

# Abstracts

## Eleventh Annual

### Medical Student Research Day

#### November 11, 2005

Medical student research is now a part of our school's culture. Whereas once students focused on delivering the highest quality of care *currently available* to their patients, many now want to be involved in the development of new treatments for disease. Others, seeing how crucial early diagnosis can be, want to identify novel diagnostic approaches. Still others are interested in health outcomes research to determine the impact of these efforts. Taken together, these young researchers will contribute to easing suffering and improving quality of life for large numbers of people.

In this regard, Mount Sinai again finds itself in the forefront of a large group. Within the last few years, year-long programs to train medical students in how to do research have proliferated, even if there are still too few to satisfy demand. A majority of our students first do research the summer following their first year of medical school, giving them an early view of how clinical medicine and research work together. This helps them decide whether they want to take a scholarly leave during medical school and obtain more in-depth research training. The diversity of student research shows the special opportunities our students have. The quality of the abstracts shows how they avail themselves of them.

These programs would not be possible without the support of Dean Kenneth Davis and Dr. Dennis Charney, Dean for Research. As physician-scientists, they are role models for our students. Dean of Medical Education David Muller is an ardent supporter of the research program and has suggested new ways to broaden it so that students with an even wider variety of interests want to participate. I thank them all for their continued support of medical student research. Grace Oluoch, Administrator, Medical Student Research Office, has worked very hard on the abstract book and to organize today's schedule. Her experience and overview have helped make this day a success. A special thanks to Jairo Munoz, Roberto Alvarez, and Merrill Schindler for developing a mechanism to permit online abstract submission. They saved us countless hours of work. I would also like to thank Annabelle Rinaldo, Associate Director of Student Affairs, for her excellent assistance with organizing Research Day so that it proceeds smoothly. We thank Michelle Sainte, Assistant Dean for Academic Administration, for her continued help and support. Finally, I would like to thank the MSSM Alumni Association for providing medical student research stipends, as well as today's buffet lunch.

Karen Zier, PhD  
Associate Dean for Medical Student Research

---

**Comparative Analysis of the Petro-Occipital Fissure in Humans and Rats: Implications for Understanding the Anatomy of Age-Related Hearing Loss.** Armand L. Balboni, Joy S. Reidenberg, Andrew D. Bergemann, and Jeffrey T. Laitman. Center for Anatomy and Functional Morphology, and Department of Pathology, Mount Sinai School of Medicine, New York, NY.

The petro-occipital fissure (POF) lies within a critical interface of cranial base growth and development. The POF of the human skull narrows with age due to an ossification of its soft tissue components. The timing of this closure closely matches the onset of age-related hearing loss (AHL). The POF is closely related to the inner ear, both morphologically and functionally, suggesting that the ossification could be pathogenic for AHL (Balboni et al., 2005). Although of significant importance during growth and development, little attention has been focused on assessing the age related changes to this region. Therefore, this study investigates the POF in both humans and rats in order to assess: 1) the comparative nature of developmental changes, 2) value in age assessment, and 3) potential use as a model system for describing the onset of AHL. Observational analysis was conducted on 14 human cadavers, 73 human crania, and 50 rat crania in order to define and describe developmental changes to the POF. Results in humans and rats show that characteristic changes of POF ossification are present and allow for sorting of crania by age. Our examination of the POF in humans and rats has identified an age related ossification that is temporally unlike other ossifying regions of the cranial base. These findings indicate a basic morphologic similarity of the POF between rats and humans. Given the hard tissue-soft tissue interface within the POF, our

data suggest that both biomechanical and molecular forces may influence the mechanism and timing of POF ossification. The further development of an animal model for the aging of the POF will be critical to elucidating the contribution of these processes to pathologies such as AHL.

**In Vivo Electrical Propagation in Connexin40 Deficient Atrial Tissue.** Baron L. Elvera, David E. Leaf, Cindy Yu, and Gregory E. Morley. Department of Medicine, Mount Sinai School of Medicine, New York, NY.

Impulse propagation in cardiac tissue is the result of cell excitability, intercellular coupling, and tissue geometry functioning in concert. Changes in these parameters during cardiac disease may lead to slowing of conduction and an increased risk of cardiac arrhythmias. Cardiac myocytes are connected electrically and metabolically through gap junction channels. Connexin40 (Cx40) and Cx43 are both highly expressed in the adult murine atria, while Cx45 predominates in the sinus node. In the current study, high-resolution optical mapping of voltage dye fluorescence was used on the right (RAA) and left atrial appendages (LAA) of isolated Langendorff-perfused murine hearts. Cx40<sup>+/+</sup> (WT) and Cx40<sup>-/-</sup> 2–4 week old and 4–21 week old mice were studied to assess the effect of reduced Cx40 expression on conduction velocity (CV) at different pacing cycle lengths (100 msec, 60 msec, 30 msec). In the RAA of 2–4 week old mice, a significant increase in propagation velocity was found in Cx40<sup>-/-</sup> (0.705±0.007 and 0.625±0.006 m/sec at BCL 100 msec; 0.689±0.004 and 0.606±0.017 m/sec at BCL 60 msec, Cx40<sup>-/-</sup> (n=4) and WT (n=4), respec-

tively). In the LAA of 2–4 week old mice, however, no significant change in CV was found at all pacing cycle lengths in Cx40<sup>-/-</sup>. Interestingly, neither the RAA nor the LAA of the 4–21 week old mice showed significant differences in CVs between Cx40<sup>-/-</sup> (n=10) compared to WT (n=10). In conclusion, optical mapping studies suggest that atrial Cx40 deletion increases electrical propagation velocity in 2–4 week old mice. These data suggest that the relative contribution of Cx40 to conduction in 2–4 week old mice is greater than that in the 4–21 week old mice. This raises an interesting possibility that the coexistence of Cx40 and Cx43 in atrial tissue has a negative effect on cell-to-cell communication and cardiac conduction.

**Disclosure of Sexual and Physical Abuse in Adolescents: A Preliminary Assessment of Effective Screening Methodologies.** Dominique F. Bayard, Angela Diaz, and Mary Rojas. Division of Adolescent Medicine, Department of Pediatrics, Mount Sinai School of Medicine, New York, NY.

**Background:** The American Academy of Pediatrics (AAP) recommends routine screening for child maltreatment and abuse. Though recent data suggests that among adolescents, one in five girls (21%) and one in eight boys (13%) report experiencing either physical or sexual abuse, it has also been shown that adolescents do not willingly or spontaneously report past or current victimization events. The methods of face-to-face interview, self-administered questionnaire, and computer interview, have been validated for reporting anxiety and sexual behavior in adolescents. Whether the disclosure of sexual and physical abuse in an adolescent population improves with either of these methods has yet to be established.

**Objective:** This study will examine different methods for eliciting disclosure of physical and/or sexual abuse experiences, and evaluate the effectiveness of these methods among adolescents.

**Methods:** Sample: Our study will include a total of 200 adolescent patients aged 12–21 years who are presenting to the Adolescent Health Center (AHC), a comprehensive integrated program of physical health, reproductive health, and mental health. Only patients presenting for an initial history and physical examination will be included. Design: Each subject will be randomly assigned to receive one of four versions of the Childhood Maltreatment Interview Schedule—Short Form (CMIS-SF): (1) Self-administered questionnaire, (2) physician administered questionnaire, (3) Audio Computer-Assisted Interview, or (4) physician-directed inquiry.

**Analysis:** We will analyze the frequency of abuse disclosure in each screening methodology using a chi-square test to determine if there is an association between disclosure and screening methodology.

**Implications:** Identifying which interviewing method yields the greatest disclosure is essential to develop and employ standardized, effective, and reliable screening methodology to meet the AAP's recommendation of routine screening for child maltreatment and abuse in adolescents.

**Genetic Predisposition of Breast Cancer Patients with ATM Sequence Variance to Adverse Radiotherapy Responses.** Hamed B. Lari, David P. Atencio, Jamie A. Cesaretti, Richard G. Stock, Sheryl Green, and Barry S. Rosenstein. Department of Radiation Oncology, Mount Sinai School of Medicine, New York, NY.

This is a case-control multi-center study to identify single-nucleotide changes in the ATM (ataxia telangiectasia mutated) gene that may be associated with increased radiotherapy (RT)-induced morbidity in breast cancer patients. The ATM protein regulates the cell cycle checkpoints and DNA repair in response to the induction of DNA damages by ionizing radiation. This group has previously reported that in a cohort of forty-six breast cancer patients, those who develop late RT reactions are more likely to possess ATM mutations than patients with normal radiation response. The goal of this retrospective study is to elucidate the association of specific polymorphism in ATM and late RT-induced reactions. We have included seventy-seven women who underwent lumpectomy and adjuvant RT. The RT-induced adverse effects are quantified according to Radiation Therapy Oncology Group/European Organization for Research and Treatment of Cancer. Blinded to patients' clinical outcome, we have isolated DNA from blood lymphocytes of each patient. Polymerase chain reaction assays were used to amplify each of the coding exons along with short neighboring introns both upstream and downstream of the exons. Utilizing denaturing high-performance liquid chromatography (DHPLC), we have identified specific base pair mismatches, small deletions, or insertions in the aberrant exons in comparison with wild-type ATM gene. Aberrant exons will be sequenced for comprehensive statistical analysis, and the findings will be compared with the clinicopathologic data collected on the study subjects. By elucidating the influence of specific ATM sequence variants causing susceptibility to adverse radiotherapy reactions, future screening for such sequences can be used to predict which patients are most likely to develop complications resulting from radiotherapy. These patients may be encouraged to seek non-radiation treatments for their cancers, or alternatively, may still benefit from radiotherapy, but performed with lower treatment doses.

**Spine Density in MAG-Deficient Mice.** Lucas Bejar, Devorah Segal, and Patrick Hof. Department of Neuroscience, Mount Sinai School of Medicine, New York, NY.

Gene expression levels of myelin related genes such as MAG, have been shown in gene microarray experiments to be significantly decreased in schizophrenia, which indicates a possible role for dysmyelination in this disease. Many neuropsychiatry disorders have neuronal dysfunction that may be linked to alterations of dendritic spine. To analyze whether spine density is altered by dysmyelination due to loss of the MAG gene, we compared MAG KO and WT animals. We visualized layer III pyramidal cells in the prefrontal cortex of 20–24 month old mice, via intracellular loading with Lucifer Yellow and confocal microscopy. We constructed dendrograms and calculated spine densities. We were able to analyze 2 KO animal and one WT animal. In the two KOs, we analyzed 2 neurons in one animal and 5 in the other. In the WT animal, 3 neurons were evaluated. We analyzed basal and apical dendrites separately. Apical dendrite spine densities were not significantly altered in the KOs. Spine density in basal dendrites was significantly lower in the MAG KO animals ( $p = 0.03$ , one-sided t test). This data indicates spine density is affected by dysmyelination caused by the lack of the MAG gene. This change in basal spine density may reflect circuit specific pathology affecting certain pathways selectively, and play a role in some of the functional deficits seen in patients with schizophrenia.

**The Need for and Attitude towards Counseling Services in Urban Kenya: A Study towards Providing Counseling Services in a Free Community-Based Clinic.** Matthew Swan, Kimberly Bowman, Dale Runcie, Ann Ellis, and Gary Rosenberg. Department of Community and Preventative Medicine, Mount Sinai School of Medicine, New York, NY.

**Introduction:** Studies have demonstrated levels of psychiatric morbidity in sub-Saharan Africa ranging from 10–25% in hospital/clinic patients, levels equal to or exceeding those of the Western world, but with a severe lack of resources to provide care.

**Purpose:** This study assesses perceptions of counseling, desires for counseling services and the need for counseling as indicated by the presence of anxiety and/or depression in patients visiting a community-based free clinic in Nairobi, Kenya.

**Methods:** Quantitative surveys were administered in English and Swahili to a convenient sample (N=372) recruited from the RAFIKI Clinic. Participants were aged 18 and over and were predominantly mothers with an average income below \$3 (200Ksh) per week. The Hospital Anxiety and Depression Scale (HADS) were used to measure the presence of anxiety and depression. Participants were queried about their interest in counseling services in five categories: depression, anxiety, childcare, family planning, and chronic illness. Patients were deemed to have a strong desire for counseling if they would utilize counseling services at the clinic for at least three of the above categories.

**Results:** Of the study participants, 88.3% expressed a strong desire for counseling. By HADS criteria 19.6% were depressed and 30.9% had an anxiety disorder. At the time of taking the questionnaire 18% of those with a strong desire for counseling were depressed, as well as 14.8% of those ages 18–30, and 31.3% of participants over 30. Focus groups revealed that participants had not previously used counseling services, but because they valued confidentiality and professional advice, would utilize them if available.

**Conclusion:** Counseling services are desired by this population and would be utilized if implemented. To further understand how this need may have been affected by population dynamics, a comparative study will be conducted in East Harlem in a population of patients utilizing free community-based clinics.

**Polypharmacy in the Elderly: The Patient's View.** Ariel C. Bulua, and Beatriz Korc. Brookdale Department of Geriatrics and Adult Development, Mount Sinai School of Medicine, New York, NY.

Polypharmacy is a major cause of morbidity and mortality, particularly in the geriatric population (age  $\geq 65$ ). In a study at the Mount Sinai Hospital, patients in a geriatric outpatient practice consumed a mean of 10.48 medications per patient. This is of particular concern because geriatric patients are the most vulnerable to adverse drug reactions and drug-drug interactions. Polypharmacy results in increased admissions to hospitals, non-adherence, and increased costs. Little research has been done to determine how geriatric patients feel about this practice. To this end, we formulated two hypotheses: many people feel they are taking too many medications, and many people are non-adherent. Possible risk factors for these two statements were determined. The study consisted of 100 patient surveys administered one on one in the Coffey Geriatrics Clinic of the Mount Sinai Hospital. Descriptive statistics were applied, including chi square analysis,

to calculate the frequencies and percentages of each variable in relation to feelings about medication and compliance. Nearly half of all patients felt they were taking too many medications. This feeling was found to correlate positively with the actual number of medications prescribed, and negatively with both the level of trust in one's doctor and a higher rating of one's health. About 40% of patients admitted to being non-adherent. Non-adherence was found to correlate positively with a higher rating of one's health, and negatively with the level of trust and comfort in one's doctor, and the amount of helpful information offered. In summary, the results showed that a significant number of patients both think they are taking too many medications and are non-adherent. Specifically, people who have a better relationship with their doctor and a better feeling about their health are more likely to feel satisfied with their medications, and more likely to adhere with their drug regimen.

**Targeting *In Vivo* Delivery of siRNAs to Study the Role of KLF6-SV1 in Epithelial Ovarian Cancer.** Michelle C. Carley, Analisa Difeo, Goutham Narla, Olga Camacho-Vanegas, and John A. Martignetti. Departments of Human Genetics and Medicine, Mount Sinai School of Medicine, New York, NY.

Epithelial ovarian cancer (EOC), the most lethal of all gynecologic cancers, is the fifth most common cause of cancer death in women. As many ovarian cancers are asymptomatic in early stages, patients often present late in the course of their illness with widespread, disseminated disease. Despite concerted clinical and research efforts, survival rates of patients with late stage EOC have not substantially improved over the last two decades. Therefore, a better understanding of the underlying genetic factors responsible for the initiation, progression, and recurrence of EOC is essential to define novel therapeutic targets and pathways. Our recent studies have identified the tumor suppressor KLF6 and its alternatively spliced isoform, KLF6-SV1 as critical regulators of the development and progression of EOC. Most notably, KLF6-SV1 is over expressed in virtually all late-stage EOC. Cell lines engineered to down regulate KLF6-SV1 exhibit decreased proliferation, invasion, and tumor formation *in vivo*. Therefore, as a starting point for defining a future rational therapeutic strategy, our studies were primarily designed to explore the effect on *in vivo* tumor growth and behavior of siRNA-mediated treatment targeting KLF6-SV1. State-of-the-art, serum-stable siRNA molecules were designed and tested *in vitro* for their eventual use *in vivo*. Our results clearly demonstrate that siRNA targeted to KLF6-SV1 expression in SKOV-3 cells, a highly aggressive ovarian carcinoma cell line, altered gene expression profiles, markedly decreased cellular proliferation and increased apoptosis. We believe that these results provide ample support for the next phase of these long-term studies: *in vivo* experiments to define the therapeutic potential of siRNA-mediated targeting of KLF6-SV1 in ovarian cancer.

**Sexual Health Needs Assessment in Gran Roque, Venezuela.** Elliot M. Charen, Elizabeth J. Garland, Philip J. Landrigan, Stephen E. Goldstone, Maria Elena Marin, and Jordana Sosa. Departments of Community and Preventive Medicine, Surgery, and Medicine/Infectious Disease, Mount Sinai School of Medicine, New York, NY, Hospital de Clínicas Caracas, Escuela de Medicina José María Vargas, Venezuela.

**Background:** Gran Roque Island of the National Park of Los Roques, is located 70 miles from the mainland Venezuela, has a population of 1,400 people, yet over 55,000 tourists visit each year. Tourism has recently introduced HIV to the island. The purpose of this study was to conduct a needs assessment to discover what the extent of the sexual health problem is, what services are in place, what sexual health resources are available to the residents, and whether there is room for improvement.

**Methods:** Informal conversations took place between the researcher and the residents representing a broad spectrum of occupations including store owners, medical professionals, teachers, government personnel, bartenders, and others.

**Results:** All residents approached willingly participated in conversations, with 37 discussions greater than 5 minutes. Preliminary results show that there are some developed sexual health services in place on the island, including cheap contraception (birth control pills) and condoms given out free upon request. There exists a basic form of sexual education in the schools, yet the number of sexually transmitted infections (STI's) is high and the age of first sexual intercourse is young. Two major barriers to health care (expensive drugs and medical care) found in the United States are absent on this island. Mision Barrio Adentro, a government sponsored program designed to help underserved communities, removes the first barrier by offering 85% discounts on drugs. The second barrier is avoided because all treatment by the doctor on the island is paid for by the government.

**Conclusions:** Obstacles to state of the art medical care exist on Los Roques since there is no testing on the island. Addition of Rapid HIV, VDRL tests, and a microscope would improve the care for the population.

All the evidence points toward conducting investigations focused on developing educational programs.

**Factors Identified by Early-Stage Breast Cancer Patients to Help Cope with Post-Surgical Treatments.** Jessica L. Cohen, and Nina Bickell. Department of Health Policy, Mount Sinai School of Medicine, New York, NY.

Breast cancer patients' feedback on their own recent experiences provides the most insight into what factors would increase use and completion of post-surgical treatments. While adjuvant treatments for breast cancer, including radiation, hormonal therapy, or chemotherapy, have been shown to reduce mortality rates by 20–30%, many patients do not complete courses of therapy. Alleviating women's concerns may help them through particularly vulnerable times. The patient population included 20 women with early-stage breast cancer, 6 months after their last definitive surgical breast procedure. Hour long telephone interviews determined the use of efficacious therapies and assessed the women's experiences, knowledge, and beliefs about breast cancer, along with barriers to completing care. Aiming to explore venues that could have helped patients better navigate their adjuvant treatment following surgery, the interviews concluded with an open-ended question asking women to think back over their breast cancer care, and what, if anything, would have improved the process. Qualitative analysis identified 4 common themes: earlier mammograms, insurance, doctors' attitudes, and process of care. Four women wished they had gone in earlier for mammograms; three women identified insurance difficulties, including avoiding expensive medications and needing to buy Medicaid cards for coverage; four women identified issues with doctors' attitudes, especially doctors' ignoring psychological issues of cancer; seven women wished the process of getting care had been easier, specifically regarding difficulties with scheduling/coordinating appointments, long wait times, finding information on the disease and support networks, and poor communication with technicians; six women did not identify any problem areas, which may be due to inability to recall or express concern, rather than an actual lack of suggestions for improvement. Targeting these problem areas with further research focused on interventions during adjuvant treatments may increase completion of post-surgical therapy and improve breast cancer patients' chances for survival.

**Autism and the Glutamate System: Potential Pharmacological Treatments.** Geoffrey A. Collins, Eydokia Anagnostou, and Eric Hollander. Seaver and New York Autism Center of Excellence, Department of Psychiatry, Mount Sinai School of Medicine, New York, NY.

**Background:** Autism spectrum disorders (ASD) are a diverse group comprising behavioral and cognitive variations in which patients notably feature repetitive behaviors/restricted interests as well as impairments in language and social skills. There is strong evidence suggesting that autism is primarily a genetic disorder. Many candidate genes and their protein products pertain to the glutamate system, suggesting that glutamatergic interventions may ameliorate some autistic traits.

**Methods:** The following database was searched: MEDLINE (1966 to Sept 2003). The following terms were used: glutamate, glutamate receptors, autism, AMPA, kainate, NMDA, metabotropic receptors, GluR2, GluR6, mGluR8, GAD65, amantadine, d-cycloserine, lamotrigine and memantine.

**Results:** Pathology specimens, genetic screening and imaging studies all suggest that the glutamate system is implicated in autism. Preliminary trials with glutamatergic agents (amantadine, d-cycloserine and lamotrigine) show some effect in reducing certain autistic behaviors.

**Conclusions:** Based on an understanding of the mechanisms of glutamate signaling, medication trials with other glutamatergic agents, such as memantine, would be of value. Additionally, new research into the function of metabotropic glutamate receptors may provide novel approaches for pharmacological intervention.

**Identification of a Novel Tfap2 Co-Factor.** Catherine Constable, Cheryl Tan, and Bruce Gelb. Department of Human Genetics, Mount Sinai School of Medicine, New York, NY.

The Tfap2 family of transcription factors has been shown to be associated with heart development. The critical role of Tfap2a in normal neural tube and cardiac development has been demonstrated in mice deficient in this gene. These mice exhibit severe developmental defects, including persistent truncus arteriosus. Also, TFAP2B has been identified as the causative gene for Char Syndrome, which is characterized by familial patent ductus arteriosus. Our lab identified Tfap2d, which differs from other members of the Tfap2 family in protein structure and in expression pattern. While pre-

viously identified Tfp2 proteins are specifically expressed in the neural crest, Tfp2d is the only known Tfp2 protein expressed exclusively in the myocardium of the developing heart. To further elucidate the role of this protein, we performed a yeast two-hybrid screen, which yielded several unique candidate interactors, including Ash2L, a chromatin-remodeling protein. This interaction was confirmed by co-immunoprecipitation of tagged proteins in eukaryotic cells. Currently, we are seeking to characterize the nature of this interaction through co-immunoprecipitation assays, first of all to ensure that Tfp2d interacts with endogenous Ash2L and additionally, that the interaction is specific for the Tfp2d protein. We are also using a CAT (chloramphenicol acetyltransferase) reporter assay to determine whether Ash2L is a co-activator of Tfp2d. In this assay, Tfp2d is inserted in a eukaryotic expression vector downstream from the RSV promoter. This plasmid is co-transfected with a CAT reporter containing three tandem copies of the hMtl1a-180 AP-2 binding sequence. The CAT concentration in the presence of Tfp2d is compared with that of controls to determine the level of transactivation.

**The Synergistic Immunotoxicity of Benzo[a]Pyrene and Ultraviolet A Impair Langerhans Cell Functions.** Jason A. Cordero, Dayuan Gao, Xueyan Zhou, and Huachen Wei. Department of Dermatology, Mount Sinai School of Medicine, New York, NY.

Accumulating evidence indicates that environmental factors contribute to the increasing incidence of skin cancer. Previously our group demonstrated that benzo[a]pyrene (BaP), a ubiquitous pollutant, synergistically increased skin cancer incidence when combined with ultraviolet A (UVA). BaP and UVA significantly depressed contact hypersensitivity and down regulated Langerhans cell (LC) migration induced by fluorescein isothiocyanate, whereas epidermal LC numbers were not altered. These results strongly suggest an impairment of LC function by BaP and UVA. The present study focused on the effect of BaP and UVA on LC functions *in vitro*. To examine the cytotoxicity, XS106 cells, a murine LC cell line, were incubated with various concentrations of BaP followed by 5 kJ/m<sup>2</sup> of UVA. Viability was measured by MTT assay. The lethal dose of BaP was found at 0.312  $\mu$ M and LD50 was about 0.16  $\mu$ M. LC migration was assessed by a chemotaxis assay. The BaP plus UVA groups significantly inhibited LC migration induced by CXCL12 in a BaP concentration dependent manner. Together, the cytotoxicity and chemotaxis assay data suggest that synergistically BaP and UVA is toxic to LC and impair the immune system by down regulating LC function.

**The Role of Donor TLR2 Signaling in Murine Islet Cell Transplantation.** William N. Coward, Jr., Nan Zhang, and Bernd Schroppel. Departments of Medicine/Renal, Gene and Cell Medicine, Mount Sinai School of Medicine, The Recanati/Miller Transplant Institute of Mount Sinai Health, New York, NY.

We hypothesize that the Toll-like receptor 2 (TLR2) recognizes self-derived intrinsic ligands that are present during cellular injury, such as necrotic cells. This signaling mediates proinflammatory responses in early post-transplantation of islets. Murine islets were isolated after collagenase digestion and discontinuous Ficoll centrifugation. To assess the function of TLR2, islets were cultured overnight with or without the specific TLR2 ligand peptidoglycan (PGN) [10  $\mu$ g/mL]. Additional islets were cultured with or without pancreatic necrotic cells (NC) to simulate conditions present in prolonged islet culture. Marginal mass isografts (n=200 islets) were transplanted under the renal capsule of STZ induced diabetic mice. Islet function was assessed with glucose monitoring and glucose tolerance testing. **RESULTS:** Screening for TLRs with QPCR reveals that TLR2, TLR3, TLR4, and TLR9 are expressed on isolated islets and on an established  $\beta$  cell line ( $\beta$ -TC3). PGN stimulation of islet TLR2 causes a significant increase in MCP-1, TNF- $\alpha$  and IL-6 expression (p<0.05). NC co-culture led to similar increases in these proinflammatory mediators. MyD88 and TIRAP, downstream signaling proteins of TLRs, were increased 3.5 fold in the presence of PGN and NC. Reduction in post-transplant blood glucose was significant in control isografts on day 1 and day 2, but not in PGN or NC pretreated isografts (p<0.05). Glucose tolerance was impaired in PGN and NC isografts compared to controls.

**Conclusions:** Murine islets express functional TLR2. Pancreatic necrotic cells are able to stimulate chemokine/cytokine expression similar to the specific TLR2 ligand peptidoglycan. Islet exposure to pancreatic necrotic cells is detrimental to glycemic control by murine islet isografts possibly through TLR2 signaling.

**The Quantification of Pericardial Effusion Volume Determined by 2D-Echocardiography Compared to Pericardiocentesis.** Christopher L. Cummings, Martin E. Goldman, and Lori B. Croft. Department of Medicine/Cardiology, Mount Sinai School of Medicine, New York, NY.

**Background:** Pericardial effusion (PE) may develop acutely or chronically over time, reaching relatively large sizes (>1000mL), and perhaps resulting in life threatening pericardial tamponade. 2D-echocardiography (2D-echo) is the most rapid and accurate method to diagnose PE. However, it provides only a semi-quantitative categorization (small<1cm, moderate 1–2cm, or large>2cm) based on the separation of visceral and parietal pericardium. Accurate, noninvasive quantification of PE volume would allow closer monitoring of PE progression and perhaps predict imminent tamponade.

**Objective:** To compare estimated PE volume using 2D-echo with the volume of fluid drained at pericardiocentesis.

**Methods:** Patients who underwent pericardiocentesis in the catheterization laboratory were retrospectively analyzed. Inclusion criteria were documented PE volume drained and a 2D-echo within 48 hours prior to drainage. Exclusion criteria were acute PE or poor quality 2D-echo images. The 2D-echos were analyzed by an independent observer who was blinded to the results of pericardiocentesis. PE volumes were calculated in apical 4 chamber, apical 2 chamber, or subxiphoid views using the method of disks. Final estimated PE volume was taken as the average of three measurements. Results: 16 patients with PE drainage volumes ranging from 250–1300mL were analyzed. There was excellent correlation between volumes by 2D-echo and pericardiocentesis:  $y = 0.65x + 245$  mL ( $r = 0.89$ ,  $P < 0.0001$ ). Standard error of the estimate=101mL; intraobserver variability=9.5%. Bland-Altman analysis showed a mean difference of  $-45 \pm 150$ mL. PE volume differed between 2D-echo and pericardiocentesis by an average of 19% (absolute volume difference=125  $\pm$  89mL).

**Conclusions:** This preliminary study demonstrated that 2D-echo can accurately quantify PE volume compared with the pericardiocentesis volume. Further studies are needed to apply and validate this noninvasive technique in a larger patient population.

**Structural Changes in Cortical Bone and Their Role in Fractures of the Distal and Ultra Distal Radius.** Gary B. Deutsch, Danielle Casagrande, Richard Ghillani, Roger Levy, and Karl Jepsen. Department of Orthopaedics, Mount Sinai Hospital, New York, NY.

Osteoporosis, characterized by structural weakening of bone and a marked decrease in bone mass, can eventually lead to bone fragility. Non-traumatic fractures of the distal radius, known as Colles' fractures, are often the first manifestation of osteoporosis and indicate that the person has twice the relative risk of developing a hip fracture within fifteen years. Women are four times more likely than men to develop the illness. In previous studies, geometric properties of bone, for example endosteal diameters, periosteal diameters, and moments of inertia, have been correlated with gender, age, and menopausal status. To further define this relationship, thirty-eight cadaver radii were harvested for radiographic and histological investigation. The age and gender of each cadaver was noted. Zero degree AP X-rays were taken of the forearms and digitized for computer analysis. Using the MATLAB program, measurements of the x-rays were obtained, including ulnar variance, cortical thickness, and radial width. For histological examination, cross sections were taken at the thirty percent site of the distal radius and eventually dehydrated and embedded in Caroplastic in order to preserve the fine architecture of the bone. Using a band saw, two millimeter slices were cut from the original cross sections and polished. These thin slides were placed under a microscopic digital camera and high-resolution images were captured for further analysis. The histological coronal images will be studied using Scion Image, allowing us to measure endosteal and periosteal diameters, cortical porosities, and any recognizable resorption spaces. We will use these measurements to determine if significant correlations exist between selected cortical bone properties and age and gender. Recognizing characteristics of cortical bone that become compromised with age may lead to new diagnostic measures that can identify these problems early and new therapies that could target these areas at the onset of osteoporosis to prevent future fractures.

**Mutations of Trefoil Factor 1 Prevent Its Tumor Suppressive Activity while Enhancing the Invasiveness of Human Gastric Cancer Cells: An Investigation Guided by Molecular Modeling.** Matthew Diamond, Xianyang Yio, Jie-yu Zhang, Lu-Hai Wang, Harel Weinstein, and Steven Itzkowitz. Departments of Physiology and Biophysics, Medicine, and Microbiology, Mount Sinai School of Medicine, Weill Medical College of Cornell University, New York, NY.

Trefoil Factor 1 (TFF1) is a key gastric tumor suppressor gene. Like the other members of the TFF family, it is vital for mucosal homeostasis and

healing, and it shares the distinct structural fold of the trefoil domain, a three-loop architecture connected by disulfide bonds between six conserved cysteines. TFF1 is unique among the TFFs in that TFF1 knockout mice develop gastric adenomas and carcinomas, and human gastric cancers typically lack TFF1 expression. TFF1 mutations have been found in human gastric cancers and are so far the only naturally occurring mutations reported for any TFF gene. A theoretical estimate of the structural stability of those mutants, as well as comparative studies of related proteins, focused our interest on a surface of the TFF1 Loop 1 edge. Molecular modeling of a number of Loop 1 mutants predicted significant changes to the electrostatic properties of that surface without a disruption of the global fold of the molecule. These computational studies then guided site-directed mutagenesis experiments. Two mutants, A10D and E13K, were found to have lost their ability to inhibit cell growth and block etoposide-induced apoptosis while gaining an ability to promote cancer cell invasion. Although invasion induced by both mutants was blocked by inhibiting PI3-kinase or phospholipase-C, inhibiting ROCK blocked only E13K-induced invasion. This is the first evidence for a functional role of TFF1 mutations in human gastric cancer, demonstrating loss of tumor suppressive activity and gain of cancer cell invasiveness from single point mutations. These studies, the first site-directed mutagenesis experiments of any TFF (other than cysteine substitution), provide the tools to probe both signal transduction mechanisms as well as structural elements responsible for trefoil factor function.

**Model for Prediction of Physician Drug Utilization and Cost in Clinical Anesthesia.** Ankur M. Doshi, David Wax, Tanuj Palvia, Marina Krol, and David L. Reich. Department of Anesthesiology, Mount Sinai School of Medicine, New York, NY.

**Background:** Several studies have compared the cost effectiveness of anesthetic agents. While some investigators concluded that anesthetic drug selection significantly affects long-term costs, there are limited data regarding the predictors of more expensive anesthetic agent usage. The purpose of the current investigation was to identify predictors of perioperative anesthetic drug cost.

**Methods:** An IRB-approved retrospective analysis was performed using 9,823 electronic anesthesia records from cases performed in a six-month period. The total cost of anesthetic and anesthetic adjuvant medications administered by intravenous bolus, intravenous infusion or inhalation was calculated for each case using the hospital formulary price list. Predictors of cost related to the patient, surgical setting, and practitioner were tested. Univariate linear regression was used to identify potential predictors of anesthetic expense per case.

**Results:** The strongest univariate predictors of anesthetic expense were determined to be anesthetic technique (general anesthesia was most expensive), increasing length of anesthetic, subspecialty of procedure (neurosurgery was most expensive) and patient class (day-of-admission surgery was most expensive), all of which had  $r^2 > 0.05$  and  $p$ -values  $< 0.0001$ . Patient age and weight, American Society of Anesthesiologists (ASA) physical status and nurse anesthetist involvement demonstrated a smaller degree of association, with  $0.011 < r^2 < 0.05$ , but with  $p$ -values  $< 0.0001$ . The lowest degree of statistically significant univariate association was noted with resident involvement, emergency status of procedure, and attending years of experience.

**Discussion:** Identifying predictors of current usage patterns should help reduce costs by enabling the establishment of benchmarks and ongoing monitoring of expenditures. Modifying the drug selection behavior of outlier practitioners using this methodology may have beneficial effects on anesthetic drug expenditures.

**Abdominal Diameter Index and 10-Year Coronary Heart Disease Incidence in Male Bridge and Tunnel Workers in NYC.** Adam C. Ehrlich, and Donald A. Smith. Department of Medicine/Cardiovascular Institute, Mount Sinai School of Medicine, New York, NY.

Many studies have shown that increased abdominal adiposity is associated with increased risk of cardiovascular disease. Visceral, or central, obesity produces insulin resistance and hyperinsulinemia which then produces hypertension, increased triglycerides, decreased HDL-cholesterol, and eventually type II diabetes mellitus in genetically susceptible individuals. All of these are risk factors for coronary heart disease, and thus it has been suggested that visceral obesity may be linked to coronary heart disease by this pathway. Recent studies have suggested that the anthropometric measurement of abdominal diameter index, recumbent abdominal height divided by thigh circumference, may be the best measure of central obesity's risk for cardiovascular disease. Telephone interviews were conducted with bridge and tunnel officers in the Triborough Bridge and Tunnel Authority who previously participated in a cross-sectional study in 1993–1994 that examined a multitude of risk factors for predicting preva-

lent coronary heart disease, including several anthropometric measurements. In that study, abdominal diameter index was the best risk predictor of prevalent coronary heart disease. This follow-up study includes a questionnaire that assesses incident coronary heart disease in the last 10 years in study participants who had no coronary heart disease at that time and who fell into the highest and lowest quartiles of abdominal diameter index. Interviews are still being conducted; thirty-seven subjects (36%) in the lowest quartile and 51 subjects (49%) in the highest quartile have been contacted. No statistical analysis has been done thus far. If there is a significant difference in the ten-year incidence of coronary heart disease in these two groups, it may confirm the hypothesis that abdominal diameter index is the best anthropometric measure of insulin resistance that can be used to predict future cardiovascular disease. This might be useful in large population screenings and underserved communities as a low-cost, quick method of determining cardiovascular risk.

**A Retrospective Cohort Study of the Adverse Event Profile of Trimethoprim-Sulfamethoxazole during the First 30 Days following Pediatric and Adult Liver Transplantation.** Ann Ellis, Roberto Posada, Sachin Kulkarni, Shirish Huprikar, and Betsy Herold. Departments of Pediatrics and Infectious Diseases, Mount Sinai School of Medicine, New York, NY.

Following liver transplantation, patients are usually placed on Trimethoprim-sulfamethoxazole (TMP-SMX) for PCP prophylaxis. TMP-SMX is considered superior to alternative agents. However, because of hepatic or hematologic adverse events, TMP-SMX is often discontinued soon after transplantation and alternative agents are used, although the causality relationship between the use of TMP-SMX and the occurrence of these events has not been demonstrated. The hypothesis of this study is that the use of TMP-SMX does not result in significantly higher adverse events than alternative agents, and that the abnormalities in liver function and bone marrow parameters are due to confounding factors. The aim of this study is to provide data regarding the incidence of cholestasis or bone marrow suppression following liver transplantation; the timing of these events in relation to the time of transplant, initiation of TMP-SMX, and other confounding variables; how often patients are changed to alternative PCP regimens; and if there are laboratory changes following the switch in PCP prophylaxis. A retrospective cohort study was conducted of liver transplant recipients during the first 30 days following transplantation. One cohort includes subjects in whom TMP-SMX was initiated, subsequently discontinued, and switched to an alternative agent. The other cohort includes subjects in whom TMP-SMX was initiated and not interrupted within the first month following liver transplantation. Trends in liver function, peripheral blood counts, and adverse events were compared in both groups. If it is found that the incidence of adverse events is not higher than that seen with other agents, it could be concluded that these adverse events are not secondary to the use of TMP-SMX. Data from this study will be critical in better understanding whether an association exists between the use of TMP-SMX and the occurrence of adverse events. No studies are currently available that examine this issue in liver transplant recipients.

**Identification of Induction and Suppression Signals for Foxp3+ Treg Differentiation.** Irene Epelboym, Yaozhong Ding, Jonathan S. Bromberg, and Jonathan S. Bromberg. Department of Gene and Cell Medicine, Mount Sinai School of Medicine, New York, NY.

The cytokine and costimulatory signals that drive or interfere with the differentiation of CD4+ T cells into Foxp3+ regulatory T cells (Tregs) can be precisely defined. Foxp3 is a transcription factor, the expression of which has been demonstrated as being integral to the differentiation and proliferation of CD4+ T cells into CD4+CD25+ Tregs. The specific signals that are activated in the Foxp3+ cells which lead to their differentiation toward the Treg lineage are unknown. Prior studies show that this process is stimulated by TGF $\beta$  through upregulation of Foxp3, and that it is subject to IL-4-mediated inhibition. It is the focus of this study to determine other input signals that trigger stimulatory or inhibitory effects on the Treg generation. Primary culture of murine CD4+CD25- T lymphocytes was maintained for 3 days in the presence of cytokines and monoclonal antibodies to costimulatory molecules that are known to serve an important function in T cell development and differentiation. These were IFN $\gamma$ , IL-12 (Th1 lineage determinants), IL-4, IL-5, IL-6, IL-10 (Th2 lineage determinants), and anti-CD28, anti-CD2, anti-CTLA4, anti-CD80, anti-CD86, anti-CD40, anti-PD-1 (mAb to costimulatory factors). Expression and transcriptional activation of Foxp3 was quantified using real-time PCR. We found that Foxp3 is induced by TGF $\beta$ , and that IL-5 and anti-CD28 suppress the TGF $\beta$ -mediated induction of Foxp3. Tregs are capable of suppressing the inflammatory response in a manner more specific and elegant than immunosuppressive therapy, and they may be an alternative for preventing graft rejection in transplantation. Since Treg proliferation and differentia-

tion can be affected by cytokines secreted by the neighboring Th1 and Th2 cells, it is important to investigate further the signals responsible for modulating Treg response. In our future studies, we will look at time as a factor in TGF $\beta$ -mediated Foxp3 induction and we will examine how TGF $\beta$  signaling cascade affects activation of the Foxp3 promoter.

**The Production of VEGF and Loss of Anti-tumor Immunity.** Steven J. Esses, Christina D. Swenson, and Karen Zier. Department of Medicine/Clinical Immunology, Mount Sinai Medical Center, New York, NY.

Solid tumors, such as the murine fibrosarcoma, CMS5, have developed a variety of mechanisms to evade the immune system, for example, via secretion of inhibitory factors, i.e. VEGF, or the recruitment of cells, i.e. the immature Gr1+/CD11b+ myeloid cells, that suppress immunity. This lab has shown that Gr1+/CD11b+ cells infiltrate the spleens of mice with CMS5 tumors. Mice with small tumors have levels of Gr1+/CD11b+ comparable to naive mice. In contrast, mice with large tumors have increased levels of these cells. Since VEGF can recruit Gr1+/CD11b+ cells from the bone marrow, our goal was to determine whether CMS5 cells secreted this factor. First, we tested whether VEGF was detectable in supernatants of confluent CMS5 cells. We showed that CMS5 cells secreted 2334 pg/ml. To see if VEGF was produced by other tumor cells, three additional lines were tested. All were positive for the factor. In order for VEGF to play a role in immune suppression, it would have to be active *in vivo*. To test this, mice were inoculated with CMS5 cells and serum was collected from non-tumor-bearing mice, early tumor-bearing mice that still had tumor immunity, and late tumor-bearing mice that had lost anti-tumor immunity, and tested for VEGF. Our findings revealed that, whereas the control and early tumor bearing mice had similar serum levels of VEGF, 77 and 74 pg/ml, respectively, the serum level of late tumor-bearing was substantially greater at 125 pg/ml. Tumor resection has been shown to lead to the return of anti-tumor immunity. Future experiments will examine whether tumor resection leads to a normalization of serum VEGF levels. In conclusion, the tumor CMS5 secretes VEGF, and the production of this factor may play an important role in the loss of anti-tumor immunity.

**Changes in Color Vision Following Cataract Surgery.** Shlomit Feit Sandler, Julius Shulman, and Scott E. Brodie. Department of Ophthalmology, Mount Sinai School of Medicine, New York, NY.

**Background:** Artists' color palettes have been known to shift from the blue to the red end of the spectrum as they age. In several well-known cases, this color-shift was reversed, following cataract removal, and sometimes colors in the blue end of the spectrum were enhanced. With age, and especially with cataracts, yellow/brown pigments accumulate in the lens of the eye. It has been argued that the presence of these pigments causes a "filtering effect" on the artist's vision and perception of color, which may account for the change in the artist's color choices. However, this hypothesis fails to account for the similar "filtering effect" on pigments found in the artist's paint itself.

**Hypothesis:** To account for the artist's altered color palette, we propose that the color palette is a "metameric match" with real-world colors, meaning the human vision process perceives pigments with distinct spectral light distributions as identical colors. Changes in retinal exposure to ultra-violet light following cataract surgery would therefore exaggerate the phenomenon, accounting for enhanced shades following cataract surgery.

**Study Design and Methods:** We plan to test this hypothesis in subjects who have a cataract in one eye and have had a cataract removed from the other eye: subjects will compare color matches between natural objects and artist pigments. They will undergo standard color vision testing, be asked to match the color of natural objects against standard color samples, and draw flowers from a large palette of colored pencils. Tasks will be performed with each eye separately, under natural and artificial light.

**Results:** Preliminary results suggest differences in color vision between eyes with and without cataracts through standard color vision testing. Drawings of natural objects demonstrated the use of different colored pencils to depict the same natural hue in indoor and outdoor settings with cataract and non-cataract eyes.

**A Comparison of Conditioned Fear Extinction between Patients with Panic Disorder and Normal Controls.** Mariel B. Fisher, Jose Martinez, Katherine Nearing, Elizabeth Phelps, and Jack Gorman. Laboratory of Clinical Psychobiology and Department of Psychiatry, Mount Sinai School of Medicine, New York University, New York, NY.

Panic disorder can be explored using fear-conditioning, which involves exposure to a neutral stimulus paired with an aversive unconditioned stimulus (US). The neutral stimulus becomes a conditioned stimulus (CS) after

repeated pairings with the US. The CS elicits fear, the conditioned response (CR), in anticipation of the US, a process known as acquisition. These learned associations can fade with repeated exposure to the CS without the US, known as extinction, however they can also be recovered with contextual retrieval cues. The learned associations become pathological when the CS elicits the CR in the absence of the CS/US pairing. In this study, we hypothesize that fear-conditioning will differ among panic patients and healthy controls in the strength of newly acquired conditioned relationships, their tendency to generalize these associations to different contexts, and their ability to extinguish acquired fear. The fear-reinstatement paradigm will be used to study individuals' responses. Subjects will first undergo acquisition and extinction of a CS/US association (blue square image/mild shock) in a particular spatial context. Next, half of the patients and controls will undergo fear-reinstatement (shock alone without blue square) in the same room, whereas the other half will experience reinstatement in a different environment. Skin conductance responses will determine the subjects' intensity of anxiety. Presenting the blue square alone, in the original spatial context as the acquisition and extinction, will test recovery of the fearful response to the blue square. If contextual conditioning does differ between panic disorder patients and normal controls, then we would anticipate seeing altered skin conductance responses during the reinstatement phase of the experiment. Because animal experiments have shown that the contextual portion of fear-conditioning requires hippocampal activation, in another experiment we will use fMRI to compare hippocampal activation during a contextual fear memory task. Both of these experiments are now ongoing.

**The Kinetics of Skin Cancer: Progression of an Actinic Keratosis to a Squamous Cell Carcinoma.** Aaron E. Fuchs, and Ellen S. Marmur. Department of Dermatology, Mount Sinai School of Medicine, New York, NY.

Actinic Keratoses (AKs) are intraepidermal skin tumors that have the potential to progress to squamous cell carcinomas (SCCs). SCCs are the second most common cancer with more than 200,000 cases in America each year, and many SCCs arise from pre-cancerous AKs. It is estimated that 10% of AKs progress to SCC. The progression from an AK to an SCC is thought to be due to chronic exposure to sun, specifically ultraviolet-B sunlight. This cumulative exposure causes cellular DNA mutations, especially in the p53 tumor suppressor gene. p53 mutations are positively associated with cell proliferation and negatively associated with apoptosis, which subsequently leads to clonal expansion. Understanding the kinetics of this developmental process can help physicians better evaluate, and subsequently treat pre-cancerous AKs. In order to determine the timescale for an AK to progress to an SCC, we examined the clinical histories of all patients diagnosed pathologically with a squamous cell carcinoma between January 1, 2004 and June 30, 2005. Out of a total patient population of 5191, 68 were determined to have had a pathologically confirmed diagnosis of an AK at the same site as the subsequent SCC. The length of time for an AK to progress to an SCC was determined to be 25.56 months (95% CI: 21.03-30.09). While a more controlled *in-vivo* study is indicated, this data provides a good estimate of the time course from an AK to an SCC. In summary, of the estimated 10% of AKs that will develop into a SCC, the progression will take approximately two years.

**Uncovering the Intricacies of Complicated Grief: A Cross-Cultural Prevalence and Risk Factor Analysis.** Benjamin E. Goldsmith, R. Sean Morrison, Lauren C. Vanderwerker, and Holly G. Prigerson. Departments of Geriatrics and Medicine, Epidemiology and Public Health, Center for Psycho-oncology and Palliative Care Research, Mount Sinai School of Medicine, New York, NY, Yale University School of Medicine, Harvard Medical School, Boston, MA.

**Background:** Complicated grief (CG) has been established as a debilitating disorder distinct from classifiable Major Depressive Disorder, Post-Traumatic Stress Disorder, and Anxiety disorders, but little is known about its prevalence and manifestations across racial and ethnic groups.

**Objective:** To establish the prevalence of CG in white and non-white populations, to identify factors associated with the development of CG, and to compare the prevalence of grief symptoms between these groups.

**Design:** Secondary analysis of data collected from a study 205 cancer patients and their caregivers (Coping with Cancer, 2002-2004) and 267 caregivers from the Yale Bereavement Study.

**Analysis:** Multivariate logistic regression was used to identify risk factors associated with CG.

**Results:** The prevalence of CG was found to vary significantly across ethnic groups. The prevalence of CG was 9.8% in whites, 19% in blacks, 40% in Asians, and 11.1% in Hispanics. CG was found to vary significantly between whites and non-whites 9.8% vs. 22.5% ( $p = .029$ ). Factors associated with the development of CG in multivariate analysis

included ethnicity (OR: 3.70, 95% CI: 1.41-9.74) and suddenness of death (OR: 2.87, CI: 1.36-6.07). Non-whites were found to be significantly more likely to report distrust toward others following the death of a loved one ( $p = .045$ ). There were no other significant differences in CG symptoms.

**Conclusions:** Our data suggests that non-whites experience CG at a significantly higher rate than white survivors, but that little variation exists in the symptoms of CG grief experienced between whites and non-whites.

**The Delivery of Breast Cancer Care by Community-Based Organizations.** Julie D. Gribetz, Alicia Cohen, Kruti Shastri, and Nina Bickell. Department of Health Policy, Mount Sinai School of Medicine, New York, NY.

The goal of this project was to assess the ability of community-based patient assistance programs to identify and address the needs of women with early-stage breast cancer who contact and utilize them. Breast cancer is prevalent in today's society. When diagnosed at an early stage, proven effective adjuvant therapies exist. Nevertheless, a percentage of women do not receive these therapies, especially minority women, due to a variety of reasons. Currently, it is unclear whether community based organizations can help reduce that under use by helping overcome barriers to care and by improving women's experiences during the course of cancer treatment. We sought to measure women's satisfaction and overall experiences with community-based organizations. We were able to speak with patients and staff members from 6 community-based organizations that serve women with breast cancer in the New York area. We surveyed 7 staff members and 35 patients who use their services. Patients were interviewed about their initial needs and expectations of the patient-assistance services, how well their needs had been identified and addressed, as well as their overall experiences with the services. Patient satisfaction was assessed and modifying factors such as age, ethnicity, and stage of breast cancer among others, were explored. One staff member from each organization was interviewed in order to compare the program's goals with patients' perceptions of care. We analyzed the data to categorize these needs and identify common themes. This project aims to explore patient experiences and satisfaction with community-based organizations, and in doing so we hope to enable and empower women of different racial backgrounds diagnosed with early stage breast cancer to obtain life prolonging therapies.

**Molecular Characterization of Interactions between ERK and Transcription Factor ATF2 in Head and Neck Squamous Cell Carcinoma.** Sachin Gupta, and Dianne Duffey. Department of Otolaryngology, Mount Sinai School of Medicine, New York, NY.

This study of head and neck squamous cell carcinoma (HNSCC) examined the role of ERK, an epidermal growth factor receptor (EGFR) pathway protein, in activating transcription factor ATF2. ERK is an important regulator of the G1/S cell cycle progression that when activated, leads to translocation and activation of transcription factors in the nucleus. In HNSCC, EGFR is often over expressed, increasing ERK activity downstream in the EGFR signal cascade. ATF2 has recently been implicated in HNSCC oncogenesis. Support for a potential upstream role of ERK in ATF2 activation comes from studies in other cell lines. By understanding the signaling interactions between ERK and ATF2, gene therapy and additional molecular targeted therapy can be developed for HNSCC. Our hypothesis is that ERK has an upstream role in the regulation of ATF2 in HNSCC. To study effects on cell proliferation and survival, a MTT cell proliferation assay was performed with UM-SCC9 cells and MEK inhibitor U0126 to generate a dose-response curve. Preliminary results suggest that after 48 hours, 25uM U0126 is not toxic to UM-SCC9 cells. To study the relationship between ERK and ATF2 activation in UM-SCC9 cells, western immunoblotting examined the expression of phosphorylated ERK and phosphorylated ATF2 at baseline and following treatment with 10uM MEK inhibitor U0126 for one, six, and twenty-four hours. Preliminary results suggest that the MEK inhibitor inhibits ERK phosphorylation. Results of phosphorylated ATF2 expression following treatment with the MEK inhibitor will be reported. Future studies will examine synergistic or antagonistic effects when the MEK inhibitor and chemotherapeutic agents (i.e., paclitaxel and cisplatin) are used concomitantly. ATF2 will be inhibited to observe how the MEK inhibitor enhances the cytotoxic effects induced by paclitaxel and cisplatin. These studies will hopefully give deeper insight into the signaling interactions between ERK and ATF2 and provide additional therapeutic targets for HNSCC.

**Is Increased Age a Risk Factor for Emergency Department (ED) Oligoanalgesia?** Ben Harris and Ula Hwang. Departments of Emergency Medicine and Geriatrics, Mount Sinai School of Medicine, New York, NY.

Many studies attribute disparities in ED analgesia administration to patient age. Little is known about the quality of ED pain management in older adults. **OBJECTIVES:** To characterize the differences in ED analgesia between older (>e y.o.) and younger (18-64 y.o.) adults presenting to an academic urban ED with painful conditions.

**Methods:** Patients,  $\geq 18$  y.o., were prospectively enrolled by reviewing the presenting illness. Study eligibility was based on both chief complaint and final ED diagnosis of conditions requiring analgesic management. Variables collected included: age, gender, triage status, medications administered and prescribed, and times of patient activity (e.g., arrival, assessment, ordering of medication).

**Results:** From July 1 to July 21, 2005, there were 4,190 ED visits. Of these, 805 patients had conditions with chief complaint and diagnosis warranting pain management: 559 were 18-64 y.o., and 101 were >e y.o. A subset of these patients with injuries was analyzed (ND). Patients >e y.o. ( $n=$ , mean age  $y.o. \pm 10$ ) were compared to patients 18-64 y.o. ( $n=$ , mean age  $y.o. \pm 13$ ). Each group was 77% female. Older patients were more acutely ill by triage score (severity index  $3.1 \pm 0.6$  v.  $3.6 \pm 0.6$ ,  $p=0.02$ ) and had more fractures (7 v. 2 fractures,  $p=0.06$ ). Older patients had less pain assessment (patients with no pain score at triage: 8 v. 3 patients,  $p=0.04$ ); took longer to get analgesic medication (206 v. 93 minutes,  $p=0.07$ ); received less analgesia (patients receiving no analgesia: 9 v. 5 patients,  $p=0.20$ ; NSAIDs: 0 v. 4 patients,  $p=0.04$ ); and were discharged without analgesic prescription: 9/15 patients v. 3/21 patients,  $p=0.004$ .

**Conclusion:** In this study, older adults received less analgesia and less pain assessment for similar conditions than younger and less acutely ill adults. Future studies will include more patients with a broader range of presentations and diagnoses and additional analyses of analgesia.

**STI Risk Assessment in Gran Roque Island, Venezuela.** Jonathan S. Hausmann, Elizabeth J. Garland, Philip J. Landrigan, Stephen E. Goldstone, Maria Elena Marin, and Jordana Sosa. Departments of Community and Preventive Medicine, Surgery, and Medicine/Infectious Diseases. Mount Sinai School of Medicine, New York, NY, Ambulatorio Dr. Tulio Villalobos, Los Roques, Hospital de Clinicas Caracas, Escuela de Medicina Jose Maria Vargas, Venezuela.

**Background:** Gran Roque Island (GRI) is the major inhabited island in Los Roques National Park, Venezuela, with 1,400 residents. Tourism brings 55,000 people to the island every year, and along with it, the possibility of introducing infectious diseases. The purpose of this study was to assess the risk of sexually transmitted infections (STI) in the community and implement plans for treatment, prevention, and education.

**Methods:** Out of 721 eligible adults, 103 permanent residents of GRI, aged 18-49, were randomly chosen from a 2004 census list. Of these, 74 enrolled in the study; the other 29 were unavailable. An anonymous, confidential, validated questionnaire based on the HIV/AIDS/STD Behavioral Surveillance Survey was administered in Spanish to participants. Two out of four HIV positive residents were also informally interviewed.

**Results:** Most adults were not married but lived with a sexual partner, and although they did not use condoms with their partner, they could name several places on the island where they could obtain them. Everybody had heard of STIs, but only a handful could correctly name any symptoms. Some young men reported having sex with female tourists, and this source of transmission was responsible for infecting one man, and later his wife, with HIV. Educational and condom distribution sessions were conducted on the island. Plans were made with the government to conduct blood tests for HIV, hepatitis, and syphilis to all willing residents in September 2005.

**Conclusions:** The high flux of people on the island and the lack of knowledge about STIs combine to make the incidence of STIs on Gran Roque Island particularly alarming. Of concern is the potential under-reporting of information on sensitive subjects in a survey that was not self-administered. Future efforts should focus on increasing awareness of STIs, especially on recognizing symptoms and promoting health-seeking behaviors.

**Infra-Red Coagulation for the Treatment of High-Grade Anal Dysplasia in HIV-Negative Men Who Have Sex with Men.** Joshua S. Hundert, and Stephen Goldstone. Department of Surgery, Mount Sinai School of Medicine, New York, NY.

**Research Question:** Is the IRC (Infra-Red Coagulator) more effective at preventing recurrences and progression to cancer of anal HSILs in HIV-negative MSM than it is in HIV-positive MSM.

**Background and Methods:** We performed a retrospective chart review on HIV-negative MSM treated for HSIL treated with the IRC.

Patients were screened with anal cytology and standard anoscopy. Those with abnormal findings underwent High Resolution Anoscopy (HRA), in which biopsies were taken. If biopsies returned as HSIL, patients were offered IRC ablation of those dysplastic areas. All patients had at least 6 months follow-up. Patients were surveyed to see if lesions had been cured, persisted, or if new (metachronous) lesions developed. Persistent and metachronous lesions were treated with IRC.

**Results:** 68 patients met enrollment criteria. Mean patient age was 39.6 years. 143 lesions were treated. The mean number of lesions per patient was 2.2. The length of follow-up ranged from 150 days to 1618 days, with an average of 753. 100 lesions were treated on the first IRC treatment. The average number of lesions at first treatment was 1.5. 27 patients underwent a second IRC treatment. 19 patients (28%) had persistence of their primary lesion at or after their 6-month post-treatment follow-up visit. 34 patients (52%) developed at least one new lesion in a different location. In the study HIV-positive subjects, the percentage of patients with persistent lesions was the same as in this study (28%). However, the percentage of patients that reported new lesions was lower in the HIV-negative population (52%) than in the HIV-positive population (65%).

**Conclusions:** IRC is a safe, ambulatory, effective treatment for anal HSILs with minimal associated morbidity. Our data suggests that IRC is as effective, if not more so, for treatment of anal HSIL in HIV-negative subjects as it is in HIV-positives.

**Xenobiotic Phenols in Early Pregnancy Amniotic Fluid.** Stephanie M. Engel, Brynna Levy, Zhisong Liu, Dana M. Kaplan, and Mary S. Wolff. Departments of Community and Preventive Medicine, Human Genetics, Pediatrics, and Ob/Gyn. Mount Sinai School of Medicine and Tris Pharma Inc., New York, NY.

Hormonally active chemicals, such as bisphenol A (BPA) and phytoestrogens, have been detected in amniotic fluid. Phytoestrogens and BPA are weak hormone agonists. Phytoestrogens also possess anti-estrogenic activity possibly by competitive binding to the estrogen receptors, and can reduce genotoxic damage to cells by antioxidant and other mechanisms. They can also inhibit cellular growth and proliferation by inhibiting tyrosine kinase cell-signaling activity and by down regulating certain membrane receptors (e.g. erbB2, EGFR). Consequently, concern has been mounting that prenatal exposure to hormonally active agents may result in reproductive or neurological effects. We examined the concentration of three phytoestrogens (enterolactone, daidzein and genistein) and BPA in residual amniotic fluid samples that had been collected early in pregnancy from a population of women in the United States. We found detectable levels of enterolactone, daidzein, genistein and BPA in 21 residual amniotic fluid specimens that were collected before 20 weeks gestation. Samples were obtained by amniocentesis from women who were referred to the Mount Sinai Medical Center because of advanced maternal age. Phytoestrogens were present in higher concentrations than BPA. Enterolactone was detected at the highest concentration (median 95.9 ug/L), followed by daidzein and genistein (9.5 and 1.4 ug/L, respectively). BPA was present at very low concentrations (10% > LOD of 0.5 ug/L). The relative concentration of the chemicals measured in amniotic fluid were identical to those in urine reported by other studies, i.e., enterolactone > daidzein > genistein >> BPA. Amniotic fluid is a source of fetal exposure to polar xenobiotics that come from the mother. The results of this analysis are described in an upcoming article in *Reproductive Toxicology*: Stephanie M. Engel, Brynna Levy, Zhisong Liu, Dana Kaplan, Mary S. Wolff, "Xenobiotic Phenols in Early Pregnancy Amniotic Fluid." In press. Volume 21:1. *Reproductive Toxicology*.

**The Photoprotective Efficacy of Genistein in Human Skin.** Anna I. Kirkorian, Julian O. Moore, Stephanie Diamantis, Mark G. Lebwohl, and Huachen Wei. Department of Dermatology, Mount Sinai School of Medicine, New York, NY.

Skin cancer is the most common cancer in the United States with an estimated incidence of one million new cases in 2004. The most important environmental factor in the development of skin cancer is exposure to UV irradiation resulting in DNA damage. Genistein, the most abundant isoflavone of the soy derived phytoestrogen compounds, has been previously shown to have antiphotocarcinogenic properties. These include the capacity for scavenging reactive oxygen species, inhibiting DNA damage, and down regulating UVB-induced signal transduction cascades associated with carcinogenesis. Genistein is also a potent antioxidant and an inhibitor of tyrosine kinase. The aim of our study is to investigate the photoprotective efficacy of genistein in vivo in human skin, in response to acute doses of UVB. Dorsal skin samples from twenty-eight healthy human subjects, Fitzpatrick skin types I through IV, were pre-treated with both genistein and a vehicle control prior to exposure to UVB radiation equivalent to one minimal erythemal dose (MED). Punch biopsies were obtained and the

cyclobutane pyrimidine dimer (CPD) profiles were assessed via immunohistochemical analysis of paraffin-embedded skin specimens. CPD represents the primary DNA lesion induced by exposure to UV irradiation. A preponderance of such lesions results in the mutation of critical genes implicated in carcinogenesis. Genistein inhibited the immunoreactivity expression profile for UV-induced DNA damage as evidenced by the decreased formation of CPDs in the genistein-treated samples when compared to the vehicle-treated skin. Our results represent the first characterization of the photoprotective effect of genistein against UV-induced DNA damage in vivo in human skin. These results serve to further validate our conclusion that genistein may serve as a potent chemo preventive agent against photocarcinogenesis.

**Doubletime Affects Wingless Signaling and Planar Cell Polarity by Regulating Dishevelled Signal Specificity.** Thomas J. Klein, Andreas Jenny, and Marek Mlodzik. Department of MCDB, Mount Sinai School of Medicine, New York, NY.

Canonical Wnt/Frizzled (Wnt/Fz) and non-canonical Frizzled/Planar Cell Polarity (Fz/PCP) signaling networks regulate a vast array of biological processes, from cell growth and division to tissue polarity and differentiation. Mutations of several signaling molecules in these pathways have been associated with a number of human diseases, including lung, breast, colon, and prostate cancer. Thus, identifying factors that regulate these two related pathways is of importance to the understanding of both development and disease. Several molecules, including the transmembrane receptor Frizzled and the cytoplasmic protein Dishevelled (Dsh), have been shown to signal to both pathways. The mechanism by which these factors selectively signal to one pathway versus the other is poorly understood. Upon stimulation by either pathway, Dsh becomes hyperphosphorylated, an event that is important for downstream signaling events and may impart signal specificity. A number of kinases have been identified that can both bind to and phosphorylate Dsh, including Casein Kinase I epsilon (CKIε). *Xenopus* studies and cell culture experiments have shown that CKIε affects both canonical and non-canonical signaling. Here we report that double-time (dbt; a.k.a. discs overgrown, dco), which encodes the *Drosophila* CKIε homolog, is important for both Wnt/Fz and Fz/PCP signaling. Using loss-of-function studies in the fly eye and wing, we demonstrate that dbt is necessary for both pathways. Using over expression studies, we show that dbt is sufficient to induce Wnt/Fz and Fz/PCP phenotypes in these tissues. Genetic interactions supported by biochemical data demonstrate that dbt promotes Wnt/Fz signaling while inhibiting Fz/PCP.

**PTTG1, a Novel Repressed Target of KLF6 Tumor Suppressor—a New Pathway of Carcinogenesis?** Ursula Lang, Sigal Kremer-Tal, Goutham Narla, Andrew Paris, Steven Yea, and Scott L. Friedman. Department of Medicine/Liver Diseases, Mount Sinai School of Medicine, New York, NY.

Background: KLF6, a Krüppel-like transcription factor, is a tumor suppressor dysregulated in a number of human cancers. While p21 is a key transcriptional target, many other downstream targets of KLF6 are unknown. Microarray analysis of a KLF6<sup>+/−</sup> and KLF6<sup>+/+</sup> mouse livers was used to uncover new KLF6-regulated genes. Of these, the most differentially induced (~2-fold) in KLF6<sup>+/−</sup> mice was the pituitary tumor transforming gene (PTTG1). PTTG1 inhibits sister chromatid separation, and drives malignant transformation; its over expression disrupts cell division, generates chromosomal instability, leading to further mutations. The aim of our study was to validate microarray data by quantitative real-time PCR (QRT-PCR). We analyzed liver and prostate tissues from KLF6<sup>+/+</sup> mice and KLF6<sup>+/−</sup> littermates. We also analyzed hepatocellular carcinoma (HCC) patient samples and cell lines stably expressing KLF6 to validate the correlation between KLF6 and PTTG1 mRNA levels. Results: By QRT-PCR, KLF6 mRNA was reduced by > 80% in 14 KLF6<sup>+/−</sup> mouse livers compared with 10 KLF6<sup>+/+</sup> livers, which correlated with a mean 1.2 fold increase in PTTG1 mRNA in KLF6<sup>+/−</sup> animals. In prostates from these same KLF6<sup>+/−</sup> mice, KLF6 mRNA was reduced ~50%, with a 2-fold increase in PTTG1 mRNA. In 12/19 patient samples there was a mean ~70% decrease in KLF6 mRNA and 2-fold increase in PTTG1 mRNA. In HepG2 hepatoblastoma cells, stable infection with KLF6 retrovirus increased KLF6 mRNA 15-fold, associated with a 40% decrease in PTTG1 mRNA. In Huh7, a HCC cell line, stable infection with KLF6 retrovirus led to a ~1.8 fold increase in KLF6 mRNA and 25% decrease in PTTG1 mRNA. Conclusion: An inverse relationship between KLF6 and PTTG1 suggests that PTTG1 may represent a transcriptionally repressed target of KLF6. Thus, inactivation of KLF6 in human cancer may lead to dysregulated PTTG1 and contribute to tumorigenesis.

### Development of an International Maternal-Child Health Education Program for Mothers in New York City and Santa Cruz, Bolivia.

Alexandra P. Leader and Andrea Rothenberg, Department of Health Education, Mount Sinai School of Medicine, New York, NY.

The purpose of the project was to develop an adaptable maternal-child health curriculum for distinct communities that are historically underserved and disadvantaged. The project involved two phases. In the first phase, we synthesized the information and skills garnered through participating in a local community health initiative in order to prepare a comprehensive and versatile health education curriculum for pregnant women, new mothers and infants living in a local, underserved and disadvantaged community. As translator, facilitator and co-instructor for the Prenatal Care and Assistance Program at Mount Sinai-Queens, a program that prepares pregnant women for labor and delivery and provides instruction and guidance for early parenting and infant care, we developed a curriculum that aims to merge clinical and educational aspects of mother-child health for mothers living in the community of Long Island City, New York. The curriculum constitutes an educational module that is adaptable to meet the specific needs of pregnant women who are ready for labor and delivery and lack adequate health services. The second phase of the project involved taking the curriculum to mothers and infants living in Santa Cruz, Bolivia, a community that shares the basic social, economic and health characteristics of our target community in New York. We worked to formally identify the specific, recognized needs of pregnant women and infants in Santa Cruz so as to focus this health education module accordingly. The curriculum was utilized to teach a six-week program of prenatal health classes in five different clinical and non-clinical settings throughout the city of Santa Cruz and we are currently analyzing our data to evaluate the efficacy of the curriculum in providing pregnant women and infants of Santa Cruz with the knowledge, skills and resources to support a healthy pregnancy and transition into early parenting.

### Multimarker Molecular Detection of Metastasis in Pathologically Negative Lymph Nodes from Melanoma Patients.

Diana P. Leon, Cristina Mangas, Josep M. Hilari, Ferrandiz Carlos, Cindy Yueh, Liqiang Xi, and Tony E. Godfrey, Departments of Medicine/Hematology/Oncology, and Dermatology, Mount Sinai School of Medicine, New York, NY, Hospital Universitari Germans Trias i Pujol, Barcelona, Spain.

Sentinel lymph node (SLN) status is the most important factor in melanoma staging and patient prognosis. Prognosis for lymph node-negative subjects (AJCC Stages I and II) should be very good, but unfortunately up to 20% of these patients suffer disease recurrence. One possible explanation for this is the presence of occult metastatic disease that is undetected by routine pathology. Previous studies have shown that molecular analysis of SLN increases the sensitivity of lymph node metastasis detection in individuals with node-negative melanoma but at the cost of specificity. We hypothesized that a multimarker Real Time quantitative PCR assay would maintain the high sensitivity of previous studies but improve specificity and therefore provide more accurate prognostic information. We obtained 370 dissected lymph nodes from 195 patients who underwent SLN biopsy at the HUGTIP in Barcelona. All nodes were tumor-negative by standard histopathological and immunohistochemical techniques. Half of each node was stored frozen and RNA was isolated. Quantitative RT-PCR was used to quantify the expression of the melanoma-associated mRNAs MART-1, Tyrosinase, SSX-2, MAGE-A3, GALNaC and PAX-3. Sensitivity and Specificity of these markers for predicting recurrence were examined using ROC curves. QRT-PCR results were compared with disease recurrence to determine clinical relevance. Median patient follow-up was 49 months and 11 of the 195 patients recurred. Kaplan-Meier survival estimates did not show significant differences in survival based on individual markers or marker combinations. Quantification of mRNA should increase the specificity of SLN staging by decreasing the number of false positive results. However, we found that specificity was still a problem and that not all recurrences were identified by the markers. Marker positivity was not significantly correlated with recurrence. However, the frequency of recurrence in this data set was low compared with other studies and our study may be underpowered despite having a large sample size.

### Fluorophotometry to Evaluate the Cornea in Patients Utilizing CRT to Correct Myopia.

Huma Naikoo, Bernard Tinio, Chakravarthy Koonapareddy, Michael Ahdoot, Tony Leung, Shmuel Mahgarefeth, and Penny A. Asbell, Department of Ophthalmology, Mount Sinai School of Medicine.

Corneal Refractive Therapy (CRT) is a non-surgical procedure that reduces myopia by reshaping the cornea to allow light to focus properly. An FDA clinical study has shown CRT to be a safe, reversible, and effective method to correct low to moderate myopia. Since CRT utilizes rigid

gas permeable contact lenses to mold the corneal shape from prolate to oblate, this study will test the health and integrity of the corneal epithelium. Our hypothesis is that CRT will have no damaging effects on the epithelium. This study employs fluorophotometry, a technique documented to be safe and highly sensitive, to evaluate corneal barrier function, an indicator of epithelial health. 0.5% fluorescein eye drops are placed in each patient's eyes, and the amount of fluorescein that seeps into the cornea is quantified with a fluorophotometry camera. Corneal epithelium health is inversely proportional to the amount of fluorescein absorbed. Baseline measurements will be taken prior to CRT fitting, and follow-up measurements with the patients will take place 1 day, 1 week, 1 month, and 3 months after the fittings. Statistical analysis of these measurements will determine the effects of CRT on the health of the corneal epithelium. Preliminary results have shown that the fluorescence of control eyes, which have not undergone CRT, remains stable and is reproducible among patient populations. If the final results show that CRT does not significantly alter fluorescence, and thus have limited damage to the corneal epithelium, then this treatment can be confidently recommended to short-sighted patients as a new alternative to refractive surgery and other conventional corrective options such as eyeglasses and contact lenses.

### The Efficacy of Antenatal Corticosteroids between 32 and 34 Weeks in Patients with Preterm Premature Rupture of Membranes.

Heather I. Levin, Enrique Soto, Thomas Musci, Natali Aziz, Yvonne W. Cheng, Andrea Weintraub, Errol Norwitz, Keith Eddleman, Joanne L. Stone, Aaron B. Caughey, and Larry Rand, Departments of Obstetrics and Gynecology, Mount Sinai School of Medicine, California Pacific Medical Center, University of California, San Francisco, Yale University.

**Objective:** Administration of antenatal corticosteroid (ACS) to women with preterm premature rupture of membranes (PPROM) at 32–34 weeks gestation is controversial. Authorities debate the theoretical risk of infection against the unclear benefit at that gestational age, despite the high prevalence of respiratory distress syndrome (RDS). Our aim is to evaluate risks and/or benefits of ACS administration to patients with PPRM between 32 and 34 weeks gestation.

**Study Design:** A retrospective cohort study of patients at three teaching institutions with PPRM at 32–34 weeks between 1993–2005 was conducted. Those who received ACS were compared to those who did not. A course of ACS was defined as receiving  $\geq 24$  hours of steroids prior to delivery. Patients were excluded if they had a prior course of ACS, a fetal anomaly, or chorioamnionitis on admission. The primary outcome variable was a reduction in the incidence of neonatal RDS, powered to detect a 50% decrease. Secondary outcomes included chorioamnionitis, neonatal sepsis, intraventricular hemorrhage (IVH), necrotizing enterocolitis (NEC) and hyperbilirubinemia.

**Results:** Of 856 patients with PPRM at 32–34 weeks who met inclusion criteria, 500 (58%) received ACS and 356 (42%) did not. Patients who received ACS at 32-0/7 to 32-6/7 weeks had a 44% reduction in RDS compared to those who did not (OR, 0.50; 95% CI, 0.31–0.81). At 33-0/7 to 33-6/7 weeks there was no significant difference. There were no statistically significant differences in any of the secondary outcomes at either gestational age.

**Conclusion:** There is benefit without apparent risk to the administration of ACS at 32 weeks gestation in patients with PPRM. No such benefit was demonstrated after 33 weeks. This should serve as the basis for a prospective randomized controlled trial looking at the effect of giving ACS between 32–34 weeks in PPRM.

### Association of Traditional Cardiovascular Risk Factors and Coronary Calcification in Elderly Japanese-American Men: The Honolulu Heart Program.

Sandy C. Liang, Kamal Masaki, Randi Chen, Bradley Willcox, Alvin Ikeda, Katsuhiko Yano, J. David Curb, and Robert Abbott, Division of Biostatistics and Epidemiology, Brookdale Department of Geriatrics & Adult Development, Department of Geriatric Medicine, Mount Sinai School of Medicine, New York, John A. Burns School of Medicine, University of Hawaii, Pacific Health Research Institute, Honolulu, Hawaii, Kuakini Medical Center, Honolulu, Hawaii, University of Virginia.

**Background:** Coronary artery calcification (CAC) as assessed by multi-slice computed tomography (MSCT) has been proposed as a noninvasive method to assess coronary artery disease. While studies have shown relationships between traditional risk factors for cardiovascular disease (CVD) and CAC, there were no studies done in the elderly. This report examines the associations between CVD risk factors and CAC in a population of very old Japanese-American men.

**Methods:** The Honolulu Heart Program is a longitudinal cohort study initiated in 1965 to study CVD in Japanese-American men in Hawaii. From 2004 to 2005, MSCT was performed to assess CAC in 222 men ages 84 to 96 years (mean age=87). CVD risk factors were available from examinations given 12 years prior to scanning.

**Results:** After adjusting for age, prevalence of diabetes increased significantly by CAC quartiles (14.4% in the first quartile to 25.4% in the fourth quartile,  $p=0.059$ ). There was also a significant positive relationship between CAC quartiles and fasting glucose ( $p=0.03$ ), pack-years of cigarette smoking ( $p=0.02$ ), and physical activity index ( $p=0.01$ ). Other traditional risk factors showed positive associations with CAC quartiles, but statistical power was limited by a small sample size.

**Conclusions:** This study in very old Japanese-American men shows that diabetes, fasting glucose, pack-years of cigarette smoking, and physical activity index are significantly associated with CAC. These findings are consistent with the observation that effects of CVD risk factors, particularly diabetes, persist in the very old. It remains to be determined whether CAC has the potential to predict CVD events in extreme old age.

**The Effect of Hemi-Sync Music on Intra-operative Stress Reduction in Patients Having Awake-Surgery for Parkinson's Disease or Dystonia.** Michelle M. Liao, Irene P. Osborn, David C. Kramer, Francis B. Sullivan, and Ron L. Alterman. Departments of Anesthesiology and Neurosurgery, Mount Sinai School of Medicine, New York, NY.

The goal of this study is to determine whether Hemispheric Synchronization (Hemi-Sync) music will reduce intra-operative anxiety in patients undergoing deep brain stimulation (DBS). DBS is a surgical procedure that is used to treat neurological symptoms of Parkinson's disease and dystonia, such as tremor, rigidity and walking difficulty. During this procedure, patients are kept awake and unsedated with their heads pinned and fixed into a frame. While local anesthetic is administered, general sedation is not allowed because patients must be conscious for the assessment of neural and motor function. Therefore, patients undergoing the DBS procedure often experience increased baseline anxiety, which poses a significant challenge in maintaining blood pressures below the safe limit of 140 mmHg. Hemi-Sync is a binaural beat music designed specifically to induce brain-wave states that promote relaxation. Thus, we hope to determine whether listening to Hemi-Sync intra-operatively can improve patients' well-being during awake-surgery. Patients will be randomly assigned to one of two groups. For 10 minutes intra-operatively, patients will receive either 1) Hemi-Sync through noise-canceling headphones or 2) noise-canceling headphones alone. Patients will take a State-Trait Anxiety Inventory questionnaire before and after this 10-minute period to assess anxiety. Blood pressure, heart rate, bispectral index, and pharmacologic regulation of blood pressure will also be recorded. Group differences pre-intervention and post-intervention will be analyzed. Through this study, we hope to determine whether the use of Hemi-Sync represents a novel non-pharmacologic alternative that provides comfort and sedation for patients during awake-surgery.

**Establishing Normative Data for the Anatomic Localization of Memory Strategies and Emotional Response to Musical Stimuli of Differing Emotional Value: 3TESLA f-MRI Analysis of Classically-Trained Musicians.** Wen Lin, Cheuk Y. Tang, Jin Fan, and Thomas P. Naidich. Departments of Radiology and Psychiatry, Mount Sinai School of Medicine, New York, NY.

**Rationale:** (1) Musicians with "absolute pitch" (AP) use associative memory to immediately identify the pitch of any tone or tone pair. Musicians with "relative pitch" (RP) use working memory to identify the relationship between any pair of tones (the interval), but cannot identify the precise pitch of either. (2) Specific tone pairs and chords carry distinct emotional values.

**Hypotheses:** (1) Presentation of single tones, tone pairs, and chords to classically-trained musicians, who differ only in the way they process pitch (AP vs. RP), will disclose the site(s) of working memory for tonality. (2) Presentation of tone pairs and chords with differing emotional "valence" (harmonious vs. dissonant intervals; major vs. minor chords) will disclose the sites activated by the musicians' appreciation of these different emotional valences.

**Materials and Methods:** The investigators will recruit 20 classically-trained musicians, (10 AP and 10 RP) who are native English speakers matched for age, gender, and the tonality of their parental languages. Musical stimuli will be presented visually ("silent hearing") by marking keys on a projected piano keyboard to ensure uniformity of the stimuli presented despite the noisy MRI environment. Event-related, blood oxygen dependent (BOLD) three Tesla functional magnetic resonance imaging (f-MRI) (Siemens, Erlangen Germany) will be used to assess the cerebrovascular responses of these musicians' brains as they perceive the individual tones, tone pairs and chords. General linear modeling (GLM) and statistical parametric mapping (SPM) of the f-MRI datasets from each participant will be used to identify the anatomic sites of tonal and emotional processing.

**Results:** Pending. IRB approval of the project has been received. GCRC funding has been approved conditional upon clarification and

amplification of specific queries. Initial data and conclusions are expected by late Fall 2005.

**Development of a Surgical Implant to Prevent Laryngopharyngeal Reflux by Increasing Resistance to Retrograde Flow at the Level of the Upper Esophageal Sphincter.** Michael J. Lipan, Joy S. Reidenberg, and Jeffrey T. Laitman. Center for Anatomy and Functional Morphology, Mount Sinai School of Medicine, New York, NY.

**Background:** Laryngopharyngeal reflux (LPR) is a manifestation of symptoms and signs resulting from abnormal exposure of the laryngeal and pharyngeal mucosa to gastric secretions refluxing through the upper esophageal sphincter (UES). Medical treatment failures, and patients with life-threatening conditions associated with reflux, are being increasingly treated with anti-reflux surgery involving fundoplication at the lower esophageal sphincter. In contrast, surgical intervention at the UES has not been attempted. The objective of this study is to determine the efficacy of a retropharyngeal implant at the UES to augment the anti-reflux properties of this barrier.

**Methods:** Cadaveric heads ( $n=3$ ) were harvested and the distal end of the proximal esophagus was tied over a catheter for water infusion. The retropharyngeal space at the level of the UES was exposed to allow insertion of implants. Implants were made of silicone rubber in various widths and either cylinders (diameters: 0.6, 0.8, 0.9cm) or half-cylinders (radii: 0.3, 0.45, 0.6cm) in shape. Maximal intraesophageal pressure was measured with a water manometer during water infusion using no implant and then using each successively larger implant in place.

**Results:** Using no implant resulted in the lowest maximal pressure (21.7 cm H<sub>2</sub>O). Increasing width of the implant correlated with increasing maximal pressure (range 46-117 cm H<sub>2</sub>O). The only exception to this trend was that the half-cylindrical implant of 0.6cm width had a higher pressure than a cylindrical implant of 0.8cm width (76 vs. 69 cm H<sub>2</sub>O respectively).

**Conclusions:** Increased resistance to liquid flow past the level of the UES can be achieved using any of the implants tested. Increased resistance correlated with increased width of the implant for those of the same shape. Half-cylindrical implants achieved greater resistance than cylindrical implants of the same width. The initial success of this method shows promise for future development of an implant for patients with LPR.

**Airway Management of Acromegalic Patients: A Retrospective Study.** Joyce C. Lo, Irene Osborn, and David Kramer. Department of Anesthesiology, Mount Sinai School of Medicine, New York, NY.

Acromegaly is an endocrine disorder in adults that is caused by an adenoma of the pituitary gland that secretes excess growth hormone (GH). Excess GH produces serious systemic changes such as organomegaly, diabetes, cardiovascular disease, and hypertension, and untreated, will lead to a shortened lifespan. Thus, treatment is essential in acromegalic patients, typically with transphenoidal resection of the pituitary gland. Other morphologic changes, such as prognathism, soft tissue overgrowth (including pharynx, tongue, lips, epiglottis, and larynx), and recurrent laryngeal nerve dysfunction, alter the airway. These alterations may be associated with airway obstruction, difficulty in ventilation, and obscured visualization of the larynx during laryngoscopy, which increase the difficulty of securing an anesthetic airway. To provide these patients with optimal care, it is important to determine the preferred method of airway management. Therefore, in this study, we characterized the methods used in airway management of approximately 200 acromegalic patients and the specific success rates of each of these methods by conducting a retrospective study that spanned a 13-year period and evaluated over 1000 patients aged 18-65 who underwent pituitary surgery. In particular, we compared the technique used for intubation, the number of intubation attempts required for success, determined failure rates, and reviewed complications to airway management, including airway trauma. Intubation methods compared include traditional direct laryngoscopy, fiberoptic intubation (asleep and awake), glidescope, intubating laryngeal mask airway, and surgical airway. We believe that our data will indicate that while acromegalic patients may pose more challenging airway management issues, current methods and devices available allow for safe and proper management of these patients. Furthermore, our patient pool is larger than any study previously published on the acromegalic airway, and, therefore, we believe that our results will provide important information on optimal airway techniques to utilize in the management of acromegalic patients.

**The Effects of Jasmonic Acid and Methyl Jasmonic Acid on Melanoma Metastasis.** Margarita S. Lolis, Yongyin Wang, and Huachen Wei. Department of Dermatology, Mount Sinai School of Medicine, New York, NY.

Melanoma is currently the fastest growing of all cancers and has a strong tendency to metastasize to the brain, liver, lungs, and bone. The prognosis of metastatic melanoma is poor, with a median survival time of 7 months and limited treatment options. Jasmonic acid (JA), a growth inhibitor produced ubiquitously in plants, may be effective in the inhibition of tumor metastases. The purpose of this study is to determine whether jasmonic acid (JA) and its methyl ester, methyl jasmonic acid (MJ) decrease the rate of metastasis of melanoma cells *in vitro*. The antimetastatic effects of JA and MJ were evaluated on the migration and invasion of a highly metastatic B16F10 melanoma cell line. Toxicity assays, dose response and temporal response experiments were performed to determine the effects of JA and MJ. Migration and invasion assays were designed using filters that were precoated with fibronectin and/or matrigel (reconstituted basement membrane) and incubated with 105 B16F10 cells with or without JA and MJ. JA and MJ were found to significantly inhibit the migration of B16F10 melanoma cells into extracellular matrix components and their invasion into reconstituted basement membrane (matrigel). Since JA is a known protease inhibitor, its ability to inhibit migration and invasion of melanoma cells may be modulated by hydrolyzing aminopeptidases in tumor cells. This *in vitro* data suggests that JA and MJ may be able to inhibit tumor cell migration and invasion possibly through a mechanism involving aminopeptidase inhibition in tumor cells. Future experiments aimed at elucidating the mechanism of action of JA/MJ, such as an aminopeptidase assay, will be performed.

**Determination of the Causes of Ocular Toxicity Secondary to the Prostaglandin Ocular Hypotensive Analogues.** Edward I. Marcus, Michael Ahdoot, Seth P. Epstein, and Penny Asbell. Department of Ophthalmology, Mount Sinai School of Medicine, New York, NY.

**Purpose:** To test whether toxicity of prostaglandin ocular hypotensive analogues (POHA) are secondary to the preservative, not the active agent.

**Background:** Glaucoma is usually treated with POHAs. To date, there is no direct comparison of the ocular surface toxicity of the different POHAs or whether the observed toxicity is due to the active ingredients or the preservatives used.

**Methods:** Toxic agents will proportionately reduce the conversion of MTT viable dye to formazan crystals by corneal epithelial cells (CEPI 17) and conjunctival cells (P61 Clone). Formazan is quantified by absorbance at 570nm. Ninety-six groups of latanoprost, bimatoprost, travoprost and unoprostone in concentrations of 0.001% to 1%, with and without the preservatives benzalkonium chloride, benzododecinium bromide, sodium perborate, and stabilized oxychloro-complex in concentrations of 0.01% to 0.10% will be examined. Media alone and 10% formalin will be utilized as controls. Seven to ten wells per group will ensure reproducibility/statistical significance. Cells will be seeded at  $1 \times 10^3$  cells/well in 96 well tissue culture plates with 200  $\mu$ L of suitable media. When confluent, after decanting, 100  $\mu$ L of the appropriate test solution will be added. After 1 hour and decanting the solution, 150  $\mu$ L of MTT will be added for 4 hours. After decanting, the precipitate will be dissolved by 100  $\mu$ L of acid isopropanol and the absorbance of each determined.

**Conclusion:** Preservatives proved to exhibit the majority of the toxicity exhibited by the commercial POHAs: bimatoprost > latanoprost > travoprost.

**Significance:** Patient compliance is of utmost importance for successful glaucoma therapy. Determining the relative toxicities of the antiglaucomatous agents should enable physicians to maximize compliance by selectively prescribing the least toxic agent.

**ERM Proteins Regulate Axon Guidance.** C. David Mintz, Ioana Carcea, Meghann Burke, Daniel McNickle, Stephen Salton, and Deanna L. Benson. Fishberg Department of Neuroscience, Mount Sinai School of Medicine, New York, NY.

The establishment of functional connectivity during brain development requires that growing axons follow an elaborate set of extracellular chemo-tactic cues that serve as an addressing system for appropriate synaptic targets. Numerous guidance cues and their transmembrane receptors have been identified, but the system which mediates the complex intracellular response of the growth cone remains unelucidated. We asked whether the ERMs, a highly homologous family of membrane-cytoskeletal linker proteins that have been implicated in cellular motility, are involved in axon guidance. Using well characterized dominant negative and constitutively active ERM mutants and an *in situ* axon guidance assay conducted in developing rat neocortical brain slices, we demonstrate that intact ERM

function is required for appropriate axon targeting. In the slice guidance assay appropriate axon trajectory is known to be dependent on the guidance cue Semaphorin 3A and its receptor, Neuropilin-1. We show that C-terminal threonine phosphorylation of the ERMs, which tightly regulates their activity, is responsive to extracellular application of Semaphorin 3A. Furthermore, we demonstrate that ERMs regulate the endocytosis of L1, a transmembrane protein that determines the plasma membrane expression of Neuropilin-1. These results identify ERMs as a new class of regulators of axon guidance. Additionally, they allow us to construct a model in which ERMs play a pivotal role in regulating cellular adaptation to guidance cues, a phenomenon that has been widely described, but not adequately explained at a molecular level.

**Quantitative Evaluation of CNS Neuronal Loss Secondary to Glaucoma in DBA/2 Mice Using MRI and Correlation with Histological Evaluation.** Steven Naymagon, Melissa Kujawski, Patrick Hof, Cheuk Tang, Thom Mittag, and John Danias. Departments of Ophthalmology, Neurobiology and Radiology, Mount Sinai School of Medicine, New York, NY.

**Background:** Glaucoma is a group of diseases in which optic nerve degeneration can lead to impairment or vision loss. The loss of optic nerve axons is followed by the loss of retinal ganglion cells (RGC). There also appears to be neuron loss in the central nervous system (CNS) targets of RGCs. This relationship has been documented for the human disease but not for the DBA/2 mouse, a rodent glaucoma model that develops high intraocular pressure and RGC death starting around 12 months of age.

**Purpose:** To study the relationship between the death of RGCs and loss of CNS neurons in a mouse model of glaucoma. To investigate whether magnetic resonance (MR) imaging can be used as a non-invasive method for quantifying glaucomatous neuronal loss in the CNS.

**Methods:** Young (pre-pathologic) and aged (glaucomatous) DBA/2 mice were perfused under anesthesia with 4% paraformaldehyde. Their brains were removed and further fixed in the same solution. MR imaging of the brains was performed in a 9.4T magnet with a custom coil. The brains were cryopreserved in 30% sucrose and sectioned with a cryostat. Serial sections through the colliculi were Nissl stained. MR images and histological sections were analyzed to determine the volume of the superior and inferior colliculi using stereological methods. The ratio of superior/inferior colliculus volume (CVR) was used to determine differences between young and aged DBA/2 animals.

**Results:** CVR mean( $\pm$ SD) in aged animals as determined by histological analysis were 1.46( $\pm$ 0.22) and 1.44( $\pm$ 0.21) for right and left colliculi respectively ( $p > 0.05$ ). MR image analysis as well as comparison of CVRs of young and aged mice is ongoing.

**Conclusions:** No significant differences were detected between left and right colliculi in this group of aged DBA/2 mice. Evaluation of MR imaging as a means of non-invasive measurement of neuronal loss secondary to glaucoma is ongoing.

**The Effect of Massive Operative Transfusions on Liver Transplant Outcome.** Greg J. McKenna, Eunice Hahn, Peter J. Neuburger, Sander S. Florman, Gabriel E. Gondolesi, Sason Roayaie, Charles M. Miller, Myron E. Schwartz, and Sukru Emre. Baylor University Transplant Institute, Medical School, Recanati/Miller Transplant Institute. Baylor University Medical Center, Mount Sinai School of Medicine, Tulane University, Cleveland Clinic, Mount Sinai Hospital, New York, NY.

**Introduction:** Usually unfavorable, massive operative transfusions in liver transplant (OLT) recipients may be beneficial given a transfusions immunosuppressive nature and the effect of a de facto total plasma exchange on HBV/HCV viral loads. We examined OLT recipients with operative of >50U PRBC.

**Material and Methods:** We studied OLT recipients from 06/89-07/03 to find those with operative transfusions of >50U PRBC, analyzing demographics, complications, rejections, outcomes and postop HCV/HBV viral loads.

**Results:** 70 (48 M, mean age 50.3y, mean donor age 43.3y) of 1890 OLT recipients were transfused >50U PRBC (mean 73.6 PRBC). Early mortality was high, with 30d patient and graft survival of 57.1% and 47.1% respectively. Factors associated with massive transfusions include marginal donors (64%), previous surgery (37%), re-OLT (24%) and iatrogenic injury (7%). Re-OLT specifically for HCV had no impact (15.7% survived >30d vs 15.6% <30d). Complications were high (PNF 14%, HAT 7%, sepsis 47.9%, cardiac/MI 24%, ARDS 18.3%, re-op 31%). For >30d survivors, the 1, 3, 5-yr patient and graft survival was 97%, 88%, 71% and 97%, 84%, 67% respectively, exceeding overall 1,3,5-yr patient and graft survival for all OLTx patients (83%, 78%, 69% and 73%, 67%, 58% respectively). The incidence of transplant specific infection was 6.6%, biliary complications 6.6%, acute rejection 36% (mean 1.7 episodes). 100%

(8/8) of HBV+ and 36% (4/11) of HCV+ >30d survivors had undetectable viral loads at the latest clinical visit.

**Conclusions:** After massive transfusion many OLTx recipients die in the first 30d from complications (i.e. sepsis, ARDS, MI). However, the outcome of those that survive 30d are optimal with excellent graft and patient survival rates, low rejection rates and clearance of HBV and HCV in many recipients.

**Barriers to Lead Screening in East Harlem and Bushwick.** Rachel E. Otterson, Nathan Graber, Deborah Vasquez, Maida Galvez, Vinay K. Aakalu, and Ray Cornbill. Department of Community and Preventive Medicine, Mount Sinai Medical Center, New York, NY.

Lead damages the developing brain. Manifestations include decreased intelligence and an increase in behavioral problems. Though the incidence of lead poisoning has declined in recent years, it is still a very real problem in some New York City (NYC) neighborhoods. Crucial in the prevention of lead poisoning are the screening and education provided by well-child health care providers. Doctors in NYC are legally required to test the blood lead level (BLL) of children at 1 and 2 years of age, assess lead exposure risk by questioning until the age of 6 and obtain a BLL on any child without a previous documented BLL if they are receiving Medicaid benefits. In 2002, only 72% of children in NYC had even one BLL screening by the age of 2. In the Bushwick and East Harlem neighborhoods the rates were only 60%. Our aim in this study has been to identify barriers to universal screening for exposure to lead. We created a 30-question, self-administered survey for pediatric health care providers in East Harlem and Bushwick. Using lists compiled by the Citywide Immunization Registry, we located, contacted and distributed surveys to these practitioners. The survey addresses knowledge, belief and practice as they pertain to risk factors, services to prevent and manage lead poisoning, screening, treatment and perceived barriers. As of August 5, 2005, we have collected data from 37 out of 60 practitioners who received surveys in East Harlem and 35 out of 50 in Bushwick. We expect to continue collecting from both neighborhoods and to accrue sufficient data to represent the vast majority of practitioners in these neighborhoods, offering a generalizable data set. This information will enable us to design interventions to overcome the identified barriers.

**Genetic Variability in the Morphology and Cellular Content of the Periosteum.** Nirmimesh C. Pandey, Christopher Price, and Karl J. Jepsen. Leni and Peter W. May Department of Orthopaedics, Mount Sinai School of Medicine, New York, NY.

The periosteum is an organ that covers bone and is composed of a condensed fibrous tissue and a neurovascular network of osteogenic and fibroblastic cells. Osteogenic stimulation of the periosteal surface can potentially increase the strength and antifracture efficacy of long bones better than current agents that target endosteal and trabecular cells. Advances in understanding the nature of the periosteum can thus be of immediate use in fighting degenerative bone disease, osteoporosis, osteomalacia and periostitis. Because periosteal growth through various stages of mammalian life has a later impact on bone strength, we undertook a comparative morphological study of periosteal growth for three genetically distinct strains of inbred mice. The inbred strains, A/J, BL/6J and C3H, were examined because they exhibit unique cortical bone geometries and molecular content as previously studied by the lab. We tested the hypothesis that variability in adult bone properties are derived in part from variability in the function of the periosteum. Femurs with intact periosteum were harvested at two age intervals and administered vital tetracycline labels to study cellular kinetics. Mice were examined at 32 days, during the greatest rate of outer surface bone growth, and 63 days, during the slowing of growth. We sectioned and stained the femurs for each genotype (n=10/strain/age), and tested for variation in specific morphologic and cellular traits of the periosteum, including cell layer thickness, vascularity, regions of osteoclastogenesis, and osteogenic vs. bone reabsorbing areas along the length of the femur. Based on continued analysis, we expect to see strain- and age-specific variability in the aforementioned traits.

**The KLF6 Tumor Suppressor Regulates Expression of GADD45 $\gamma$ , a Cell Cycle Regulatory Protein, In Vivo and In Vitro.** Andrew J. Paris, Sigal Tal-Kremer, Goutham Narla, Steven Yea, Ursula Lang, Rachel Schwartz, and Scott L. Friedman. Department of Medicine/Liver Diseases, Mount Sinai School of Medicine, New York, NY.

**Hypothesis:** KLF6 regulates GADD45 $\gamma$  expression in vivo and in cultured tumor cells.

**Background:** The KLF6 tumor suppressor is a transcription factor whose activity has been linked to activation of p21 and interaction with

cyclin D1. GADD45 $\gamma$  is a growth suppressor, induced by DNA damage, which activates MTK1 causing G2/M arrest and apoptosis by increasing p38/JNK activity. GADD45 $\gamma$  was identified as a possible KLF6-regulated gene as its expression by cDNA microarray was decreased in tissues from KLF6 +/- mice compared to KLF6+/+ littermates. Specifically, in KLF6 +/- liver samples there was a 51% reduction of GADD45 $\gamma$  expression and a good correlation (R=.62) between GADD45 $\gamma$  and KLF6 mRNAs. Since KLF6 is dysregulated in 87% of human hepatocellular carcinoma (HCC), we compared GADD45 $\gamma$  mRNA expression in 18 HCC tumors to surrounding non-tumor tissue. We also extended our studies to PC3M cells, a metastatic prostate cancer cell line, by evaluating the impact of KLF6 downregulation on GADD45 $\gamma$  mRNA following stable expression of KLF6 si-RNA.

**Results:** By real time PCR and immunoblot, KLF6 mRNA and protein were significantly decreased in KLF6 +/- livers relative to the wt littermates: average KLF6 (p=0.05) and GADD45 $\gamma$  mRNAs (p=0.001) were decreased 85% (n=24 mice) in the KLF6 +/- livers. Similar results were obtained in the prostate and stomach. In 18 HCC patient samples, 89% (16/18) had decreased KLF6 mRNA expression and 72.2% (13/18) of tumors had decreased GADD45 $\gamma$  expression relative to surrounding tissue. On average, HCC tumors expressed 70% less GADD45 $\gamma$  (p=0.02). In PC3M cells, stable expression of KLF6 si-RNA reduced KLF6 mRNA by 75% and GADD45 $\gamma$  by 50%.

**Conclusions:** This data suggests a novel role for KLF6 in regulating GADD45 $\gamma$  expression. Future studies will employ promoter deletion analysis and ChIP to investigate GADD45 $\gamma$  as a direct transcriptional target of KLF6.

**High Molecular Weight Seminal Plasma Proteins Interfere with the Anti-HSV Activity of Candidate Topical Microbicides in Clinical Development.** Sarju S. Patel, Marla Keller, Ehsan Fam, Kathleen Hogarty, Natalia Chesenko, Cindy Goldberg, Ana Tuyama, Josephina Carlucci, and Betsy Herold. Department of Pediatrics and Infectious Diseases, Mount Sinai School of Medicine, New York, NY.

**Background:** HSV infection increases the risk of HIV acquisition, and coinfection with HIV and HSV increases both HIV transmission and replication. As these epidemics continue to expand, novel preventative strategies are urgently needed. This study evaluates three candidate topical microbicides, pharmacologic compounds designed for vaginal application to prevent acquisition and transmission of HIV and HSV. By binding viral glycoproteins, these compounds inhibit infection in cell culture, explants, and animal models. While these compounds retain their activity in cervicovaginal secretions, no studies have assessed activity in the presence of seminal plasma. The purpose of these studies is to test the anti-viral activity of candidate microbicides in seminal plasma.

**Methods:** Clinical specimens were obtained from consenting, healthy individuals, ages 18-50. HSV plaque assays were performed on human cervical epithelial cells. Microbicides evaluated include PRO 2000, a sulfonated naphthalene compound currently in large-scale Phase II/III trials; SAMMA, a non-sulfonated anion; and SPM8CHAS, a sulfonated amphiphilic umbrella compound. Cells were pre-treated for 1 hour at 37°C with one of the drugs diluted in PBS or cervicovaginal lavage fluid (CVL). HSV-2 isolates were then introduced in PBS, seminal plasma, or a control HEPES buffer adjusted to the pH and total protein concentration of seminal plasma. The cells were again incubated for 1 h at 37°C. Infection was monitored by counting plaques at 48 h. Results: Seminal plasma significantly interferes with anti-HSV activity of all three compounds and reduces the intrinsic anti-viral activity of CVL fluid. Fractionation studies using Centricon preps suggest that the interfering proteins are of higher molecular weight (>100kD). Mass spectrophotometry studies to identify the mediator(s) are ongoing.

**Conclusion:** Seminal fluid reduces the effectiveness of anionic microbicides in cell culture. If validated in ongoing clinical trials, identifying the protein(s) and mechanism of action should facilitate development of new formulations to overcome this phenomenon.

**Comparative Morphological Study of Tendon-Bone Insertions.** Jason S. Pruzansky, Damien M. Laudier, Vincent M. Wang, Mitchell B. Schaffler, and Evan L. Flatow. Department of Orthopaedic Surgery, Mount Sinai School of Medicine, New York, NY.

Tendon failure at its insertion into bone is a common and debilitating orthopedic injury, yet relatively little is known regarding the relationship between tendon morphology and function. Furthermore, different tendons have been shown clinically to have differing susceptibilities to damage. The aim of the current project is to compare the anatomy and morphology of normal rat patellar, Achilles, and supraspinatus tendon-bone insertions. Rat tendons were harvested fresh immediately following animal sacrifice and processed for light microscopic histological examination. To charac-

terize potential differences among tendons, collagen fiber network, cellular phenotype and density, and fibrocartilaginous dimensions will be quantified. Preliminary data has suggested distinct anatomic variants among the three different insertion sites. Among the tendons examined, the thickness of calcified fibrocartilage varies widely in shape and thickness, as does the quantity of non-calcified fibrocartilage. The cellularity noticeably changes between insertion sites and the morphometry of the tidemark differs as well. Additional samples are presently being processed for further analysis. By analyzing the morphometry of insertion sites qualitatively and quantitatively we hope to find a relationship to functional properties, which may provide insight into the etiology of clinical tendon pathologies. This research on normal tendons will also provide a foundation for future analyses of the morphologic alterations due to damage or injury.

**Effect of Community-Based Asthma Education Programs on the Asthma Outcomes of Inner-City Children: A Literature Review.** Taisha Y. Roman and Carl Johnson. Departments of Ambulatory Pediatrics and Medical Education, Mount Sinai School of Medicine, New York, NY.

**Introduction:** Asthma is the most common chronic childhood disease in the United States. Health care disparities exist for minority children with asthma. In recent years, enormous efforts have been implemented to reduce gaps in asthma care. Community-based asthma education is one intervention that aims to educate parents and children on the self-management of asthma using familiar community settings. However, despite such efforts, asthma continues to be a leading cause for child hospitalizations in poor inner-city neighborhoods such as East Harlem.

**Objectives:** To determine the extent of community-based asthma education programs for children in inner cities. Community-based asthma education is defined as educational programs NOT performed in the hospital setting. A critical review of the literature sought to determine: 1. The extent of community-based asthma education programs for children in inner cities, 2. The effectiveness of these programs, and 3. The limitations of community-based asthma education programs. **Methods:** A Medline search was conducted using the key word terms 'asthma education programs' and 'community-based,' for publications from 1995-present.

**Results:** 12 articles relevant to community-based asthma education were reviewed. Of these, 4 studies (in St. Louis, Harlem, West Philadelphia and Boston) assessed the effectiveness of community-based asthma education programs for inner-city youth. Common outcome measures were asthma control and the frequency of Emergency Department visits. Each study concluded that asthma education has a positive affect on asthma care.

**Conclusions:** Despite inner-city communities having some of the highest prevalence and hospitalization rates of asthma, there are few publications about community-based asthma education programs. This finding may play a role in asthma health care disparities for children from inner-city communities. Future interventions should focus on the implementation of effective community-based asthma education programs that use uniform and proven asthma outcome measures and should consider collaborations with parents and children living with asthma.

**Cost-Effectiveness of Probiotic Treatment in Preventing Hospital-Acquired Clostridium Difficile-Associated Diarrhea.** Allyson L. Rovetto, Cheuk Yin Lai, and Henry Sacks. Department of Community and Preventive Medicine, Mount Sinai School of Medicine New York, NY.

**Hypothesis:** Prophylactic treatment with the probiotic *saccharomyces boulardii*, a live, non-pathogenic yeast, is cost-effective in preventing antibiotic-associated diarrhea (AAD) in hospitalized patients.

**Background:** AAD occurs in 5-30% of hospitalized patients given antibiotics; the most worrisome is that caused by *clostridium difficile* (CDAD), which can cause toxic megacolon and death. A recent study gave a conservative cost estimate (not including doctors' costs nor post-hospital care costs) for CDAD of \$1.1 billion per year in the US. Increasing antibiotic resistance and recurrence rates indicate a need for a cost-effective preventive therapy. There is growing evidence that probiotics such as *s. boulardii* can prevent AAD and recurrent CDAD.

**Results:** Base-case estimates and ranges: Probability of AAD, given antibiotics 20% (5-30%); effectiveness of *s. boulardii* in preventing AAD 63% (48%-74%); increase in hospital costs \$3669 per patient with AAD; probability of relapse of AAD 20% (5-45%), mortality of CDAD 1% (0.5-4%). Major adverse events from *s. boulardii*, primarily bloodstream infections (BSI), appear rare but increasing, although firm estimates are lacking. For a course of *s. boulardii* costing less than \$50 per patient, the model yielded an average cost saving of \$712 per patient. The most likely to benefit were patients over age 65 and those hospitalized longer than 2 weeks. Sensitivity analyses showed that preventive treatment with *s. boulardii* will save lives, unless BSI occur in more than 4/1000 treated patients, which seems unlikely.

**Conclusion:** In hospitalized patients being started on antibiotics, simultaneous administration of *s. boulardii* can reduce costs by over \$700 per patient and probably save lives. Better data are needed on the rates of severe adverse events due to *s. boulardii*, but appear highly unlikely to outweigh the benefits.

**Needs Assessment of Women's Health Issues in Delhi, India Conducted with Peer Educators.** Shonali Saha, Kasturi Gupta, Suneel Vatsayan, and Henry Sacks. Departments of Medical Education, Sociology, Community and Preventative Medicine, Mount Sinai School of Medicine, New York, NY, Maxwell School of Syracuse University, Nada India Foundation.

The purpose of this study was to conduct a three-fold assessment of the needs of the women of Chattarpur by partnering with the non-profit Nada India Foundation. The study recommends programming strategies for women's health in Chattarpur, an "urban village" in South Delhi. The 10-week community needs assessment had three components: (1) What do female community members' perceive their health needs to be? (2) What are the medically determined needs? (3) What are the observed needs from a third party perspective? Researchers partnered with women of the community to train them in health related data collection, formulate a research agenda, and carry out the study, which aims to determine whether community participation improves the quality and impact of health related research. Women acted as peer educators and researchers, interviewing over fifty community members regarding health related issues. Peer educators reported findings in a weekly focus group. Appreciative inquiry was used in interviews and focus groups. Local doctors were interviewed to determine medical needs and identify discrepancies between their views and those of community members. The principle investigator lived in the community to gain a third party perspective. Preliminary findings indicate that health care services and basic necessities are inadequate for women living in Chattarpur. Women interviewed felt they lacked proper health information and wished available diagnostic and treatment services were expanded. Doctors agreed that services needed expanding but did not deem it necessary to provide any information because they consider most women in the community incapable of understanding it. In response to these findings, Nada India Foundation will continue to train peer educators in health related topics to conduct outreach that will educate women and connect them to care. Findings will be shared with community members, local health care providers, the research community, and government agencies.

**PTSD and Adherence to Treatment in HIV Patients.** Mary Ann Cohen, Jeffrey Weiss, Anupana Reddy, Erin Samuels, and Jack Gorman. Department of Psychiatry, Mount Sinai School of Medicine, New York, NY.

The present study is an examination of the relationship between Post-Traumatic Stress Disorder and nonadherence to treatment among patients with HIV. Successful HIV treatment requires a high degree of adherence, which includes taking at least 95% of scheduled HAART doses, as well as attending a multitude of regular and time consuming medical appointments. It is therefore crucial for both doctors and patients to recognize and understand PTSD and its potential impact on adherence.

**Methods:** 352 patient charts were non-systematically selected from the charts of the 1005 patients referred for psychiatric consultation by their primary HIV physicians between 1998 and 2003 and were then coded. In order to examine the associations with adherence, the medical charts of 62 of the 352 persons were reviewed for adherence data, such as number of scheduled medical appointments attended, CD 4 count and viral load in the one-year period post-psychiatric consultation.

**Results:** While the results in this small sample do not reach significance [ $\chi^2=1.9$ ,  $p=0.295$ ], there was a higher percentage of nonadherence in patients with PTSD (67%) than in patients without PTSD (42%). These preliminary findings suggest a trend such that in the larger sample of 1005 patients these differences would achieve significance, and further studies are thus warranted. If we further break the groups down into both PTSD and substance abuse ( $n=9$ , 78% non-adherent), PTSD alone ( $n=3$ , 33% nonadherent), substance use alone ( $n=17$ , 53% nonadherent), neither diagnosis ( $n=9$ , 22% nonadherent) the finding becomes somewhat more significant ( $p=0.114$ ) and points in the direction of comorbid PTSD and substance abuse being the strongest risk factor for nonadherence, suggesting this more specific question as an important area of future investigation in its own right.

**The Incidence of Iatrogenic Splenic Injury in Laparoscopic versus Open Colectomy: A Comparison Study during the Ten-Year History of Laparoscopic Colectomy at The Mount Sinai Medical Center.** Adam L. Sandler, Marcus Malek, and L. Brian Katz. Department of Surgery, Mount Sinai School of Medicine, New York, NY.

**Background:** Iatrogenic splenic injury necessitating splenectomy is a well-recognized, and potentially serious, complication of colon resection. Iatrogenic splenectomy is associated with significant morbidity and mortality, including bleeding and the Post-Splenectomy Sepsis Syndrome, which results from increased susceptibility to encapsulated organisms. Our study aims to compare the incidence of iatrogenic splenic injury in laparoscopic colon resection with that of open colon resection over a ten-year period at Mount Sinai.

**Hypothesis:** An initial review of medical records and spleen specimens analyzed by the Department of Pathology suggests a higher incidence of iatrogenic splenectomy during open colon resections. We hypothesize that, controlling for other factors, including the larger volume of open procedures, the higher incidence among patients undergoing the open procedure is due to its more invasive nature as compared to the laparoscopic approach.

**Study Methods and Design:** We conducted a retrospective chart review of all the medical records of Mount Sinai patients who underwent colectomy in the last ten years. The goal was to identify those who suffered iatrogenic splenic injury as a result of the procedure. Confirmatory evidence of splenic injury was garnered from pathology reports of splenic injury following colon surgery. Finally, we hope to relate our findings to the relevant clinical literature on iatrogenic splenic injury.

**Results/Significance:** As a result of our review, we found twelve cases of iatrogenic splenectomy occurring during open colectomy and none during laparoscopic colectomy. The indication for colon resection in the patients who suffered iatrogenic splenic injury included colon adenocarcinoma, ischemic bowel, familial adenomatous polyposis, and diverticulitis. Laparoscopy, in general, has many well-recognized advantages over open procedures, including post-operative recovery time and length of stay. This retrospective review of our experience at Mount Sinai presents yet another potential advantage of laparoscopy during colon resection.

**Association of Surgical Education Database.** Celia M. Divino, Scott Q. Nguyen, Luke R. Scalcone, and Linda P. Zhang. Department of General Surgery, Mount Sinai School of Medicine, New York, NY.

**Purpose:** Propose an adjunct to conventional surgical education for medical students and surgical residents.

**Background:** The Association of Surgical Education (ASE) plans to pilot a database composed of various surgical topics. A gamut of surgical topics are represented in PowerPoint format. These power points will aid in the education of surgical residents and medical students. Senior residents, chief residents, or attending faculty may access specific surgical topics via the ASE website (<http://www.surgicaleducation.com/>). All power points are downloadable Microsoft PPT formatted files. The PowerPoint presentation may be used as basis for discussion or formal lecture.

**Methods:** The construct of the database is based on uniformity and systematic presentation of surgical material. Uniformity is maintained via skeleton power points—this assures continuity from presentation to presentation. All database power points have been standardized including background, clinical presentation of information, charts, etc. Each PowerPoint presents surgical cases in clinical vignette style. The case presentation challenges the student/resident to think clinically and propose a logical management and work-up of a simulated patient.

**Results:** Included is a list of completed presentations: Incidental Adrenal Mass: Rebecca Evangelista, MD Jaundice: Hilary Sanfey Inguinal Hernia: Karen Brasel, MD, MPH Abdominal Pain: Barry Mann, MD; Philip Wolfson, MD Intussusception: Philip Wolfson, MD Care: Kimberly Ephgrave, MD, FACS Acute Mesenteric Ischemia: Scott Q. Nguyen, MD; Celia M. Divino, MD Pulmonary Embolus: Linda P Zhang; Scott Q. Nguyen, MD; Celia M. Divino, MD Tension Pneumothorax: Luke R Scalcone; Scott Q. Nguyen, MD; Celia M. Divino, MD.

**Conclusions:** The preliminary compilation of PowerPoint presentations is promising. Various contributors from several medical academic institutions have complete pilot PowerPoint presentations. The database is slated for trial in the near future. A component of the database will allow for revision/comments regarding power points.

**Investigating Parents' Knowledge of Pediatric Environmental Health Issues.** Melissa L. Schapiro, and Leo Trasande. Departments of Pediatrics, and Community and Preventive Medicine, Mount Sinai School of Medicine, New York, NY.

Exposure to environmental pollutants is linked to a number of pediatric health problems, including asthma, allergies, and learning disorders. Par-

ents who are unaware that pollutants can harm children are unlikely to take steps to protect their children from exposure, so it is important to ascertain parents' knowledge. Our goal is to study parents' concerns about pollutants, as well as their understanding of the potential effects these pollutants can have on their children's health. We will visit pediatric clinics in two neighborhoods, one with low SES and one with high SES, to administer a questionnaire to 100 parents of children ages 2–12 years. We will compare the responses of parents living in the low and high SES neighborhoods, as well as the responses of parents whose children do and do not suffer from the various health problems commonly linked to pollutant exposure. We hypothesize that most parents do not understand some of the connections between pollutants and children's health. This study is intended to enable us to make recommendations for future community education campaigns on children's health issues. Additionally, we believe findings from this study may provide new information for local government officials to better understand community members' concerns about pollution and its impact on children's health.

**Pilot Study of the Use of Intravenous Immunoglobulin in HIV-Associated Myelopathy.** Lauren D. Schiff, Katia Cikurel, David Dorfman, and David Simpson. Departments of Neurology and Psychiatry, Mount Sinai School of Medicine, New York, NY.

HIV-associated myelopathy is characterized by white matter vacuolization predominantly of the posterior and lateral columns of the thoracic spinal cord. It is the most common cause of spinal cord disease in HIV/AIDS; however there is no effective treatment currently known. Although the etiology of HIV-myelopathy is unknown, it shares similarities with HTLV-1-associated myelopathy which has been shown to improve with intravenous immunoglobulin (IVIg). Based on this evidence we sought to evaluate the safety and efficacy of IVIg treatment in patients with HIV-associated myelopathy. Seventeen patients with HIV-associated myelopathy received 2 daily infusions of IVIg twice over a 56-day study period, on days 1–2 and 29–30. Patients were evaluated at baseline and at days 14, 28, and 56 for changes in spasticity, strength, deep tendon reflexes, sensation, urinary function, and clinical disability. We found a statistically significant improvement in composite Medical Council Research (MRC) strength scores 28 days following the first infusion ( $p = 0.021$ ). Although the second infusion did not produce a statistically significant improvement in strength, there was no significant reduction from peak strength. We found no other significant changes from baseline. These data suggest that IVIg may improve and maintain strength in patients with HIV-associated myelopathy. Based on this pilot data, we suggest a controlled study of the efficacy of IVIg in treating HIV-associated vacuolar myelopathy.

**Internal Hernias: Clinical Presentation, Classification, and Management.** Avi Schlager, Saber Ghiassi, and Celia Divino. Department of General Surgery, Mount Sinai School of Medicine, New York, NY.

**Introduction:** Internal hernia (IH) is the protrusion of a viscus through a peritoneal or mesenteric aperture. They account for up to 1% of all cases of small bowel obstruction and may be increasing in frequency. Symptoms of IH are often vague and nonspecific making clinical diagnosis difficult. Delay in diagnosis may result in a catastrophic outcome. This study describes the characteristic clinical presentation, the subtypes, and the surgical management of 49 cases of surgically proven IH at The Mount Sinai Medical Center.

**Methods:** A retrospective chart review of patients at our institution with the diagnosis of IH between 1994 and 2004 was conducted. Patients with previous Roux-en-Y procedures were excluded. The review yielded 49 cases of surgically confirmed IH. Data obtained included clinical signs and symptoms, radiographic findings, surgical management, and subtypes of IH.

**Results:** The most common subtype of IH was transmesenteric (60.0%), followed by paraduodenal and transomental (10% each). A history of prior abdominal surgery was present in 83.7% of cases. The majority of cases presented with obstructive symptoms of abdominal pain (79.6%), nausea (77.6%) and vomiting (71.4%). The most common physical exam findings were abdominal tenderness (81.6%) and distention (46.9%). The most common radiographic findings were dilated loops of small bowel (54.2% of obstructive series, 56.0% of CT scan, and 62.5% of Small bowel series), and transition zones (40% of CT scans).

**Conclusion:** Previously, paraduodenal hernias were reported as the most common type of IH. This study demonstrates that transmesenteric hernias are the most prevalent types of IH, especially in patients with previous abdominal surgeries. These patients often present with clinical and radiographic findings of small bowel obstruction. CT is not sensitive for detecting transmesenteric hernias. Clinicians should be mindful of IH in patients with previous abdominal surgeries and those with chronic abdominal pain without clear etiology.

**The Impact of Donor Surgery Organ Extraction Time on Transplant Liver Allograft Outcomes.** Avi Schlager, Anthony Patrello, Gautam Siram, and Greg McKenna. Transplant Surgery, Mount Sinai School of Medicine, New York, NY, Baylor University Medical Center.

**Introduction:** During a transplant donor harvest, there is a period after flushing the liver with cold preservation fluid where the organ is dissected free from the surrounding tissues and removed from the body. Often during this extraction time, the organ may be sub-optimally cooled and preserved. Cold ischemia time, the time the organ spends on ice prior to implantation, and warm ischemia time, the time from the start of organ implantation to reperfusion have been shown to affect allograft outcome. No reports have described the impact of Organ Extraction Time on donor allograft outcome.

**Methods:** We retrospectively obtained the data regarding donor cross-clamp times and organ removal times for over 900 cadaveric donor allograft livers for transplants performed at The Mount Sinai Hospital as well as the labs (Peak and Day-7 AST/ALT/T-Bil/PT). Data was also obtained retrospectively from a prospectively obtained database regarding donor parameters, patient and graft survival. Multivariate Cox-regression analysis was performed on the data. Results: Donor organ extraction times >30 min was associated with significantly improved 1-yr, 5-yr and 10-yr patient survival ( $p=0.001$ ) and graft survival ( $p=0.01$ ). Organ extraction time >30 min was associated with improvements in peak AST (585.5 vs. 666.5  $p=0.04$ ) and peak T-bili (5.40 vs. 6.3  $p=0.007$ ). Univariate analysis showed organ extraction time <30 min to be a predictor of worse allograft patient survival (Hazard ratio 1.45 with 95% CI Limits) and graft survival (Hazard ratio 1.30 with 95% CI Limits 1.057-1.607) Multivariate analysis showed organ extraction time <30 min to be an independent predictor of worse allograft function (Hazard ratio 1.36 with 95% CI Limits 1.036-1.79).

**Conclusion:** The data shows that not only does prolonged donor organ extraction time (>30 min) not worsen survival, but rather results in improved patient and graft survival. The explanation for this finding is currently being investigated.

**A Video Project to Improve Medical Communication between Ethiopian Immigrant Patients and Health Care Providers in Israel.** Joshua Schulman-Marcus, Nurit Guttman, and Anat Jaffe. Departments of Communications and Endocrinology, Mount Sinai School of Medicine, New York, NY, Tel Aviv University, Hillel Yaffe Medical Center, Hadera, Israel.

The immigration to Israel of nearly 100,000 Ethiopian Jews since 1985, most of whom came from rural villages, has presented serious communication challenges within the Israeli medical system. Many of the Ethiopian immigrants had no knowledge of Western perspectives on health or of health problems such as chronic diseases, preventive medicine, medical specialization, and nutrition. High rates of illiteracy, limited language proficiency, and different expectations of the doctor-patient relationship have led to widespread communication deficiencies that reduce the quality of care and medical outcomes. In order to aid health professionals in overcoming communication challenges with Ethiopian patients, a series of short videos will be made that both highlight common causes of miscommunication and suggest improvements. To assure that the content of the videos be as realistic as possible, interviews with doctors, nurses, patients, and health care liaisons were conducted at nine clinics across Israel that treat many Ethiopian patients. The analysis of the interview data provided incidents that will serve as the basis for the video scenarios. Several common sources of frustration and/or miscommunication were identified: 1) language barriers contributing to neglect of patient needs, 2) patients having difficulty describing their symptoms, 3) patients not understanding the purpose or instructions for prescriptions and medical tests, 4) patients frustrated because their physician didn't touch them or look at them directly, 5) not following treatment recommendations for chronic diseases such as Type II diabetes which did not exist in Ethiopia, 6) patient lack of understanding of the relevance to disease of preventive medicine and diet. From these findings several prototype scenarios will be filmed and shown to both Israeli health professionals and members of the Ethiopian immigrant community. This project is also relevant to all health professionals coping with cultural barriers to effective communication and care as a result of immigration.

**Arab American Health Needs Assessment and Outreach.** Sara U. Schwanke, Mary E. Foley, Elizabeth J. Garland, and Philip J. Landrigan. Department of Community and Preventive Medicine, Mount Sinai School of Medicine, New York, NY.

**Background:** In the last five years, Arab American (AA) communities have come under greater scrutiny than ever before. A thorough literature review, however, yields limited research regarding the health needs of Arab residents in the US, including those of the AA community in New

York City (NYC). As the number of Arab Americans in the New York metro area continues to grow, and increasing public attention is directed toward Arab communities throughout the US, more information must be obtained.

**Hypothesis:** AA in NYC face unidentified barriers to health care services that may be influenced by a combination of social, economic, and cultural factors.

**Methods:** The focus group interview is the primary research method employed. The focus group interview guide, developed from individual interviews with community leaders and social outreach providers, explores personal health perceptions and needs among community members. Two focus groups, segregated by gender, will be held at central locations in each of two Arab neighborhoods in NYC. Eligible participants must be at least eighteen years old, have immigrated to the US from an Arab country within the last 20 years, and have lived in one of the study neighborhoods at least two years.

**Results:** Focus group discussions will be analyzed for a variety of factors, including socioeconomic status, immigration history, proximity to care, language capabilities, and cultural beliefs that may affect accessibility and utilization of health care by members of the AA community in NYC. Given the qualitative nature of the research method, the results will be presented primarily in summary form.

**Conclusions:** Preliminary discussions with community leaders suggest that mental health services for the AA community are severely inadequate. A lack of Arabic-speaking providers is another frequently cited problem. The NYC AA community would benefit from health care services specifically designed to address such unmet needs.

**The Effect of TFF1 Mutations on Malignant Behavior of Human Gastric Cancer Cells.** Andrew D. Schweitzer, Jie-yu Zhang, Xianyang Yio, and Steven Itzkowitz. Departments of Medicine/Gastroenterology and Oncological Sciences, Mount Sinai School of Medicine, New York, NY.

Trefoil factor family-1 (TFF1) is a tumor suppressor gene in the stomach. TFF1 knockout mice all develop adenomas, with 30% progressing to invasive carcinoma. One study described eight mutations of TFF1 among 61 human gastric cancers. Two such mutations, E13K and A10D, were shown by us to lose their growth suppressor function while enhancing cancer cell invasion. This is the first example of a functional role for a mutation in any trefoil factor. The T8I and T8K mutants reported in human gastric cancer have not yet been characterized. The aim of this study is to determine how mutations at the eighth residue of TFF1, T8K and T8I, affect the behavior of human gastric cancer cells. The changes from hydrophilic threonine to either hydrophobic isoleucine (T8I) or to positively-charged lysine (T8K) are hypothesized to change the biological function of TFF1. T8I and T8K TFF1 mutants were generated by site-directed mutagenesis of E. coli cells (SURE II) that had been transfected with wild type TFF1, sequenced to verify correct point mutation, and purified from the cells. Once sufficient amounts of recombinant protein are produced, T8K and T8I will be tested in various in vitro assays including cell proliferation, apoptosis, motility and invasion through a reconstituted basement membrane (matrigel). These experiments will determine whether point mutations of the eighth residue of TFF1 that have been described in gastric cancer have functional consequences. If so, experiments will be conducted to analyze the effects of these mutations in vivo and to analyze how these mutations affect the structure of TFF1 using computational methods.

**Risk Factors for Hospitalization in the First Year of Enrollment in a Home-Based Primary Care Program.** Alexandra Shaw, Jeremy Boal, Joan Penrod, Tsivia Hochman, Katherine Ornstein, and Linda DeCherrie. Department of Medicine, GRECC, Brookdale Department of Geriatrics and Adult Development, Mount Sinai School of Medicine, New York, NY, Bronx VA Medical Center.

**Background:** Home-based primary care is growing as a model of care for homebound patients. One of the goals of such programs is prevention of unnecessary hospitalization.

**Objective:** To identify risk factors for hospitalization within the first year of enrollment in a home-based primary care program.

**Methods:** We used a retrospective chart review of n=660 patients in an urban visiting doctors program enrolled between 1/03 and 6/04 to collect demographic characteristics and health and functional status of patients at enrollment. We used a multi-variable logistic regression to examine these baseline factors as predictors of hospitalization within 12 months of enrollment.

**Results:** Males (1.9, 95% CI, 1.3-2.8), those recently hospitalized (1.6, 95% CI, 1.0-2.4) and Latinos (1.7, 95% CI, 1.1-2.7) were at increased risk of hospitalization. Patients with palliative goals of care (0.5, 95% CI, 0.3-0.9) were less likely to be hospitalized in the first 12 months after enrollment. In a subgroup analysis of patients who had no recent hospital-

izations, males (1.8, 95% CI, 1.1-2.9), Latinos (1.7, 95% CI, 1.0-2.7) and those with 7 – 8 ADL limitations (1.8, 95% CI, 1.0-3.0) were at increased risk of hospitalization. Those with palliative care goals (0.4, 95% CI, 0.2-0.8) and urinary incontinence (0.7, 95% CI, 0.4-1.0) were less likely to be hospitalized.

**Conclusions:** Patients who are sicker at enrollment, i.e. those with more comorbidities and recent hospital stays, are at higher risk of hospitalization and may benefit from interventions to prevent hospitalization. Patients with palliative care goals are less likely to be hospitalized, which is consistent with common palliative goals. Gender and ethnicity influence hospitalization risk. More research is needed to examine potential causes for the link.

**Cognitive Enhancement Through Central Thalamic Deep Brain Stimulation.** Prasad R. Shirvalkar, Malika I. Seth, Nicholas D. Schiff, and Daniel G. Herrera. Departments of Psychiatry, Neurology and Neuroscience, Mount Sinai School of Medicine, New York, NY, Weill Cornell Medical College.

The biological substrates of consciousness must support states of perceptual awareness, working memory and directed attention. Previous reports have established that the central thalamus (intralaminar nuclei (ILN) and paralaminar regions) links brainstem arousal systems to cerebral cortical and basal ganglia networks crucial to the organization of wakeful behaviors; this region has also been implicated in supporting normal and pathological thalamocortical rhythms. Therapeutic treatment of neuropsychiatric disorders increasingly relies on Deep Brain Stimulation of various nuclei, although knowledge of underlying mechanisms is limited. Using precise behavioral assays and postmortem histological processing of animal brain tissue, it is possible to investigate the impact of electrical stimulation in this system. Here we focus on the central thalamus which has been proposed as a Deep Brain Stimulation target for the treatment of impaired cognitive function following non-progressive brain injuries. We studied behavioral and gene expression effects of electrical stimulation of the centrolateral nucleus (CL) of the intralaminar nuclei of the rat thalamus. Unilateral high-frequency (100 Hz) electrical stimulation of CL in awake animals produced significant improvements in performance and learning of a visual object recognition task compared to control animals. To evaluate the functional activation patterns associated with CL stimulation, we examined patterns of immediate-early gene (IEG) expression in cortical and subcortical structures. In a separate series of experiments, similar electrical stimulation of CL produced ipsilateral upregulation of *c-fos* and *zif268* expression with laminar specificity in the motor cortex (mCtx), anterior cingulate cortex (ACC) and caudate-putamen (CP), and bilateral elevation in hippocampi at two hours following stimulation. In vivo stimulation of CL activates a wide cerebral network and may influence basic cognitive processes associated with attention and memory.

**Role of Vpr in HIVAN Pathogenesis.** Alexandra Snyder, Mohammad Husain, Michael J. Ross, Paul Klotman, and Mary Klotman. Department of Medicine, Infectious Diseases, and Nephrology, Mount Sinai School of Medicine, New York, NY.

HIV-associated nephropathy (HIVAN), primarily affecting HIV-infected people of African descent, leads to glomerulosclerosis and microcystic tubulointerstitial disease. Although the mechanism of HIV-1 entry remains unclear, HIV-1 RNA has been found in renal epithelial cells. In HIVAN, glomerular epithelial cells, or podocytes, show a dysregulated phenotype, including dedifferentiation, hyperproliferation and apoptosis, as do renal tubular cells. Previously we have shown that HIV-1 accessory protein Nef is the major determinant of HIVAN pathology, while others report that Vpr causes mild glomerulosclerosis. We want to investigate a specific role for Vpr in renal epithelial cells. Vpr was cloned into a lentiviral vector (pHR-CMV-IRES-GFPdeltaB), which was then used to produce pseudotyped virus by transfection of 293T cells, providing gag/pol and a vesicular stomatitis virus glycoprotein (VSV.G) envelope in trans. The pseudotyped virus was used to infect immortalized human proximal tubular epithelial cells (HPT-1, established in our lab) under differentiated and undifferentiated conditions. Preliminary data demonstrates an increased apoptotic index among Vpr-infected undifferentiated HPT1 cells relative to controls. Vpr has been shown to induce G2 arrest and/or apoptosis depending on cell type, however, its mechanism has not been elucidated in kidney epithelial cells. Recently, in our lab ubiquitin-like protein Fat10 has been shown to be upregulated in HIV-infected HPT-1 cells. In ongoing studies we will investigate the role of Fat10 and Fas/FasL, which is upregulated in diseased epithelium, in the mechanism of Vpr-induced apoptosis. We hypothesize that together Nef and Vpr may induce the proliferation and apoptosis that ultimately lead to the glomerulosclerosis and tubulointerstitial disease characteristic of HIVAN.

**The Regulation of Sprouty1 in Prostate Cancer.** Gabriela Soriano, Analisa DiFeo, John Martignetti, Goutham Narla, Scott Friedman, Jonathan Licht, and Debra Morrison. Departments of Medicine, Hematology, Oncology, Human Genetics, and Liver Disease, Mount Sinai School of Medicine, New York, NY.

Abnormal response to growth factor signaling is a major contributor to the development and progression of many cancers. Sprouty1, a general inhibitor of the receptor tyrosine kinase/Ras/Map kinase signal transduction cascade, has been shown to be down-regulated in a variety of cancers, including prostate cancer. The attenuation of Sprouty1 expression in prostate cancer may be due to transcriptional regulation or epigenetic silencing. Previously, Sprouty1 was demonstrated to be directly regulated by the Wilms' tumor suppressor gene WT1 in the kidney. KLF6, a tumor suppressor gene in the same family as WT1, also regulates the Sprouty1 promoter in transient transcription assays. Interestingly, KLF6 is lost or mutated in a large percentage of prostate cancer cases. Due the correlation between KLF6 and Sprouty1 expression and the presence of a KLF6 binding site in the Sprouty1 promoter, we hypothesized that KLF6 regulates Sprouty1 in the prostate by directly binding to its promoter. To demonstrate a connection between these two proteins, KLF6 was transiently over-expressed in the prostate cancer cell lines PC3 and LNCaP. A variable effect on the level of Sprouty1 expression was observed by qRT-PCR. Subsequently, the opposite experiment was performed. PC3 cells were treated with small interfering RNA (siRNA) oligos to knockdown KLF6 expression. Preliminary data suggests that Sprouty1 levels decrease by approximately 30% following an 80% reduction in KLF6 expression. Given this conflicting data it is not yet possible to draw a conclusion. Next, we considered that silencing of Sprouty1 is through hypermethylation of CpG islands located in the Sprouty1 promoter. Therefore, PC3 cells were treated with the demethylating agent 5-aza-2-deoxycytidine, which activates genes that may have been abnormally hypermethylated in the process of tumorigenesis. A 2–3 fold induction of Sprouty1 was observed by qRT-PCR. Future studies will investigate this epigenetic mechanism.

**Extended Criteria Donor Livers and Graft Outcome.** Anne M. Stey, Jon Chan, Ilhan Karabicak, and Sukru Emre. Recanti Miller Transplant Institute, Liver Transplant, Mount Sinai Hospital, New York, NY.

The use of extended criteria organs offers hope to transplant candidates. We analyzed a number of criteria that may determine the success of these organs as grafts including donor age, BMI, LFTs, serum sodium and bilirubin levels. Linear regression was used to determine the correlation of each of the above with postoperative length of stay, postoperative graft function as determined by postoperative LFTs and prothrombin time and length of host survival in days. We found that donor age is negatively correlated with host survival in days ( $m = -7.9 \pm 1.74$ ,  $p = 0.0001$ ). It was not related to postoperative length of stay or any parameters of postoperative graft function. Similarly, donor BMI showed a negative correlation with host survival which approached significance ( $m = -.27 \pm .17$ ,  $p = 0.11$ ). However, it was also negatively correlated with postoperative length of stay ( $m = -5.5 \pm .88$ ,  $p = 0.0001$ ). This may display the dichotomous effect of energy storage in the liver. Interestingly, measures of donor liver function, namely donor serum LFTs and bilirubin, were not correlated to postoperative graft function, host survival or postoperative length of stay. There was, however, a clear negative correlation between donor serum sodium and all measures of postoperative graft function (SGPT: $m = 18.9 \pm 7.6$ ,  $p = 0.01$  SGOT: $m = 24.5 \pm 9.2$ ,  $p = 0.008$  prothrombin time: $m = 15.04 \pm 6.6$ ,  $p = 0.02$ ). Donor hypernatremia has been cited in the literature to predispose grafts to dysfunction. However, this correlation did not extend to a correlation with survival or postoperative length of stay. In conclusion, donor age, hypernatremia and elevated BMI related to poor host survival or postoperative graft function. Unexpectedly measures of donor liver function were unrelated. This reaffirms that we must challenge what we consider factors for extended criteria organs.

**The Effect of Weightlifting Exercises on Intraocular Pressure in Glaucoma Patients.** Leah R. Strugatz, Lee A. Polikoff, Raul Chanis, Ashish Toor, and Janet B. Serle. Department of Ophthalmology, Mount Sinai School of Medicine, New York, NY.

**Purpose:** Increased intraocular pressure (IOP) is the most important risk factor in the development and progression of glaucoma. When performing certain weightlifting exercises, IOP elevation occurs due to increased choroidal volume and obstructed venous outflow. As more people perform routine weightlifting exercises, it is important to assess the effects of weightlifting exercises on IOP in glaucoma patients.

**Methods:** Previously diagnosed glaucoma patients who performed weightlifting exercises at least twice a week were enrolled. Eleven patients (10 Caucasian and 1 African American; mean age  $\pm$  SD: 63.7  $\pm$  12.6

years), all on medical therapy for glaucoma, have participated in the study. Diagnoses included POAG 5, PDS 2, NTG 2, OHT 1, and CACG 1. IOP was measured using a pneumatometer. Five repetitions were performed of each exercise: bench press, leg press, triceps extension, seated rows and stomach crunches. IOP for both eyes were averaged for pre-exercise, and one minute post-exercise measurements. Only the OD was used for intra-exercise IOP calculations. Statistical analysis was performed using a two-tailed t-test.

**Results:** Post-exercise IOP was similar to pre-exercise IOP ( $p=0.149$ ), following bench press, seated rows, stomach crunch and leg press. IOP decreased ( $p=0.029$ ) post-triceps extensions compared to pre-exercise. IOP increased intra-exercise for bench press ( $p=0.016$ ), from a mean of 18.32 mmHg to 21.05 mmHg, as compared to pre-exercise. Seated row ( $p=0.042$ ) IOP also increased intra-exercise, compared to pre-exercise IOP, from a mean of 15.27 mmHg to 16.91 mmHg.

**Conclusions:** Five repetitions of exercises, such as bench press, leg press, triceps extension, seated rows and stomach crunches do not appear to raise IOP in glaucoma patients within one-minute following exercise. Certain exercises, such as flat bench press and seated rows, cause transient increases in IOP. The effects of multiple repetitions during many sets of weightlifting exercises are still unknown.

**Predictors of Mitochondrial Toxicity among Treatment-Experienced HIV/HCV Co-infected Patients.** Malini D. Sur and Douglas T. Dieterich. Department of Medicine, and Liver and Gastroenterology, The Mount Sinai Medical Center, New York, NY.

**Question:** Is the risk of mitochondrial toxicity (MT) among treatment-experienced HIV/HCV co-infected patients increased by use of nucleoside reverse transcriptase inhibitors (NRTIs), age, or severity of hepatic fibrosis and steatosis?

**Background:** Mitochondrial toxicity of nucleoside analogs is a serious clinical concern in HIV treatment today. These drugs include NRTIs used in antiretroviral therapy and ribavirin used with peginterferon to treat Hepatitis C virus (HCV) infection. Patients receiving treatment for both HIV and HCV infection have been shown to be at an elevated risk for MT. The biochemical aging process, potentially linked to increased mitochondrial oxidative stress, may further exacerbate the risk of MT in the HIV/HCV co-infected patient, along with hepatic fibrosis and steatosis.

**Methods:** We examined laboratory data for 102 HIV/HCV co-infected patients, previously unsuccessfully treated for HCV, enrolled in Hepatitis Resource Network Study 004 and assigned to receive peginterferon alfa-2a and ribavirin. Serum lactate values at weeks 0, 12, and 24 after start of treatment were used to identify patients with hyperlactatemia ( $>2.2$  mmol/L), an indicator of MT. Binomial logistic regression was used to determine if hyperlactatemia was associated with age over 50 years, concomitant use of ddI or d4T, and baseline hepatic fibrosis and steatosis.

**Results:** Thirteen patients (13.5%) at week 0, 12 patients (12.5%) at week 12, and 11 patients (11.5%) at week 24 showed hyperlactatemia. Regression analysis showed neither age, use of ddI or d4T, nor severity of fibrosis or steatosis to be significantly associated with hyperlactatemia.

**Conclusions:** We did not observe a significantly greater risk of developing hyperlactatemia among treatment-experienced HIV/HCV co-infected patients who were above 50, used ddI or d4T, or had greater fibrosis or steatosis at start of HCV therapy. MT remains a concern in co-infected patients, and further research to identify risk factors for developing MT is recommended.

**It's Like Crossing a Bridge: Barriers to Physicians Discussing Deactivating Implantable Defibrillators at the End of Life.** Ezra N. Teitelbaum, Nathan E. Goldstein, Davendra Mehta, Elizabeth H. Bradley, and R. Sean Morrison. Department of Medicine/Cardiology, Brookdale Department of Geriatrics. Mount Sinai School of Medicine, New York, NY, Yale University School of Epidemiology and Public Health, Boston, MA.

**Background:** Implantable cardioverter defibrillators (ICDs) can prevent premature death from arrhythmias. However in the setting of advanced illness, these devices might make the dying process more painful. To avoid this, some patients may wish to have their device deactivated. Research has shown that in the context of other end-of-life discussions, physicians broach the subject of ICD deactivation with less than 30% of patients.

**Objective:** To identify the factors that impede physicians from engaging in ICD deactivation discussions.

**Methods:** Electrophysiologists, cardiologists and generalists (internists and geriatricians) were interviewed using open-ended questions to determine physicians' past experience with discussing deactivating ICDs. Transcripts of these interviews were analyzed using the qualitative method of constant comparison until no new concepts emerged in successive conversations (i.e., thematic saturation).

**Results:** 11 physicians (6 women and 5 men) from three states were interviewed. Physicians believed that conversations about deactivating

ICDs were different than other discussions regarding end-of-life care because once the device had been deactivated, it was "like crossing a bridge" from which there was no return. Barriers to discussing device deactivation included the absence of an established physician-patient relationship, difficulty applying the theoretical importance of such discussions to practical clinical scenarios and a lack of training in end-of-life care.

**Discussion:** A variety of factors deter physicians from initiating conversations about ICD deactivation. Findings from this project can be used to develop strategies to enhance the quality and frequency of physician initiated ICD deactivation discussions.

**Cardiac Involvement and Rate of Disease Progression in Fabry Disease—Hemizygous Males And Heterozygous Females.** Jeremy J. Thaden, Maryam Banikazemi, and Martin Goldman. The Zena and Michael A. Wiener Cardiovascular Institute, The Department of Human Genetics, Mount Sinai Medical Center, New York, NY.

Fabry Disease is an X-linked lysosomal storage disorder that results from a deficiency of the enzyme alpha galactosidase A. Afflicted individuals often have angiokeratomas, peripheral pain, hypohidrosis, and suffer from a progressive small-vessel disease of the kidney, heart, and brain. Disease progression is relatively well characterized in hemizygous men, but less is known about the clinical manifestations in heterozygous women. This study will involve analyzing a database of collected echocardiograms to evaluate disease and disease progression in hemizygous males and heterozygous females. Several studies have indicated that left ventricular hypertrophy and diastolic dysfunction serve as reliable markers of disease progression in affected individuals. We expect that hemizygous males and heterozygous females will have greater left ventricular mass and diastolic dysfunction compared to normal. Additionally, because of the disease's X-linked inheritance, we expect the disease to progress more rapidly in hemizygous males than in heterozygous females. Finally, because there is a progressive and lifelong accumulation of glycolipid in afflicted cells, we expect that, among the same gender, older individuals will be more severely afflicted than younger individuals. We will compare transmitral flow (E/A ratio), an indicator of diastolic function, and left ventricular mass to age and gender-matched controls in order to characterize the changes in diastolic function and left ventricular mass relative to normal. Also, by comparing heterozygous females to age-matched hemizygous males, we will be able to better characterize disease pathology in men relative to women. Additionally, by comparing rate of change of these same parameters between hemizygous men and heterozygous women, we will be able to evaluate the rate at which the disease progresses in women with respect to men. Finally, by comparing younger individuals with older individuals of the same gender, we will be able to evaluate how the disease progresses with respect to age.

**The Effect of Medicaid Eligibility Policies on Medicaid Enrollment by Low-Income Seniors.** Ryan C. Ungaro and Alex D. Federman. Department of Medicine/General Internal Medicine, Mount Sinai School of Medicine, New York, NY.

**Background:** Many elderly Medicare beneficiaries who are eligible for Medicaid are not enrolled. With states looking to reel in rising Medicaid spending, various policy changes have been made to curtail Medicaid growth. However, little is known about the effect of state policies on Medicaid enrollment for Medicare beneficiaries.

**Objectives:** To determine the effect on Medicaid enrollment by Medicare beneficiaries of the Omnibus Budget Reconciliation Act (OBRA) of 1986, which liberalizes income thresholds, and section 209(b) of the Social Security Act Amendments of 1972, which allows states to establish more restrictive income and asset eligibility criteria. In addition, the effect of requiring separate State Supplemental Income (SSI) and Medicaid applications on Medicaid enrollment was investigated.

**Methods:** Cross-sectional analysis of the 2001 Medicare Current Beneficiary Survey examining Medicare beneficiaries 65 or older with incomes less than 100% of the federal poverty level. We modeled Medicaid enrollment as a function of residence in states applying OBRA or 209b policies, controlling for demographic and health status characteristics. Medicaid enrollment was also modeled as a function of residence in states with separate SSI and Medicaid applications.

**Results:** Restrictiveness of state Medicaid eligibility criteria did not appear to affect Medicaid enrollment for low-income seniors. The adjusted relative risk ratio (RR) of Medicaid enrollment for seniors living in OBRA states was 1.18 (95% CI 0.89, 1.54). The RR for subjects living in 209(b) states was 1.13 (95% CI 0.73, 1.68). The RR for subjects living in states with separate applications for SSI and Medicaid was 1.08 (95% CI 0.73, 1.55).

**Conclusions:** Our results suggest that 209b and OBRA policies may not significantly affect Medicaid enrollment by low-income seniors. The separation of SSI and Medicaid applications also may not affect enroll-

ment. More research is needed to identify barriers to Medicaid enrollment for this population.

**Clinical, Hormonal, and Genetic Variations in Male Pseudohermaphroditism.** Peter J. Vasquez, Susan W. Baker, Robert C. Wilson, and Maria I. New. Department of Pediatric/Endocrinology, Mount Sinai School of Medicine, New York, NY.

**Objectives:** This study aims to characterize the clinical and hormonal profiles of subjects with male pseudohermaphroditism, and to correlate these findings to the underlying molecular genetic defect.

**Background:** Male pseudohermaphroditism (MPH) is defined by the presence of a 46,XY karyotype, male gonads, and ambiguity of the external and/or internal genitalia caused by incomplete virilization *in utero*. MPH can result from decreased synthesis of testosterone or from the impairment of response to androgens. Defects in androgen action are the most common cause and include mutations in the androgen receptor gene and mutations in the steroid 5 $\alpha$ -reductase 2 gene. Defects in androgen synthesis are due to autosomal recessive mutations that impair any of the enzymatic reactions involved in the conversion of cholesterol to testosterone, as well as impaired stimulus of testosterone production due to defects in the hCG/LH receptor. The clinical and hormonal profiles of male pseudohermaphrodites are heterogeneous and may be correlated to specific genetic mutations. To date, the correlation of phenotype and genotype in MPH has not been fully characterized. We are evaluating an established clinic population of male pseudohermaphrodites. Retrospective medical record review is being done to obtain relevant clinical and hormonal data. If possible, subjects are asked to undergo repeat clinical, hormonal, and genetic evaluation to obtain current information. The data will be compiled and analyzed to identify genotype/phenotype correlations. **Results:** At this time we are in the process of gathering and analyzing data. We hope to demonstrate a correlation between genotype and phenotype in MPH. This will aid physicians in diagnosing and treating patients with MPH, and will provide a better understanding of these complex conditions to patients, their families, and physicians.

**Pharmaceutical Innovation and Population Health.** Steven Y. Wang and Salomeh Keyhani. Department of Health Policy, Mount Sinai School of Medicine, New York, NY.

The high price of drugs has been justified to ensure continuing pharmaceutical innovation. However the focus of current drug development has never been examined and it is unclear if current drug development serves society's health needs. This is a retrospective study examining pharmaceutical innovation in the past 14 years. A drug is innovative if it is a new molecular entity (never been marketed before in the US) and if it is given priority review by the FDA. A priority drug is considered a significant therapeutic advance, while standard review denotes a "me-too" drug. We examined trends in innovation over time and classified drugs by pharmacologic class, indication and general disease area. We also explored the association between the number of drugs developed for a disease area and the disease burden in the population. For a measure of disease burden, we used the World Health Organization's estimates of disability adjusted life years (DALY) in North America as a measure of population health. There were 366 NME's approved for 98 different indications between 1991 and 2004. One third of the drugs approved were in the infectious disease and cardiovascular categories. The most common indications for which new drugs were approved in these disease categories were bacterial infections followed by hypertension. Over 95% of drugs approved for these two indications were "me-too" drugs. In fact, the majority of all drugs developed in the past 14 years (60%) were "me-too" drugs. Moreover, we found no association between the burden of disease as measured by DALY's and the number of drugs approved for a disease area.

**Polyoma Virus Infection is a Risk Factor for Subsequent Development of Bladder Carcinoma in Immunocompetent Individuals.** David B. Weinreb, Garrett T. Desman, David E. Burstein, James Godbold, and Edward Johnson. Departments of Pathology, and Community and Preventive Medicine, Mount Sinai School of Medicine, New York, NY.

Despite various reports of polyoma virus (PV) DNA sequences in tumors, there has been no study statistically linking PV infection to tumor etiology. Here, we have performed a cross-sectional study of 3782 immunocompetent patients having had urine cytologic analyses. One hundred and thirty-three of these patients were reported to have PV-infected urothelial cells in the urine, a finding previously considered to be clinically insignificant in immunocompetent patients. We determined that PV infection of urothelial cells is associated with a diagnosis of bladder carcinoma (Odds ratio =

4.813,  $p < 0.001$ ). Additionally, we considered only patients for whom the PV-infected cells were identified prior to the earliest diagnosis of bladder carcinoma; the association remains statistically significant (Odds Ratio = 3.419,  $p < 0.001$ ). We conclude that identification of PV-infected cells is highly predictive of a subsequent diagnosis of bladder carcinoma. The polyoma T-antigen binds to the p53 gene product, inhibiting its function but also stabilizing it such that an increase in p53 can be detected by immunohistochemistry. Here, we examine six cases of renal transplant patients with allograft dysfunction resulting from PV infection of the non-native kidney. In all cases, immunohistochemistry demonstrated p53 expression specific to the renal tubular cells with cytopathologic features indicative of PV infection. This result suggests that binding of p53 by T-antigen occurs in PV infected cells. Collectively, these data suggest that PV infection is a risk factor for bladder carcinoma and that sequestration of p53 by T-antigen may be part of the mechanism by which PV infection promotes oncogenesis.

**A Community Outbreak of Legionnaires' Disease.** Kristin M. Wilson, George James, Rosalyn O'Loughlin, Lon Kightlinger, Hill Nicholas, Matt Wery, Josh Clayton, and Mathew R. Moore. Department of Community and Preventive Medicine, Mount Sinai School of Medicine, New York, NY, Respiratory Diseases Branch Division of Bacterial and Mycotic Diseases, Centers for Disease Control and Prevention, South Dakota Department of Health.

**Background:** Seven cases of community acquired Legionnaires' disease were reported in Rapid City, South Dakota. Dates of onset for these cases ranged from May 23 to July 7, 2005. Five patients were hospitalized, 1 died. An epidemiologic and environmental investigation was conducted to attempt to identify the source of the outbreak.

**Methods:** Aerosol producing devices that could act as potential sources of Legionella in the town were identified. Water samples and biofilm swabs of these potential sources, as well as samples from the case patients' homes were obtained and sent to the CDC Respiratory Diseases Legionella Laboratory for analysis. A case control study was conducted with the 7 cases matched to 4 controls each by race and underlying medical condition. Cases and controls were asked about exposures to potential aerosol producing devices, places they had traveled to in town and the routes they used to get there.

**Results and Conclusions:** All 7 cases were positive for Legionella pneumophila serogroup 1 (Lp1) by urine antigen tests. A clinical isolate available from one patient was found to be Lp1 MAB pattern (1,2,5,7). 50 environmental samples were obtained, including water samples and swabs from the 6 case homes, 6 area cooling towers, and 1 decorative fountain. All of the cooling towers and two patient homes tested positive for Legionella, but none matched the Mab pattern of the suspected outbreak strain. In the matched case control study analysis, no statistically significant differences were found between the cases and controls that could implicate a source of the outbreak. At this time, no source of the outbreak has been identified either through environmental sampling or epidemiologic analysis. Recommendations regarding remediation of the positive cooling towers and residences have been made.

**Measuring Patient Satisfaction: An Emergency Department Experience.** Leigh M. Wright, Jennifer V. Norton, and Ruben E. Olmedo. Departments of Nursing, Toxicology, and Emergency Medicine, Mount Sinai School of Medicine, New York, NY.

Patient satisfaction is a subjective quantity, having less to do with the quality of medical care received than the perception of how well that care was delivered. Customer satisfaction is becoming an important factor in measuring successful medical care. It is commonly accepted that patient satisfaction levels are indicators of future patient behaviors and health care choices. In emergency departments, patient satisfaction takes on added significance since often a patient's primary contact with an institution occurs within the emergency department. In 2003, the Department of Emergency Medicine (ED) at Mount Sinai Hospital initiated a Customer Service Design Team to implement strategies for improving patient satisfaction. Some of the strategies focused on key areas of personnel courtesy, patient overcrowding, patient waiting times, and communication during the ED visit. The present study evaluated which factors may have contributed to overall patient satisfaction and determined areas in need of improvement. A customer satisfaction instrument was created in English and Spanish. The survey was distributed to a convenience sample of 220 patients at the time of discharge. Answers were given using a 5-point Likert scale, free response and self-reported arrival/discharge times and demographic information. When asked to rate their overall satisfaction level, more than 80% of the patients responded with "satisfied" or "very satisfied." Doctor, nurse and registrar courtesy also achieved high satisfaction ratings. However, only 50% of patients stated that the speed of their visit was "faster" or "much faster" than the amount of time they expected to spend in the ED. This may indicate that improving on patients' ED length of stay is a potential source for improving patient satisfaction.