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University of Maryland School of Medicine

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Thirty-Second Annual Medical Student Research Day

***September 24, 2009
Southern Management Corporation
Campus Center
621 W. Lombard Street, Baltimore, MD***

MSRD Organization Committee

Ashley S. Huber, MSIV
Alpha Omega Alpha Medical Honor Society

Jordan E. Warnick, Ph.D.
Assistant Dean & Professor
Office of Student Research

Sponsors

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University of Maryland School of Medicine

Acknowledgments

We would like to express our gratitude to Dr. E. Albert Reece for providing the financial support for Medical Student Research Day - 2009. Our special thanks to the faculty and medical student judges who so willingly provided their time and knowledge.

MSRD Judges

Poster Presentation:

Dr. Samuel Alaish
Dr. Abdu Azad
Dr. Svetlana Chapoval
Dr. Matthew Frieman
Dr. Yongjun Guan
Dr. Rao Gullapalli
Dr. Britta Hahn
Dr. Bret Hassel
Dr. Julie Hotopp
Dr. Laura Hungerford
Dr. Stephen Jacobs

Dr. Ashwani Khanna
Dr. Miriam Laufer
Dr. Alan McMillan
Dr. Istvan Merchenthaler
Dr. Rosangela Mezghanni
Dr. Mike Miller
Dr. Anindo Roy
Dr. Violeta Rus
Dr. Tonya Webb
Dr. Xianfeng Zhao

Oral Presentations:

Session 1 (Ballroom 210B)

Dr. Xianfeng Zhao
Dr. George Fantry
Dr. Erin Hager
Ashley Huber, MSIV
Mira Herman, MSIV

Session 2 (Room 349)

Dr. Yuko Ota
Dr. Prasad Rallabhandi
Dr. Dan Schulze
Dr. Kathy Squibb
Stephanie Cha, MSIV

Audio Visual:

Kyle Hatten, MSIV
Meghna Trivedi, MSIV

Event Photography:

Miriam Ayub, MSIV

**32nd Annual Medical Student Research Day
September 24, 2009**

11:30 a.m.	<i>(Poster Presentation set-up)</i>
Noon – 3:00 p.m. Ballroom 208A	Welcome <i>Ashley Huber, MSIV</i> <i>Jordan E. Warnick, PhD</i> Poster Presentation & Judging
2:30 p.m.	<i>(Oral Presentation set-up)</i>
3:00 – 5:40 p.m. Oral 1 – Ballroom 210B Oral 2 – Room 349	Oral Presentation & Judging
6:00 p.m. Ballroom 208A	Welcome Address <i>Ashley Huber, MSIV</i> <i>Jordan E. Warnick, PhD</i> Dinner
6:45 p.m.	Keynote Address “The Role of Lipid Rafts in Developmental Toxicity” <i>Cynthia F. Bearer, MD, PhD</i> Mary Gray Cobey Professor of Neonatology Chief, Division of Neonatology
7:30 p.m.	Presentation of Awards & Certificates

Poster Presentation Schedule

<i>Abstract No.</i>	<i>Name</i>	<i>Time</i>	<i>Location</i>
<i>P.01</i>	Groleau, Patricia	Noon – 3:00 p.m.	Ballroom 208A
<i>P.02</i>	Gordon-Lipkin, Eliza	Noon – 3:00 p.m.	Ballroom 208A
<i>P.03</i>	Nigam, Shikha	Noon – 3:00 p.m.	Ballroom 208A
<i>P.04</i>	Stauffer, Craig	Noon – 3:00 p.m.	Ballroom 208A
<i>P.05</i>	Kerns, Michelle	Noon – 3:00 p.m.	Ballroom 208A
<i>P.06</i>	Kerns, Michelle	Noon – 3:00 p.m.	Ballroom 208A
<i>P.07</i>	Pandelidis, Katherine	Noon – 3:00 p.m.	Ballroom 208A
<i>P.08</i>	Nadel, Robyn	Noon – 3:00 p.m.	Ballroom 208A
<i>P.09</i>	Levine, Andrea	Noon – 3:00 p.m.	Ballroom 208A
<i>P.10</i>	Kvarta, Mark	Noon – 3:00 p.m.	Ballroom 208A
<i>P.11</i>	Miller, Brian	Noon – 3:00 p.m.	Ballroom 208A
<i>P.12</i>	Gause, Colin	Noon – 3:00 p.m.	Ballroom 208A
<i>P.13</i>	Eisenberg, Lindsay	Noon – 3:00 p.m.	Ballroom 208A
<i>P.14</i>	Atwood, Joel T	Noon – 3:00 p.m.	Ballroom 208A
<i>P.15</i>	Schratz, Kristen	Noon – 3:00 p.m.	Ballroom 208A
<i>P.16</i>	Nelson, Jonas A.	Noon – 3:00 p.m.	Ballroom 208A

Students are to be present for the entire 3-hour period
to allow judges to meet with them

Oral Presentation Schedule (Concurrent Sessions)

Abstract No.	Name	Session	Time	Location
O.01	Gregory Bittle	Oral 1	3:10	Ballroom 210B
O.02	Timothy Feeney	Oral 1	3:20	Ballroom 210B
O.03	Michael Grant	Oral 1	3:30	Ballroom 210B
O.04	Ali Hamedani	Oral 1	3:40	Ballroom 210B
BREAK (10 minutes)				
O.05	Andreas Saltos	Oral 1	4:00	Ballroom 210B
O.06	Jennifer Emberger	Oral 1	4:10	Ballroom 210B
O.07	Robert LeGros	Oral 1	4:20	Ballroom 210B
O.08	Nicole Mahdi	Oral 1	4:30	Ballroom 210B
BREAK (10 minutes)				
O.09	Bryce Olenczak	Oral 1	4:50	Ballroom 210B
O.10	Maxim Orlov	Oral 1	5:00	Ballroom 210B
O.11	Hemal Sampat	Oral 1	5:10	Ballroom 210B
O.12	Kyle Wilson	Oral 1	5:20	Ballroom 210B
O.13	Aleksandra Gajer	Oral 1	5:30	Ballroom 210B
O.14	Jordan Ambrose <i>and</i> Jessica Ton	Oral 2	3:00	Room 349
O.15	L. Latéy Jones	Oral 2	3:10	Room 349
O.16	Daniel Smith	Oral 2	3:20	Room 349
O.17	Erica Chapin	Oral 2	3:30	Room 349
BREAK (10 minutes)				
O.18	Adam Fisch	Oral 2	3:50	Room 349
O.19	Tuo Li	Oral 2	4:00	Room 349
O.20	Matthew Smith	Oral 2	4:10	Room 349
O.21	Monica Charpentier	Oral 2	4:20	Room 349
O.22	Janelle Cooper	Oral 2	4:30	Room 349
BREAK (10 minutes)				
O.23	Ashley Devonshire	Oral 2	4:50	Room 349
O.24	Eitan Friedman	Oral 2	5:00	Room 349
O.25	Aparna Ramaseshan	Oral 2	5:10	Room 349
O.26	Daniel Smith	Oral 2	5:20	Room 349
O.27	Claude Muresan	Oral 2	5:30	Room 349

Presentations MUST remain on-time: 8 min talk 2 min Q&A.

Alphabetical by Student Name

<i>Name</i>	<i>Abstract No.</i>
Ambrose, Jordan	O.14
Atwood, Joel T	P.14
Bittle, Gregory	O.01
Chapin, Erica	O.17
Charpentier, Monica	O.21
Cooper, Janelle	O.22
Devonshire, Ashley	O.23
Eisenberg, Lindsay	P.13
Emberger, Jennifer	O.06
Feeney, Timothy	O.02
Fisch, Adam	O.18
Friedman, Eitan	O.24
Gajer, Aleksandra	O.13
Gause, Colin	P.12
Gordon-Lipkin, Eliza	P.02
Grant, Michael	O.03
Groleau, Patricia	P.01
Hamedani, Ali	O.04
Jones, L. Latéy	O.15
Kerns, Michelle	P.05 / P.06
Kvarta, Mark	P.10
LeGros, Robert	O.07
Levine, Andrea	P.09
Li, Tuo	O.19
Mahdi, Nicole	O.08
Miller, Brian	P.11
Muresan, Claude	O.27
Nadel, Robyn	P.08
Nelson, Jonas A.	P.16
Nigam, Shikha	P.03
Olenczak, Bryce	O.09
Orlov, Maxim	O.10
Pandelidis, Katherine	P.07
Ramaseshan, Aparna	O.25
Saltos, Andreas	O.05
Sampat, Hemal	O.11

<i>Name</i>	<i>Abstract No.</i>
Schratz, Kristen	P.15
Smith, Daniel	O.16 / 0.26
Smith, Matthew	O.20
Stauffer, Craig	P.04
Ton, Jessica	O.14
Wilson, Kyle	O.12

Alphabetical by Research Mentor

<i>Mentor</i>	<i>Name</i>	<i>Abstract No.</i>
Allen, Jeremiah	Bittle, Gregory	O.01
Atamas, Sergei	Orlov, Maxim	O.10
Aurelian, Laure	Wilson, Kyle	O.12
Bearer, Cynthia F.	Sampat, Hemal	O.11
Black, Maureen	Jones, L. Latéy	O.15
Calebresi, Peter	Gordon-Lipkin, Eliza	P.02
Coulombe, Pierre	Kerns, Michelle	P.05 / P.06
Daumit, Gail	Levine, Andrea	P.09
Ferguson, Robert	Gajer, Aleksandra	O.13
Fink, Jeffrey	Chapin, Erica	O.17
Ford, Sidney and Peralta, Ligia	Ambrose, Jordan and Ton, Jessica	O.14
Gaspari, Anthony	Groleau, Patricia	P.01
Gould, Todd	Smith, Matthew	O.20
Griffith, Bartley	Stauffer, Craig	P.04
Griffith, Bartley and Wu, Zhongjun	Miller, Brian	P.11
Griffith, Bartley and Wu, Zhongjun	Gause, Colin	P.12
Griffith, Bartley and Wu, Zhongjun	Saltos, Andreas	O.05
Gulati, Mangla	Nigam, Shikha	P.03
Hafer-Macko, Charlene	Nadel, Robyn	P.08
Harris-Warrick, Ronald	Kvarta, Mark	P.10
Khurana, Ramesh	Eisenberg, Lindsay	P.13
Kittner, Steven	Hamedani, Ali	O.04
Krimsky, William	Atwood, Joel T	P.14
Lichenstein, Richard	Smith, Daniel	O.16 / O.26
Magaziner, Jay and Goodpaster, Bret	Devonshire, Ashley	O.23
Martin, Stuart	Charpentier, Monica	O.21
Matsuo, Koji	Cooper, Janelle	O.22
Montaner, Silvia	Friedman, Eitan	O.24
Nataro, James and Rasko, David	Emberger, Jennifer	O.06
Panigrahi, Pinaki	Ramaseshan, Aparna	O.25
Panigrahi, Pinaki	Schratz, Kristen	P.15
Poston, Robert	Grant, Michael	O.03
Rodriguez, Eduardo	Muresan, Claude	O.27
Rodriguez, Eduardo	Olenczak, Bryce	O.09
Sen, H. Nida	Mahdi, Nicole	O.08
Serletti, Joseph and Wu, Liza	Nelson, Jonas A.	P.16
Simon, Jakub	LeGros, Robert	O.07

<i>Mentor</i>	<i>Name</i>	<i>Abstract No.</i>
Tang, Cha-Min	Li, Tuo	O.19
Viscardi, Rose	Pandelidis, Katherine	P.07
Weber, David	Fisch, Adam	O.18
Wilson, Gerald	Feeney, Timothy	O.02

Poster Abstracts

- P.01 MODELING FOR INVARIANT NATURAL KILLER T-CELL/KERATINOCYTE INTERACTIONS IN ALLERGIC CONTACT DERMATITIS. Patricia F. Groleau*, Rita Fischelevich, Yuming Zhao and Anthony A. Gaspari. Department of Dermatology, University of Maryland School of Medicine, Baltimore, MD.

Invariant Natural Killer T-Cells (iNKT), cells that recognize glycolipids presented on CD1d molecules, have been shown to migrate into the epidermis during allergic contact dermatitis (ACD). Little is known about the mechanisms of interaction between iNKT-cells and CD1d-bearing Keratinocytes (KC) during ACD. The present study aimed first to characterize the roles of CD1d and α -Galactosylceramide (α -GalCer) in iNKT cell cytotoxicity during their interactions with KC, a potential mechanism of cell destruction in ACD, and second to determine if KC have a tolerizing effect on iNKT cells. Calcein-labeled HaCat KC were either mock transfected, transfected with a control negative oligonucleotide, or transfected with CD1d siRNA and were incubated with iNKT in the presence or absence of α -GalCer and fluorescence was measured to determine the levels of iNKT cytotoxicity. Cytotoxicity was found to be dependent on both α -GalCer and CD1d at high iNKT:KC ratios, but only dependent on CD1d at low ratios, indicating a possible endogenous glycolipid may play a role at low effector:target ratios. After a non-stimulatory incubation with KC and α -GalCer, iNKT showed a decrease in TNF- α and IL-4 cytokine secretion as well as Granzyme B and K gene expression when stimulated with a CD1d bearing monocytic cell line, THP-1, suggesting iNKT cell hyporesponsiveness. These data indicate that iNKT-cells can recognize CD1d on KC, and that such interactions may induce immunologic hyporesponsiveness. This may limit the scope of the damage that iNKT-cells can mediate during ACD.

- P.02 SEMI-AUTOMATIC SPINAL CORD ATROPHY QUANTIFICATION IN MULTIPLE SCLEROSIS: RELATIONSHIP TO CLINICAL DISABILITY AND OPTICAL COHERENCE TOMOGRAPHY. Eliza Gordon-Lipkin*, BettyAnn Chodkowski, Daniel Reich, Seth Smith, Kathleen Zackowski, Mathew Pulicken, Peter Calabresi. Department of Neurology, Johns Hopkins School of Medicine, Baltimore, MD.

We examine the relationship in MS among spinal cord atrophy (by semi-automatic quantification), retinal thinning (by optical coherence tomography (OCT)), and disability measures. Axial magnetization transfer weighted (MTw) images (C2-C6) were obtained on 36 MS subjects and 11 controls on a 3T MRI scanner. A semi-automatic segmentation process (approx. 5min) generated cord cross-sectional areas and CSF-normalized MTw signal (MTCSF). Brain parenchymal fraction (BPF) was estimated from cranial MRI using SIENA-X. RNFL thickness was measured by OCT. Disability was scored by EDSS. Multiple linear regression analysis was used to assess relationships among imaging and clinical parameters, accounting for age. Mean cord cross-sectional area at C2 (CA) was decreased in MS patients (62.6 mm² vs. 70.2 mm² for controls, p=0.03). CA predicted EDSS in MS (r²=0.34, p=0.007) but were not significantly associated with RNFL thickness. MTCSF at C2 was not associated with CA, EDSS, or RNFL thickness. BPF was not significantly associated with CA. MS subtype analyses were also performed. Semi-automatic quantification of cord atrophy from MTw images is fast and the results predict global disability. It may therefore be a useful tool to monitor disease for patient care and clinical trials. Cord atrophy and RNFL thinning or BPF, however, are not linked, suggesting that this is not a measure of global MS neurodegeneration. The previously described association between RNFL thinning and brain atrophy may reflect specific damage to the intracranial visual pathways rather than a global process. (Support by NMSS and Nancy Davis Foundation)

- P.03 DIAGNOSTIC DILEMMA: AOSD – AN UNCOMMON PRESENTATION OF A RARE DISEASE. Shikha Nigam* and Mangla Gulati. Division of Internal Medicine, Department of Medicine, University of Maryland School of Medicine, Baltimore, MD.

AOSD is a rare systemic inflammatory disorder of unclear etiology that typically presents with spiking fevers, evanescent rash, arthralgias or arthritis, and sore throat and lab abnormalities including neutrophilic leukocytosis, increased acute phase reactants, and marked hyperferritinemia. Diagnosis of AOSD is difficult given its low incidence, variable presentation and overlap between other diagnoses. The purpose of this case report is to present an uncommon presentation of a rare disease, AOSD. A 29 year old AAF was admitted for dyspnea, pharyngitis and fevers 2 days after a cholecystectomy for acute cholecystitis. Patient was sent home with antibiotics for pneumonia, but returned with shortness of breath, fevers, and bilateral ankle swelling; leukocytosis, hypoalbuminemia, iron-deficiency, and coagulopathy; pleural effusion with consolidation on CXR. Symptoms worsened despite broad coverage antibiotics, negative blood, urine and sputum cultures. She was transferred to our hospital for worsening condition and dubious diagnosis. Upon transfer, physical exam was significant for tachycardia, reduced breath sounds, no rashes, and exquisitely tender and swollen wrists and ankles. NSAID trial resulted in significant improvement in joint swelling, tachycardia, with decreasing supplemental oxygen requirement. Yamaguchi criteria(3) were met, AOSD was diagnosed and patient was started on steroids. Patient's condition dramatically improved as she was afebrile, able to ambulate without supplemental oxygen, tachycardia and joint swelling resolved. Variability of presenting symptoms, rarity of the disorder, along with the lack of specific markers diagnostic for AOSD, makes it a difficult diagnosis. This conundrum is exacerbated by the fact that a delay in diagnosis and treatment can result in permanent articular damage while a presumptuous diagnosis and treatment with immunosuppressive agents can have devastating results.

- P.04 PARACRINE SIGNALING OF MESENCHYMAL STEM CELLS AND THE EFFECTS OF SDF-1 ON INFARCTED MYOCARDIUM. Craig Stauffer,* A. Saltos, J. Hu, T. Li, G. Bianchi, Z.J. Wu and B. Griffith. Department of Surgery, University of Maryland School of Medicine, Baltimore, MD.

The loss of cardiomyocytes following a major myocardial infarction (MI) can lead to remodeling events such as left ventricular dilation, reduced contractility and heart failure. Mesenchymal stem cells (MSC's) are multipotent, self-renewing adult stem cells that are responsible for cell repair. Transplantation of MSC's into infarcted tissues has demonstrated improved cardiac function and attenuation of remodeling and thus offers a promising therapy of MI. The benefits of MSC's are thought to be mediated via the paracrine release of soluble factors which modify their surrounding environment. SDF-1 is a chemokine released from MSC's that is known for trophic support of cardiomyocytes, decreased apoptosis and increased neovascularization. We seek to identify the paracrine mechanism of MSC repair by comparing the effects of SDF-1 on neovascularization, apoptosis and hypertrophy of infarcted myocardium to those of MSC's. Protease-resistant SDF-1 was injected into the zone adjacent to an induced 25% MI in Dorset sheep. 12 weeks post-MI, tissues were harvested and evaluated immunohistochemically for capillary density, apoptosis and cardiomyocyte hypertrophy via PAL-E, TUNEL and hematoxylin and eosin staining, respectively. Image analysis software, Image J and Cell Profiler, were used to count and quantify capillary density, apoptosis and cardiomyocyte hypertrophy from microscopic images of stained myocardium. Preliminary data suggest comparable decreases in hypertrophy and increases in capillary density with SDF-1 and MSC treated animals. Additionally, SDF-1 treatment resulted in decreased apoptosis. The beneficial effects of MSC's appear to be in part mediated by paracrine release of SDF-1, yet further

experimentation is needed. (Supported in part by the Office of Student Research, University of Maryland School of Medicine.)

- P.05 PRELIMINARY WORK IN PREPARATION FOR CLINICAL TRIALS TESTING THE THERAPEUTIC EFFECTIVENESS OF SULFORAPHANE IN KERATIN BASED DISORDERS. Michelle L. Kerns*, Andrea Benedict, Daryle J. DePianto, Paul Talalay and Pierre A. Coulombe. Bloomberg School of Public Health, and School of Medicine, Johns Hopkins University, Baltimore, MD.

Epidermolysis Bullosa Simplex (EBS) is a rare, genetically-determined, devastating skin blistering disorder due to mutations in either the K5 or K14 gene (Coulombe et al., J. Clin. Invest., 119:1784, 2009). We previously reported that treatment with the natural chemical sulforaphane (SF) ameliorates skin blistering in a mouse model of keratin 14 (K14) deficiency, correlating with a robust induction of the K14-like keratins K16 and K17 in the basal layer of the epidermis (Kerns et al., PNAS 104: 14460-, 2007). Here we report on follow-up studies conducted in preparation of clinical trials testing the therapeutic potential of broccoli sprout extracts containing defined amounts of bioactive SF in human skin. Using SKH-1 hairless mice, we conducted a survey of various vehicles to determine the optimal formulation that fosters the penetration of the effect of SF on keratin expression down to the deepest layer of epidermis, while maintaining normal tissue functions, after topical application. Another goal was to develop reliable metrics to assess the efficacy with which treatment with natural extracts prepared from broccoli sprouts helps prevent or ameliorate skin blistering after exposure to mechanical trauma. This requires a clear understanding of the clinical presentation and course of EBS. To this end, we also interviewed 2 adults with EBS. (This work was supported by Grants AR42047 and AR44232 from the National Institutes of Health, and a grant from the March of Dimes Birth Defects Research Foundation.)

- P.06 TWO FACES OF SULFORAPHANE: DETERMINING HOW THIS CHEMOPREVENTIVE AGENT ALTERS KERATIN EXPRESSION. Michelle L. Kerns*, Daryle J. DePianto, Masayuki Yamamoto and Pierre A. Coulombe. Bloomberg School of Public Health, and School of Medicine, Johns Hopkins University, Baltimore, MD and Tohoku University Graduate School of Medicine, Japan.

We recently reported that treatment with the natural chemical sulforaphane (SF) markedly ameliorates skin blistering in a mouse model of keratin 14 (K14) deficiency, correlating with a robust induction of the K14-like keratins K16 and K17 in the basal layer of the epidermis (Kerns et al., PNAS 104: 14460-, 2007). While the best-characterized property of SF is the activation of gene expression via the transcription factor Nrf2, this small molecule also acts through alternate avenues. The studies reported here establish that SF triggers the expression of K16 and K17 via distinct mechanisms in epidermal keratinocytes *in vivo*, and remarkably, that the induction of K17 results from a transient drop in cellular glutathione levels rather than activation of Nrf2-dependent transcription. In contrast, induction of K16 proceeds through both Nrf2-dependent and independent pathways. These findings further the understanding of SF's effect on gene expression within the epidermis and how these changes are enacted. (Supported by Grants AR42047 and AR44232 from the National Institutes of Health, and a grant from the March of Dimes Birth Defects Research Foundation.)

- P.07 ROLE OF BIOFILM FORMATION IN UREAPLASMA ANTIBIOTIC SUSCEPTIBILITY, AND DEVELOPMENT OF BRONCHOPULMONARY DYSPLASIA (BPD) IN PRETERM NEONATES. Katherine Pandelidis* and Rose M. Viscardi. Department of Pediatrics, University of Maryland, School of Medicine, Baltimore, MD.

Several studies have shown an association between *Ureaplasma* respiratory tract colonization and development of BPD, a chronic lung disorder in very premature infants. Despite treating colonized infants with antibiotics, many continue to have positive cultures several weeks after treatment. *Ureaplasma* isolates from men with chronic prostatitis or urethritis can form biofilms in vitro that alter susceptibility to antibiotics. Whether *Ureaplasma* isolates from colonized infants can form biofilms is unknown. We hypothesized that *Ureaplasma* isolates vary in capacity to form biofilms that contribute to their antibiotic resistance and ability to evade host immune responses. The aims of this research were 1) to determine the ability of *Ureaplasma* isolates from premature neonates to form biofilms in vitro, 2) to compare the susceptibility of the biofilm forming and non-biofilm forming organisms to azithromycin and erythromycin, and 3) to determine the relationship of biofilm forming capacity in *Ureaplasma* isolates and the risk for BPD. Thirteen clinical isolates collected from preterm neonates and two ATCC strains were characterized for their capacity to form biofilms in vitro and antibiotic susceptibility performed on each isolate pre- and post-biofilm formation. All of the isolates analyzed formed biofilms. All isolates tested were more susceptible to azithromycin (Minimum Inhibitory Concentration, MIC50 2 µg/mL) than erythromycin (MIC50 4 µg/mL), and biofilm formation did not significantly affect antibiotic susceptibility. There was a trend towards higher MIC and minimum biofilm inhibitory concentrations (MBIC) for the clinical isolates than for the ATCC strains as well as for isolates from BPD infants than non-BPD infants. Based on the results, azithromycin may be a better candidate for clinical trials in treatment of colonized infants. (Supported in part by the Office of Student Research, University of Maryland School of Medicine.)

- P.08 FATIGUE AND QUALITY OF LIFE IN MYASTHENIA GRAVIS. Robyn Nadel* and Charlene Hafer-Macko. Department of Neurology, University of Maryland School of Medicine, Baltimore, MD.

Myasthenia gravis (MG) is an acquired autoimmune disease that is due to antibody attack at the neuromuscular junction and impaired acetylcholine transmission. The majority of myasthenic patients have generalized weakness and fatigue. Weakness affects ocular muscles, bulbar muscles, respiratory muscles, and proximal musculature. Current treatment includes symptom management and immune suppression. Fatigue in MG leads to a sedentary lifestyle and deconditioning which places these individuals at high risk for cardiovascular disease and osteoporosis. To date, there is limited research characterizing the fatigue and quality of life (QOL) in this population. As MG is no longer considered a fatal disease, we need to use these measures to focus on improving well-being and QOL in acute and chronic phases of MG. This cross sectional pilot study examines fatigue in relation to symptoms, QOL, mood, and sleep using a series of validated scales administered in clinic (MG-Symptoms, MG-QOL, Short-Form36, Fatigue Severity, Visual Analog Fatigue, Beck's Depression, and Epworth Sleepiness scales). 7 males and 9 females with chronic, stable MG, mean age of 59 (range 18-74), have an MG symptoms score of 8.5/24 (range 2-16) and daytime fatigue of 59/100 (range 10-99). Increased fatigue relates to MG symptom severity ($r=0.50$, $p=0.05$) and inversely relates to MG-specific QOL ($r=-0.75$, $p=0.001$), but not to mood or sleep. QOL inversely relates to depression ($r=-0.65$, $p=0.007$). The goal is to develop these fatigue measures to improve clinical management. We need to understand whether fatigue should be treated as an MG symptom or requires management of mood, sleep, or other contributors. (Supported in part by the Office of

Student Research, University of Maryland School of Medicine.)

- P.09 QUALITY OF CARE AND OUTCOMES FOR DIABETES MELLITUS AMONG DISABLED MEDICAID RECIPIENTS WITH AND WITHOUT SEVERE MENTAL ILLNESS. Andrea Levine*, Yiyi Zhang¹, Elena Blasco-Colmaneres¹, Saul Blecker¹, Eliseo Guallar¹, Susan dos Reis¹, Daniel Ford¹, Donald Steinwachs¹, Lisa Dixon¹ and Gail L. Daumit². University of Maryland School of Medicine, Baltimore, MD and Johns Hopkins University School of Medicine, Baltimore, MD².

Persons with severe mental illness (SMI), such as schizophrenia, bipolar disorder, and severe depression, have a higher rate of comorbidities, including cardiovascular disease and diabetes, and mortality than the general population. Previous studies indicate mixed results with regard to the quality of diabetes care received by the SMI population; some studies conducted at the VA indicate that the quality of diabetes care received by patients with and without SMI is comparable, while some studies in the general population indicate otherwise. To test the hypothesis that persons with SMI receive inferior quality of care for diabetes, resulting in poorer clinical outcomes and a higher risk of mortality, compared to diabetics without SMI, we conducted a retrospective cohort study of disabled Maryland Medicaid recipients ages 21 through 62, enrolled in Medicaid in 1992-1993, and followed through 2004. Participants had a diagnosis of SMI or were eligible for Medicaid due to medical disability at time of enrollment in the study, and had diabetes (defined as having had a prescription for diabetic medication, 1 inpatient visit, or 2 outpatient visits with diagnostic codes of 250.0-250.9, 357.2, 362.0, or 366.41). The Medicaid claims data was analyzed for quality of care measures which focused on ACE inhibitor and statin use and for clinical outcomes, including hospitalizations due to diabetes related complications and mortality. The study was comprised of 5, 817 adults with diabetes mellitus: 1,369 with SMI and 4,448 without SMI. Patients in the SMI cohort were more likely to be younger, white, and have substance abuse than their non-SMI counterparts. For both ACE/ARB use and statin use, persons without SMI were more likely to fill prescriptions for recommended medications, 47% vs. 58% ($p < 0.001$) and 28% vs. 36% ($p < 0.001$), respectively. Persons with SMI were more likely to undergo hospitalization due to short-term diabetes complications, 5.1% vs. 3.8% ($p = 0.029$). While the crude death rate for the SMI cohort was lower (4.3 deaths/100 persons) compared to the non-SMI cohort (5.3 deaths/100 persons), the mortality rate when adjusted for demographics and comorbidities is not significantly different between the two groups. Both ACE/ARB and statin use significantly decreased the risk of mortality in persons with and without SMI, as did the use of insulin or other oral hypoglycemics. The significant increase in hospitalizations for short-term complications due to diabetes among the SMI population may imply poorer access to or quality of primary care for diabetes. With regard to the rate of mortality, when adjusted for comorbidities and demographics, there was no significant difference between the rate of mortality between people with and without SMI. However, persons with SMI are known to die nearly 30-years earlier than the general population. A possible explanation for this discrepancy is that both the control and the experimental groups in this study were, in order to qualify for the study, extremely ill. This may have narrowed the otherwise large gap between mortality rates between SMI and non-SMI persons.

- P.10 SYNAPTIC DEPRESSION AND RECOVERY DYNAMICS: NEUROMODULATOR-EVOKED METAPLASTICITY WITHIN A CENTRAL PATTERN GENERATOR NETWORK. Mark D Kvarda*, Bruce R. Johnson and Ronald M. Harris-Warrick. Dept. of Neurobiology and Behavior, Cornell University, Ithaca, NY.

Previous studies have shown that neuromodulators, through action on synaptic and intrinsic properties, can effectively reconfigure central pattern generator (CPG) neural

networks that control rhythmic motor behavior, such as locomotion. To better understand the roles of these properties in determining the phasing and bursting characteristics that define motor output, and the way that this pattern can be altered as the need for a change in behavior dictates, we re-examined the neuromodulation at an isolated pacemaker-output synapse in the lobster pyloric network, a 14-neuron CPG. Although many synaptic and intrinsic changes to the pyloric network with monoamine application have been well-documented, the characterization of short-term depression and recovery dynamics in physiological saline has not, let alone the effects of monoamines on these dynamics. Photoinactivation and pharmacological block were used to isolate the pyloric dilator(PD)→lateral pyloric(LP) synapse. Voltage-clamped PD neurons were driven with both square pulses and trains of pre-recorded realistic waveforms (1.45 Hz) to examine the extent of inducible depression, as well as the rate of this change and the ensuing recovery. Serotonin significantly increased both the rate and level of depression and tended to increase recovery time. Octopamine decreased both the rate and level of depression at this synapse, with no clear effect on recovery. Finally, dopamine, at a concentration below the threshold for synaptic strength effects, had no effect on the magnitude of depression, but drastically reduced both depression and recovery times. These results suggest that monoamines not only modulate the amplitude of pyloric synapses but also change the dynamics of synaptic depression and recovery. These metaplastic effects can contribute to shaping the output from this CPG network. (Supported by NIH grant NS17323.)

P.11 DEVELOPMENT OF OPTICAL OXYGEN SATURATION AND BUBBLES SENSORS FOR AN EMBEDDED APL COMPUTER SAFETY SYSTEM. B Miller*, T Zhang, A Pampori, Z Wu and B Griffith. Department of Surgery, University of Maryland School of Medicine, Baltimore, MD.

We are developing an Artificial Pump Lung (APL) to supply the total respiratory needs of adults suffering from lung failure. We hypothesize that incorporating an embedded computer system that monitors oxygen saturation and the presence of gaseous emboli will assist in prototype development, increase patient and physician satisfaction, and decrease complications from device failure. Specific Objective: To develop optical sensors to detect oxygen saturation and gaseous emboli in non-pulsatile flow blood within the para-corporeal circuit. Methods: Our oxygen saturation sensor exploits the difference in extinction curves between oxyhemoglobin and deoxyhemoglobin at red and infrared (IR) wavelengths. We used Light Emitting Diodes (LEDs) of 660nm (red) and 940nm (IR). Using two wavelengths allows normalization for differing hematocrit levels. To detect gaseous emboli, we use the IR LED in a strobe mode, exploiting the increased translucence of blood containing an air bubble. We employed a TSL230 light-to-frequency converter to detect light levels and a Microchip PIC18F4520 programmed in C using the Microchip C18 compiler to drive the LEDs, interpret the output of the TSL230, and calculate, display, and record the oxygen saturation and presence of gaseous emboli. The saturation sensor was calibrated and tested using blood samples at differing saturation levels. Benchmarks were taken using a Profile pHox Plus L arterial blood-gas analyzer. The bubble sensor was tested using a circulatory loop with ports for injecting measured volumes of air upstream of the sensor. Results/Conclusions: Testing of the oxygen sensor yielded a strong linear correlation between sensor signal and oxygen saturation, indicating proper device function. Testing of the bubble sensor indicates detection of bubbles at least 50% of the inner diameter of the tubing. Further device tests will be used to fully quantify the accuracy of these sensors. (Supported by the Department of Surgery and NIH 1RO1HL082631.)

- P.12 ALTERATIONS OF BLOOD COAGULATION ASSOCIATED WITH LEFT VENTRICULAR ASSIST AND ARTIFICIAL LUNG DEVICES. C. Gause*, J. Hu, A. Saltos, Z. Wu and Bartley Griffith. Division of Cardiac Surgery, Department of Surgery, University of Maryland School of Medicine, Baltimore, MD.

Cardiovascular disease (CVD) and lung disease are both major contributors to death and disability in the United States. Left ventricular assist devices (LVADs) and artificial pump lung devices have been used and are under development as safe and effective treatment options for individuals suffering from heart or lung disease. Clinical complications associated with these devices, including hemolysis, thromboembolism, and blood element activation may arise due to the shear stress induced by the device or the interaction of circulating cells with the artificial surface. Specific Objectives: To identify biomarkers of blood coagulation induced by ventricular assist devices and artificial lungs in humans and animals, and to establish an association between these biomarkers, clinical complications, and device design/type/operation. Methods: Flow cytometry was used to determine the degree of platelet activation in Dorsey sheep blood using antibodies against CD41/61 and CD62p. ELISA assays were used to measure p-selectin and thrombin activity in plasma. Results: Initial data suggest an increase in platelet activation and thrombin activity immediately in the post-operative period. P-selectin, thrombin, TNF α , and IL-8 concentrations appear to be associated with thrombus formation. Ongoing experimentation will yield additional data for CFD correlations and statistical calculations. Conclusion: The surgical stress of device implantation and long-term embolic events are correlated with markers of coagulation. (Supported in part by the Office of Student Research, University of Maryland School of Medicine and by the American Association for Thoracic Surgery's Summer Intern Scholarship.)

- P.13 ORTHOSTATIC HEADACHE IN POSTURAL TACHYCARDIA SYNDROME (POTS). Lindsay Eisenberg* and Ramesh Khurana. Division of Neurology, Union Memorial Hospital, 201 E University Pkwy, Baltimore, MD.

The objective was to examine the relationship between POTS and headache and to increase awareness of these co-morbidities. POTS, a form of orthostatic intolerance, causes dizziness, palpitations, fatigue, panic-like symptoms and heart rate increase ≥ 30 bpm (Khurana, 1995 & 2006). It may afflict 500,000 Americans (Robertson, 1999). Mokri and Low (2003) reported orthostatic headache without CSF leak in 4 POTS patients. However, there is no systematic study of headache in POTS. Methods: POTS patients (n = 24; 19 women, 5 men; age range, 17 – 48 years) were prospectively interviewed about preexisting headache, and orthostatic headache during daily activities and head-up tilt (HUT). They were assigned a headache diagnosis based on the International Classification of Headache Disorders (ICHD-II). Cardiovagal and adrenergic functions were assessed using heart rate response to deep breathing, the Valsalva maneuver and HUT (Neurology 1996). Occurrence of orthostatic headache was queried during the HUT. Results: All 24 patients had orthostatic intolerance > 6 months and orthostatic tachycardia (range, 30 to 65 bpm; normals, 18.79 ± 2.27 bpm). All patients except one (95.8%) had preexisting migraines. Orthostatic headache affected 58.6% of patients during daily activities and 62.5% during HUT. Conclusions: Headache is a frequent and disabling co-morbid condition to POTS. Migraine prevalence is greater in POTS patients than in the general population. Patients with complaint of orthostatic headache should be clinically evaluated for orthostatic intolerance and orthostatic tachycardia. (Supported by the Union Memorial Hospital Summer Clinical Research Program.)

- P.14 A TRIAL OF SPRAY CRYOTHERAPY IN MALIGNANT AIRWAY DISEASE: FIRST PATIENT EXPERIENCES. Joel T Atwood* and William S. Krimsky. Department of Interventional Pulmonology, Franklin Square Hospital, Baltimore, MD.

Cells exposed to flash freezing undergo necrosis secondary to direct cellular damage by ice crystals, as well as vascular and endothelial injury with consequent ischemia and subsequent infarction. Spray cryotherapy is a novel, non-contact method of destroying unwanted tissue using low-pressure liquid nitrogen. This FDA cleared device has been used in over 3,000 treatments and on more than 1,000 pts with Barrett's Esophagus, dysplastic lesions, and esophageal cancers. Based on those results as well as the results of animal and prior study, treatment was delivered to five patients with malignant airway disease. We sought to evaluate if there would be any bystander effect on non-diseased tissue. All five patients had increased luminal patency. Of the patients who had repeat airway examination, there was no evidence of scarring or stricturing. Spray cryotherapy appears to be a safe and effective modality in the treatment of malignant airway disease.

- P.15 SURVEILLANCE OF ESBL GENE CARRIAGE AMONG INDIAN NEONATES. Kristen Schratz*¹, Dinesh Chandel¹, Dipti Mohanty², Pravas K Misra² and Pinaki Pangrahi¹. ¹Dept of Pediatrics, Univ of Maryland School of Medicine, Baltimore, MD 21201; ²Asian Institute of Public Health, Bhubaneswar, India.

Extended spectrum β -lactamase (ESBL) producing bacteria are of increasing clinical concern worldwide. Increasing resistance to 2nd and 3rd generation cephalosporins has been mainly attributed to the emergence of ESBL strains expressing TEM, SHV, & CTX-M phenotypes. Since ESBL-producers express co-resistance to common drugs, including 3rd generation cephalosporins, they pose a formidable clinical challenge with limited therapeutic options. There have been increasing reports of bloodstream infections in neonates caused by ESBL positive *Klebsiella pneumoniae* and *E. coli*, which negatively affect treatment outcomes. ESBL-producing bacteria have also been implicated as an emerging cause of community acquired infections. Therefore, effective surveillance and isolation to control the spread of ESBL-producers is crucial. In this study, we investigated the prevalence of these genes in stool samples of hospital and community-born Indian neonates. Serial samples were collected from 48 babies at months 2/3, 5/6, and 9/12. Multiplex PCR-based identification of the ESBL genes was conducted on 209 isolates. In hospital-born babies the rate of carriage was 71, 78 and 78% at months 3, 6, and 12 respectively. The rates were 74, 59, and 76% in the community. SHV, TEM, CTX genes were present in 26%, 41%, and 24% of the isolates in the hospital and 20%, 47%, and 22% in the community respectively. Two or more genes were present in 20% of these isolates. Over 70% of the *Klebsiella* isolates carried SHV, but rarely (2-3%) TEM or CTX. To the contrary, SHV, TEM, and CTX were isolated from 11%, 37%, and 53% *E. coli* isolates respectively. Our study, for the first time, reports such high rates of ESBL genes in fecal isolates from young infants in the Indian community, acquired as early as 2/3 months of age. Indiscriminate use of antibiotics (available without a prescription) may promote colonization of mothers and adults with drug resistant bacteria and further spread to other community members, including infants. Our results, demonstrating a high carriage rate of ESBL genes in the community, should alarm local health officials. (Funded in part by IDSA and the Office of Student Research, University of Maryland School of Medicine.)

- P.16 **COMPLICATIONS IN DIEP AND MSFTRAM FLAPS IN BREAST RECONSTRUCTION: A SINGLE SURGEON'S RECENT EXPERIENCE.** Jonas A. Nelson*, Yifan Guo, Seema S. Sonnad, Liza C. Wu and Joseph M. Serletti. Division of Plastic Surgery, University of Pennsylvania School of Medicine, Philadelphia, PA.

Questions continue to surround the optimal choice of free flap for breast reconstruction. Much of the discussion has centered on the DIEP flap and the msfTRAM flap and balancing abdominal donor site morbidity and risk of flap loss. The purpose of this study was to critically examine complication rates in a consecutive series of DIEP and msfTRAM flap breast reconstructions. The authors performed a retrospective review of the senior author's experience with DIEP and msfTRAM flaps from July 2006 to July 2008. Information collected included demographics, bmi, medical history, and intraoperative and postoperative complications including vessel thromboses, total and partial flap loss, hernia, seroma, hematoma, and delayed healing. Ninety one women underwent 123 msfTRAM flap reconstructions, 53 women underwent 71 DIEP flap reconstructions and 31 women underwent bilateral reconstruction with one DIEP and one msfTRAM flap. In comparing total DIEP and msfTRAM flaps, a small difference was noted in immediate major postoperative complications, a category which included thromboses and full or partial flap necrosis (DIEP=3.9%, msfTRAM=0%, p=0.03). There was one flap loss and one partial flap loss, both in DIEP flaps. No other differences were noted. Breast reconstruction with DIEP and msfTRAM flaps can be performed safely with low complication rates. DIEP flaps may, however, benefit from an increased postoperative level of awareness. The choice of flap type should ultimately be made intraoperatively, based on anatomic findings, on a patient by patient basis. (Supported by the Doris Duke Clinical Research Fellowship.)

Oral Abstracts – Session 1

- O.01 OUTCOMES FOLLOWING MAJOR ABDOMINAL SURGERY IN LEFT VENTRICULAR ASSIST DEVICE PATIENTS. Gregory J. Bittle*, Jeremiah G. Allen, Eric S. Weiss, Ashish S. Shah, Stuart D. Russel, Christopher L. Wolfgang and John V. Conte. Division of Cardiac Surgery, Department of Surgery, and Division of Cardiology, Department of Medicine, The Johns Hopkins University Medical Institutions, Baltimore, MD.

As left ventricular assist devices (LVADs) are implanted with increasing frequency for end-stage heart failure, more LVAD patients will develop conditions requiring major abdominal surgery. We reviewed our institutional outcomes following major abdominal procedures in LVAD recipients to thoroughly address the concerns of general surgeons faced with operating on such patients. From December 2001 to January 2008, 69 patients received a Thoratec, Heartmate XVE, or Heartmate II LVAD. This population was divided into patients who had undergone major abdominal surgery (n = 19), and a control group comprised of patients who had not (n = 50), in order to compare survival (30-day, 90-day, 1-year, and cumulative), heart transplantation rate, and post-LVAD implant complications. In all, these 19 abdominal surgery patients underwent 24 major procedures at an average of 90.2 ± 130.8 days after device implantation. Baseline demographics, device characteristics, and indicators of acuity were comparable to the control group. Similarly, no differences were found when comparing the abdominal surgery group to the control group with regard to total LVAD support (353.3 ± 339.3 vs. 210.6 ± 252.8 days) or rate of heart transplantation (26.3% vs. 34.0%). A log-rank comparison of the cumulative survival estimates reinforces these findings (p = 0.299). This suggests that in spite of the high acuity and comorbidity in the LVAD patient population, major abdominal surgery does not appear to affect survival, likelihood of receiving a heart transplant, or post-implant complications. On the contrary - given the favorable outcomes observed, it is clear that general surgeons play an integral role in the optimal care of LVAD patients by operating on them when standard indications for surgical intervention are present. (This work was supported in part by the National Institutes of Health, NIH 2T32DK007713-12 ESW).

- O.02 INVESTIGATION OF miRNA-DIRECTED CONTROL OF LDL RECEPTOR EXPRESSION. Timothy Feeney* and Gerald Wilson. Department of Biochemistry and Molecular Biology, University of Maryland School of Medicine. Baltimore, MD.

Low Density Lipoprotein (LDL) is the primary vehicle for transport of cholesterol from the liver to peripheral tissues. However, despite LDL's physiologic necessity, high levels of LDL in the circulation are associated with increased risk of atherosclerosis and cardiovascular disease. Dietary intake and/or genetic predisposition can both contribute to elevated LDL levels. For instance, in familial hypercholesterolemia a deficiency in the number of functional LDL receptors (LDLR) impairs cellular uptake of LDL, thus elevating LDL concentrations in the circulation. A major research objective is to increase hepatic LDL uptake by increasing expression of LDLR, since LDL-cholesterol internalized by the liver can be excreted by conversion to bile acids. Preliminary data in the Wilson lab indicate that LDLR production can be increased by disrupting miRNA pathways that normally destabilize LDLR mRNA. Therefore, it is hypothesized that LDLR mRNA is destabilized through interactions between one or more miRNAs and the LDL receptor mRNA. To begin to test this hypothesis, macromolecular binding activities from cultured cell extracts were analyzed for LDLR mRNA binding using electrophoretic mobility shift assays (EMSA). Additionally, expression vectors were constructed to help identify subdomains of LDLR mRNA that are necessary for protein/miRNA binding and destabilization. The data indicate that specific macromolecular binding interactions do occur with LDLR mRNA, and that these interactions are occurring in

a functionally important region of the transcript. (Supported by the University of Maryland School of Medicine MD/PhD program.)

- O.03 MAKING THE CASE FOR PAR-1 INHIBITION IN CABG: RESULTS FROM A RANDOMIZED DOUBLE-BLIND PLACEBO CONTROLLED TRIAL WITH APROTININ. Michael C. Grant* and Robert S. Poston. Division of Cardiac Surgery, Department of Surgery, University of Maryland School of Medicine, Baltimore, MD.

Off-pump coronary bypass grafting (OPCAB) provides an ideal environment to initiate a harmful thrombin activation cascade that can lead to early thrombosis and subsequent graft failure. A non-selective serine protease inhibitor, aprotinin, may prevent these harmful sequelae through inhibition of the platelet activator site PAR-1. Although previous trials with aprotinin have established a favorable safety profile, recent database analyses suggest an increased risk of adverse thrombotic events. Given this controversy, our group sought to better characterize both the antithrombotic action and negative outcome associated with aprotinin. OPCAB patients randomly received saline (n=61) or full dose aprotinin (n=59). Aprotinin patients demonstrated diminished RBC transfusion ($P<0.04$) and reduced postoperative hemorrhage (603 ± 330 vs. 810 ± 415 cc, $p<0.004$). Platelets sampled from the coronary sinus after revascularization showed less activation in the aprotinin group, evidenced by reduced formation of platelet-leukocyte conjugates ($P<0.02$) and platelet derived microparticles ($P<0.05$) and specific inhibition of thrombin-induced platelet aggregation ($p=0.007$). The aprotinin group showed a reduction in thrombin generation (F1.2) and contact activation (XIIa) in the coronary sinus but not skin wounds. Over the first postoperative year, more patients from the aprotinin group remained free of major adverse cardiac or cerebrovascular events (MACCE) defined by myocardial infarction (elevated troponin I or EKG changes), SVG occlusion (CT angiography at early and late follow-up), stroke (clinical exam) and death (11.8 vs. 34.4%, $p<0.005$); the hazard ratio for MACCE in placebo patients was 2.87 (95% C.I. 1.25–5.57). Compared to placebo, the aprotinin group developed a significant lower eGFR on day3 ($P<0.006$), but this difference resolved by day5. Peak aprotinin level correlated with the degree of eGFR decline noted on day3 ($R=0.56$, $p<0.03$) and independently predicted postoperative acute kidney injury (AKI) (OR 8.8, $P<0.008$). ROC analysis demonstrated that peak aprotinin level strongly predicts AKI (AUC=0.86, 95% CI 0.69-1.00) with harmful dose established at 271 KIU/ml. This provided a narrow window to allow antithrombotic benefit and prevent injury. Simultaneous to hemostatic benefits, aprotinin appears to protect OPCAB patients from the amplification of thrombin production within saphenous vein grafts and reduced the risk of adverse outcome. However, administration of aprotinin was associated with a narrow therapeutic window and increased incidence of AKI. Further investigation of alternative PAR-1 inhibiting peptidomimetics is necessary to maximize both efficacy and safety. (Supported in part by the NIH, Grant #RO1- HL084080-01A1.)

- O.04 FACTOR V LEIDEN AND ISCHEMIC STROKE RISK: THE BALTIMORE-WASHINGTON YOUNG STROKE STUDY. Ali G. Hamedani*, John W. Cole, Yuching Cheng, Mary J. Sparks, Jeffrey R. O'Connell, Marcella A. Wozniak, Barney J. Stern, Braxton D. Mitchell and Steven J. Kittner. Department of Neurology, University of Maryland School of Medicine, Baltimore, MD.

The Factor V Leiden mutation (rs6025) has been associated with venous thromboembolism in young adults and ischemic stroke in children, but its relation to ischemic stroke in young adults remains uncertain because prior studies have been based on small numbers of cases. We therefore examined the association between Factor V Leiden and ischemic stroke in participants of the Baltimore Young Onset Stroke Study, specifically among oral contraceptive users, smokers, cryptogenic strokes, and stroke cases

without other vascular risk factors. Through a population-based case-control study, we identified 365 women and 509 men aged 15–49 years with first-ever ischemic stroke and 957 controls, frequency-matched for age, race, and gender. Factor V genotypes were determined using the Illumina 50K CVD SNP chip. Historical risk factor information was obtained using a standardized questionnaire, and stroke subtype was determined through adjudication by two neurologists. Logistic regression was used to calculate odds ratios for the entire population as well as for subgroups stratified by individual risk factors, the presence or absence of any stroke risk factor (smoking, oral contraceptives, hypertension, diabetes, and myocardial infarction), and stroke subtype, adjusted for age, race, and gender. The prevalence of Factor V Leiden was not increased among ischemic stroke patients overall (3.64%) or among the subgroup of cryptogenic stroke patients (3.85%) compared to controls (3.65%). However, Factor V Leiden was associated with ischemic stroke in those with hypertension (OR = 7.9, $p = 0.0475$) and in those with one or more risk factors (OR = 2.438, $p = 0.0419$). The lack of association between Factor V Leiden and ischemic stroke in the overall population is discordant with conventional clinical wisdom and suggests that Factor V Leiden may act more as a weak modifying risk factor for stroke among patients predisposed to vascular disease rather than as a strong proximate cause of ischemic stroke. (Supported in part by an Alpha Omega Alpha Carolyn L. Kuckein Student Research Fellowship and an American Medical Association Foundation Seed Grant.)

O.05 EFFECT OF NOVEL THERAPIES ON REDUCING CARDIOMYOCYTE APOPTOSIS FOLLOWING MYOCARDIAL INFARCTION. Andreas Saltos*, Craig Stauffer, Tieluo Li, Zhongjun Wu and Bartley Griffith. Department of Surgery, University of Maryland School of Medicine, Baltimore, MD.

Following myocardial infarction, profound cell death in and nearby the infarcted tissue (infarct and border zones, respectively) prompts the pathological remodeling process that leads to the heart failure phenotype. While the cell death that occurs in the infarct zone is primarily necrosis due to ischemia, much of the cell death in the border zone is by apoptosis. With appropriate intervention, undesirable cell signaling and apoptotic cell death could potentially be reduced and/or prevented. Stromal cell-derived factor-1 (SDF-1) is a cytokine that has been demonstrated to prevent apoptosis and support survival of cardiomyocytes. In addition, the purification and introduction of myocardial stem cells (MSC's) into infarcted tissue is emerging as a promising new therapy. Myocardial infarctions of 25% left-ventricular mass were induced in adult Dorset sheep; the sheep subsequently received either an injection of SDF-1 or purified MSC's in the border zone, or no treatment (control). After 12 weeks post-infarct, the sheep were terminated, and the myocardial tissue sampled for biochemical analysis. TUNEL staining was used to evaluate apoptosis histologically, and western blotting was used to evaluate the presence of the pro-apoptotic proteins calcineurin and BAD. TUNEL analysis revealed reduced apoptosis in the border zone in sheep treated with SDF-1 or MSC's as compared to control. In addition, expression of calcineurin and BAD in the border zone was generally lower in both groups of treated sheep as compared to control. The results indicate the experimental therapies may be effective in limiting cell death after myocardial infarction.

O.06 MICROARRAY PROFILING OF *SHIGELLA* spp. Jennifer B. Emberger*, David Rasko¹ and James Nataro^{2,3}. ¹Institute for Genome Sciences, University of Maryland School of Medicine, Baltimore, MD. ²Center for Vaccine Development and ³Department of Pediatrics, University of Maryland School of Medicine, Baltimore, MD.

Shigella spp. are diverse pathogens that have important implications worldwide. They are transmitted via the fecal oral route and are responsible for many deaths per year in developing countries where access to clean food and water is limited. This study involved

the analysis of forty two Shigella strains collected from hospitalized children in Kenya using a multi-genome microarray that contains the complete genomes of 32 isolates. This array allows powerful interrogation of the Kenyan isolates in a complete species context. There were twelve mortalities in the group, however we chose to do the experiments in a blinded fashion so we do not know which isolates are from the lethal outcomes. DNA was extracted from 20 of the 42 strains. The DNA was then digested and labeled with biotin. A gel shift assay was run to ensure proper labeling. The DNA samples were then hybridized to pan E.coli/Shigella microarrays. The data from the arrays was scanned and analyzed. Preliminary analysis revealed that there were several distinct lineages present among the examined isolates. Furthermore, the presence of various toxin-encoding (eg. those that encode Type III secretion systems and SPATEs) genes were detected and compared between samples through the generation of MEV plots. Once all 42 strains have been hybridized, the clustering will become clearer and the final goal will be to correlate the numbers of toxin-encoding genes with clinical severity. (Supported by Infectious Disease Society of America.)

O.07 IMMUNOLOGICAL CORRELATES OF PROTECTION FROM SHIGELLA. Robert P. LeGros* and Jakub K. Simon. Center for Vaccine Development, University of Maryland School of Medicine, Baltimore, MD.

Shigella infection is a major cause of human morbidity and mortality, leading to an estimated 165 million cases of shigellosis and 1.1 million deaths each year. Consequently, the development of an effective vaccine against Shigella could lead to a significant reduction in disease prevalence and a concomitant quality-of-life improvement in countries in which Shigella is endemic and epidemic. While no such vaccine is in use presently, the Center for Vaccine Development (CVD) at the University of Maryland School of Medicine has several candidate vaccines in development. The specific aim of this research is to identify immune parameters that are correlated with protection from Shigella. These parameters have been investigated through the use of a functional antibody assay which we are currently optimizing and ELISA. CVD is already in possession of frozen blood serum samples from subjects in case-control studies conducted in Chile. In order to identify immune correlates of protection from Shigella, we have measured the levels of serum IgG and IgA anti-lipopolysaccharide (anti-LPS) in symptomatic cases and asymptomatic controls. While we have found no difference in serum IgA levels between cases and controls at time of presentation (Means: 11,372 ng/ml for cases, 10,034 ng/ml for controls), serum IgG anti-LPS levels at the time of first clinical examination are dramatically higher in controls (Means: 4,811 ng/ml for cases (95% CI -3,904-13,526 ng/ml); 29,126 ng/ml for controls (95% CI 6,286-51,966 ng/ml)). These data suggest that IgG anti-LPS may play an important role in conferring protection from Shigella on patients. (Supported in part by the Office of the Dean, University of Maryland School of Medicine and NIH grant 5K23AI065759-04 to JKS.)

O.08 THYROID ADENOMA IN A PATIENT WITH AUTOIMMUNE RETINOPATHY. Nicole Mahdi,* H. Nida Sen and Lisa Faia. Laboratory of Immunology, National Eye Institute, National Institutes of Health, Bethesda, MD.

This report describes a unique presentation of autoimmune retinopathy (AIR) associated with a thyroid adenoma. A 51-year old Caucasian woman presented with a rapid decline in vision. Extensive testing for anti-retinal antibodies, as well as, visual field testing and electrophysiology, confirmed the diagnosis of autoimmune retinopathy without an underlying malignancy. Conventional local and systemic immunosuppressive therapies failed to halt the progression. Rituximab treatments were initiated and a slowing of visual loss was seen, as evidenced by improvements in visual field testing. Continued surveillance for malignancy revealed a thyroid adenoma. This case presentation of AIR associated with a thyroid

adenoma highlights the need for continued surveillance for malignancy in AIR, and the possible new use of rituximab for the treatment of AIR. In addition, this case may influence future investigation as to the underlying cause of malignancy in interesting cases of AIR.

- O.09 DOXORUBICIN CHEMOTHERAPY AS IMMUNOSUPPRESSION FOLLOWING ORTHOTOPIC FASCIOCUTANEUS FREE FLAPS. Bryce Olenczak* and Eduardo Rodriguez. Division of Plastic Surgery, Department of Surgery, University of Maryland School of Medicine, Baltimore, MD.

With over 2,500 new cases of bone cancer each year, composite tissue allotransplantation is the ideal solution for reconstructing these large extremity defects after tumor extirpation. The chemotherapeutic agents currently utilized for adjunctive therapy after oncological resection have devastating immunosuppressive effects on the patient, with doxorubicin and cisplatin utilized as the standard of care for the treatment of Osteosarcoma. By utilizing the adverse immunosuppressive effects of doxorubicin we propose immunosuppression in a small animal model undergoing composite tissue allotransplantation. Methods: We used an abdominal wall composite tissue allograft flap consisting of skin, fat, and fascia based off the superficial inferior epigastric vessels in a rat model to determine the feasibility of this innovation. Rats were divided into three groups: 1) autotransplant, 2) allotransplant, 3) allotransplant with doxorubicin. Rats in group 3 were administered a standard dose on the day of surgery and on post operative days 7, 14, and 21. Histological analysis was performed to compare composite tissue graft across the groups. Results: Group 1 showed no signs of composite tissue rejection with all rats surviving. Group 2 began to show signs of tissue rejection between days 3 and 4, with complete rejection identified by day 7. Analysis of Groups 3 is incomplete but preliminary data suggests a reduced severity of lymphocyte infiltration in the flap. A short course of chemotherapy with doxorubicin may result in immunosuppression in the small animal model, creating an immunological environment in which the allograft will survive, ultimately accomplishing the endpoint of limb salvage. (Supported in part by the Office of Student Research, University of Maryland School of Medicine.)

- O.10 STEM CELLS DRIVE TENDON REPAIR THROUGH MCP-1 AND TIMP-1. Maxim Orlov*, Irina G. Luzina, Lew C. Schon and Sergei P. Atamas. Division of Rheumatology and Clinical Immunology, Department of Medicine, University of Maryland School of Medicine, Baltimore, MD.

We treat tendonopathies and bone non-unions by supplementing standard surgical techniques with local instillations of enriched autologous non-red bone marrow cells. In more than 200 patients treated to date, such treatment leads to a faster recovery compared with traditional surgery alone, with beneficial effects seen as early as three days after the procedure. We hypothesized that such a rapid beneficial effect is not due to stem cell differentiation into mature connective tissue cells, but that the instilled bone marrow cells likely act via production and secretion of anti-inflammatory and profibrotic mediators. We found that bone marrow cells do indeed produce MCP-1 and TIMP-1, which are known potent regulators of collagen production and turnover in other tissues. We investigated whether MCP-1 and TIMP-1 may regulate collagen production in primary human tenocytes. Our approach included a Cell Titer assay to investigate changes in tenocyte proliferation and Q-RT-PCR to investigate changes in collagen production. Tenocytes were cultured with concentrations of MCP-1 and TIMP-1 ranging from 1ng/ml to 400ng/ml. Results show a dose dependent increase in cell proliferation when exposed to TIMP-1 and MCP-1 as well as a dose and time dependent increase in collagen production. The currently ongoing experiments address the ability of bone marrow cells to directly regulate collagen production by tenocytes in co-cultures. Future experiments will utilize neutralizing antibodies to block

MCP-1 and/or TIMP-1 and thus to determine whether these two factors are indeed the mediators of the observed healing effect of bone marrow on tenocytes. We also plan to identify the cell surface receptors on tenocytes for these two factors, and to delineate the intracellular signaling pathways leading to transcriptional activation of collagen. (Supported in part by the Maryland Stem Cell Research Fund.)

O.11 BILIRUBIN-MEDIATED DISRUPTION OF L1 CELL ADHESION MOLECULE FUNCTION IN NEURONS. Hemal N. Sampat* and Cynthia F. Bearer. Division of Neonatology, Department of Pediatrics, University of Maryland School of Medicine, Baltimore, MD.

Hyperbilirubinemia occurs in approximately 60% of healthy neonates and nearly all preterm neonates born in the U.S. While most of these cases resolve without consequence, in approximately 1 in 650 to 1000 full-term neonates and an estimated higher number of preterm neonates, the hyperbilirubinemia can become severe and prove toxic to neurons, resulting in a condition of neurological deficit called kernicterus. The exact mechanism of bilirubin-mediated toxicity of neurons is not known, although it is suspected that the lipophilic bilirubin, which readily crosses the blood-brain barrier when not conjugated to glucuronic acid, may cause disruption in neuronal lipid membranes. We propose that bilirubin disrupts protein-protein interactions within lipid rafts of the neuronal plasma membrane. The cell adhesion molecule L1 is trafficked through lipid rafts, is known to be involved with mitogen-activated protein kinase signaling cascades, and has previously been implicated in neurocytotoxicity associated with fetal alcohol syndrome. We demonstrate here that bilirubin disrupts L1-mediated activation (phosphorylation) of ERK1/2 using both primary cerebellar neurons and the transformed mouse neuronal cell line CAD. This provides evidence that bilirubin may cause disruption of protein-protein interactions in lipid rafts as a possible mechanism of bilirubin-mediated neurocytotoxicity. (Supported in part by the Office of Student Research, University of Maryland School of Medicine.)

O.12 HSV-2 PROTEIN ICP10PK POTENTIATES THE NEUROPROTECTIVE ACTIVITY OF STEM CELLS. Kyle Wilson*, Jennifer Laing and Laure Aurelian. Department of Pharmacology and Experimental Therapeutics, University of Maryland School of Medicine, Baltimore, MD.

NMDA excitotoxicity leads to apoptosis via caspase 3 activation. Excitotoxic injury has been demonstrated to occur in epilepsy, ischemia, and post-traumatic disease processes and it is believed to cause apoptosis in other neurodegenerative diseases. Gene therapy and stem cell replacement have been proposed as potential therapies, however, neither have yet met clinical expectations. Clinical challenges of gene therapy include the identification of a valid target, gene delivery and specific prolonged expression of the therapeutic gene in an appropriate and non-mutagenic fashion. Therapeutic challenges faced by stem cells therapy include appropriate and effective engraftment as well improved neuroprotective activity. The proposed studies are based on the hypothesis that stem cell modification by transfection of optimal neuroprotective genes could enhance their ability to engraft and reconstruct interrupted survival pathways through effective combination of gene and stem cell therapies. The HSV-2 protein ICP10PK has a robust and wide therapeutic activity in neurons. It blocks caspase 3 activation and apoptosis and inhibits caspase-independent programmed cell death through the activation of multiple non-redundant signaling pathways including activation of Ras and its downstream pathways MEK/ERK and PI3-K/Akt, and the adenylate cyclase/PKA pathway. Furthermore, when expressed in hippocampal neurons infected with the ICP10PK vector Δ RR, ICP10PK induces the release of VEGF, which directly promotes the survival of uninfected ICP10PK negative neurons, and FKN, which modulates the balance of IL-10/TNF- α cytokines expressed by microglia. We proposed that ICP10PK expression in stem cells may improve engraftment efficiency and

encourage neuroprotection through these mechanisms. Herein, we demonstrate that ICP10PK expression in different stem cell lines does not interfere with differentiation during engraftment and potentiates their neuroprotective activity in organotypic hippocampal models of NMDA excitotoxicity.

- O.13 THROMBOPHILIA TESTING IN PATIENTS WITH DEEP VENOUS THROMBOSIS AND/OR PULMONARY EMBOLISM. Aleksandra Gajer*, Robert Ferguson, Anna Patkowska, Bashar Farjo and Laura Park. Department of Internal Medicine, Union Memorial Hospital, Baltimore, Maryland 21218.

The purpose of our study is to determine the utility of inherited thrombophilia testing in patients who have experienced deep vein thromboses or pulmonary embolisms, and to devise an algorithm to guide physicians when to order a work up and what to do with the results. To date we have completed a retrospective chart review of 262 patients who had a diagnosis of deep venous thrombosis (DVT) and/or pulmonary embolism (PE) during an admission to Union Memorial Hospital between 9/1/2003 and 2/28/2005 (18 months). In this stage of the study we reviewed data related to thrombophilia work-ups done in an acute post-DVT/PE hospital setting. Patient data considered in review includes demographics, chief complain on admission, ordering physician, history of previous DVT/PE, whether the event was idiopathic and risk factors that may have contributed to the event, symptoms, family history, if thrombophilia work-up was done and what was included, how the patient was treated and their future testing and treatment plan. The next phase of the study will include looking at patients' follow-up records to determine if testing was done at a later date and if the results changed management. A positive family history was the most important motivator for a thrombophilia work-up. 86% of patients with a positive family history had a thrombophilia work-up (n=7). 22/46 or 48% of the thrombophilia work-ups done showed some abnormal result. The clinical significance of abnormal results is sometimes difficult to establish. The outcome considered in this phase of the study was planned treatment duration. For most patients the planned anticoagulation treatment duration was non-specified. Abnormal results are difficult to interpret when tests are ordered immediately following a thrombotic event. The only tests that should be run in an acute post DVT/PE setting are Factor V Leiden, and Prothrombin Gene Mutation (Factor V Leiden mutation rare in non-whites). For at risk patients, a thrombophilia work-up should be done 6 months after their event when they are off anticoagulation therapy.

Oral Abstracts – Session 2

- O.14 THE COMMERCIAL EXPLOITATION OF AMERICA'S CHILDREN: HELPING TO STOP MODERN DAY SLAVERY. Jordan Ambrose*, Jessica Ton*, Sidney Ford and Ligia Peralta. Division of Adolescent and Young Adult Medicine, Department of Pediatrics, University of Maryland School of Medicine, Baltimore, MD.

The sex trafficking of women, children and men is a crime that occurs not only internationally, but in the United States as well. DMST (domestic minor sex trafficking) plagues many cities in the US, including our own - Baltimore. An estimated 200,000-300,000 American children aged 10-17 are vulnerable to exploitation and forced into commercial sex every year. This includes prostitution, stripping and the production of pornographic images and films. The mental and physical trauma of being forced into prostitution during adolescence is immense, yet the justice system currently does not provide rehabilitation once these children are detained. Our project, SafeStart, aims to bring together services and support to young men and women who are survivors of domestic minor sex trafficking, to provide early intervention services to at-risk youth and to promote community awareness. Partnering with the Division of Adolescent Medicine at the University of Maryland, we have gained access to at-risk youth and worked to educate them about risk factors that can lead to sexual exploitation, including sex trafficking. In collaboration with a Baltimore outreach group YANA (You Are Never Alone) and members of the Maryland Human Trafficking Task Force, we have initiated and coordinated the production of an hour-long National Public Radio segment on sex trafficking and attended sentencing hearings of admitted sex traffickers in support of the minor victims and the victims' families. We have also put in motion a mentorship program for adolescent victims of sex trafficking crimes to offer them support and a sense of normalcy in their lives. As members of the Maryland Human Trafficking Task Force, we have helped train law enforcement officers on how to better understand child sex trafficking victims, and collected toiletry items and clothing donations for victims who are rescued. By interacting directly with those involved in commercial sex, we've come to understand adult sex trafficking survivors as people rather than as prostitutes. In addition, we are strategizing to help minor victims access appropriate shelter options after they are rescued, as their current choices are extremely limited. We've built a strong rapport with those who work closely with these victims and are now more equipped to assist them in the many ways outlined above. (Supported in part by the Arnold P. Gold Summer Service Fellowship, The Baltimore Albert Schweitzer Fellowship and the Office of Student Research, University of Maryland School of Medicine.)

- O.15 EXPLORING HOW HOUSING AND ENERGY INSECURITY ARE RELATED TO CHILD AND CAREGIVER HEALTH AND WELL-BEING AMONG FAMILIES IN BALTIMORE. L. Latéy Jones*, Anna Quigg, Maureen M. Black. Growth & Nutrition Division, Department of Pediatrics, University of Maryland School of Medicine, Baltimore, MD.

Children's HealthWatch is a multi-site collaboration among public health and pediatric clinicians and researchers from 7 urban medical centers, including the University of Maryland Department of Pediatrics. Children's HealthWatch monitors the relation between economic conditions and the health and well-being of young children. This project describes housing and energy insecurity among 3,074 families from the Baltimore site, focusing on how maternal and child health and well-being are related to housing and energy insecurity, and the role of housing and energy assistance. Caregivers of children under the age of 3 years were interviewed at the Pediatric Ambulatory Center and Pediatric Emergency Department. Children were weighed and measured and caregivers completed a 15-20

minute interview which included self-report measures of maternal health and mental health, child health, hospitalizations, and development, household demographics and access to public assistance. Covariates representing child, caregiver, and household variables were identified and logistic regressions were performed to examine relations between the predictors and outcomes. Over half (56%) of the children from the Baltimore site live in homes that are either housing insecure (at least 2 moves in the past year, crowded, temporarily living with others, or unable to pay rent/mortgage) or energy insecure (threatened or actual utility cutoff, heat with cooking stove, or lack of heat). Housing insecurity was associated with maternal fair/poor health, maternal depression, and child fair/poor health. Energy insecurity was associated with maternal fair/poor health, maternal depression, child fair/poor health and child risk for overweight. Results suggest a negative association between housing and energy insecurity and multiple indicators of child and caregiver health and well-being. Assistance programs were not sufficient to alleviate housing or energy insecurity. (Supported by the W.K. Kellogg Foundation. Children's HealthWatch)

- O.16 EVALUATING THE ATTITUDES AND BEHAVIORS OF TEENS AND PARENTS TOWARD PARENT-TEEN DRIVING AGREEMENTS. Daniel Smith* and Richard Lichenstein. Division of Pediatric Emergency Medicine, Department of Pediatrics, University of Maryland School of Medicine, Baltimore, MD.

Even with the implementation of the Graduated Licensing Program, new teenaged drivers continue to have disproportionately high injury and fatality rates from motor vehicle crashes. Parent-teen driving agreements (PTDAs) have been shown to significantly reduce risky driving practices in teens. Recently, schools in a Maryland county have started offering PTDAs to students during mandatory driver safety presentations. To gauge the effectiveness of and attitudes toward the PTDA, 109 county teens and 92 parents were surveyed from 12 county high schools. The majority (80% teens, 86% parents) of participants signed a driving contract. Most (59% teens, 90% parents) participants believe the PTDA makes teens better drivers. Similarly, most (56% teens, 63% parents) participants would feel safer on the road if PTDAs were mandatory for new drivers. Teens were also surveyed for three common risk factors associated with increased teen crash rates: driving with other minors without supervision, speeding, and using a cell phone while driving. Only 23% of the teens reported no risky behaviors. Unfortunately, teens that displayed more than 1 risk factor were less likely to think the PTDA would benefit them ($p < 0.05$). However, no correlation was found between risky teen driving habits and whether or not the teen signed a PTDA. A follow-up survey in six months will analyze changes in parent and teen attitudes toward the PTDA and corollary changes in teen driving habits. Government traffic records for the county will also be reviewed for 2009-2010 to determine if giving out PTDAs had a significant effect on teen driver safety.

- O.17 ADVERSE SAFETY EVENTS IN CHRONIC KIDNEY DISEASE: THE FREQUENCY OF "MULTIPLE HITS." Erica Chapin*, Jeffrey Fink, Min Zhan, Van Doren Hsu, Stephen Seliger, and Loreen Walker. Division of Nephrology, Department of Medicine and Epidemiology and Preventive Medicine, University of Maryland Medical System, Baltimore, MD.

Chronic kidney disease (CKD) lacks standardized patient safety indicators (PSIs); however, undetected safety events are likely to contribute to adverse outcomes in this disease. This study sought to determine the proportion of CKD patients who experience multiple potentially harmful safety events from varied causes and to identify risk factors for the occurrence of "multiple hits". A sample of patients with CKD ($n = 70,154$) in the Veterans Health Administration (VHA) were retrospectively examined for the occurrence of

one or more safety events from a set of indicators defined a priori, including: Agency for Health Care Research and Quality (AHRQ) PSIs, hypoglycemia, hyperkalemia, and dosing for selected medications not accounting for CKD. Approximately half of the cohort participants suffered from one or two adverse safety events, while 7% had three or four (multiple) distinct events. Individuals with three or four of the pre-designated safety events were more likely to be diabetic, non-Caucasian, have an estimated glomerular filtration rate (eGFR) < 30 ml/min/1.73m², and ≤ 65 years of age. A “Safety Risk Index” was developed based on these characteristics, and those that had all four traits were 25 times as likely to have 3 or 4 adverse safety events than those with none of the characteristics. Patients with CKD are at an exceptionally high risk for safety events pertinent to this disease population and a substantial number are subject to multiple events from a diverse set of safety events, which could have important consequences in disease outcomes. (Supported in part by NKF of Maryland Mini-Grant, R21DK075675).

- O.18 DETERMINING THE FUNCTION OF S100A5 VIA ITS SPECIFICITY FOR XIP. Adam Fisch* and David J. Weber. Biochemistry Department, University of Maryland School of Medicine, Baltimore, MD.

In order to provide evidence for our model that S100A5 antagonizes calmodulin in the sodium-calcium exchanger (NCX1) of olfactory sensory neurons (OSNs), we compared the specificity of S100A5 to XIP (Exchanger Inhibitory Peptide) against three other S100 proteins (S100B, S100A1, and S100A4). Isothermal Titration Calorimetry (ITC) was used to acquire information about the binding interactions between the proteins and peptide. The MicroCal ITC computer program was then used to extrapolate the dissociation constants from the ITC primary data. The results revealed the dissociation constants (K_D) of S100A5, S100B, S100A1, and S100A4 to be $2.13 \pm 0.30 \mu\text{M}$, $6.82 \pm 0.50 \mu\text{M}$, $3.27 \pm 0.11 \mu\text{M}$, and $>65 \mu\text{M}$, respectively. The fact that S100A5 bound more tightly to XIP than the other S100 proteins is preliminary evidence that XIP has some specificity for interacting with S100A5 versus other S100 proteins, which may impact NCX1 function. Thus, physiological studies are warranted next to examine the role of S100A5 in modulating NCX1 function in OSNs. (Supported by an MD/PhD grant.)

- O.19 DEVELOPING A NOVEL ATLAS OF THE HUMAN BRAIN. Tuo Li*, Syed H. Naqvi, M. Samir Jafri, and Cha-Min Tang. Department of Neurology, University of Maryland School of Medicine, Baltimore, MD.

Atlases of the human brain typically delineate the location of anatomic structures but do not provide information on the connectivity between different structures. The issue of connectivity has gained considerable recent interest. A detailed 3D atlas of brain connectivity does not currently exist and is the goal of this project. This goal faces daunting challenges. Older methods for studying connectivity using retrograde and anterior-grade tracer labeling are massively labor intensive. The new MRI technology called diffusion tensor imaging (DTI) requires relatively little manual effort, but is limited by the spatial resolution of MRI. We propose a strategy that takes advantage of an optical property of white matter, i.e. myelinated fiber tracts scatter light in a strongly angle-selective manner (optical anisotropy). Starting from a thin histological section, the strategy is to 1) measure the signal pattern of fiber tracts by illuminating the section from a full range of angles, 2) calculate the orientation of the fiber tracts based on their distinct signal patterns obtained from the different illumination angles, and 3) track fibers 3-dimensionally in a stack of histological sections. We have obtained strong proof-of-concept results. This optical anisotropy approach can identify and dissect apart neighboring fiber tracts not possible with conventional histological staining methods. It can resolve submillimeter details that are not possible with DTI. And it can accurately extract the orientation (pitch and azimuth angles)

of fiber tracts within thin histological sections. (Supported by the MD/Ph.D Program, T.L.; Maryland Stem Cell Research Fund, M.S.J.; VA Merit Review, C.-M.T.)

O.20 **ANTIDEPRESSANT LIKE EFFECTS OF CENTRALLY ADMINISTERED INSULIN IN MICE.** Matthew Smith* and Todd Gould. Department of Psychiatry, University of Maryland School of Medicine, Baltimore, MD.

Severe depression effects up to 15 percent of Americans at some point in their lives. Existing medications are inadequate for a large percentage of patients. A well supported hypothesis is that novel treatments for depression may act by increasing the activity of neurotrophic signaling pathways, and in particular those mediated by AKT-Glycogen Synthase Kinase 3 (GSK-3) signaling. Because GSK-3 is a known downstream target of the insulin receptor signalling cascade, we hypothesized that administration of insulin to the brain would result in antidepressant like effects. As insulin, like most neurotrophic factors, does not cross the blood-brain-barrier in a sufficiently rapid or efficient manner, we administered insulin directly to the CNS both intranasally and via intracerebroventricular injections and then tested mice in several well established assays for antidepressant efficacy including the forced swim and tail suspension tests. Acute administration of ICV insulin resulted in a robust antidepressant like effect in the forced swim test that was absent when tested again two hours later. This effect was neither a result of a generalized change in locomotion nor peripheral hypoglycemia induced by hypothalamic insulin signaling. This effect was not observed in the tail suspension test nor following sub-chronic administration of intranasal insulin over a period of 10 days. Our findings support our hypothesis and form a strong basis for further investigation of insulin, as well as other neurotrophic factors, as a potential therapy for depression related disorders.

O.21 **BIOLOGICAL RESPONSES OF DETACHED BREAST TUMOR CELLS PROVIDE NOVEL TARGET FOR THERAPY.** Monica Charpentier* and Stuart Martin. Department of Physiology, University of Maryland School of Medicine, Baltimore, MD.

While breast cancer screening and improved adjuvant therapies have contributed to a decline in the death rate of breast cancer, there has been a significant lack of improvement in outcome for patients with metastatic breast cancer. The cancer stem cell hypothesis provides an explanation for the limited success of current therapies for the prevention and treatment of metastatic breast cancer and suggests novel approaches for therapy based upon the unique characteristics of cancer stem cells. Cancer stem cells are a small subpopulation of the breast tumor cells that retain the stem cell characteristics of self-renewal and differentiation. Breast cancer stem cells are able to enter circulation and reach distal tissues, where they remain dormant and cell-cycle arrested, resisting conventional chemotherapeutics. The presence of these disseminated breast cancer cells predicts poor prognosis and metastatic recurrence. The Martin lab has previously reported that mammary epithelial cells are able to generate long, dynamic microtubule-based protrusions of the plasma membrane in response to detachment, termed microtentacles. The presence of these microtentacles correlates with invasiveness, supporting a role for microtentacles in metastasis. The aim of this summer research project was to further define the relationship between breast cancer stem cells and microtentacles by correlating microtentacle number and length with the expression of stem cell characteristics. Fluorescence microscopy and FACS analysis were used to separate a mammary epithelial cell line with inducible stem cell characteristics into populations expressing the cancer stem cell marker profile CD44+/CD24- and ALDEFLUOR-positive and populations that did not express this stem cell phenotype. We predicted that the population expressing the stem cell phenotype would have higher percentage and greater length microtentacles than both normal breast epithelial

cells and normal breast stem cells. Preliminary data indicates that absence of the stem cell phenotype correlates with decreased microtentacle formation. This data points to the inhibition of microtentacles as a potential target for reducing metastatic recurrence of breast tumor stem cells. (Supported in part by USPHS grant R01-CA124704 and an Exploratory Research Grant from the State of Maryland Stem Cell Research Foundation - 2008-MSCRFE-0081).

O.22 CASE REPORT: SYNCHRONOUS PAGET'S DISEASE IN BREAST AND VULVA. Janelle C. Cooper*, Kevin M. Audlin, and Koji Matsuo, Mercy Medical Center, Baltimore, MD.

Synchronous Paget's disease of breast and vulva is extremely rare and has only been reported in the literature in one other case. A 58-year-old postmenopausal woman was found to have crusting, bleeding, and discharge from left nipple as well as vulvar pruritis at the same time. Biopsy of breast lesion demonstrated Paget's disease with an underlying foci of ductal carcinoma in-situ that required total mastectomy of left breast with sentinel lymphadenectomy and breast reconstruction. For vulvar symptoms, she was initially diagnosed with dermatitis and topical ointment was prescribed. However, her symptoms persisted for the next several months, and she underwent vulvar biopsy that demonstrated Paget's disease. She then underwent partial vulvectomy. Multiple episodes of recurrent vulvar Paget's disease were noted in the postoperative course, and medical therapy with Imiquimod and a second partial vulvectomy was performed. While co-incidence of breast and vulvar Paget's disease is likely, ectopic mammary tissue in vulvar as well as secondary metastasis from a focal lesion of breast Paget's disease are possible differential diagnoses. Whenever the patient complains of vulvar symptoms in the setting of breast Paget's disease, careful evaluation of vulvar is needed. There was a delay in diagnosing vulvar Paget's disease in our experienced case.

O.23 SKELETAL MUSCLE MASS AND COMPOSITION CHANGES POST-HIP FRACTURE. Ashley L. Devonshire^{1*}, Pete Chomentowski³, Denise Orwig², Marty Eastlack⁴, Gregory Hicks², Ram R. Miller², Marc Hochberg¹, Bret Goodpaster³, Jay Magaziner². ¹University of Maryland School of Medicine, Baltimore, MD, ²Department of Epidemiology and Preventive Medicine, University of Maryland School of Medicine, Baltimore, MD, ³ Department of Medicine, University of Pittsburgh, Pittsburgh, PA, ⁴Department of Physical Therapy, Arcadia University, Glenside, PA.

The loss of lean body mass following hip fracture repair has been described previously. Despite their importance to the recovery of lower extremity function, less is known about post-fracture changes in muscle mass and muscle composition of the legs. The purpose of this study was to examine specific changes in muscle mass and muscle fat infiltration that occur in the fractured (FX) and unfractured (UNFX) legs following repair of hip fracture. Twenty-one Baltimore Hip Studies participants had computed tomography (CT) images of the mid-thigh in both the FX and UNFX legs analyzed for muscle and intermuscular fat cross-sectional area (CSA) at 2, 6, and 12 months post-fracture (SliceOmatic, Version 4.3). Participants were aged 80.1 ± 9.4 years. At 2, 6, and 12 months post-fracture, muscle CSA was lower in the FX vs. UNFX leg. There was higher thigh intermuscular fat CSA in the FX leg compared to the UNFX leg at all three time points. Over the course of 12-months, post-hip fracture, muscle mass in both the FX and UNFX leg increased. It is important to note that the FX leg persistently displayed lower muscle mass parameters when compared to the UNFX leg. Muscle fat content decreased in the FX leg but not the UNFX leg. These findings regarding changes in muscle mass and muscle fat infiltration may underlie the decline in lower extremity function that persists long after the period of fracture healing. (Supported by Pittsburgh MSTAR – Medical Student Training in Aging Research T35 AG026778).

- O.24 DOWNSTREAM TARGETS IN KSHV vGPCR PARACRINE NEOPLASIA. Eitan R. Friedman* and Silvia Montaner. Department of Oncology and Diagnostic Sciences, University of Maryland, Baltimore, MD.

Kaposi's sarcoma (KS), a malignancy arising from endothelial cells, commonly occurs in HIV-infected patients. KS-associated herpes virus (KSHV) is the etiologic agent for this disease. Of the many proteins expressed by KSHV, the viral G protein-coupled receptor (vGPCR) is sufficient to induce a highly-related disease when introduced into murine endothelial cells in vivo. vGPCR is constitutively active and stimulates the PI3K/Akt pathway. Akt in turn activates mTOR, to increase protein translation, and other proteins that favor cell growth. vGPCR also causes endothelial cells to secrete angiogenic factors that induce the proliferation of neighboring endothelial cells via paracrine signaling, to contribute to tumor formation. To determine the genes up-regulated upon vGPCR expression, RT-PCR was performed from mRNA isolated from stable endothelial cell lines expressing empty vector, vGPCR, or a mutated vGPCR (R143A). We found that *agp2*, *sphk1*, *efna3*, *thbs2*, *il6*, *col18a1*, and *tgfa* are up-regulated by vGPCR and that *fgfr3* is down-regulated. Also, Angiopoietin Like 4 (AGPL4) was found up-regulated, by RT-PCR, Western blot analysis and ELISA in human microvascular endothelial cells (HMEC1) and primary human microvascular ECs (HMVECs), upon expression of vGPCR. To determine the genes that vGPCR up-regulates in a paracrine manner, nude mice were injected with a 1:9 ratio of vGPCR TK endothelial cells and endothelial cells expressing both latent genes vFlip and vCyclin. Tumors were allowed to grow until their size was 150 mg, and then ganciclovir was administered daily, to eliminate the vGPCR-expressing cells. Fixed tumors will be used to perform immunohistochemistry for AGPL4. Genes induced by vGPCR may serve as novel therapeutic targets for Kaposi's sarcoma. (Supported in part by the Office of Student Research, University of Maryland School of Medicine.)

- O.25 SURVEY OF ATTITUDES TO CERVICAL CANCER PREVENTION AND EMERGING HPV TECHNOLOGIES IN ORISSA, INDIA. Aparna Ramaseshan*¹, Niharika Khanna², Surendra Senapati³, Krushna Ballav Das³, and Pinaki Panigrahi¹. ¹Departments of Pediatrics, and Epidemiology & Preventive Medicine, ²Family & Community Medicine, UMB; ³AH Regional Cancer Center, Cuttack, India.

India, with the highest number of yearly cervical cancer cases, harbors a quarter of the world's burden of cervical cancer. The risk of death due to cervical cancer is growing, and is 2.4% for women in India compared to 1.3% for the world in general. However, there are no organized surveillance programs or interventions to reduce the impact of this cancer. Despite the remarkable promise of HPV (human papillomavirus) vaccines, there are socio-cultural barriers to vaccination programs in India. This study was designed to investigate the awareness of Indian women on cervical cancer and its link with HPV, and different socio-cultural factors that may ultimately influence HPV vaccine decision making. With the support of the Acharya Harihar Regional Cancer Center in Orissa, the field study was conducted in and around the city of Bhubaneswar. The questionnaire was administered to women in the reproductive age (18 to 49 yrs) living in urban, rural, and urban slum areas. 286 women participated in the study with a mean age of 34. Approximately 47% of the women believed that cervical cancer lead to death; however, 70% had never heard of HPV. 66% of the participants were uninformed that HPV infection is the primary cause of cervical cancer, while 62% were unaware that it could be prevented by a vaccine. 58% of the women believed that their communities would accept the HPV vaccine. While ~ 70% of the women

were likely to get their daughters vaccinated, they cited their husbands as key players in the decision making. It was reassuring that 84% of the women knew and believed that vaccines, in general, are effective in preventing diseases. These data indicate that there is a lack of awareness about HPV, cervical cancer, and the availability of a vaccine to prevent this cancer. Educational intervention holds the key for the acceptance of HPV vaccination in this community. There is also a need for piloting prevention projects including HPV vaccination before large scale screening, treatment, and vaccination programs can be undertaken. (Funded by the Arnold P. Gold Foundation, USA.)

- O.26 IMPROVING INFLUENZA VACCINE DELIVERY FOR AT-RISK PATIENTS IN A PEDIATRIC EMERGENCY DEPARTMENT (PED). Daniel Smith* and Richard Lichenstein. Division of Pediatric Emergency Medicine, Department of Pediatrics, University of Maryland School of Medicine, Baltimore, MD.

Influenza vaccination rates continue to be low for asthmatic children in urban populations. Despite educational efforts, many parents decline flu shots for their at-risk children. We analyzed parent knowledge, attitudes and practices toward the flu shot to determine barriers for vaccination. All parents were given a short survey and CDC education about the benefits of the flu shot. Subjects were asked about 1) risks of flu disease and vaccination 2) cost of vaccine 3) sources of influenza information, and 4) site to receive vaccine. Flu vaccine administration was subsequently recorded for each patient. Data was collected from 12/8/2008- 2/14/2009. 48 parents participated in the study with children (mean 8 yrs, SD=5). 17 (35%) of parents believed that their children were at risk for the flu this season. 11 (23%) parents believe the vaccination shot makes their children sick. 17 (35%) would not get the flu shot at any cost. Most (90%) parents believed physicians were the best source for flu information, and most (90%) wanted to get their children vaccinated in the clinic. 32 (67%) patients received the flu shot while in the PED. Parents that believed the flu shot would make their child sick were less likely to request the flu shot ($p < 0.05$). Less strong predictors of flu shot refusal were young children ($p = 0.052$) and the parent's unwillingness to get the flu shot at any cost ($p = 0.070$). Parents' perception that the flu shot causes disease is a significant barrier to vaccination. Therefore, educational efforts should aim to dispel myths for parents of high risk patients. This will become increasingly important as H1N1 vaccination protocols are implemented.

- O.27 FOREHEAD AESTHETIC SUBUNIT RESTORATION WITH MICROVASCULAR FLAPS. Claude Muresan*, Helen Hui-Chou and Eduardo D. Rodriguez. Division of Trauma Plastic Surgery, Department of Surgery, University of Maryland School of Medicine, Baltimore, MD.

The forehead is a highly visible and dynamic facial aesthetic unit which may be embarrassed by a variety of etiologies. The literature has described multiple forehead reconstructive approaches however; there is lack of uniformity describing the forehead aesthetic subunits. We sought to define the aesthetic forehead subunits as it relates to the large forehead defect restoration with microvascular flaps. Eight consecutive patients underwent free flap reconstruction for large forehead defects over a four year period (2005-2009) at R. Adams Cowley Shock Trauma Center, University of Maryland Medical Center or Johns Hopkins Hospital. Data collection included age, sex, etiology, location, and size of defect, follow-up time and complications. The forehead aesthetic units treated included: one paramedian (P); two central and paramedian (C/P); two central, paramedian and lateral (C/P/L); and three laterals (L). Seven patients presented with defects as a result of a carcinoma and the remaining patient had a forehead defect from a traumatic gunshot wound. All but one patient were female with an average age of 54.5 years. Seven patients had ulnar forearm flaps (UFF) and one an anterolateral thigh (ALT) flap. The average flap size was 12.6 x 7.8 cm. The success rate was 100 percent. Three patients had secondary

minor revision procedures. A forehead subunit classification system has been devised for the treatment of large forehead defects. This approach provides a suitable option for cases that benefit from distant tissue replacement in a single stage, while preserving the principles of aesthetic subunit replacement.