrium. The presence of severe TR in mitral valve disease patients is a straight-forward indication to perform tricuspid valve repair (TVR) concomitant with mitral valve repair or replacement (MVR). There is currently little prospective data in the literature supporting either tricuspid repair or neglect in MVR patients with moderate TR. The objective of this study was to determine the clinical worth of TVR concomitant with MVR in patients with moderate TR through a randomized clinical trial. Forty patients undergoing mitral valve surgery with moderate TR at the University of Maryland Medical Center were enrolled in the study (N=22 MVR only; N=18 MVR with TVR). All patients underwent preoperative tests and assessments, including a transthoracic echocardiogram (TTE), a transesophageal echocardiogram, and a cardiac MRI. Patients were seen at 1, 6, 12, and 24 months post-operation, at which time additional imaging exams were completed. Various outcomes measured by TTE and MRI were recorded and compared in the two groups. The primary outcome was TR grade at 12-months post-surgery. There was a statistically significant difference in TR grade at the pre-discharge and 24-month follow-up time points (P=0.003 and P=0.002, respectively). However, at the primary study endpoint (12 months) TR grade showed no statistically significant difference between the two groups (P=0.39). Tricuspid annular plane systolic excursion (TAPSE) and RV systolic pressure demonstrated no significant difference at any of the study time points between the two groups. Fractional area change and RV fractional shortening both demonstrated significant increases in RV performance at 12-months in the MVR only group compared to the MVR with TVR (P=0.02 and P=0.04, respectively). The trial is in its initial stages and all comparisons are based on preliminary analyses. A more accurate difference in TR grade can be observed once the entire cohort of patients complete all follow-up appointments.

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

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EVALUATION OF PATIENTS WITH VASOVAGAL SYNCOPE AND HEADACHE DURING HUT-TEST. Sara Van Meerbeke* and Ramesh Khurana, Department of Neurology, MedStar Union Memorial Hospital, Baltimore, MD.

The aim of this study was to evaluate the association between vasovagal syncope and headache. This aim stems from the results of numerous recent studies that have shown a high co-occurrence of vasovagal syncope and headache. One recent questionnaire-based study found that syncope may have a migrainous basis. Based on the answers to questionnaires, the authors of this study noted that migraine immediately precedes or follows syncope in a high proportion of patients. We hypothesized that a similar proportion of patients developing syncope during a head-up tilt test (HUT-test) in our laboratory would experience migraine as opposed to headache. Further, we hypothesized that patients developing syncope concurrent with headache would have greater autonomic dysfunction than patients developing syncope alone. In order to test this hypothesis, we performed a retrospective analysis on the charts of 25 patients that experienced syncope or pre-syncope during HUT-test during laboratory evaluation. We evaluated the frequency of headache or migraine during examination as well as the location, severity, duration, and timing of headache or migraine in reference to the onset of syncope to better elucidate cause and effect. Further, we evaluated laboratory values and symptoms before, during, and after HUT-test to assess if any of these variables predict the occurrence of headache in syncope patients. Of the 25 patients that underwent HUT-test, 10 experienced headache symptoms concurrent with syncope and 15 experienced syncope alone. In our study, we did not observe any patients that experienced syncope that was concurrent with migraine. Heart rate response to deep breathing was found to be significantly lower for the HUT-induced headache negative group by 6.5 bpm compared to the HUT-induced headache positive group (p-value=0.03). Valsalva ratio, IV phase of Valsalva maneuver, and HUT heart rate increase did not differ significantly between groups. No symptoms predicted the occurrence of HUT-induced headache. Based on the absence of occurrence of migraine, we provide evidence that supports the idea that most episodes of syncope do not have a migrainous basis.

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CAN WEBSITE INFORMATION BE USED TO IDENTIFY GUIDELINE-CONCORDANT WEIGHT LOSS PROGRAMS IN THE COMMUNITY? Benjamin Bloom*, Ambereen Mehta[2], and Kimberly Gudzune[1], [1]Welch Center for Epidemiology, Prevention, and Clinical Research, [2]Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, MD.

Weight loss has been demonstrated to prevent diabetes mellitus. Guidelines recommend that primary care providers (PCP) refer patients with obesity to high intensity weight loss interventions; however, many PCPs may be unaware of locally available programs. Our objective was to determine the reliability of web-based information regarding guideline-concordant practices of community weight loss programs in Maryland. We conducted a systematic online search for community-based weight loss programs, and performed a content analysis to abstract weight management practices from their websites. We then randomly selected 50 of these programs for a telephone survey to obtain actual program components and practices. We compared the accuracy of web and telephone data among this vanguard group to determine reliability of web-based information using cross-

tabulations. We identified 191 programs and recruited 41 for the telephone survey. Among this vanguard, 41% were physician delivered and 98% were in-person interventions. From the website, we could abstract program intensity (frequency of contacts) reliably among 37% of programs. Most misclassified programs were graded as a lower intensity as compared to phone report. Content analysis correctly identified programs containing dietary components (71%), exercise components (53%), and any behavioral component (51%). Both exercise and behavioral components were often not reported on the websites, despite use of these guideline-based practices as reported by phone. We accurately identified 90% of programs that used FDA-approved anti-obesity medications; however, 29% of programs that dispensed nutraceuticals were misclassified. Typically, websites failed to mention the use of these non-guideline-supported supplements (43%), despite endorsement by program staff of their use. Evaluation of weight loss programs' web-based content can reliably reflect some measures of guideline-concordant care and underestimates other aspects. This information could potentially be used to create a decision aid to facilitate PCPs' assessment of local weight loss programs, thus enhancing referrals to guideline-concordant programs.

Supported by the NIDDK Medical Student Research Program in Diabetes at the JHU-UMD Diabetes Research Center (P30DK079637).

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ASSOCIATION BETWEEN TOTAL CHOLESTEROL AND AT-RISK PSYCHOSIS SYMPTOMS AMONG HELP-SEEKING ADOLESCENTS.. Xavier Diao*, Caroline Demro[1], Elizabeth Thompson[1], Jason Schiffman[1], and Gloria Reeves[2], [1]Department of Psychology, University of Maryland, Baltimore County and [2]Division of Child and Adolescent Psychiatry, Department of Psychiatry, University of Maryland School of Medicine, Baltimore, MD.

Schizophrenia is a potentially devastating mental illness, characterized by perceptual disturbances (e.g. hallucinations), delusional thoughts, and/or disorganized symptoms. The primary pharmacologic treatment, antipsychotic medication, can also cause physical health problems through metabolic side effects (e.g. weight gain, new-onset diabetes). However, there is evidence that metabolic abnormalities may be present in individuals with first-episode psychosis prior to antipsychotic medication exposure, including hyperglycemia. It is unclear how early these metabolic abnormalities can be detected over the course of mental illness, and also if there is any association between specific psychotic symptoms and metabolic parameters. In this study, we assessed metabolic syndrome criteria in a sample of 52 antipsychotic-naïve adolescents (15.49 ± 2.68 yrs old) receiving mental health services. Youth were screened for "at-risk" psychosis symptoms using the Structured Interview for Psychosis Risk Syndromes (SIPS), and metabolic parameters (total cholesterol, HDL-C, LDL-C, glucose, blood pressure, insulin, triglycerides, weight, height, waist circumference) were measured after an overnight fast. We examined the relation between at-risk psychosis symptoms and fasting metabolic parameters. We found that disorganized communication was significantly correlated with total cholesterol (r = –0.39, p = .005) and LDL-C (r = –0.29, p = .040). The correlation with total cholesterol remained significant after controlling for waist circumference (r = –0.35, p = .015) and BMI (r = –0.38, p = .006), and when participants with current stimulant use were excluded from analyses (r = –0.41, p = .015). Fasting glucose also inversely correlated with disorganized symptoms (r = –0.29, p = .040). The results of this pilot study, if replicated, indicate a possible association between total cholesterol and disorganized symptoms that can be detected in adolescence. Longitudinal studies are needed to assess the causal relation between this metabolic parameter and psychiatric symptom over a course of illness.

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HYDROPHOBICALLY MODIFIED BIOPOLYMER FOR CONTROL OF MASSIVE HEMORRHAGE. Apurva Chaturvedi*, Matthew Dowling[1], Srinivasa Raghavan[2], and Ian MacIntire[3], and Mayur Narayan[4], [1]Department of Bioengineering and [2]Department of Chemical and Biomolecular Engineering, University of Maryland, College Park, College Park, MD, [3]Department of Research and Development, Remedium Technologies, Inc., College Park, MD, and [4]Division of Trauma, Critical Care, Acute Care and Emergency General Surgery, Department of Surgery, University of Maryland School of Medicine, Baltimore, MD.

Alginate is a biocompatible polysaccharide that is commonly used in the pharmaceutical, biomedical, cosmetic, and food industries. Though lyophilized alginate rapidly absorbs water, it is not an effective hemostat. The purpose of this study is to attempt to increase the hemostatic capabilities of alginate by hydrophobically-modifying alginate. Previous studies have illustrated modifying chitosan in this way greatly enhances its hemostatic effect as well as cellular adhesion, and it was hypothesized that hydrophobically-modifying alginate would demonstrate the same effects. Fifteen Yorkshire swine were randomized to receive hydrophobically-modified (hm) alginate pads ($n = 5$), unmodified alginate pads ($n = 5$), or standard Kerlix™ gauze dressing ($n = 5$) for hemostatic control. Following a splenectomy, arterial puncture (6 mm punch) of the femoral artery was made in groin. Wounds were allowed to freely bleed for 30 seconds at which time dressings were applied and compressed for 3 minutes in a randomized fashion. Fluid resuscitation was given to preserve the baseline mean arterial pressure. Wounds were monitored for 180 minutes after arterial puncture, and surviving animals were euthanized. Blood loss for the hm-alginate group was significantly less than control groups ($p =< 0.0001$). In addition, eighty percent of hm-alginate pads were able to sustain hemostasis for the full 180 minutes with only one pad whereas control groups of unmodified alginate and Kerlix™ gauze dressings were not even able to achieve initial hemostasis. Hydrophobic-modification of alginate dramatically increases hemostatic effect of when compared to unmodified alginate and Kerlix™ gauze dressings for decreasing blood loss and achieving/sustaining hemostasis from a lethal femoral artery puncture. This is a similar result as has been previously described when hydrophobically-modifying chitosan. When taken in conjunction, both works suggest that hydrophobic-modification of polymers can significantly increase their hemostatic capabilities.

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REPLICATION OF ASSOCIATION OF A LOSS-OF-FUNCTION MUTATION IN HORMONE-SENSITIVE LIPASE WITH METABOLIC TRAITS IN THE AMISH. Donique Parris*, Toni Pollin, Alan Shuldiner, and Coleen Damcott, Division of Endocrinology, Diabetes, and Nutrition, Department of Medicine, University of Maryland School of Medicine, Baltimore, MD.

Lipolysis is a metabolic pathway that regulates energy homeostasis through degradation of intracellular triacyglycerol (TAG) and release of fatty acids for use as energy substrates or lipid mediators in cellular processes. Both excess (e.g. obesity) and insufficient (e.g. lipodystrophy) white adipose tissue (WAT) stores, the primary energy depot, are associated with insulin resistance and

increased risk for type 2 diabetes. Thus, maintenance of normal WAT function is critical in preserving whole body insulin sensitivity and energy homeostasis. Hormone-sensitive lipase (HSL) is a key lipolytic enzyme with high affinity for diacylglycerol, but which also hydrolyzes TAG, cholesterol esters, and retinol esters. Recently, a 19-base pair deletion in the LIPE gene, which encodes HSL, was identified in the Amish. The mutation was associated with absence of the HSL protein, dyslipidemia, hepatic steatosis, systemic insulin resistance, and type 2 diabetes. The objective of this study was to identify additional carriers of the HSL mutation in a second Amish cohort and determine its effects on metabolic traits, such as fasting total cholesterol, triglycerides, high-density lipoprotein (HDL) cholesterol, and low-density lipoprotein (LDL) cholesterol. We genotyped 1,076 DNA samples from Amish participants in the Wellness Study and identified 33 heterozygote carriers (ID) and 1 homozygote (DD). Association analyses were then performed to determine which metabolic traits were significantly associated with the HSL mutation while taking relatedness of the participants into account. Of the metabolic traits analyzed, triglycerides and HDLs were statistically significant associated with the HSL mutation. The presence of the D allele was associated with higher serum triglycerides ($p=0.009$) and lower HDL cholesterol levels ($p=0.03$). These data provide replicating evidence of the reported effects of the HSL mutation on metabolic traits and further highlight the importance of HSL in maintaining systemic lipid homeostasis.

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ACCURACY OF CONTINUOUS NONINVASIVE HEMOGLOBIN MONITORING FOR THE PREDICTION OF BLOOD TRANSFUSIONS IN TRAUMA PATIENTS. David Hanna* and Samuel Galvagno, Jr., Division of Trauma Anesthesiology and Critical Care Medicine, Department of Anesthesiology, University of Maryland School of Medicine, Baltimore, MD.

Post-traumatic hemorrhage is the most common cause of preventable death in military and civilian settings. Standard vital signs are difficult to measure during acute resuscitation. The aim of this study was to examine whether continuous noninvasive total hemoglobin (SpHb) can predict the need for blood transfusion in the first 24 hours of trauma patient resuscitation. We hypothesized that SpHb levels, combined with patient-specific factors, can identify the immediate need for transfusion in trauma patients. Subjects were enrolled if they were directly admitted to the Trauma Resuscitation Unit (TRU) at the R Adams Cowley Shock Trauma Center, >18 years of age, and had a Shock Index (heart rate/systolic blood pressure) >0.60. Upon admission, A Masimo Radical-7 co-oximeter (Masimo Corporation, Irvine, CA) was applied, providing SpHb levels. The primary outcome of interest was the administration of at least one unit of packed red blood cells within 24 hours after admission.677 subjects had continuous vital signs waveforms available. When SpHb was monitored for 15 minutes, SpHb did not contribute additional sensitivity and specificity for the predictive model. The highest AUROC for the prediction of blood product administration within the first 3 hours of admission was recorded when the following variable were considered: age, sex, prehospital stroke index, admission heart rate, SpHb and SpO2. When data from 30 minutes of continuous monitoring were analyzed, significant improvement in AUROC occurred as more variables were added to the model. However, the addition of SpHb alone to the model did not improve AUROC significantly for prediction of transfusion within the first 3 hours of admission. The results from this study demonstrate that SpHb monitoring, accompanied by continuous vital signs and patient-specific data has good accuracy for the prediction of need for transfusion. However, as an independent variable, SpHb did not enhance predictive models for blood transfusion. Considering the high mortality associated with hemorrhagic shock, robust and reliable

methods for assessing the need for transfusion are urgently needed to ensure optimal patient outcomes.

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ACUTE LOWER EXTREMITY ISCHEMIA AS A POTENTIAL MAJOR COMPLICATION AFTER CARDIOTHORACIC (CT) SURGERY. Angelina She*, Dr. Robert S. Crawford[1], Donald Harris[2], and Adriana Laser[2], [1]Division of Vascular Surgery, [2]Department of Surgery, University of Maryland School of Medicine, Baltimore, MD.

Acute lower extremity ischemia is a potential major complication after cardiothoracic (CT) surgery. We evaluated the incidence, management and outcomes of this event. Patients at a high volume cardiovascular center with acute leg ischemia after CT surgery were identified from billing and clinical databases for retrospective review. The primary outcome was the composite of amputation or inpatient death. Between 2004 – 2014, 74 patients had acute leg ischemia after CT surgery. Index CT procedures were: 36 (49%) coronary bypasses, 26 (35%) valve, 23 (31%) transplant or device, and 17 (23%) aorta. 23 (31%) patients had an aortic balloon pump and 27 (37%) cases were emergent. Limb ischemia occurred at a median of 2 days (IQR 1 – 5) after CT surgery, and 11 (15%) cases were bilateral. 57 (77%) patients had a pulse deficit and 35 (47%) had gross signs of malperfusion. While 11 (15%) were attributed to pre-existing peripheral arterial disease, the remainder were from an aortic balloon pump (20%), femoral cannulation (19%), a direct effect of cardiac or aortic disease and surgery (16% and 12%, resp.). 11% were of uncertain etiology. 9 (12%) patients had unsalvageable ischemia, 1 (1%) was treated non-operatively, and 64 (87%) underwent a lower extremity vascular procedure. Of these, 61 were reperfused, by thromboembolectomy (57%), bypass (31%), or endovascular intervention (12%). 22 (30%) patients had fasciotomies. 16 (22%) patients required amputation and 32 (43%) patients died, with 38 (51%) meeting the composite endpoint. While there was a trend toward increased risk for amputation or death with an aortic balloon pump after CT surgery (18% vs 3%, $P = 0.06$), patient comorbidities, and CT and vascular surgical factors did not appear to contribute to limb morbidity or mortality in these patients. Acute lower extremity ischemia after CT surgery is relatively infrequent, but is associated with significant morbidity and inpatient mortality. Further study is required and warranted to identify risk factors for initial ischemia, and for subsequent adverse outcomes.

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IS INCISIONAL NEGATIVE PRESSURE WOUND THERAPY ASSOCIATED WITH DECREASED SURGICAL SITE INFECTIONS? Nina Semsarzadeh*, Karan Chopra[1], Kashyap Tadisina[2], John Maddox[1], and Devinder Singh[1], [1]Division of Plastic Surgery, Department of Surgery, University of Maryland School of Medicine, Baltimore, MD and [2]University of Illinois at Chicago College of Medicine, Chicago, IL.

Negative pressure therapy (NPT) has been used to treat open wounds for the past two decades. More recently, studies have reported the use of NPT over closed incisions to decrease surgical site occurrences. To assess cumulative status of reported findings, we conducted a meta-analysis of the current literature to evaluate the effectiveness of incisional negative pressure wound therapy (iNPWT) in lowering the incidence of surgical site infections (SSIs) as compared to standard dressings. PubMed, the Cochrane Library, and Cumulative Index to Nursing and Allied Health Literature (CINAHL) were searched through August 2014 for publications comparing iNPWT to standard care. A meta-analysis including 4631 participants from 14 published studies was performed. The overall rates of surgical site infection in the iNPWT and control groups were 6.61% and 9.36%, respectively. Individual Odds Ratios or relative SSI likelihood rates by incision site location were 56% ($p = 0.01$) for the abdomen, 37% ($p = 0.002$) for the chest, 19% ($p = 0.0001$) for the groin, and

55% for the lower extremity (p = 0.022). The use of iNPWT was found to decrease SSI rate by 56% across all incision site regions considered together (p < 0.0001). However, a sensitivity analysis of heterogeneity (i.e., sub-group analysis) resulted in the three groin area studies being dropped and a final result that yielded an odds ratio of 0.504 (p = 0.0001), indicating a 50% reduction in SSI rate with iNPWT relative to standard care. Additionally, 9 of the 14 studies reported dehiscence rates among the two groups. Overall rates of dehiscence in the iNPWT and control groups were 5.32% and 10.68%, respectively. Heterogeneity was very high (I2 = 84%) and consequently data were not considered for further analysis. However, the effect size, Odds Ratio = 0.5 (CI 0.30 to 0.85), was significant, suggesting a correlation between iNPWT and lower dehiscence. The results of the quantitative meta-analysis suggest that iNPWT is an effective method for reducing SSIs. It also appears that iNPWT may be associated with a decreased incidence of dehiscence although the evidence is still inconclusive.

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DOES MARIJUANA USE LEAD TO POOR OUTCOMES AFTER KIDNEY TRANSPLANTATION? Garrett Greenan*, Silke Niederhaus[1], Jonathan Bromberg[1], Megan Anders[2], and Alexia Leeser[3], [1]Department of Surgery and [2]Department of Anesthesiology, University of Maryland School of Medicine and [3]Sandy Spring Friends School, Baltimore, MD.

Though marijuana use is being legalized in several states, the effect of marijuana use on kidney transplantation is unknown. Despite this dearth of knowledge, many transplant programs refuse to offer kidney transplants to patients using marijuana. The purpose of our study is to examine whether marijuana use results in worse outcomes after kidney transplantation, such as poorer patient or graft survival, or poorer graft function. We are performing a retrospective chart review of the 1226 adult kidney transplant recipients transplanted over a five-year period from 1/1/2008 to 1/1/2013. We are comparing one-year patient and graft survival, and one- and five-year kidney function in transplant recipients with or without a history of marijuana use. The marijuana use history is being extracted from urine drug screens obtained at pre-transplant evaluation, and from patients' self-reported histories of marijuana use. So far, 863 charts have been reviewed. Across the 863 charts, 521 had urine toxicology data available. Of these, 487 (93.5%) were negative, and 34 (6.5%) were positive for marijuana. Among those with negative toxicology screens, 55 admitted to past use, and 6 to current use. Among those with positive screens, 16 denied ever using marijuana, 6 admitted to past use only, and 10 confessed to current use. Two positive toxicology screens were later repeated and found to be negative; one admitted to marijuana use and one did not. Patient survival was 98.2% in the non-marijuana group and 100% in the marijuana positive group. If graft failure was considered as a GFR (glomerular filtration rate, by MDRD) <20 ml/min, then 35 (7.2%) of grafts failed in the non-marijuana group versus 2 (5.9%) in the marijuana group. The average one-year creatinine was 1.83±1.47 mg/dL in the non-marijuana group, and 2.02±1.8 mg/dL in the marijuana group. When kidney function was adjusted for muscle mass by using the MDRD calculation for GFR, the average GFR was identical in both groups at 51 ml/min at one year. While data collection is ongoing and statistical analysis is pending, it does not appear that marijuana use adversely affects outcomes after kidney transplantation.

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OUTCOMES OF TROCHANTERIC OSTEOTOMIES FOR ACETABULAR FRACTURE SURGERY. Andrew Dubina*, Niluka Wickramaratne[1], Robert O'Toole[2], and Theodore Manson[2], [1]Department of Surgery, Virginia Commonwealth University Health System, Richmond, VA and [2]Department of Orthopaedics, University of Maryland School of Medicine, Baltimore, MD.

Trochanteric osteotomies are used to improve surgical exposure during open reduction and internal fixation of acetabular fractures when used in conjunction with standard approaches. The total hip arthroplasty literature has reported non-union rates as high as 30% with trochanteric osteotomies, however few data exist regarding the outcomes of trochanteric osteotomies for acetabular fracture surgery. Our hypotheses were (1) patients receiving trochanteric osteotomies during ORIF of acetabular fractures have low rates of nonunion of the osteotomy fragment and (2) hip abduction precautions are not necessary with digastric type osteotomies. A retrospective review was conducted to identify patients with all acetabular fractures between July 2002 and June 2010 (n=734 fractures) who required trochanteric osteotomies (n=64, 9% of fractures). Forty-seven met inclusion criteria of adequate follow-up (>56 days) to evaluate healing; no excluded patient experienced a complication. Fractures were classified by the attending orthopedic surgeon using the Letournel-Judet classification system. The primary outcome measure in this study was complete radiographic union of the osteotomy site and maintenance of hardware of the trochanteric osteotomy site at final follow-up. All study patients demonstrated radiographic union of the trochanteric osteotomy site (100% union rate, n=47). The study cohort of patients included 12 unigastric and 35 digastric osteotomies. Only 20% of the digastric trochanteric osteotomies were given hip abduction precautions post-operatively yet they all (n=35) healed uneventfully. No significant difference was found in the number of patients who had their trochanteric osteotomy screws removed between our data and a historical control (13% vs. 20%, p=0.43). Despite the infrequent application of abduction precautions that are intended to protect the osteotomy site and reduce the risk of nonunion or fixation failure, our data demonstrate a 100% union rate (n=47) of trochanteric osteotomies at 8 weeks post-operatively. Additionally, it appears it may be safe to not use hip abduction precautions in patients with digastric trochanteric osteotomies.

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AN INVESTIGATION OF THE COST OF GLAUCOMA-BASED DISEASE SURVEILLANCE. Emily Schehlein* and Osamah Saeedi, Department of Ophthalmology and Visual Sciences, University of Maryland School of Medicine, Baltimore, MD.

Glaucoma is the leading cause of irreversible blindness worldwide and requires frequent monitoring to prevent progression of the disease and loss of vision. These frequent office visits cost billions in direct costs, but the indirect and societal costs of these visits have not been assessed in the United States. Alternative models of glaucoma care utilizing telemedicine are in use in other countries and have been proposed in the United States. Knowledge of the indirect and societal costs of glaucoma monitoring is critical to assessing the cost-effectiveness of alternative models of glaucoma health care delivery. This project examines the societal and indirect costs of glaucoma care. Specifically, we have designed and distributed a survey which assesses in detail the costs associated with each individual visit including cost of transportation, time, and loss of work for the individual and caregiver. Demographic and clinical variables are being collected and will be correlated with these variables. We are conducting this pioneering research with the aim of drawing attention to the need for improvement in patient care, reduced health care costs, and increased convenience to the patient.

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