

AL DABAGH, BISHR

1. Title	Toll Like Receptors in Fusarium Keratitis
2. Student Presenter:	Bishr Aldabagh
3. Co-workers and Collaborators:	Ahmad Tarabishy, M.D
4. Advisor:	Eric Pearlman, Ph.D
5. Departments:	Ophthalmology, Pathology
6. Institutions:	Case Western Reserve University, University Hospitals
7. Support:	MSTP Program
8. Please choose your academic program:	MD PHD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Purpose: Fusarium keratitis is an ulcerative corneal disease which is destructive to the ocular structures and detrimental to vision. Fusarium will penetrate the cornea and Descemet's membrane if untreated and contiguously spread into the anterior chamber and eventually lead to endophthalmitis. This study examines Toll Like Receptor (TLR) responses to clinical isolates of Fusarium keratitis using TLR2, TLR4, TLR2/4, and MyD88 null mice.</p> <p>Methods: The corneal epithelium was abraded and exposed to heat killed Fusarium (conidia and hyphae) at a concentration of 5×10^6 CU/mL diluted with hydroxypropyl methylcellulose ophthalmic demulcent and covered with plastic or filter membrane to secure the fungal solution. Confoscan analysis and immunohistochemistry were performed at 24 hour time points. In vivo analysis was performed using Green Fluorescent Protein positive bone marrow chimeric mice to track the kinetics of the host response in vivo. Neutrophils and macrophages were isolated from wild type and TLR mice using a continuous gradient after intra-peritoneal injection of casein and stimulated with Fusarium to determine a dose response to fungal load.</p> <p>Results/Conclusion: In vitro studies show a decreased chemokine response to Fusarium (both hyphae and conidia) in both the TLR2 null and TLR4 null mice. Heat killed Fusarium did not induce a response in vivo but showed a decreased response compared to the control. Thus, Fusarium may be inhibiting the immune response.</p>

ALFORD, RAPHAEL

1. Title	: PARACEST agents for DCE MRI studies of tumor angiogenesis.
2. Student Presenter:	Raphael Alford
3. Co-workers and Collaborators:	Byunghee Yoo, Meser Ali
4. Advisor:	Mark Pagel
5. Departments:	Department of Biomedical Engineering
6. Institutions:	Case Western Reserve University, University Hospitals
7. Support:	This project was funded by the American Cancer Society through the Case Comprehensive Cancer Center in September 2004-December 2005.
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Changes in tumor angiogenesis are an early biomarker of aggressive cancer growth and chemotherapeutic efficacies. It has been shown that vascular permeability is correlated with angiogenesis. However, standard MRI methods that measure tumor angiogenesis are qualitative or semi-quantitative, due to biological variabilities. PARACEST agents are paramagnetic lanthanide complexes that can be selectively detected with MRI, so that the multiple agents can be measured during one MRI scan. We hypothesize that PARACEST agents with different diameters can be simultaneously applied to a tumor animal model and sequentially detected, so that DCE MRI vascular permeability characteristics can be measured from all imaging probes during a single MRI scan session. The assessment of multiple agents during the same scan session will reduce or eliminate problems with biological variabilities. PARACEST agents were characterized in vitro to optimize image enhancement parameters. Preliminary tests with a PARACEST agent that targets liver tissue were also conducted to optimize in vivo imaging. MCF-7, MCF-7C3, and MB-468 tumor models were developed for ongoing studies of PARACEST agents for DCE MRI applications.</p>

ANNABERDYEV, SHOHRAT

1. Title	Nutrition in Polytrauma Patients
2. Student Presenter:	Shohrat Annaberdyev
3. Co-workers and Collaborators:	
4. Advisor:	Dr. Heather Vallier, M.D.
5. Departments:	Dept. of Orthopaedics at MetroHealth Hospital
6. Institutions:	
7. Support:	T35
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Background and Rationale: Trauma causes increased stress on patients, which consequently leads to increased GI acid production as well as increased translocation of bacteria across the gut. This poses a greater risk of bleeding and infection. The problem of providing adequate nutrition to support the healing process is further complicated by the hypercatabolic response elicited by major trauma. Patients frequently require operations and are frequently made NPO perioperatively. Diminished nutritional status of hospitalized trauma patients results in slower fracture and wound healing, and increased risks of infection. In states of acute malnutrition, protein catabolism for prolonged periods is associated with increased strain on cardiac, pulmonary, hepatic, GI and other organ systems, making patients more susceptible to infections, which is detrimental to wound and fracture healing.</p> <p>Hypothesis: Early enteral feeding will reduce complications, length of stay, and costs, when compared with delayed enteral nutrition, or parenteral nutrition (e.g. i.v. proteins, lipids, sugars).</p> <p>Methods: The study is a retrospective review of 419 patients with multiple system injury, including orthopaedic trauma, defined as unstable spine, pelvis, acetabulum, or femur fracture requiring surgery, or a surgical repair involving greater than or equal to two extremities. Data is collected through chart review, and patients are contacted to conduct an outcomes questionnaire – MFA (Musculoskeletal Function Assessment).</p> <p>Results: The data collection is still not complete. While extensive chart review and data was collected on 114 patients, it is still early for concrete analysis or preliminary results.</p> <p>Conclusions: Upon conclusion of the study, the specified patient population will be evaluated for complications, number of days spent on ventilator, number of days in ICU, and MFA outcomes. These will be analyzed for associations with type of feeding (PO vs NPO) that was administered to the patient, as well as early vs delayed initiation of PO feeding.</p>

AUBERT, PAMELA

1. Title	Palliative care in orthopaedic surgical oncology
2. Student Presenter:	Pamela M. Aubert
3. Co-workers and Collaborators:	
4. Advisor:	Dr. Richard J. O'Donnell
5. Departments:	Orthopaedic Surgery Oncology
6. Institutions:	University of California San Francisco, Comprehensive Cancer Center
7. Support:	
8. Please choose your academic program:	MD MA
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Hundreds of thousands of Americans are affected every year by skeletal complications of oncologic disease. Recent developments in medical oncology, radiation oncology and radiology, particularly with respect to the use of bisphosphonate medication and radiofrequency techniques, have served to greatly lessen the morbidity associated with metastatic skeletal disease. Similarly, there has been significant advancement in the field of orthopaedic oncology in the areas of internal fixation, endoprosthetic implant design, and minimally-invasive kyphoplasty technology. Given the palliative intent of intervention in this patient population, the goal of treatment of skeletal metastases must be optimization of limb function and ultimately, quality of life.</p>

BAZICK, JESSICA

1. Title	Expression of Cyclin A in Alzheimer's Disease
2. Student Presenter:	Jessica Bazick
3. Co-workers and Collaborators:	Gemma Casadesus
4. Advisor:	Mark Smith, Ph.D.
5. Departments:	Department of Pathology
6. Institutions:	Case Western Reserve Institute
7. Support:	Crile Fellowship
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Alzheimer's disease (AD) is a chronic disorder with progressive neurodegeneration. It is characterized by typical pathological hallmarks including β-amyloid deposition, neurofibrillary tangles, and disturbances in the expression of various cell cycle proteins. Recent findings have suggested that aberrant mitotic re-entry plays a role in the etiology of AD. This study investigates the importance of cell cycle control in AD pathology by focusing on a particular cell cycle protein, cyclin A. Cyclin A forms a complex with CDK2 implicated in eukaryotic cell cycle control. During S phase, CDK2/cyclin A phosphorylates different substrates allowing DNA replication and the inactivation of G1 transcription factors.</p> <p>Immunocytochemistry assays were used to analyze the nuclear expression of cyclin A in neurons in the hippocampi of normal mice and transgenic APP23 mice and in the hippocampi of age-matched human control subjects and patients suffering from AD. The mouse subjects, normal and transgenic, were composed of two different age groups: 3 month old and 12 months old in order to determine whether there was a change in cyclin A levels depending on the age of the mouse. Immunohistochemical analyses demonstrated no significant difference in cyclin A expression in control subjects and transgenic APP23 mice of either age group. Levels of cyclin A expression were not significantly different in the human control subjects and patients with AD. Even though our analysis did not demonstrate differences in immunosignaling of cyclin A in controls and case subjects, it does not rule out the importance of cyclin A in AD pathogenesis. Levels of the protein from tissue specimens are in the process of being analyzed will provide more information about the expression of cyclin A levels between cases and controls.</p>

BEATTY, CHRISTOPHER

1. Title	Relation of Ventricular Dilatation to Outcome in Infants with Posthemorrhagic Ventricular Dilatation
2. Student Presenter:	Christopher Beatty
3. Co-workers and Collaborators:	Maureen Hack, Nori Minich, Dee Wilson
4. Advisor:	Shenandoah Robinson
5. Departments:	Divisions of Pediatric Neurosurgery and Neonatology
6. Institutions:	Rainbow Babies and Children Hospital
7. Support:	Crile
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Objective: Since the 1990's survival of preterm infants has improved markedly, but children with post-hemorrhagic ventricular dilatation (PHVD) continue to have poor neurodevelopmental outcomes. These children suffer intraventricular hemorrhage (IVH) and other complications of prematurity. The contribution of post-hemorrhagic hydrocephalus to the risk of cerebral palsy and learning disabilities is unclear. We hypothesized assessment of ventricular enlargement and outcomes could clarify the contribution of PHVD to neurodevelopmental outcomes.</p> <p>Methods: Records of 54 preterm infants from the Rainbow Neonatal High Risk Program database with PHVD were examined. Infants with PHVD without adequate records, imaging, or 20 months (corrected) follow-up were excluded. Severity of illness, dates of ventricular dilatation and treatment, and outcomes were recorded. Lateral ventricular width was measured on coronal head ultrasounds using the standard method of Levine, and noted to be either above or below the 97%+4mm and 97%+50mm lines according to gestational age. Statistical analyses were performed, with $P < 0.05$ considered significant.</p> <p>Results: Twenty-five infants requiring a permanent shunt were compared to 29 who recovered without a shunt. Infants not requiring a shunt were diagnosed with dilatation significantly earlier (median 12 days) than those needing a permanent shunt (median 26 days, $P < 0.001$). Using the 97%+4mm line, PPV=49% and NPV=80%. With the 97%+50mm line, PPV=80% and NPV=83%, suggesting infants with dilatation >97%+50mm are likely to require shunting. Multiple statistical analyses failed to demonstrate that PHVD adds significantly to the deficits these children are prone to develop, compared to other risk factors such as IVH.</p> <p>Discussion: The accepted threshold (97%+4mm) for ventricular dilatation is not as strong a predictor for requiring a permanent shunt as 97%+50mm. This study shows for the first time a clinically predictive threshold for requiring a shunt in preterm infants. Statistical analyses demonstrated that ventricular dilatation and duration of dilated ventricles did not affect outcomes, unlike IVH.</p>

BELDING, JONATHAN

1. Title	OCT Imaging of the Embryological Quail Heart
2. Student Presenter:	Jonathan Belding
3. Co-workers and Collaborators:	Michael Jenkins, Pankti Patel, Ajay Basavanhally, Osman Chughtai
4. Advisor:	Dr. Michiko Watanabe and Dr. Andrew Rollins
5. Departments:	Department of Pediatrics, Genetics, and Anatomy Department of Biomedical Engineering
6. Institutions:	Case Western Reserve University School of Medicine Rainbow Babies and Children's Hospital Case Western Reserve University
7. Support:	NIH T35 Training Grant AHA Student Scholarship in Cardiovascular and Cerebrovascular Disease
8. Please choose your academic program:	MD MS
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Optical Coherence Tomography (OCT) imaging is a relatively new modality that is being adapted to study the normally and abnormally developing beating heart. The goal of this project was to provide a detailed atlas of normal quail heart morphology during early developmental stages when it attains its tubular structure and loops to the right (HH stage 10-18) to provide a baseline from which to compare experimentally manipulated hearts. Fixed embryos were studied because resolution and contrast is better than in living hearts. Quail eggs were chosen because they are easy to procure and widely used. Fertilized coturnix eggs were incubated at 100 degrees F and 40% humidity for various times between 36 and 72 hours. The eggs were cracked and the embryos dissected away from the yolk and extraembryonic tissue. They were fixed in 4% formalin for several hours, and washed in PBS solution. The embryos were imaged first by video microscopy and then according to OCT protocol. These files were processed to create a 3D reconstruction of the heart. To date, stage 16, 17 and 18 hearts have been imaged and processed. These images show trabeculae carnae formation in the developing ventricle, dextral looping of the heart, endocardial cushion formation with low cellular density Wharton's Jelly material and the beginning of septation of the outflow tract by these cushions. 3D reconstructions of these hearts show that the external morphology of the mature quail heart is already apparent in these relatively early stages. We believe that this illustrates OCT's ability to see morphological defects even at these early stages. In conclusion, OCT is a highly useful modality for viewing the normal development of quail hearts at early stages because it is able to image the heart with high resolution. We have the potential to use this technique to rapidly and non-invasively image embryos that have been experimentally manipulated.</p>

BEVERSLUIS, DAVID

1. Title	Mapping Religious Health Assets in Central America
2. Student Presenter:	David Beversluis
3. Co-workers and Collaborators:	
4. Advisor:	Dr. Henry Mosley
5. Departments:	Population and Family Health Sciences
6. Institutions:	John Hopkins University School of Public Health; Christian Connections for International Health
7. Support:	Crile Grant
8. Please choose your academic program:	MD MPH
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>This Crile project was carried out in conjunction with the ongoing investigations of the Global Religious Health Assets Mapping (GRHAM) project of Christian Connections for International Health (CCIH), a DC-based networking and information sharing organization. GRHAM is an ambitious initiative to quantify, through surveys and onsite GPS mapping, the faith based contribution to primary health care in developing nations, but has not previously worked in Central America.</p> <p>This researcher participated in a number of activities which have begun the process of mapping FBO involvement in selected Central American countries, including Honduras, Guatemala, El Salvador, Nicaragua, Costa Rica, and Haiti. Significant time was spent compiling contact lists of faith based organizations (FBOs) working in these countries. This was done through the use of internet queries, email correspondence with CCIH contacts in known FBOs, phone interviews with project managers, and access of non-profit and hospital directories, such as Guidestar.org. This effort was coordinated with other interested organizations already active in Central America, such as Medical Mission Exchange.</p> <p>Training in the use of geographic information systems (GIS) software was also undertaken, and significant effort was put toward geo-referencing approximately 2500 hospital and project sites. This work was carried out by cross-referencing geonet GPS data with known hospital and town locations to produce GIS maps of selected FBO involvement. The World Health Organization's Healthmapper software was used; this data will eventually be integrated into GRHAM's online database.</p>

BROWN, CRYSTAL

1. Title	Determination of a role for MCMV to counteract siRNA mechanisms
2. Student Presenter:	Crystal E. Brown
3. Co-workers and Collaborators:	
4. Advisor:	Adam P. Geballe M.D
5. Departments:	Human Biology
6. Institutions:	Fred Hutchinson Cancer Research Center
7. Support:	Crile Research Fellowship
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Viruses have evolved mechanisms to counteract host cell anti-viral factors including protein kinase R (PKR), oligoadenylate synthetases (OAS) and short interfering RNAs (siRNA). For example, the vaccinia virus E3L gene and the human cytomegalovirus (HCMV) TRS1 and IRS1 genes bind dsRNA and PKR inhibit the PKR/OAS pathway. Interestingly, the E3L protein also counteracts siRNA mechanisms, most likely binding siRNA and preventing formation of the RNA-induced silencing complex. Recently, two murine cytomegalovirus (MCMV) genes, m142 and m143, were found to encode dsRNA binding proteins which can also block the PKR pathway. Because MCMV is a useful model for studying the pathogenesis of HCMV infections, I designed experiments to determine whether MCMV infection also blocks siRNA function in host cells. I cotransfected a plasmid expressing secreted alkaline phosphatase (SEAP) along with a plasmid expressing an siRNA targeting SEAP (psiRNA-SEAP) into NIH 3T3 cells. Twenty-four hours post-transfection, the cells were mock-infected or infected with MCMV and SEAP activity was assayed twenty-four hours later. I found no significant difference in the knockdown of SEAP activity by psiRNA-SEAP between mock-infected and MCMV-infected cells in several experiments. For example, in one experiment, I detected a 3-fold knockdown of SEAP activity in mock-infected cells compared to a ~4-fold knockdown in infected cells. It remains possible that MCMV might have mechanisms for antagonizing other siRNAs or that function in other cell types or at other stages of infections. However, these preliminary results suggest that MCMV does not block siRNA effects and therefore siRNAs might be useful therapeutic agents against cytomegaloviruses.</p>

CAMPBELL, LAURA

1. Title	Access to Community Services for Children with Special Health Care Needs: Referral Practices and Familiarity with Services of Physicians in Northeast Ohio
2. Student Presenter:	Laura Campbell
3. Co-workers and Collaborators:	
4. Advisor:	Dr. Carolyn Green
5. Departments:	Child Neurology
6. Institutions:	Rainbow Babies and Children's Hospital
7. Support:	none
8. Please choose your academic program:	MD MA
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Seven percent of children in Ohio have special healthcare needs. In addition to complex medical care, these children need community services such as special education, financial assistance, and family support. The goal of this study was to determine in what ways physicians are addressing the community resource needs of their patients: (1) what systems they are using in their practices to coordinate access to community resources; (2) how familiar they are with important community organizations; and (3) what tools would improve resource access for their special-needs patients. A survey was mailed to 282 family practice physicians and pediatricians in the University Hospitals Primary Care Practice network in Northeast Ohio. The response rate was 13.5%. The most common resource coordination systems were: pamphlets/posters available in the office (55%), referrals to social workers (33%), designated office care coordinators (21%), websites (17%), family advocacy programs (11%), and giving phone numbers (11%). Familiarity with important resources varied but was generally lower than expected; only 70% were familiar with the Ohio Bureau for Children with Medical Handicaps, and only 55% were familiar with resources available through the County Board of Mental Retardation and Developmental Disabilities. Respondents were enthusiastic about receiving additional tools to help with community resource coordination – 95% would use a printed list of resources and 87% would use a website. While approaches to coordination of community resource access varied, all survey respondents acknowledged this need and had a system in place to address it. However, a less than 100% familiarity with established community resources suggests that the current system is not adequate for most practices. In response to the survey, we recognize a need to increase access by formalizing these systems. The most widely suggested tool from the survey was the provision of a web and paper-based database of resource information. As a result we have created a web-based resource directory for Rainbow Babies & Children's hospital, and will evaluate its impact on resource access and care coordination for children with special health care needs.</p>

CELIGOJ, FRANK

1. Title	Prediction of Parasympathetic Responses from Sinus Rhythm Electrogram Analysis
2. Student Presenter:	Andrew Celigoj
3. Co-workers and Collaborators:	Nicolas Lellouche, David Cesario, Kalyanam Shivkumar
4. Advisor:	David Cesario
5. Departments:	UCLA Cardiac Arrhythmia Center Division of Cardiology, Department of Medicine
6. Institutions:	David Geffen School of Medicine at UCLA
7. Support:	NHLBI, R01HL084261
8. Please choose your academic program:	MD
9. What year are you in the program?	3
10. Body of Abstract (300 words or less)	<p>Background: Complex fractionated electrograms and high frequency activity sites have been described in the left atrium during atrial fibrillation (AF). However, the patterns of electrograms (EGM) in the left atrium during sinus rhythm in patients presenting with paroxysmal AF have not been studied. The aim of this study was to define the different patterns of EGM observed in the left atrium during AF ablation in sinus rhythm and their relationship to the local vagal tone. Methods and Results: We retrospectively analyzed 30 patients who underwent paroxysmal AF ablation in sinus rhythm. During the procedure, pulmonary vein isolation was performed. If necessary, additional lines (root and mitral annulus line) were also performed. Before ablation, we analyzed electrogram patterns by quantifying the total number of deflections, the amplitude and the duration. Then, before and during each ablation, we analyzed the heart rate and the atrial-His (AH) interval. A significant vagal response during radiofrequency application was defined as an increase in AH > 10 ms and/or a decrease of heart rate >20% or 10 beats per minute (bpm) if baseline heart rate was less than 50 bpm. A vagal response was associated with a specific pattern of left atrial electrogram: EGM with at least 4 deflections, a duration > 40 ms and an amplitude > 0.7 mV. The ablation sites associated with vagal response were located in specific areas of the left atrium, mainly in the posterior wall and in the septum.</p> <p>Conclusions: Vagal tone activation during AF ablation is associated with pre-ablation high amplitude complex fractionated electrograms.</p>

CHAMBERLAIN, RYAN

1. Title	Impact of Prenatal Brain Injury on the Cerebellum of Adult Rats
2. Student Presenter:	Ryan Chamberlain
3. Co-workers and Collaborators:	Qing Li
4. Advisor:	Dr. Shenandoah Robinson, MD
5. Departments:	Neurosurgery
6. Institutions:	University Hospitals of Cleveland, Case Western Reserve University School of Medicine
7. Support:	T-35 NIH grant
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Premature infants often suffer perinatal brain injury that impairs neurodevelopment. Recent research has shown alterations in cerebellar development contribute to observed deficits. After prenatal transient hypoxia-ischemia, infant rats show altered cerebellar development with a preferential loss of neural cells arising at the time of the insult. We propose that alterations observed during cerebellar development will irreparably alter the mature cerebellum. Specifically we predict that excess loss of cell populations arising at the time of the insult will persist into adulthood.</p> <p>Uterine arteries were occluded for 60 minutes on embryonic day 18, and pups were born at term. Sham controls had surgery without arterial occlusion. Immunolabeling of midline sagittal cerebellar vermis from adult rats was performed. For neurons, anti-calretinin antibodies immunolabeled molecular layer unipolar-brush cells arising at E17-E18. Anti-parvalbumin immunolabeled P15 Purkinje cells and postnatal molecular layer basket and stellate cells. O4 antibodies labeled pro-oligodendrocytes arising at E17-18. Independent observers were blinded to the insult status. Labeled cells from approximately 5 animals from each group were counted. Means were compared using student t-test, with $P < 0.05$ considered significant.</p> <p>As predicted, a decreased number of unipolar-brush cells that arise around E18 were observed. Purkinje cell numbers were not affected, as they arise before the injury. Basket and stellate cells showed a trend toward decreasing cell number, an unexpected result. These changes may be secondary to damage to the oligodendrocytes or granule cells. Our O4 immunolabeling showed a trend towards decreasing pro-oligodendrocyte density, similar to loss observed in neonatal rats. Overall, the changes observed in neonatal rats persisted into adulthood, and additional loss of basket and stellate cells occurred.</p> <p>These findings show that a prenatal systemic insult can alter cerebellar development. A better understanding of the impact of the lesion on brain development will guide the investigations for novel therapy.</p>

CHAN, VINCENT

1. Title	In vivo investigation of Dystrophic epidermolysis bullosa in knockout mouse models
2. Student Presenter:	Vincent Chan
3. Co-workers and Collaborators:	Jennifer Remington MD, Julie Burnette
4. Advisor:	Mei Chen PhD, David Woodley MD
5. Departments:	Dermatology
6. Institutions:	University of Southern California
7. Support:	
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Dystrophic epidermolysis bullosa (DEB) is an inherited skin disease characterized by chronic blistering and scarring of the skin and mucous membranes. DEB is caused by mutations in the type VII collagen (C7) gene, COL7A1. C7 is the major component of the anchoring fibrils, which are attachment structures located beneath the lamina densa in the epidermal basement membrane zone (BMZ) that mediate dermal-epidermal adherence. COL7A1 gene mutations may result in absent or dysfunctional anchoring fibrils, causing instability within the BMZ and dermal-epidermal separation.</p> <p>DEB knockout mouse models were used to compare the therapeutic efficacy as well as the immune response of intradermal and intraperitoneal injections of purified recombinant C7 (protein-based therapy) and lentiviral transfer vectors (vector-based therapy). Affected homozygous pups were injected once daily and observed for reduced blister formation and general well-being (i.e. weight). Skin biopsies were taken at different time intervals post-injection. Skin samples were analyzed by H&E staining to verify the presence of intact skin, and immunofluorescence staining, using an antibody to human C7, to detect C7 deposition in the BMZ. Positive human C7 samples were then sent to a collaborator for immuno-EM, which verified restoration of anchoring fibrils.</p> <p>The intradermal route produced a superior therapeutic response when compared to the intraperitoneal route, judging by phenotypic correction of skin blistering and the amount of BMZ C7-staining. While intradermal protein and lentiviral-based therapy produced similar levels of C7-staining, intraperitoneal protein-therapy was more effective than intraperitoneal lentivector therapy.</p> <p>Upon analysis of immune response, it was found that intradermal injections triggered a CD4 response in the dermis within one week of life, while intraperitoneal injections did not elicit a CD4 response until the second week. Anti-human C7 antibody production was verified by ELISA.</p>

CHEN, ANDREW

1. Title	Effect of clock protein deletion on cardiac hypertrophy, remodeling, and gene expression in hypertension
2. Student Presenter:	Andrew Chen
3. Co-workers and Collaborators:	David J. Chess, William C. Stanley
4. Advisor:	William C. Stanley
5. Departments:	Physiology
6. Institutions:	Case Western Reserve University
7. Support:	T35 (NIH)
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Previous studies have shown the existence of internal clocks in mammalian cardiac tissue which allow for optimized cellular responses to external stimuli. In these studies, metabolic genes – including those regulating carbohydrate utilization, fatty acid oxidation, and mitochondrial function – exhibited diurnal variation with their activity peaking at night. In the setting of pressure overload-induced hypertrophy, however, this diurnal variation was abolished. Thus, a loss of the clock mechanism may be important in the development of left ventricular hypertrophy and systolic dysfunction in the setting of hypertension. To elucidate the role of clock proteins in cardiac remodeling, the present study evaluated the effects of transverse aortic constriction (TAC) on mice with clock and <i>bmal1</i> deletions. These genes encode transcription factors responsible for induction of other clock-related components. Following the banding procedure, animals were subjected to two-dimensional and Doppler echocardiographic studies for analysis of end systolic and diastolic diameters, relative wall thickness, velocity of circumferential shortening (an index of myocardial contractility), cardiac output, ejection fraction, and fractional shortening. Upon terminal surgery, hearts were harvested and assessed for left ventricular mass, alpha and beta myosin heavy chain content, and atrial natriuretic factor (ANF) expression. The activities of medium chain acyl-CoA dehydrogenase (MCAD) and citrate synthase were measured as an index of fatty acid oxidation and myocardial oxidative capacity, respectively. Additionally, mRNA levels for peroxisome proliferator-activated receptor alpha- (PPARα) regulated genes encoding carnitine palmitoyl transferase-I (CPT-I) and uncoupling protein 3 (UCP3) were quantified using RT-PCR. Finally, plasma free fatty acids and serum insulin concentrations were determined using spectrophotometric techniques.</p>

CHEN, SAMUEL

1. Title	Overview of home care services provided by Jichi Medical University Hospital in Japan
2. Student Presenter:	Samuel Chen
3. Co-workers and Collaborators:	
4. Advisor:	Drs. Yuko and Koki Tsuruoka
5. Departments:	Department of Community and Family Medicine
6. Institutions:	Jichi Medical School
7. Support:	
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>The model for primary and family care in Japan has evolved differently from that of the United States as a result of the accessibility of universal health care and cultural differences in familial and societal structure. Long-term care insurance (kaigo hoken) helps to pay for the costs of care for eligible patients through a collective pool maintained by insurance premiums and tax. The development of this system is a reflection of the Japanese emphasis on societal unity and a way to alleviate familial stress that may arise from prolonged elderly nursing care. Through interview and observation of patients receiving long-term care insurance, I was able to construct first an overview of the Japanese home care services provided by Drs. Yuko and Koki Tsuruoka's team at Jichi Medical University Hospital in Japan. The level of care ranged from health maintenance to terminal care and always involved working closely with the patient's family and visiting helpers and nurses. Through participant observation, I was then able follow the care of a specific patient, Mr. Y, and aid in the production of an observational study. The study looks at Mr. Y's weekly home visits, familial obligations and participation in his care, and services provided by external support groups, notably that of a portable bathing service. For bedridden patients such as Mr. Y, having the opportunity to soak in a bathtub greatly improves his quality of life, and must be understood in the cultural context that most Japanese consider a daily soak in the bathtub to be an irreplaceable part of the day. This research project emphasizes the importance of understanding the cultural and societal context of how home care is delivered in Japan.</p>

CHIANG, SILVIA

1. Title	Evaluation of Human Beta-Defensin Expression in HIV-Infected Women versus Non-Infected Women
2. Student Presenter:	Silvia Chiang
3. Co-workers and Collaborators:	Ana Vasquez, PhD Candidate (Dr. Miguel Quinones's lab, CCF)
4. Advisor:	Dr. Michael Lederman
5. Departments:	Department of Medicine Department of Obstetrics and Gynecology
6. Institutions:	University Hospitals
7. Support:	NIH T35 Grant
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Protective mechanisms against HIV acquisition at mucosal sites are incompletely understood. The role of human β-defensins (hBDs), which are antimicrobial peptides, in host defense against HIV is a promising area of study that may illuminate mechanisms underlying disease progression and susceptibility to opportunistic infections. Characterization of hBD-2 and hBD-3 expression in the oral and cervicovaginal epithelia of HIV patients and controls will help define the effects of HIV infection on the expression of these important defenses, as well as elucidate the relationship between defensin levels and mucosal infections such as oral candidiasis, that often complicate HIV infection. Samples will be collected from HIV-infected and non-infected women undergoing routine pelvic examinations. Oral epithelial samples will be obtained by scraping with a plastic loop. Cervicovaginal epithelial samples will be obtained by vaginal scraping for the epithelial cells, and cervicovaginal secretions will be obtained with Sno-strip wicks. Using real-time PCR, this study will compare mRNA expression levels of hBD-2 and hBD-3 between the epithelial cells of HIV-infected vs. non-infected women. Defensin protein levels in cervicovaginal secretions of HIV-infected vs. non-infected women will be measured by ELISA. Messenger RNA and protein expression levels will then be correlated with HIV status, CD4 cell count, and plasma viral load. The Wilcoxon Rank sum test will be used to compare defensin levels between the infected and non-infected groups, and Spearman's correlations will be used to identify possible associations between defensin levels and clinical variables. IRB approval has been obtained. Collaborators from the Departments of Medicine and Obstetrics/Gynecology have agreed to obtain informed consent and collect specimens from patients. In addition, ELISA and real-time PCR procedures have been developed and tested. The rationale behind this study and the clinical and laboratory procedures have been presented to the clinician-researchers of the AIDS Clinical Trials Unit of University Hospitals.</p>

CHUANG, DEBBY

1. Title	Impact of Socioeconomic Status on Critically Ill Stroke Patients
2. Student Presenter:	Debby Chuang
3. Co-workers and Collaborators:	
4. Advisor:	Dr. Gwendolyn Lynch
5. Departments:	Department of Neurology
6. Institutions:	UHHS, CWRU
7. Support:	T35 Fellowship
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Background/Objective: Recent studies have supported the notion that lower socioeconomic status is associated with increased stroke risk, greater stroke severity, and poorer overall outcome (1). Our retrospective study set out to determine potential associations between socioeconomic status and the clinical presentation, disease severity, clinical course, and/or discharge status of a single-center population of critically ill stroke patients in the Cleveland, OH area.</p> <p>Methods: A retrospective analysis of the 2001 University Hospitals of Cleveland Neurointensive Care (UH-NSU) Hyperglycemia Database was conducted. Subjects were included in the study if the following inclusion criteria were met: age >18 years, admission diagnosis of stroke (cerebral infarction, subarachnoid hemorrhage, and intracerebral hemorrhage), length of stay greater than 24 hours, and available medical records, zip codes, and income category for analysis. The variables included in the analysis were age, sex, race, zip code, past medical history, NSU admission details, NSU vital statistics (blood glucose level, temperature, heart rate, and blood pressure), in-hospital complications, discharge status, and cost of care. The identified zip codes from the data set were used to collect Zip Code Tabulation Areas (ZCTAs) and their associated median family income, median household income, and median non-family income data from the online version of the 2001 US Census database. Once the incomes were categorized into eight \$10,000-increments, the patients in our sample were subsequently categorized into their respective income categories through matching zip codes with ZCTAs. Univariate and multivariate statistical analyses were then performed to determine possible associations between the income categories and the stroke patient variables.</p> <p>Results/Conclusions: 221 patients admitted for stroke due to cerebral infarction, intracerebral hemorrhage, or subarachnoid hemorrhage were identified and included in the analysis. 90 different zip codes were collected from the patient sample and correlated to ZCTAs. The statistical analysis and other results are pending.</p> <p>(1) Cox, Anna M, Christopher McKeivitt, Anthony G Rudd, Charles D A Wolfe. Socioeconomic status and stroke. <i>Lancet Neurology</i> 2006;5: 181-8</p>

COBB, INGRID

1. Title	Influence of socioeconomic status and sedentary activity on the relationship between body mass index and cardiovascular comorbidities in overweight children
2. Student Presenter:	Ingrid M. Cobb
3. Co-workers and Collaborators:	
4. Advisor:	Dr. Leslie Heinberg
5. Departments:	Biostatistics and Epidemiology
6. Institutions:	Case Western Reserve University School of Medicine
7. Support:	
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Studies have shown that increased obesity in children is associated with an increased risk of medical co-morbidities. For example, increased BMI is associated with increased cardiovascular risk factors such as for dyslipidemia, hypertension, and glucose impairment. Low socioeconomic status (SES) and increased sedentary behavior are risk factors for the development of obesity. Participants (n=163) were enrolled in the Healthy Kids/Healthy Weight (HKHW), which is a clinical research program at Rainbow Babies and Children's Hospital in Cleveland, Ohio that is dedicated to helping and guiding overweight children and their families build healthy and physical lifestyles. The female to male percentage was 57% to 43%. The participants ages ranged from 4- 17, however the largest percent of the participants were in the 10-14 age range. The BMI for the participants were at the 85th percentile which identifies them as at risk for overweight or overweight. This study will examine the possible moderating role of SES and sedentary activity on the relationship between BMI and the risk for cardiovascular factors in a pediatric overweight population. It is hypothesized that lower SES will be related to a greater association between BMI and cardiovascular risk factors. A similar moderating relationship is hypothesized for sedentary behavior.</p> <p>Using a linear regression model, SES and sedentary behavior moderated the relationship between the SES and sedentary hypothesis and BMI for the comorbidities of insulin resistance, systolic blood pressure, and triglycerides and BMI. However, the hypotheses were not demonstrated for glucose intolerance, diastolic blood pressure, total cholesterol, LDL, HDL, dyslipidemia, hypercholesterolemia, hypertriglyceridemia, and mixed dyslipidemia and BMI. This data represents a possible link to understanding the moderating factors in the role of SES and sedentary activity on the relationship between body mass index and co-morbidities. Future research in this area will further elucidate the factors involved in the increasing medical issue of pediatric obesity.</p>

DELOS SANTOS, GRACE

1. Title	Pc 4 Binding to Cardiolipin: A Study in Liposomes
2. Student Presenter:	Grace B. Delos Santos
3. Co-workers and Collaborators:	Dr. Myriam E. Rodriguez
4. Advisor:	Dr. Nancy L. Oleinick
5. Departments:	Radiation Oncology
6. Institutions:	Case Western Reserve University
7. Support:	National Institutes of Health T35 Short-term Research Training Grant to G.B. Delos Santos: "Research Training in Heart, Lung, Blood, & Sleep Disorders", grant number HL082544. National Cancer Institute R01 to N.L. Oleinick: "Cardiolipin in Photodynamic Therapy", grant number CA106491.
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Porphyryns and related macrocycles are currently employed as photosensitizers in photodynamic therapy (PDT), which is a non-invasive and highly specific cancer treatment modality that uses singlet oxygen to exert cytotoxic effects on cells. Cells that have been treated with PDT have been shown to undergo apoptosis or necrosis, although the initiating events of apoptosis that are unique to PDT have yet to be elucidated. Pc 4, a phthalocyanine photosensitizer first synthesized at Case and now in clinical trial at University Hospitals, has been shown to bind preferentially to mitochondrial membranes and to exert photodamage to certain membrane molecules. Cardiolipin (CL) is a major phospholipid in the mitochondrial inner membrane. Fluorescence resonance energy transfer (FRET) studies have shown colocalization of Pc 4 and cardiolipin in the mitochondrial membrane, which points to CL as a possible binding site and target site for Pc 4. Herein are reported the binding constants of Pc 4 in liposomes of increasing cardiolipin content. Unilamellar liposomes were used as membrane models to test the incorporation of the dye. It was shown that Pc 4 does not display preferential binding to cardiolipin. Moreover, binding affinities appear to be independent of the lipid composition of the liposomes. The behavior of the Pc 4 analogues, Pc 181, Pc 12, and Pc 135, was also investigated in liposomes; each contains two alkyl-siloxy ligands linked axially to the central silicon in contrast to Pc 4, which has one such ligand. Each displayed a higher binding affinity than did Pc 4 due to a greater extent of disaggregation. Nonylacridine orange (NAO), a molecule reported to preferentially bind to cardiolipin, did not display preferential binding to cardiolipin in the liposomal system. This does not preclude cardiolipin as a binding site for Pc 4 but rather suggests that the binding affinity is system dependent and that the liposomal system is better at detecting differences in disaggregation over differences in binding affinities.</p>

DERAKHSHAN, JAMAL

1. Title	Active Catheter Tracking and Vessel Wall Imaging with a 5 French MRI Catheter
2. Student Presenter:	Jamal J. Derakhshan (1)
3. Co-workers and Collaborators:	Jens O. Heidenreich M.D. (2), Simi Paul M.D. (2), Ingmar Viohl Ph.D. (3), Jeffrey L. Sunshine M.D., Ph.D. (2), Jeffrey L. Duerk Ph.D. (1,2)
4. Advisor:	Jeffrey L. Duerk, Ph.D.
5. Departments:	1-Biomedical Engineering 2-Radiology
6. Institutions:	1-Case Western Reserve University 2-University Hospitals of Cleveland 3-Interventional Imaging Inc. (I3 MRI)
7. Support:	NIH R41 HL082076 Siemens Medical Solutions-MRI NIH T32 GM007250 Case MSTP
8. Please choose your academic program:	MD PHD
9. What year are you in the program?	5
10. Body of Abstract (300 words or less)	<p>Introduction: In diseases such as atherosclerosis, it is necessary to accurately depict the blood vessel wall for the diagnosis of pathology and for vascular interventions such as angioplasty and stent placement. A startup company specializing in devices for MRI (Interventional Imaging Inc., Cleveland, OH) has developed a 5 French disposable catheter for imaging the vessel wall using MRI. The aim of this study was to assess the catheter sensitivity in phantom experiments and to test the ability to actively track and image arteries in vivo.</p> <p>Methods: All experiments were performed in a new 1.5 T interventional MRI scanner (Magnetom Espree, Siemens Medical Solutions, Erlangen, Germany). The catheter was placed in a tub of doped water and high resolution/small field-of-view images were acquired. In 13 healthy, 100 pound, anesthetized pigs, the catheter was introduced through a sheath in the femoral artery. The catheter was advanced under real-time MRI guidance to the femoral, iliac, subclavian and carotid arteries using the Interactive Real Time Tip Tracking pulse sequence (Siemens Medical Solutions, Chicago, IL). Once at the targeted vascular locations, images of the vessel wall were acquired using the catheter.</p> <p>Results: In phantom experiments the catheter sensitivity was determined to be 1-2 cm axially and 2 cm longitudinally. In vivo, it was possible to actively track the catheter to the targeted locations. The catheter was able to access medium sized arteries (as small as 3 mm). The catheter had a sensitivity radius of 1 cm in vivo. Images with 160 μm in-plane resolution and 5 mm slice thickness were acquired. Using these images it was possible to differentiate the vascular lumen, the vessel wall as well as surrounding tissue.</p> <p>Conclusion: The new 5 French catheter can be actively tracked to targeted anatomy and can be used to generate high resolution vessel wall images in vivo.</p>

DONG, FEI

1. Title	Has PSA-Induced Stage Migration Ended?
2. Student Presenter:	Fei Dong
3. Co-workers and Collaborators:	Alwyn M. Reuther, Cristina Magi-Galluzzi, Ming Zhou, Patrick A. Kupelian
4. Advisor:	Eric A. Klein
5. Departments:	Glickman Urological Institute, Taussig Cancer Center, Department of Anatomic Pathology (CCF); Department of Radiation Oncology (MDA Orlando)
6. Institutions:	Cleveland Clinic Foundation, M.D. Anderson Cancer Center Orlando
7. Support:	None
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Purpose: Serum prostate-specific antigen (PSA) screening has led to pathologic stage migration. We examined patients treated by radical prostatectomy between 1987 and 2005 to establish temporal trends in rates of extraprostatic extension (EPE), organ-confined disease (OC), and clinically insignificant disease.</p> <p>Methods: Surgical pathology of 3364 patients treated consecutively at a single institution was analyzed for EPE and OC. In addition, 2256 specimens removed between 1999 and 2005 were evaluated for clinically insignificant disease (tumors < 0.5 cc, surgical Gleason grade < or = 6, and no EPE). Trends were statistically evaluated from 2005 to the earliest year at which the Cochran-Armitage Test was not significant, using Bonferroni's adjustment with cutoff of $p = 0.0029$.</p> <p>Results: From 1987 to 2005, pathologic staging showed a decreasing trend for EPE and increasing trend for OC (both $p < 0.0001$). There was no trend in the proportion of EPE ($p = 0.025$) or OC ($p = 0.007$) from 1998 to 2005. The proportion of clinically insignificant disease showed no trend for the entire period for which data was available, from 1999 to 2005 ($p = 0.829$).</p> <p>Conclusion: Trends of pathologic stage migration of the early PSA era have diminished since 1998, while the proportion of clinically insignificant disease remained constant. These findings suggest that the reservoir of undetected prostate cancers may be depleting, and that PSA-associated pathologic stage migration has plateaued. The current rate of detection may more accurately reflect the true incidence of disease.</p>

EDWARDS, TERESA

1. Title	Prevalence of Smoking Cessation Counseling at a Public Inner-city Hospital
2. Student Presenter:	Teresa M. Edwards
3. Co-workers and Collaborators:	N/A
4. Advisor:	Dr. John Daryl Thornton
5. Departments:	Pulmonary and Critical Care
6. Institutions:	Case Western School of Medicine MetroHealth Medical Center
7. Support:	NIH Heart, Lung and Blood Fellowship
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Background: Several studies have documented the effectiveness of inpatient smoking cessation counseling in a trial setting, but few have documented how often this occurs or its effectiveness in clinical practice.</p> <p>Methods: We interviewed 77 consecutive patients who had been admitted for at least 48 hours into a public inner-city hospital. Patient demographics and smoking status were ascertained, and patients were asked whether they were counseled to quit by their current providers, and their willingness to quit. Medical records were reviewed to determine which providers documented smoking status, whether nicotine replacement therapy (NRT) was prescribed, and whether cessation clinic referrals were made. Patients were called one week following discharge to determine change in smoking status.</p> <p>Results: 33 patients (43%) were current smokers and 20 (26%) former smokers - all 53 had smoking-related comorbidities. Of the 33 currently smoking patients, the average pack-years was 27+/-26. Smoking status was documented by ER staff for 9 (27%) patients, admitting nurse for 29 (88%), resident for 21 (64%) and attending for 6 (18%). Only 10 (30%) patients were counseled to stop smoking; 6 (18%) were counseled by a physician. None were offered NRT, and only 9 (27%) were referred to an ambulatory smoking cessation program. However, 21 (64%) desired aid with quitting. One-week post discharge, 3 more had been offered NRT or counseling prior to discharge, but 8 (24%) had subsequently quit spontaneously citing concerns about their health.</p> <p>Conclusions: In this ongoing study, smoking status of inpatients was quite prevalent but variably assessed. Among smokers, few were offered cessation therapy despite expressing a desire to quit. Further work is needed to determine the factors associated with inpatient smoking assessment and intervention.</p>

ELLIOTT, PATRICK

1. Title	Acculturation status and health care beliefs: a pilot study in minority populations
2. Student Presenter:	Patrick Elliott
3. Co-workers and Collaborators:	
4. Advisor:	Dr. Joseph Sudano
5. Departments:	Medicine
6. Institutions:	MetroHealth Community Hospital
7. Support:	Crile Grant
8. Please choose your academic program:	MD MPH
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Objectives: Little data exists on relationships between acculturation and healthcare beliefs regarding the nature of healthcare itself and medical encounters. Elucidating these relationships may contribute to improved understanding in minority population doctor-patient relationships and may also improve cultural competency.</p> <p>Methodology: I collected survey data from 342 subjects from outpatient clinic areas in an urban public hospital. I developed a 16-item survey that included 6 demographic and socioeconomic items and 10 health belief items. These latter items assessed patients' opinions and beliefs about the nature of healthcare (response options strongly disagree, disagree, neutral, agree, strongly agree) healthcare is a right, a privilege, should be ensured by government, etc.) and physician relationships (doctor takes my concerns seriously, charges too much, etc.). Acculturation was dichotomized--more/less acculturated--and operationalized by interview language--English or Spanish-speaking, respectively. I provide 1) descriptive statistics of demographic, socioeconomic, and health belief items; 2) psychometric properties of health belief items stratified by acculturation.</p> <p>Results: English-speaking respondents (n=186) were younger, had higher education levels, and were more likely insured compared to their Spanish-speaking counterparts (n=156). Spanish-speakers responded significantly more positively to the following: doctors charge fair prices; people should be personally responsible for obtaining healthcare; healthcare is a privilege. In contrast, English-speakers responded significantly more positively to the following: healthcare is a right, government should ensure healthcare. Factor loadings differed, as well. The average inter-item covariance was 0.13; scale reliability coefficient was 0.61.</p> <p>Discussion: Spanish and English-speakers have significantly different views on health care in several areas. I originally hypothesized that Spanish-speakers would be more likely to view healthcare as a right and something that government should ensure; however, the data suggests English-speakers are more likely to hold these views. These differences may be explained by a stronger sense of entitlement among the English-speakers compared to Spanish-speakers.</p>

EPPICH, JULIE

1. Title	Abnormal Pap Follow-up in a Suburban Family Practice
2. Student Presenter:	Julie Eppich, BS, MSII
3. Co-workers and Collaborators:	Patricia Kellner, MD and Susan Flocke, PhD
4. Advisor:	Susan Flocke, PhD
5. Departments:	Department of Family Medicine
6. Institutions:	Case Western Reserve University
7. Support:	Crile Research Fellowship
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Background: The focus of previous research on improving follow-up of abnormal Pap smears has been on low-income, minority women in urban, academic settings. However, follow-up rates of middle income women are between 50 – 70% and represent an important missed opportunity to prevent the progression of cervical cancer. This study was designed to evaluate a simple, yet systematic office reminder and tracking program in the setting of a suburban family practice and its effectiveness at improving the rate of follow-up of abnormal Pap smears.</p> <p>Methods: A retrospective chart review was conducted in a single suburban Family Medicine practice in Northeast Ohio. Sixty-five women with abnormal Pap test results were studied, 37 pre-intervention and 28 post. The main outcomes of interest were rate of adherence to recommended follow-up and delay in follow-up.</p> <p>Results: Overall, adherence to recommended follow-up during this time period was 92.1 %. There was no significant difference in follow-up rates detected after the implementation of a systematic reminder program; however there was a trend toward decreased delay in follow-up subsequent to the intervention (7.1 % vs. 24.3 %, $p = 0.533$). Of those receiving follow-up, 19.6 % were delayed, taking more than 3 months past the recommended follow-up to receive care. Patients with lower grade abnormalities were more likely to receive delayed follow-up care, while those who received a recommendation for colposcopy were less likely to have a delay in follow-up. Final collection of outcome measures for 14 cases is currently in progress and will be complete by presentation date and incorporated into these results.</p> <p>Conclusions: A simple reminder system that requires few resources can have a significant impact on the follow-up of abnormal test results. Busy family physicians can use this model as evidence for application in their own practices.</p>

ESTROVICH, IGOR

1. Title	The Vestibulo-Ocular Responses in Progressive Supranuclear Palsy
2. Student Presenter:	Igor E. Estrovich
3. Co-workers and Collaborators:	Ke Liao
4. Advisor:	R. John Leigh
5. Departments:	Departments of Neurology and Biomedical Engineering
6. Institutions:	Veterans Affairs Medical Center
7. Support:	Supported by NIH grant EY06717, the Office of Research and Development, Medical Research Service, Department of Veterans Affairs, and the Evenor Armington Fund.
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>PSP patients suffer from a high rate of falling early in the progression of the disease, and this tendency is a leading cause of morbidity. However, in contrast to the epidemiology and clinical sequelae of falling episodes, the underlying pathophysiology of why patients fall is not a completely solved body of knowledge. This study attempted to isolate the specific impairment of the vestibular reflexes that cause this propensity to fall. These experiments demonstrate that the angular vestibulo-ocular reflex (aVOR), which depends on the labyrinthine semicircular canals, is intact in PSP, while the translational vestibulo-ocular reflex (tVOR), which depends on the otoliths, is impaired. We measured eye rotations induced by horizontal head-and-body rotations (yaw) or vertical translations (bob), and combination of the two in five PSP and 15 control subjects. Subjects viewed small targets located either at 2 m or 15 cm while their eye movements were measured using the magnetic search coil technique and head movements were measured by infrared reflectance method.</p> <p>Control subjects showed increased gain of aVOR and tVOR during viewing of a near versus far target, as dictated by geometric factors. PSP patients showed an appropriate modulation of aVOR gain during near viewing, but a deficient tVOR during all viewing conditions. This study presents evidence that, in PSP, there is selective failure of translational vestibular ocular responses which sense linear accelerations, while angular vestibular ocular reflexes are preserved. Whereas this deficit in otolith vestibular ocular reflexes provides insight into the pathology of PSP, further experimentation is needed to determine if there is a corresponding deficit in the otolith-spinal reflexes, which are ultimately responsible for the falls.</p>

FELDMAN, KATHRYN

1. Title	Effect of cryopreservation on ovarian vessels' microvascular autografting
2. Student Presenter:	Kathryn Feldman
3. Co-workers and Collaborators:	Amr Kader, MD, Rakesh Sharma, PhD, Tommaso Falcone, MD, FRCSC, FACOG
4. Advisor:	Tommaso Falcone, MD, FRCSC, FACOG
5. Departments:	Obstetrics and Gynecology, Plastic Surgery
6. Institutions:	Cleveland Clinic Foundation
7. Support:	Crile Fellowship
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Background: Cryopreservation and autotransplantation of ovaries is an experimental strategy to preserve fertility. Present techniques result in severe ischemic damage of the auto-graft. Vascular grafting of cryopreserved whole ovaries was developed with the aim of improving post-transplantation ovarian ischemia. Our hypothesis is that cryopreservation may cause vascular endothelial damage increasing the risk of thrombosis, leading to post-transplantation vessel occlusion.</p> <p>Objective: to study the effects of cryopreservation and thawing techniques on ovarian vessels' structure, patency, and thrombus formation after microvascular anastomosis.</p> <p>Methods: Three ewes underwent bilateral oophorectomy. The right ovarian vessels were immediately grafted to the deep inferior epigastric vessels on the ipsilateral side. The left ovarian vessels were cryopreserved for approximately 2 weeks and consequently thawed. After thawing, these vessels were grafted to the left deep inferior epigastric vessels. Two weeks later, all vascular grafts were explored and excised. Vessels were checked for structural changes, patency, and thrombus formation.</p> <p>Results: Sheep #1 developed a seroma at the site of the fresh graft. The thawed vessels were so edematous that the grafting could not be performed. Sheep #2 had a functioning fresh graft, but did not recover from anesthesia. Sheep #3 had a successful fresh graft but only the cryothawed ovarian artery was grafted as the vein was varicosed and incompatible with the host vessel. On final exploration, the grafted fresh ovarian artery was functioning, and the vein was thrombosed. The grafted cryo-thawed artery was totally obliterated.</p> <p>Conclusion: The preliminary observations on this technique showed severe limitations. First, the technique of cryopreservation used appears to cause edema of the vessels post thaw that makes microvascular anastomosis very difficult. The technique of cryopreservation needs to be altered to avoid this effect. Second, even if the microvascular anastomosis is technically possible the cryopreservation process seems to have caused endothelial damage resulting in graft occlusion. Third, the technical limitation of discrepancy between the vessels anastomosed may require a different anatomical site.</p>

FORTUN, CHAD

1. Title	Effects of Keratan Sulfate on Proteolytic Cleavage of the Aggrecan Core Protein
2. Student Presenter:	Chad M Fortun
3. Co-workers and Collaborators:	
4. Advisor:	Dr. Thomas Hering
5. Departments:	Department of Orthopaedics
6. Institutions:	Case Western Reserve University
7. Support:	AFAR
8. Please choose your academic program:	MD MS
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>To date no data related to the initial hypothesis has been produced. Over the summer we performed a pilot study to determine the methods necessary to produce aggrecan substituted with KS and aggrecan deficient of KS.</p> <p>We determined the most appropriate cell line to be a wild type MDCK cell line and a mutant MDCK cell which are substituted with KS and KS deficient respectively. We also determined it is necessary to utilize a nucleofector to nucleofect our MDCK cell lines in order to increase our efficiency in transiently transfecting them with the plasmid carrying the genes for aggrecan production.</p> <p>This pilot study will allow us, in the coming months, to produce a large quantity of aggrecan substituted with KS and deficient in KS. This stock of aggrecan will allow us to carry out our original hypothesis.</p> <p>“Hypothesis: We hypothesize that the substitution pattern of keratan sulfate on the aggrecan molecule, which may vary according to age, anatomical location or pathology, will modulate the proteolytic cleavage of aggrecan.”</p> <p>Over the next few months and over the course of my research block the remaining questions will be addressed and answered.</p>

FRANCO, MARLENY

1. Title	Provider-level factors associated with HPV vaccine delivery to low-income residents in Cleveland.
2. Student Presenter:	Marleny Franco
3. Co-workers and Collaborators:	Stephen Asiimwe, MBChB, MS and Ann K. Avery, MD.
4. Advisor:	Ajay K. Sethi, PhD, MHS.
5. Departments:	Department of Epidemiology and Biostatistics at Case Western Reserve University, Department of Infectious Diseases at Metrohealth Center.
6. Institutions:	Case Western Reserve University, University Hospitals of Cleveland, Metrohealth Center.
7. Support:	T35 National Heart, Lung, & Blood Institute Research Opportunities for Minority Students Grant.
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Human papillomavirus (HPV), which causes cervical cancer, is thought to be the most common viral sexually transmitted infection (STI) in the United States. Cervical cancer is the third most common cancer in women in the U.S. In June 2006, the U.S. Food and Drug Administration approved Gardasil, a vaccine against strains 6 and 11 as well as 16 and 18, which cause approximately 90% of cases of genital warts and 70% of all cervical cancers, respectively. Although, prior to the vaccine's release, studies showed physicians' general approval and intention to recommend it, no studies have been published exploring these issues since the vaccine's availability. Our goals were to assess healthcare providers' attitudes, perceived barriers to vaccination and intention to recommend the vaccine to patients aged 9 to 26 years seeking low-cost or free health care in Cleveland and East Cleveland. Healthcare providers working in community health centers around the city were invited to complete a self-administered 68-item questionnaire. Due to delays in IRB approval, the data collection is currently still ongoing. Data collection and analysis is expected to be complete by December 2006. The results could potentially show significant discrepancies between providers' reported intent to recommend the vaccine prior to its release compared to their intent and attitudes now that the vaccine is available. Additionally, results will reveal providers' opinions regarding the age at which they feel it is appropriate to recommend the vaccine as well as the barriers they expect to encounter when recommending the vaccine to different age groups. This information would shed light on the attitudes that influence providers' level of compliance with HPV vaccination guidelines and would be useful in designing appropriate interventions to enhance compliance.</p>

FULLER, MOLLY

1. Title	The Role of BMP4 in Astrogliosis and Scar Formation following Spinal Cord Injury
2. Student Presenter:	Molly L. Fuller
3. Co-workers and Collaborators:	Rae Wang, Brian Rothstein, Anne DeChant
4. Advisor:	Robert H. Miller
5. Departments:	Department of Neurosciences
6. Institutions:	School of Medicine, Case Western Reserve University
7. Support:	This research is supported by grant #NS36674 to R.H.M.
8. Please choose your academic program:	MD PHD
9. What year are you in the program?	7
10. Body of Abstract (300 words or less)	<p>Bone Morphogenetic Proteins (BMPs) are members of the Transforming Growth Factor-β superfamily of cytokines which signal through intracellular molecules called Smads. BMP4 has been shown to promote differentiation of neural precursors into astrocytes at the expense of oligodendrocytes during development. We are investigating the role of continued expression of BMP4 in the adult central nervous system (CNS), and its influence on the biology of astrocytes in the injured spinal cord. In our rat model of a demyelinating lesion of the dorsal columns, injury leads to altered astrocyte behaviors, including cell hypertrophy, increased expression of glial fibrillary acidic protein (GFAP), and formation of a scar with accumulations of chondroitin sulfate proteoglycans (CSPGs). Local GFAP-positive astrocytes contain phosphorylated Smad1/5/8 in their nuclei, showing responsiveness to environmental BMP's. These activated astrocytes are present in the lesion before and during CSPG accumulation, which begins at 2 days post-injury. In vitro analysis of astrocyte responses show that treatment with BMP4 for 60 minutes induces a translocation of Smad1/5/8 from the cytoplasm to the nucleus and a dose-dependent increase in the phosphorylation of Smad 1/5/8. After 24 hours of BMP4 treatment, quantitative RT-PCR shows increased mRNA for several CSPG core proteins, including aggrecan, brevican, and neurocan. After 48 hours of BMP4 treatment, cells produce a dose-dependent increase in the amount of CSPG's deposited on the culture substrate. We hypothesize that a demyelinating lesion of the spinal cord causes a local increase in BMP4 signaling and dysregulation of CSPG expression by resident astrocytes. Inhibition of this response could limit scar formation and allow for improved recovery after CNS injury.</p>

GALLOGLY, MOLLY

1. Title	Kinetic Comparison of Human GRx1 and GRx2 as Deglutathionylation Enzymes
2. Student Presenter:	Molly Gallogly
3. Co-workers and Collaborators:	David Starke, Amanda Leonberg, Susan Gillenberger
4. Advisor:	John Mieyal, PhD
5. Departments:	Pharmacology
6. Institutions:	Case SOM
7. Support:	NIH R01 AG 024413 (JJM), NIH P01 AG 15885 (JJM), Dept. of Veterans' Affairs Merit Review Grant (JJM), NIH T32 GM07250 (MMG)
8. Please choose your academic program:	MD PHD
9. What year are you in the program?	6
10. Body of Abstract (300 words or less)	<p>Glutaredoxin (GRx) is a thiol-disulfide oxidoreductase (TDOR) that utilizes free glutathione (GSH) to reduce protein-glutathione mixed disulfides (P-SSGs), forming protein-SH and glutathione disulfide (GSSG). GRx-mediated deglutathionylation of proteins such as actin, PTP1B, and Ras serves important roles in cellular redox balance and signal transduction (Shelton et. al., 2005). Mammalian cells contain two GRx isoforms: GRx1, found in the cytosol and mitochondrial intermembrane space (Pai et al., 2006), and GRx2, localized to the nucleus and mitochondrial matrix (Lundberg et. al., 2001). Although GRx2 displays <35% sequence identity to GRx1 (Gladyshev et. al., 2001), it has an analogous active site motif (CXXC) and glutathionyl stabilization site (Bushweller et. al. 1994, Yang et. al. 1998). Here we report that GRx2 also mimics GRx1 remarkably in its catalytic mechanism. Like GRx1, GRx2 displays ping-pong kinetics whereby the apparent KM and Vmax values for protein-SSG and GSH change in proportion to the concentration of the other substrate. We also determined the pKa of GRx2's active site cysteine thiol by examining the pH dependence of enzyme inactivation by iodoacetamide. The active site cysteine's pKa was determined to be 4.5, one pH unit higher than the corresponding pKa value for GRx1. If the catalytic principle of GRx2, like GRx1, is dependent on the pKa value of the enzyme-SH leaving group (Gilbert, 1990), Grx2 is predicted to display 25% of the activity of GRx1 for a common protein-SSG substrate. Indeed, with either BSA-SSG or cysteine-SSG, the catalytic efficiency of GRx2 is about 25% of that of GRx1. Finally, we demonstrate that while GRx2 can couple to thioredoxin reductase (TRase), as reported by Johansson et al. (2004), turnover of GRx2 by TRase is far less efficient than turnover by the preferred coupling enzyme, GSSG reductase (GRase), even when GRase and GSH are present at one-tenth of their typical intracellular concentrations. Thus, turnover by TRase is unlikely to serve as an important contributing mechanism to GRx2 activity in situ, even under low GSH ("oxidative stress") conditions.</p>

GATHERWRIGHT, JAMES

1. Title	Hydrogen Peroxide Induced Changes in the Rac-Binding Domain of the PlexinB1 Receptor
2. Student Presenter:	James Gatherwright
3. Co-workers and Collaborators:	Rebecca Alviani, Preeti Chughari
4. Advisor:	Matthias Buck
5. Departments:	Physiology & Biophysics Department
6. Institutions:	Case Western Reserve University School of Medicine
7. Support:	
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Introduction: Current models propose that the principal function of Plexin is to bind and sequester active Rac1, removing it from the pool of GTPases that can interact with effector molecules, thereby reducing actin turnover and contributing to growth cone collapse. The Rac binding domain (RBD) contains a surface loop between an α and β helix. This loop has a CxxxS sequence which is similar to the CxxS motif indicative of a thiol-dependent redox enzyme. This suggests that under oxidative conditions, the RBD of Plexin can form disulfide bonds which may have effects on enzymatic activity and/or structural conformation. Oxidative signaling has already been implicated in a variety of other proteins and it has even been hypothesized that the protein MICAL exerts its effects by increasing Reactive Oxygenation Species (ROS) in the presence of Plexin.</p> <p>Objective: To demonstrate that ROS can induce structural changes in the RBD at physiological levels and to elucidate these changes using SDS-Page, NMR, and CD techniques.</p> <p>Results:</p> <ol style="list-style-type: none">1. Both the Cys34 and Cys112 mutants formed dimers under previously demonstrated conditions, while the NoCys mutant remained in the monomeric form after exposure to Hydrogen Peroxide.2. The incubation times showed no change in the ability of dimer to form.3. Multiple exposures had no effect on the amount of dimer formed.4. The molar concentration however did have an effect on the amount of dimer formed giving optimal conditions for either mutant (Cys112 50μM; Cys34 100μM) with an incubation time of 2hrs.5. NMR data pending.6. CD data pending. <p>Conclusions: Pending</p>

GENTRY, MILLICENT

1. Title	Identification of Microsatellite Markers in the mosquito <i>Aedes Aegypti</i>
2. Student Presenter:	Millie Gentry
3. Co-workers and Collaborators:	
4. Advisor:	Dr. Ronald Blanton
5. Departments:	Center for Global Health and Diseases
6. Institutions:	Case Western Reserve University
7. Support:	
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Dengue fever (DF) is a viral illness transmitted by the mosquito <i>Aedes aegypti</i>. It is the most important mosquito-borne disease affecting humans worldwide. Dengue is endemic in more than 100 tropical and sub-tropical countries, with 2.5 billion people at risk and an estimated 50 million new infections reported each year. Since a viable vaccine has yet to be developed, dengue prevention depends entirely on vector control. At present, little is known about subpopulation diversity in natural populations of <i>A. aegypti</i>, thus our goal was to develop novel microsatellite markers that might prove to be useful molecular tools in the study of genetic variability in <i>A. aegypti</i> populations. Microsatellites are some of the best neutral markers for population genetics studies, but in contrast to other mosquitoes, <i>A. aegypti</i> is known to be microsatellite-poor. Trimeric repeats were preferred since they produce less stuttering on gels. We searched GenBank entries directly for 16-21 mers with ~40% GC content that flank perfect trinucleotide repeats and that would produce an amplicon of ~100-300 nucleotides. A single set of PCR conditions was used to eliminate many sources of error, to maximize efficiency and increase comparability across laboratories. In all we identified 4 promising microsatellites. These produced a simple pattern amplifying genomic DNA from laboratory-bred mosquitoes from Johns Hopkins University and the Oswaldo Cruz Foundation, Brazil. All markers produced either homo- or heterozygotes. They had heterozygosities of 72, 50, 25 and 88% and a maximum of 3 alleles using small samples of 8-10 individuals. The laboratory will continue to identify an additional 6 markers. These will be used to generate the genetic indices F_{st} and N_e so that the distribution of the vector and the effect of control programs could be more effectively monitored.</p>

GIBBINS, KAREN

1. Title	Effects of Exercise and Nutrition Intervention on Depression and Eating Behavior Thoughts in Endometrial Cancer Survivors
2. Student Presenter:	Karen Gibbins
3. Co-workers and Collaborators:	Vivian VonGruenigen, Heidi Gibbons, Steven E. Waggoner, Mary Beth Kavanagh, Jeffrey Janata, Kerry S. Courneya, and Edith Lerner
4. Advisor:	Vivian VonGruenigen
5. Departments:	Gynecologic Oncology
6. Institutions:	University Hospitals
7. Support:	Crile Fellowship
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Background: Endometrial cancer survivors are typically plagued by comorbidities related to obesity. Diagnosis and treatment of cancer could serve as a teachable moment for patients to make lifestyle changes that would decrease these comorbidities. Long-term changes need to address not only behavior, but also emotional thinking and concerns.</p> <p>Question: In terms of depression and thoughts regarding eating behaviors, how are the cognitions of endometrial cancer survivors changed by a six month exercise and nutrition intervention?</p> <p>Methods: 45 patients post-treatment for early stage endometrial cancer were randomized to intervention or control groups for six month exercise and nutrition counseling. Patients completed the Beck Depression Index, 3 Factor Eating Inventory (EI), and Weight-Efficacy Lifestyle (WEL) questionnaires at baseline and post-intervention.</p> <p>Results: At baseline, 15% had mild depression, 4% had moderate depression, and 4% had severe depression. At 12 months, 16% had mild depression and 3% had moderate depression, with an overall decrease in Beck score of 2.5 ($p < 0.001$). There was no difference in Beck score change between groups. EI revealed patient problems with eating restraint and did not show any difference between groups. WEL total scores were significant comparing baseline to 6 months (Difference = 29, $p < 0.05$) and baseline to 12 months (Difference = 3.5, $p < 0.05$). The significant factor subsets in the intervention group were Social Pressure and Positive Factors.</p> <p>Conclusion: The six month intervention was effective in positively changing mental state regarding efficacy in Social Pressure and Positive Factors. These cognition changes suggest feasibility of maintaining the weight and exercise changes made during intervention.</p>

GIFFORD, TYLER

1. Title	Maximizing Production of Dissociated Purkinje Neurons for use in Patch Clamp Analysis
2. Student Presenter:	Tyler Gifford
3. Co-workers and Collaborators:	Ovsepyan, S. and Friel, D.
4. Advisor:	Friel, D.
5. Departments:	Neuroscience
6. Institutions:	Case Western Reserve University School of Medicine
7. Support:	<p>Raman and Bean, Ionic Currents Underlying Spontaneous Action Potentials in Isolated Cerebellar Purkinje Neurons. <i>Journal of Neuroscience</i>, 1999. 19 (5) 1663-1674.</p> <p>Womack and Khodakhah, Dendritic Control of Spontaneous Bursting in Cerebellar Purkinje Cells. <i>Journal of Neuroscience</i>, 2004 • 24 (14) 3511–3521</p>
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Background and rationale: P/Q type Calcium channels are expressed on the surface of Purkinje cells in mouse cerebellum. Therefore the Purkinje cells are a good candidate for studying calcium current and its effect in P/Q type mutants. My work focused on developing a reproducible technique for preparing dissociated Purkinje cells and measuring current and voltage using patch clamping.</p> <p>Question or hypothesis that I addressed: What is the optimal preparation method for preparing dissociated Purkinje cells for patch clamping?</p> <p>Methods used to pursue this question: Previously established procedures for preparation of Purkinje neurons have been published by Raman and Bean (1999) and Womack and Khodakhah (2004). Based on these techniques, a procedure was developed for dissociating Purkinje neurons that maximally preserved dendritic arborization without compromising cell viability. Variables included exposure time to protease and repetitions of trituration. Outcome measures included number of live cells obtained per brain slice and preservation of dendritic tree. Cell viability was confirmed with detection of normal electrical activity detected with patch clamp.</p> <p>Results: Maximum live cells were obtained with a protease exposure time of 12 minutes. Five repetitions of rapid trituration produced adequately dissociated cells with detectable dendritic trees. Patch clamping under voltage clamp detected normal oscillations and spontaneous firing in dissociated cells.</p> <p>Conclusion: A customized technique based on methods published by Raman and Bean and materials published by Womack and Khodakhah produced the maximum number of viable cells with detectable dendritic trees and normal electrical activity.</p>

GITTINGER, MATTHEW

1. Title	Detection of Peripheral Blood Mononuclear Cells in S-phase by Flow Cytometric Analysis of Ki-67 and Cyclin A Co-expression
2. Student Presenter:	Matthew Gittinger
3. Co-workers and Collaborators:	Scott Sieg Ph.D. and Doug Bazadar
4. Advisor:	Dr. Michael Lederman M.D.
5. Departments:	Medicine and Infectious Disease
6. Institutions:	Case Western Reserve University
7. Support:	NIH and Dr. Lederman's discretionary funds
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>HIV infection is characterized by an increased proportion of circulating T-lymphocytes found in S-phase of the cell cycle. Previous studies suggest S-phase T-cells are more likely to undergo apoptosis instead of completing the cell cycle, and proportions of these cells are directly related to plasma HIV levels. We use uptake of bromodeoxyuridine (BrdU), a thymidine analogue that is incorporated into newly synthesized DNA, to identify cells in S-phase. These cells are detected by flow cytometric analysis using a fluorochrome labeled antibody to BrdU. Frozen peripheral blood mononuclear cell (PBMC) samples from HIV+ patients who have been followed in our clinic are available for research, but studies suggest frozen samples are not efficiently labeled with BrdU. These samples could provide a resource for testing the relationship between rates of CD4 cell loss and frequencies of circulating S-phase T-cells over time. The purpose of this study was to identify cellular markers that permit detection of lymphocytes in S-phase of the cell cycle when examining frozen samples.</p> <p>We reasoned that identifying T-cells expressing Ki-67, an intracellular protein present during G1, S, and G2/M phases of the cell cycle, and cyclin A, another intracellular protein characteristic of S-phase cells, might provide an alternative method for detecting cells in S-phase. We tested this approach by stimulating healthy PBMCs with anti-CD3 antibodies to induce cell cycle progression in vitro. T-cells were analyzed for co-expression of Ki-67, cyclin A, and BrdU. Analyses of CD4+ lymphocytes demonstrated that stimulated cells labeled with BrdU corresponded to cells expressing both Ki-67 and cyclin A. Cells from these samples were frozen and thawed after 1 week to test for the stability of cyclin A in freeze-thaw conditions. Expression of this marker was not altered by the freeze-thaw method, suggesting it should be stable in cryopreserved PBMC samples.</p>

GLAZER, DANIEL

1. Title	Methoxyamine and benzylguanine potentiate the therapeutic efficacy of temozolomide in a human glioma cell line
2. Student Presenter:	Daniel Glazer
3. Co-workers and Collaborators:	Alina Bulgar, John Donze, Yanling Mao
4. Advisor:	Lili Liu and Stan Gerson
5. Departments:	Hematology/Oncology
6. Institutions:	Case Western Reserve University
7. Support:	American Cancer Society and the NIH
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>This project focused on the combined cytotoxic effects of temozolomide, methoxyamine and benzylguanine on a human glioma cell line. The purpose of my work was to determine if the effect of these three drugs in combination is greater than the effect of temozolomide alone. This is an important question because malignant cells are able to repair the DNA damage caused by temozolomide using base excision repair (BER) and the protein MGMT. These two repair pathways can be blocked by the inhibitors methoxyamine and benzylguanine, potentiating temozolomide cytotoxicity. To determine the efficacy of the drugs in combination I constructed a survival curve relating the drug dose to percent survival of glioma cells. Next, I did an AP site analysis to measure the percent of abasic sites that are bound by methoxyamine and thus blocked from repair. To quantify the effect of these drugs in cell culture I used Annexin V staining and cell cycle analysis to determine the amount of apoptosis and cell cycle arrest respectively. Lastly, I used JC-1 staining to examine the level of mitochondrial damage caused by these compounds. These experiments clearly show that methoxyamine and benzylguanine potentiate the cytotoxic effects of temozolomide. In combination they are roughly ten times more potent than temozolomide alone as shown by the survival curves. AP site analysis demonstrated a 50% blocking of abasic sites by methoxyamine, leading to a greater accumulation of DNA damage than would be expected with temozolomide alone. The results from Annexin V, cell cycle analysis, and JC-1 staining were consistent with these findings, as the three drug combination proved to be superior to temozolomide alone. It is clear that benzylguanine and methoxyamine have a synergistic effect when used in combination with temozolomide. By inhibiting the BER and MGMT repair pathways, temozolomide becomes a much more effective drug.</p>

HARTUPEE, JUSTIN

1. Title	IL-17 Induces Chemokine Expression via mRNA Stabilization
2. Student Presenter:	Justin Hartupee
3. Co-workers and Collaborators:	
4. Advisor:	Thomas Hamilton
5. Departments:	Department of Immunology
6. Institutions:	Lerner Research Institute, Cleveland Clinic
7. Support:	
8. Please choose your academic program:	MD PHD
9. What year are you in the program?	4
10. Body of Abstract (300 words or less)	<p>IL-17 is a T cell derived cytokine that plays an important role in both host defense and autoimmunity by driving pro-inflammatory gene expression. However, the molecular mechanisms by which this induction occurs are not well understood. We have used the mouse chemokine CXCL1 (KC) as a model to study this process. KC expression is known to involve both the initiation of transcription as well as stabilization of the rapidly decaying mRNA. KC followed the typical pattern of IL-17 regulation in that IL-17 alone stimulated little expression, but it could cooperate with TNFα to induce a synergistic response. We have determined that IL-17 is a relatively poor stimulus for KC transcription and the activation of the transcription factor NF-κB. However, both actinomycin D chase experiments and studies using a tetracycline-regulated reporter indicate that IL-17 prolongs the half-life of the KC mRNA. Thus TNFα and IL-17 cooperate because they each provide half the requirements for full gene expression. TNFα induces transcription while IL-17 drives mRNA stabilization. IL-17 induced stabilization required the cytoplasmic adaptor Act1, which has recently been reported to interact with the IL-17R and to be required for the induction of gene expression. TRAF6 is recognized to function downstream of Act1 to mediate IL-17 induced NF-κB activation. TRAF6 also plays a role in signaling in response to other stimuli that result in KC mRNA stabilization such as IL-1 and toll like receptor ligands. This association suggested that TRAF6 may be part of a common signaling cascade that drives mRNA stabilization in response to multiple stimuli. However, using both a dominant negative construct and deficient cells we have determined that mRNA stabilization in response to IL-1 and IL-17 does not require TRAF6. This data indicates the existence of an uncharacterized TRAF6 independent signaling pathway that mediates mRNA stabilization.</p>

HEAPHY, JOHN

1. Title	Phthalocyanine 4 (Pc 4)-Photodynamic Therapy for the Treatment of Benign Viral Induced Tumors
2. Student Presenter:	John Heaphy
3. Co-workers and Collaborators:	Richard Lee M.D.
4. Advisor:	Kumar Alagramam Ph.D.
5. Departments:	Otolaryngology
6. Institutions:	CWRU
7. Support:	
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Recurrent Respiratory Papillomatosis (RRP) lacks a satisfactory treatment modality. Photodynamic therapy (PDT) is the use of light to activate an exogenous photosensitizer to initiate physical and chemical changes within a targeted cell population for therapeutic effect. Pc4, a photosensitizer, is a silicon phthalocyanine ring that works by targeting mitochondrial membranes and activating cellular pathways of apoptosis through generation of reactive oxygen species. To test the efficacy of Pc 4 PDT for the treatment of virally induced papillomas, a xenograft model where New Zealand white rabbit epithelium was grafted on to the backs of SCID mice was used. The rabbit epithelium was harvested from the backs of the rabbit's ears. Xenografts 7 mm in diameter were punched out and transplanted to the backs of SCID mice, two grafts per mouse. After the grafts healed, a subset of the xenografts were infected with Cottontail rabbit papilloma virus (CRPV). Once the papillomas formed the mice received tail vein injections of Pc 4. After 48 hours, to allow for washout of Pc 4 from tissues that do not have rapidly dividing cells, the skin grafts were exposed to laser light from a tunable Argon pumped-dye laser at a wavelength of 675 nanometers to activate the photosensitizer.</p> <p>Results and conclusion: Of the 11 mice that were treated with Pc4 PDT to remove CRPV induced papillomas, 10 were successful in complete removal of the growth. Of those 10 which were successfully treated, 8 have subsequently remained tumor free several weeks after treatment. These mice are still being monitored for potential papilloma regrowth. Data from the current study suggests that Pc 4-PDT is effective in eradicating virally induced papillomas in the xenograft model. However, long term studies are necessary to validate the efficacy of Pc 4-PDT against virally induced papillomas and their recurrence.</p>

HOSSAIN, HOMAIRA

1. Title	Changes in Body Tissue Composition in Morbidly Obese Patients Following Bariatric Surgery.
2. Student Presenter:	Homaira Ayesha Hossain
3. Co-workers and Collaborators:	Pamela Marks, Aaron Eckhauser, James Isbell, Phillip Williams, Kong Chen
4. Advisor:	Naji N. Abumrad, MD
5. Departments:	Department of Surgery
6. Institutions:	Vanderbilt University School of Medicine
7. Support:	National Institutes of Health
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Studies have shown that the risk for insulin resistance and diabetes is greatly increased in the obese. One type of treatment to bring about weight loss is bariatric surgery, which is performed on patients who are morbidly obese. The purpose of this study was to examine the changes that occur in body tissue composition following Roux-en-Y gastric bypass surgery. We utilized DEXA scans, measurements of body weight, body height, body mass index (BMI) and waist-to-hip ratio (WHR) to trace the changes that occurred from the pre-op to 6-months to 1-year following surgery. DEXA scans allowed us to calculate the changes in percent Fat Mass (FM) and percent Lean Body Mass (LBM) in various body regions of interest (e.g. arms, legs, trunk, android, and gynoid regions). We found that following RYGB, there was a 35% reduction in BMI after one year, while the WHR decreased from 0.89 to 0.82 (both significant at $p < 0.05$). In the first six months after surgery, FM loss and LBM loss were about equal and amounted to 18.3 kg and 19.5 kg, respectively. In the second six months after surgery, FM loss (9.6 kg) was greater than LBM loss (1.9 kg, $p < 0.01$). Overall, in the cumulative 1-year period, FM loss (27.9 kg) was greater than LBM loss (21.5 kg). Interestingly, the greatest percent FM loss and LBM loss occurred in the trunk and the legs. These findings have raised some interesting issues that must be addressed when considering bariatric surgery. Wouldn't it be ideal if following weight loss surgery, patients could only lose FM and not so much LBM? We need to design methods--nutritional, exercise, or otherwise--to enhance loss of FM and diminish loss of LBM. Also, since most of the LBM losses in the first year occur mostly in the trunk and legs, we need to design exercise protocols to enhance LBM preservation. Future studies could determine whether interventions such as strength training could diminish loss of LBM in those areas.</p>

HUDSON, MICHAEL

1. Title	NPP1, a Physiological Inhibitor of Calcification, in Human Pulmonary Artery Smooth Muscle Cells
2. Student Presenter:	Michael L. Hudson
3. Co-workers and Collaborators:	Domenick A. Prosdocimo
4. Advisor:	George R. Dubyak, Ph.D.
5. Departments:	Department of Physiology and Biophysics
6. Institutions:	Case Western Reserve University
7. Support:	This research was conducted with support from the Crile Summer Research Fellowship at Case Western Reserve University offered by the Dean's Office of Case Western Reserve University School of Medicine, the Crile Research Endowment, and NIH grant HL18708 (G. Dubyak, PI).
8. Please choose your academic program:	MD MS
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Nucleotide pyrophosphatase/phosphodiesterase 1 (NPP1) is a type-II transmembrane ectonucleotidase that acts as a physiological inhibitor of calcification by increasing extracellular pyrophosphate (PPi) in connective tissue matrices. This increase in extracellular PPi is opposed by the hydrolysis of PPi to phosphate (Pi) by the GPI-anchored ecto-alkaline phosphatase (ALP). Studies have shown that macrophages activated by T cell-derived cytokines such as interferon-γ (IFN-γ), in the presence of 1α,25-dihydroxyvitamin D3 (1,25(OH)$_2$D3), increase expression of ALP in human vascular smooth muscle cells (hVSMCs) through production of inflammatory mediators, specifically tumor necrosis factor-α (TNF-α) and oncostatin M (OSM). Since calcification homeostasis is influenced by regulation of NPP1 and ALP through the dynamic interplay of PPi and Pi, we hypothesized that macrophage-induced increases in ALP expression would be associated with increased NPP1 activity. To test this hypothesis, we cocultured human pulmonary artery smooth muscle cells (hPASMCs) and human monocytes (THP-1) for 4 days in the presence of IFN-γ and 1,25(OH)$_2$D3. ALP activity was measured by a colorimetric assay of whole cell lysate using a microplate spectrophotometer. NPP1 activity was assayed by the metabolism of fluorescently-derived β-MeATP (β-MeATP) via HPLC. Cocultures of hPASMCs and THP-1 cells treated with IFN-γ and 1,25(OH)$_2$D3 showed no increase in NPP1 activity when incubated with β-MeATP for 1 hour. We also did not observe an increase in ALP or total phosphodiesterase activity in the treated cocultures. Further analysis of the hPASMC cultures indicated reduced levels of α-smooth muscle actin when compared to 1$^{\circ}$ rat aortic smooth muscle cells. We speculate that the absence of predicted increases in NPP1 activity can be explained by loss of 1$^{\circ}$ smooth muscle phenotype in our relatively high passage (p. 13) hPASMCs. Additional studies are necessary to determine whether ALP upregulation in smooth muscle cells occurs concomitantly with increased NPP1 activity.</p>

HUH, EUN

1. Title	Punica granatum L. extract inhibits IL-1beta induced activation of p38-mitogen activated protein kinase and suppresses IL-1beta induced expression of ICAM-1 in Human Umbilical Vein Endothelial Cells in vitro
2. Student Presenter:	Eun Huh
3. Co-workers and Collaborators:	Meenakshi Shukla, Kalpana Gupta
4. Advisor:	Dr. Tariq Haqqi
5. Departments:	Medicine - Rheumatology
6. Institutions:	Case Western Reserve University
7. Support:	
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Background: Inflammatory cytokines produced by activated macrophages in the synovium have been identified as the major inducers of endothelial cells (EC) activation in rheumatoid arthritis (RA). Activated EC lining the blood vessels produce a number of inflammatory mediators and express cellular adhesion molecules (CAM). The expression of the adhesion molecules is central to the attachment of leukocytes to the endothelium and secreted chemokines then direct transendothelial migration of activated leukocytes to the site of inflammation. Decrease in inflammatory cytokine production and decreased expression of E-selectin and ICAM-1 have been shown to be associated with improved joint function and disease remission.</p> <p>Human umbilical vein endothelial cells (HUVEC) upregulate the expression of selectins when stimulated by IL-1? in vitro. p38-mitogen activated protein kinase (p38-MAPK) has been shown to be an important regulators of CAM expression, targeting p38-MAPK is emerging as a novel therapeutic approach for the treatment of various inflammatory disorders. Our lab has previously shown that an extract of pomegranate fruit (PFE) was highly effective in suppressing the cytokine-induced activation of p38-MAPK in human chondrocytes. In this study we set out to determine whether PFE will suppress the IL-1?-induced activation of p-38 MAPK and whether PFE will suppress the IL-1?-induced upregulation of adhesion molecules E-Selectin and ICAM-1 in HUVEC in vitro.</p> <p>Methods: HUVEC were pretreated with PFE at different concentrations (10-200 ?g/ml) for 90 minutes then stimulated with IL-1beta (2 and 5 ng/ml) for 60 minutes, 6 and 24 hours. Expression of E-selectin and ICAM-1 was quantified using flow cytometry. The expression and phosphorylation of p38-MAPK was determined by Western immunoblotting.</p> <p>Results: The HUVEC used, from Cambrex Corporation, did not express E-selectin. At high PFE concentrations (200 ?g/ml) IL-1?-induced expression of ICAM-1 was inhibited (5-20%). The same dosage of PFE was highly effective in suppressing the IL-1?-induced phosphorylation of p-38 MAPK in HUVEC.</p> <p>Conclusions: PFE or its metabolites may be beneficial in treating inflammatory activation of EC by suppressing phosphorylation of p38-MAPK and the expression of ICAM-1.</p>

INUI, TAZO

1. Title	Community-Acquired vs. Nosocomial Intra-abdominal Infections: a Retrospective Review of Origin and Outcome
2. Student Presenter:	Tazo S. Inui
3. Co-workers and Collaborators:	
4. Advisor:	Dr. Mark A. Malangoni
5. Departments:	Department of Surgery
6. Institutions:	Metrohealth Medical Center
7. Support:	NIH T-35
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>BACKGROUND: While nosocomial secondary peritonitis and intra-abdominal infections (IAIs) are assumed to be associated with greater morbidity and mortality in the surgical patient, little research has compared nosocomial IAIs with community-acquired (CA) IAIs. HYPOTHESIS: the aim of this retrospective chart review was to determine if more negative outcomes are associated with nosocomial IAIs seen and surgically treated at a large, urban, tertiary care center between 1999 and 2006. METHODS: Using a combination of ICD-9 CM codes, the electronic health records of patients who were classified as having a disease state associated with secondary peritonitis and who had undergone a surgical intervention (either via operation or radiologically-guided drainage) were analyzed for etiology of disease, intervention, associated flora, and outcome. Primary endpoints included mortality, PE/DVT, MI/arrhythmia, the need for re-operation or re-drainage. Secondary endpoints included: days in ICU, greater than 72 hrs on assisted ventilation, and associated infection (e.g. sepsis, pneumonia, UTI, additional IAIs/pelvic abscesses). RESULTS: There are currently 246 patients who meet the above criteria. Twenty-eight patients were diagnosed with nosocomial IAIs. Four of the patients with nosocomial IAIs (14%) died during the course of hospitalization, compared with 6 of the patients with CA IAIs (2.7%). Seven patients suffered MIs (5 CA IAI, 2 nosocomial); 10 had arrhythmias (5 CA IAI) after surgical intervention. 5 DVTs were reported (3 CA IAI). Sixteen of CA IAIs (7%) returned to the OR once; 15 (6.8%) required additional CT-guided drainage. Nine patients with nosocomial IAIs (32%) returned for re-exploration in the OR; 7 (25%) required additional CT-guided drainage. CONCLUSION: There is substantial additional morbidity and mortality for patients who acquire nosocomial IAIs. Further research is warranted to more precisely determine causative factors, and to identify potential avenues for reducing the risk of nosocomial IAIs.</p>

JAVAHERI, SOGOL

1. Title	The Distribution of Calsequestrin in the rat brain
2. Student Presenter:	Sogol Javaheri
3. Co-workers and Collaborators:	Zhen-zhen Wu and Dale Feng
4. Advisor:	Dale Feng and Kingman Strohl
5. Departments:	Pulmonary
6. Institutions:	VA Medical Center
7. Support:	Crile T35 scholarship
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Calsequestrin is the most abundant Ca²⁺-binding protein in the sarcoplasmic reticulum of skeletal and cardiac muscle and also exists in the brain. Our preliminary data demonstrated that when compared to age-matched rats in usual cage conditions, juvenile rats given the opportunity to exercise (wheel running) for six weeks show an increase in frontal cortical and hippocampal levels of calsequestrin-2 but not calsequestrin-1. However, there is no data about how these proteins are distributed in the brain and the neurons. We proposed to map these proteins in the entire brain in the rat by immunohistochemistry. 4 rats were killed by transcardiac perfusion with 4% paraformaldehyde in PBS buffer. Brains were removed, processed with 30% sucrose and then coronal sections were cut at 30 μ. Sections were blocked with animal serum, incubated with rabbit antibody against calsequestrin-1 and goat antibody against calsequestrin-2 and then with secondary goat antibody against rabbit and secondary horse antibody against goat. Then standard ABC procedure provided by the Vector's Lab was followed, and positive stained cells were revealed by the DAB method from the same company. Sections were mounted on slides and viewed under a light microscope. Preliminary results indicate that cells positively stained by antibodies against both calsequestrin-1 and 2 existed in the brain tissue. Cell positively stained by calsequestrin-2 are much more abundant than that of calsequestrin 1. These cells distributed thoroughly in the cortex, hippocampus, and brain stem. In the cortex most cells are in grey matter and in deeper layers such as layer IV. This implicates that the proteins coexist with neurons but not glial cells. However, characterizing the distribution of these proteins with double staining technique is needed. We plan to double-label both calsequestrin-1 and 2 with other enzymes and to use electron microscopy technology to further study these proteins.</p>

JOSEPH, SHARMA

1. Title	Nivirapine Drug Resistance Detected More Sensitive
2. Student Presenter:	Sharma Joseph
3. Co-workers and Collaborators:	Matt LaLonde
4. Advisor:	Dr. Eric J. Arts
5. Departments:	Center for AIDS Research
6. Institutions:	Case Western Reserve School of Medicine
7. Support:	
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>The purpose for the project was to employ an oligonucleotide ligation assay that was developed by Dr. Arts and his lab. This assay is unique in that as compared to the genotypic and phenotypic approaches currently employed, it is believed that mutant virus can be detected up to a sensitivity of 0.5% as compared to the current 20%.</p> <p>To address the project more specifically, the hope was to characterize NNRTI-associated mutations by single nucleotide polymorphism analysis of clinical samples obtained from a cohort of mother-child pairs in which the mothers received a single dose of nevirapine to prevent mother-to-child transmission of the virus. The mutations to be probed for were the K103N and the Y181C mutations as these are the first mutations usually seen in clinical NVP drug resistance. How drug-resistant virus is maintained over time was also hoping to be studied. The results of this second component are of course as yet unknown. I may eventually see that these resistance mutations are not fit and disappear as more competent viruses are permitted to outgrow them in the presence of drug pressure. This would be manifested in the disappearance of the drug-resistance mutations at different timepoints.</p>

KAN, CHARLENE

1. Title	Mammary Epithelial Cells Transformed by Cyclin-Dependent Kinase Hyperactivity are Partially Sensitized to p53-mediated Arrest in Response to Nutlin-3
2. Student Presenter:	CE Kan
3. Co-workers and Collaborators:	MW Jackson
4. Advisor:	GR Stark
5. Departments:	Department of Genetics and Department of Molecular Genetics
6. Institutions:	Case Western Reserve University, Case Comprehensive Cancer Center and The Cleveland Clinic Foundation, Lerner Research Institute
7. Support:	NIH RO1 funding to George Stark
8. Please choose your academic program:	MD PHD
9. What year are you in the program?	4
10. Body of Abstract (300 words or less)	<p>Cyclin D1, a key cell cycle regulator, initiates cell cycle progression from G1 to S phase by complexing with cyclin-dependent kinases (CDK) to promote the phosphorylation of RB and therefore E2F-dependent transcription. Overexpression of cyclin D1 is frequently observed in breast carcinomas and expression of constitutively active cyclin D1 has been shown to transform mink epithelial cells in vitro. We show here that CDK hyperactivity transforms immortalized human mammary epithelial cells (HMECs) independently of p53 inactivation, but that cells retaining p53 activity remain relatively sensitive to cellular arrest induced by Nutlin-3, an Hdm2 antagonist that stabilizes p53. Cells lacking p53 were resistant to Nutlin-3 regardless of cyclin D1/cdk status. Regarding cells containing functional p53, control cells exhibited a decrease in phosphorylated RB upon Nutlin-3 treatment, while D1/cdk expressing cells maintained phosphorylated RB levels. This indicates that there exist additional RB-independent mechanisms for cdc2 down regulation. Following removal of Nutlin-3, cdc2 remained suppressed in both control and D1/cdk-expressing cells. We conclude that the D1/cdk complex is able to disrupt the necessary pathways in order to cause transformation in vitro; however, the p53 pathway can still be activated to cause cellular arrest as evidenced by the partial resistance to Nutlin-3 treatment. This indicates that compounds such as Nutlin-3 which activate the p53 signaling pathway may be effective in breast cancers which over express cyclin D1 but still have wild type p53 signaling.</p>

KAN, JUSTIN

1. Title	Evaluation of Trauma Team Activation Protocol at a Level I Trauma Center
2. Student Presenter:	Justin Kan
3. Co-workers and Collaborators:	Patricia Wilczewski, RN
4. Advisor:	Jeffrey Claridge, MD
5. Departments:	Department of Surgery, Division of Trauma, Burns, and Critical Care
6. Institutions:	Metro Health Medical Center
7. Support:	Crile fellowship, MetroHealth Department of Surgery Funds, and Dr. Claridge is supported in part by the National Institutes of Health, National Institute of Child Health and Human Development, Multidisciplinary Clinical Research Career Development Programs Grant K12 HD049091
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Background: There are criteria that are used to trigger trauma team activation based on prehospital assessment of trauma patients. These trauma activations involve the mobilization of a health care team and utilization of a large amount of resources. Patients who require trauma activations are thought to need rapid assessment, potential intervention, and presumed admission to the hospital at a priority above other patients.</p> <p>Hypothesis: Certain criteria are not associated with the necessity of trauma activations.</p> <p>Methods: A prospective observational study was performed at a level one trauma center on all trauma activations between August 1, 2005 and January 31, 2006. Data collected included mechanism of injury, trauma activation criteria, age, gender, disposition, and patient identifiers. Specific Trauma team activation criteria were evaluated to identify which criteria were associated with admission.</p> <p>Results: 2067 patients were evaluated with the average age of 37.5 years. 70% were male and 87% of patients suffered blunt injury, of which motor vehicle crashes were the most common mechanism. The two most common single criteria were Glasgow Coma Score (GCS) of 12–14 seen in 27% of patients and a reported high speed motor vehicle crash (MVC > 45 mph) seen in 37.5% of patients. There was no association between GCS of 12 – 14 with admission. In patients with a GCS of 12-14, 27% were admitted and 25% were discharged (p=0.36). There was a significant inverse association between MVC > 45 mph and admission. In patients with a MVC > 45mph, 26% required admission and 39% were discharged (p<0.001).</p> <p>Conclusions: Despite the most common reasons for trauma activations, a GCS of 12-14 had no association with admission, and MVC >45 mph had an association with discharge from the hospital. Thus, patients with one of these two criteria could be a target population to decrease resource allocation.</p>

KAWAI, YU

1. Title	Cognitive and Behavioral Functioning in Children with Congenital Heart Disease: A Pilot Study
2. Student Presenter:	Yu Kawai
3. Co-workers and Collaborators:	
4. Advisor:	Dr. Patricia Klaas and Dr. Lourdes Prieto
5. Departments:	Children's Hospital - Congenital Heart Disease
6. Institutions:	Cleveland Clinic
7. Support:	None
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Children with congenital heart defects are more likely to experience acute or chronic hypoxia, especially for those who receive cardiac repair surgery, compared to children without congenital heart malformations. The hippocampus is vulnerable in hypoxic or anoxic events often resulting in memory and cognitive difficulties. Hypoxemia may also result in academic, emotional, and behavioral difficulties in children. However, no known studies have systematically investigated these factors as they pertain to children with congenital heart defects who have required cardiac repair surgery. Our primary goal is to investigate the long term effects of congenital heart defects on cognitive and behavioral functioning in children ages 6-16 who have undergone surgical intervention compared to those with congenital heart malformations who have not had any surgical intervention. The patients will be evaluated based on results from the Conner's Parent Rating Scale – Revised (S), Achenbach Child Behavior Checklist for Ages 6-18, and history questionnaire concerning early childhood development, medical history, and academic placement. The study is on-going and the data is currently being collected. It is anticipated that parents of children who required cardiac repair surgery will report greater cognitive and behavioral difficulties than those of children with cardiac conditions that have not undergone surgery. The effect of chronic cyanosis will also be evaluated by comparing children who have required cardiac surgery for cyanotic versus acyanotic heart disease. It is anticipated that children with cyanotic heart disease requiring surgery will demonstrate a higher likelihood of cognitive and behavioral difficulties on these measures than children with acyanotic heart disease requiring surgery. It is hoped that information obtained from this study will assist in developing a better understanding of the cognitive and behavioral sequelae of congenital heart defects and their surgical intervention in children and the development of early interventions aimed at reducing cognitive and behavioral difficulties.</p>

KHATRI, RINA

1. Title	The role of a single nucleotide polymorphism in the MDM2 promoter in Glioblastoma Multiforme
2. Student Presenter:	Rina Khatri, B.A.
3. Co-workers and Collaborators:	Kapila Navaratne, M.S., Robert J. Weil, M.D.
4. Advisor:	Robert J. Weil, M.D.
5. Departments:	Brain Tumor Institute
6. Institutions:	Cleveland Clinic, OH 44195
7. Support:	
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Purpose: Glioblastoma multiforme (GBM) is the most common form of primary brain tumor in adults, and has very poor outcomes (5-year survival of <5%). The aggressive behavior of these tumors makes therapeutic intervention both a challenge and a necessity. A better understanding of the molecular alterations in GBM that influence survival and response to therapy is a key step in advancing treatment efficacy. Dysregulation of the p14arf/MDM2/p53 tumor suppressor pathway has been proposed as a potential mechanism by which astrocytic cells undergo malignant transformation. Mutations in p53 have been found in 25-40% of tumors and MDM2 mutations in 10%. MDM2 serves as a negative regulator of p53 through sequestration and ubiquitination of p53. Recently, Bond et al. identified a single nucleotide polymorphism (SNP) in the mdm2 gene which increases the affinity of the promoter for the transcriptional activator Sp1, resulting in increased MDM2 expression and subsequent attenuation of the p53 pathway. This SNP has been shown to influence risk, age of onset and survival in several cancer types; however its role in GBM is unknown. We studied the role of this MDM2 SNP in GBM.</p> <p>Methods: We genotyped 98 GBM patients and 102 normal controls at the MDM2 promoter for the SNP using polymerase chain reaction (PCR). The results were analyzed using GraphPad Prism Version 3.0.</p> <p>Results: We found that GBM patients were more likely than normal control subjects to have the T/G or G/G genotype (p=0.02) and that the frequency of the G-allele was higher in GBM patients than in normal controls (p=0.04). However, we found no correlation between age of onset or survival time and MDM2 genotype.</p> <p>Conclusion: The G allele is found in higher frequency in GBM patients; however, it does not seem to confer an increased risk or a more malignant course of GBM.</p>

KIDO, MAYA

1. Title	Comparing Adverse Post-Discharge Effects of Procedural Sedation Analgesia in Pediatric Emergency
2. Student Presenter:	Maya Kido
3. Co-workers and Collaborators:	
4. Advisor:	Baruch Krauss, Alisa McQueen
5. Departments:	
6. Institutions:	Harvard University, Children's Hospital Boston
7. Support:	
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Procedural sedation and analgesia (PSA) is the use of sedative, analgesic and dissociative agents to provide anxiolysis, analgesia, sedation, and motor control for patients undergoing diagnostic and therapeutic procedures. The efficacy and safety of PSA during the procedure and post-procedure prior to discharge periods has been well documented, but adverse effects post-discharge have not been studied. In order to better understand the potential risks associated with PSA in the post-discharge period, this study proposes to examine the adverse events associated with the two most common PSA agents; ketamine and fentanyl/midazolam. Ketamine is associated with emergence delirium while the child is still in the ED, raising questions about the longer term effects post-discharge. With greater understanding of the PSA post-discharge period, physicians may be able to reduce adverse side effects and improve discharge instructions to families. The study will be a prospective, observational cohort of children undergoing PSA in the Children's Hospital Boston emergency department. Physicians will, independent of the study, determine if patients need PSA and assign an appropriate therapeutic agent. If the physician chooses either ketamine or fentanyl/midazolam the patient will be eligible for enrollment. Among eligible patients, informed consent will be obtained from either the patient or guardian for use of demographic data from the ED medical record and for a follow-up phone call in one week consisting of a validated behavioral questionnaire. Data collection is expected to be completed by June 2007. Once complete, the data will be analyzed comparing the number of maladaptive behaviors exhibited by children receiving either ketamine or fentanyl/midazolam, adjusting for preoperative anxiety and covariates such as subject age, sex, medication use and type/site of injury.</p>

KNITTEL, JUSTIN

1. Title	ADENOSINE RECEPTOR AGONISTS/ANTAGONISTS AND INSULIN SECRETION
2. Student Presenter:	Justin Knittel
3. Co-workers and Collaborators:	Marcel Toepfer, Jens Wensing, Anja Riyazi
4. Advisor:	Dr. Eugen Verspohl
5. Departments:	Department of Pharmaceutical & Medicinal Chemistry
6. Institutions:	University of Muenster Muenster, Germany
7. Support:	Crile Fellowship
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Newly developed selective agonists and antagonists have allowed for a closer examination of the 4 major Adenosine receptors (A1, A2A, A2B, A3) and their role in the mechanism of insulin release. Combinations of selective and non-selective adenosine receptor agonists and antagonists were used to measure changes in the amount of insulin secreted by rat pancreatic islet cells. We hypothesized that activation or inhibition of individual subtypes of adenosine receptors would result in differential changes in insulin secretion. Insulin secretion was measured by radioimmunoassay (RIA), using ^{125}I, in the presence of a stimulatory glucose concentration (5.6 mM). NECA (10 μM), a non-degradable adenosine analog, caused an overall increase in insulin secretion. Caffeine, a non-selective AR antagonist, was found to increase insulin release at multiple concentrations (0.1 to 100 μM). CHA (10 μM, A1 receptor agonist) was found to by itself increase insulin release and led to increased secretion when combined with higher concentrations of caffeine. It was thought that specific adenosine-receptor antagonists on their own would have no intrinsic effect on insulin release, but one A2B receptor antagonist, PSB-1115, showed varying effects across a range of concentrations. Adenosine itself, which is quickly degraded, had no effect on insulin secretion at two concentrations (10 and 100 nM). The results indicate that activation of A1 and inhibition of A2B may lead to an overall increase in insulin secretion.</p>

KOBALY, KRISTEN

1. Title	Outcomes of Extremely Low Gestational Age Infants (ELGA, <28 weeks) with Bronchopulmonary Dysplasia: Effects of Practice Changes in 2000-2003
2. Student Presenter:	Kristen Kobaly
3. Co-workers and Collaborators:	Mark Schluchter, PhD; Nori Mercuri-Minich, MA; H. Gerry Taylor, PhD; Deanne Wilson-Costello, MD; Richard Martin, MD; Maureen Hack, MD
4. Advisor:	Maureen Hack, MD
5. Departments:	Department of Pediatrics
6. Institutions:	Case Western Reserve University
7. Support:	T35 Short Term Research Training Grant, HL082544
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Objective: Extremely low gestational age (ELGA, < 28 weeks) infants with Bronchopulmonary Dysplasia (BPD) suffer poorer early childhood cognitive and neurodevelopmental outcomes than preterm and term-born controls. We sought to evaluate whether changes in neonatal intensive care unit (NICU) practices and therapies have improved BPD outcomes.</p> <p>Design/Methods: We compared early childhood outcomes of ELGA infants between two periods: Period I, 1996-1999 (n=118) and Period II, 2000-2003 (n=107). Outcomes included neurosensory abnormalities (cerebral palsy, blindness, deafness), the Bayley Scales of Infant Development Mental Developmental Index (MDI), and overall neurodevelopmental impairment (subnormal MDI and/or neurosensory abnormality). Effects of NICU changes on outcomes were examined via multivariate analyses.</p> <p>Results: NICU changes between period I and II included increased antenatal (72% vs. 83%, p=0.046) and postnatal (75% vs. 29%, p=0.000) steroid therapy, decreased severe cranial ultrasound abnormality (25% vs. 13%, p=0.012), and increased ventilator dependence (36 vs. 43 days, p=0.020). Rates of BPD did not change (52% vs. 53%).</p> <p>Follow-up at 20 months corrected age revealed fewer neurosensory abnormalities during Period II (36% vs. 16%, p=0.011), but no change in the rates of subnormal (<70) MDI (37% vs. 45%). Overall neurodevelopmental impairment did not change (50% vs. 51%). Multivariate analyses, including time period (I vs. II) as a variable, revealed significant (p<0.05) predictors of subnormal MDI to be cranial ultrasound abnormality and duration of ventilator dependence. Predictors of neurodevelopmental impairment included cranial ultrasound abnormality, increased ventilator dependence and postnatal steroid therapy.</p> <p>Conclusions: Changes in NICU practices have not improved the rates of BPD or its overall outcomes. In fact, infants spend more time on ventilators, possibly due to reduced postnatal steroid use. Further therapeutic modifications are needed to decrease both the rates of BPD and its long-term outcomes.</p>

KRINSKY, SYLVIA

1. Title	Can Reminiscence Therapy Improve Quality of Life in Alzheimer's Patients?
2. Student Presenter:	Sylvia Krinsky
3. Co-workers and Collaborators:	Danny George
4. Advisor:	Dr. Peter Whitehouse
5. Departments:	Integrative Studies
6. Institutions:	University Memory and Aging Center
7. Support:	Crile
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Currently, there is no medicinal cure for Alzheimer's disease, which has led many patients to search for alternative therapies, such as reminiscence therapy. The LifeBook project is modified form of reminiscence therapy that provides patients a valuable opportunity to create a multimedia scrapbook of their personal narratives of health and illness. In order to standardize the LifeBook experience we created a LifeBook companion guide that outlines the process and includes 13 questions aimed at determining a patient's individual beliefs and values. LifeBook allows patients to re-examine old photographs, share favorite recipes and music, and ultimately reflect on their own preferences regarding end of life care. In order to investigate the efficacy of LifeBook as a therapeutic agent we conducted pilot interviews aimed at developing a standardized yet flexible interview protocol to evaluate quality of life, a highly subjective variable. We ultimately decided to utilize a 13 question quality of life scale in combination with a 3 question qualitative survey. We then added 3 open ended questions regarding whether the finished Lifebook guided patients and caregivers through the difficult task of developing advanced directives for their end of life care. However, during patient interviews, questions still had to be altered for a given patient's mental and emotional state, especially in patients with later stage disease progression. We are currently still in the process of conducting patient interviews and analyzing data to determine whether LifeBook affected the quality of life in patients suffering from Alzheimer's disease.</p>

KRUPER, GREGORY

1. Title	Variability of heart rate and respiratory rate in rats, after exposure to chronic intermittent hypoxia.
2. Student Presenter:	Gregory J. Kruper
3. Co-workers and Collaborators:	Mikkel Fishman
4. Advisor:	Thomas E. Dick
5. Departments:	Pulmonary, Neuroscience
6. Institutions:	CWRU
7. Support:	Crile Fellowship
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>A decrease in heart rate variability predicted cardiac pathology (Pincus and Goldberger, Am J Physiol. 266: H1643-H1656, 1994). Further, cardiac arrhythmias were associated with sleep apnea (Mehra et al., Am J Respir Crit Care Med. 173: 910-916, 2006). During sleep apnea, the body experiences periods of intermittent hypoxia. We postulated that intermittent hypoxia alone decreased heart rate variability and that this would be linked with decreased breathing frequency variability due to cardiopulmonary coupling. A secondary hypothesis was whether or not a difference existed between two rodent strains which have very different hypoxic responses.</p> <p>We implanted wireless pressure transducers to monitor blood pressure in adult male rats (Sprague Dawley/Zivic Miller and Brown Norway/Harlan). Blood pressure was measured before and after conditioning with intermittent hypoxia. Hypoxic exposures consisted of ambient PO₂<10% for 15s, followed by 5min of recovery; repeated for 8h per/d for 28d. Respiratory pattern was determined using whole-body, flow-through plethysmography. The animals were allowed to acclimatize to the plethysmographic chamber then exposed to hyperoxia for 5m, then a hypoxic challenge, followed by hyperoxia for 5m and then a hypercapnic challenge followed by hyperoxia.</p> <p>Linear and non-linear variabilities in the patterns were displayed graphically by Poincaré plots. The pattern of the Poincare plots was consistent for both two species; greatest variability when the animals were breathing hyperoxia than hypoxia or hypercapnia; both before and after intermittent hypoxic conditioning. However, preliminary results indicate that animals of both species decreased their respiratory variability during the baseline hyperoxia after intermittent hypoxic conditioning. In contrast, heart rate variability increased after hypoxic conditioning.</p> <p>We conclude that the changes in respiratory control appear independent of those in heart rate. Further, decreased variability during hyperoxia without changes in hypoxic and hypercapnic variabilities indicate that the alteration in respiratory control occurred in the network controlling breath-to-breath variability and that the reflex drive dominates the network's intrinsic variability. Finally, present caveats of this study are variability needs to be quantified and sample size needs to be larger.</p>

KUMAR, ARYAVARTA

1. Title	A Novel Self-Assembling Nucleobase Scaffold Coating with Nano-Scale Control
2. Student Presenter:	Aryavarta M. S. Kumar
3. Co-workers and Collaborators:	Sona Sivakova, Justin D. Fox, Jennifer E. Green, Stuart J. Rowan, Roger E. Marchant
4. Advisor:	Roger E. Marchant
5. Departments:	Biomedical Engineering Macromolecular Science and Engineering
6. Institutions:	Case Western Reserve University
7. Support:	Funding for this research was provided by the NIH Grant No. NIBIB-EB-001466-01 and by Case MSTP grant T32-GM07250.
8. Please choose your academic program:	MD PHD
9. What year are you in the program?	6
10. Body of Abstract (300 words or less)	<p>Spacing of biological residues is important for biological function. For example, the synergistic peptide sequences RGD and PHSRN in a coating can promote cellular spreading especially when the peptide spacing mimics in vivo distances. Here we propose to design and construct a novel scaffold material to self-assemble on a hydrophobic surface. To allow nano-scale positioning of biological residues, we focused on a supramolecular system composed of small molecular weight monomers. By tuning the distances within the assembly, the scaffold could be used to recreate epitope structures and/or construct arrays of biological residues on a surface with applications ranging from nano-scale microchip technologies to improved biocompatibility of medical devices.</p> <p>The model materials in this scaffold design (G-an-G $n=12, 18$) are a novel nucleobase molecule that have a core hydrocarbon flanked by two peptide nucleic acid connectors with guanines. After adsorbing on a hydrophobic surface, these materials surface self-assemble laterally; all the interactions of the assembly are non-covalent. From molecular modeling, we suggest the guanine moieties form surface hydrogen bonded tape motifs that depend on the local environment and the steric constraints within the assembly. We have used several parameters to tune the molecular assembly at the nano-scale to show that it can potentially be used to synthetically recreate epitope structures on a surface.</p> <p>By using the G-a12-G and G-a18-G two monomer system, we can also phase separate at the nano-scale and, interestingly, the surface concentrations of the two monomers are identical to their solution concentrations even though they have a different number of methylene groups.</p> <p>If this research is successful, it will generate a novel scaffold material that is tunable that will enable spacing of biological residues to be controlled at the nano-scale.</p>

KUO, IRIS	
1. Title	Linkage Studies of Reading and Spelling Abilities in Children with SSD
2. Student Presenter:	Iris Kuo
3. Co-workers and Collaborators:	Lisa Freebairn, Amy Hansen, Dr. Sudha Lyengar, Chris Millard
4. Advisor:	Dr. Barbara Lewis, Dr. Catherine Stein
5. Departments:	Department of Pediatrics, Department of Epidemiology and Biostatistics
6. Institutions:	Case Western Reserve University
7. Support:	Crile, NIH
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Speech sound disorders (SSD) are the most prevalent communication disorders in young children. Studies show that both SSD and reading disorders (RD) have a genetic basis. Children with SSD also have a significant chance of developing RD and spelling difficulties.</p> <p>We have followed the proband (SSD) and family members and assessed their reading and spelling abilities at school age (7-12 yrs). The tests administered include the Woodcock Reading Mastery Test (WR), Wechsler Individual Achievement Test (WIAT), Test of Written Spelling (TW), and Test of Written Language (TOWL). The subtest scores were stepwise adjusted for age, sex, socioeconomic status, and birth order. Linkage analysis of those measures to genetic regions on chromosomes 1, 3, 6, and 15 was performed using Haseman-Elston regression via SIBPAL; these chromosomal regions have been linked to SSD and/or RD in previous studies.</p> <p>Results show significant linkage (p-value < 0.05) of reading and spelling measures to genetic regions on chromosomes 1, 3, 6 and 15. Chromosome 1 showed linkage to WR Word Identification (1p34.3), TW Total Score and TW Unpredictable Words subtests (1p33), TOWL Thematic Maturity subtest (1p36.11), and the TOWL Contextual Vocabulary and Contextual Style subtests (1p34.4 and 1p33). Chromosome 3 showed linkage to WR Word Attack and Word Identification subtests (3q11.2), TW Total Score and Unpredictable Words subtests (3q13.12), TOWL Contextual Vocabulary and Contextual Style subtests (3p14.1), and TOWL Syntactic Maturity (most significantly linked to 3p12.3 but also 3p14.1). Chromosome 6 was linked to TW Predictable Words (6p21.33). Chromosome 15 showed linkage to WR Word Attack (15q22.1), WR Word Identification (15q21.1), WIAT Listening Comprehension (15q22.1), and TW Unpredictable Words (15q21.1). These findings support the hypothesis that SSD and RD may have a shared genetic basis, and these chromosomes include genes that influence reading and spelling. Further research is needed to determine more precise genetic locations.</p>

KUZMA, KRISTIN

1. Title	Factors Influencing Prehospital Placement and Utilization of Peripheral Intravenous Catheters
2. Student Presenter:	Kristin Kuzma
3. Co-workers and Collaborators:	Karl Sporer, Glen E Michael, Glen Youngblood
4. Advisor:	Karl Sporer
5. Departments:	Department of Medicine, UCSF and Emergency Medicine at San Francisco General Hospital
6. Institutions:	University of California, San Francisco San Francisco General Hospital
7. Support:	None
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Study Objective: This study examined the association between IV initiation and utilization rates with paramedic impression, vital signs, skin signs, and Glasgow Coma Score (GCS).</p> <p>Methods: Electronic records for 34,585 patients transported by ambulance were evaluated for IV placement and utilization. Utilization was defined as a fluid bolus greater than 250 cc or IV medication administration. Basic statistical methods were followed by logistic regression analysis to control for age, race, and gender, paramedic impression, systolic blood pressure (SBP), heart rate (HR), respiratory rate (RR), GCS, skin sign color, and capillary refill.</p> <p>Results: 60% of the patients received IV's. 70% of the IV's were not used for treatment. Certain primary impressions had IV's that were infrequently utilized (n= number in group, % with IV placed, % unused): post seizure (n= 989, 72%, 91%); weakness/dizzy/nausea (n= 3092, 69%, 80%); syncope/near-syncope (n=2034, 81%, 74%); abdominal pain (n=1554, 70%, 86%).</p> <p>Statistically significant differences were found for paramedic impression, abnormal BP, HR, RR, GCS, and skin signs. 58% of patients with normal vital signs received IV's, while only 28% of IV's were utilized for treatment; hypotension 80% received IV (OR=1.211, p=.012) with 70% utilized; hypertension 61% received IV (OR=1.060, p=.027) with 28% utilized; bradycardia 82% received IV (OR=1.588, p<.0001) 51% utilized; tachycardia 66% received IV (OR=1.152, p=.001) 33% utilized; bradypnea 93% received IV (OR=1.638, p=.051) 86% utilized; tachypnea 70% (OR=1.120, p=.024) 33% utilized. 76% of patients with a GCS less than 15 received IV (OR= 1.672, p<.0001) with 32% utilized. The IV initiation rate for abnormal skins was 79% (OR=1.691, p<.0001) with 42% utilized.</p> <p>Conclusion: Many paramedic impression categories are associated with frequent IV initiation but infrequent utilization. High utilization was associated with hypotension, bradycardia, bradypnea, and abnormal skin signs. Insight into the prehospital patients least likely to require IV utilization could reduce the number of unnecessary IV's.</p>

LANGHAM, GEOFFREY

1. Title	Does the addition of a full-access under-body blanket to routine thermal care improve heat transfer in cardiac surgery patients?
2. Student Presenter:	Geoffrey Langham
3. Co-workers and Collaborators:	Steven Insler, Mohamed Bakri, Fady Nageeb, Edward Mascha
4. Advisor:	Daniel Sessler
5. Departments:	Department of Outcomes Research - Division of Anesthesiology
6. Institutions:	Cleveland Clinic Foundation, Cleveland OH
7. Support:	NIH T35 short-term training grant
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Introduction. Hypothermia during cardiac surgery and in the postoperative period has been associated with adverse outcomes. Conventional (over-body) forced-air warming is highly effective. An under-body cover has been developed for use during cardiac surgery, during which anterior surface access is restricted. We tested the hypothesis that combining under-body forced-air warming with standard thermal care improves core temperature and reduces post-bypass temperature drop ("afterdrop") in patients undergoing cardiac surgery.</p> <p>Methods. Patients scheduled for routine, non-emergent cardiac surgery at the Cleveland Clinic between April and July 2006 were enrolled. Patients were randomly assigned to either routine thermal management (n=29) or routine management supplemented by the Arizant Model 635 under-body cover (n=27). Routine heat conservation methods were applied in both groups. Core temperature was measured via bladder Foley catheter.</p> <p>Results. Morphometric and demographic characteristics in the two groups were similar, as were anesthetic and surgical management and pre-induction core temperatures. Minimum temperature during bypass was 35.3 ± 1.3 in the standard treatment group and 35.5 ± 1.5 in the active-warming group ($P=0.67$). The only statistically significant temperature difference between the groups was upon leaving surgery. Afterdrop was similar in the routine management and forced-air groups, and did not differ significantly.</p> <p>Conclusions. Patients undergoing routine thermal management and normothermic bypass did not become hypothermic. There was only trivial afterdrop. Lack of afterdrop indicates that normothermic bypass was effective at warming the core and peripheral tissues. Forced-air warming did not increase core temperature by a clinically important amount in our patients. We note that effective heat transfer would have increased core temperature, even in normothermic patients. Forced-air was minimally effective, presumably, because the under-body cover warms much less surface area than a standard over-body forced-air cover.</p>

LARSEN, COBY	
1. Title	An endothelial cell-specific peptide fluorosurfactant polymer on ePTFE
2. Student Presenter:	Coby C. Larsen
3. Co-workers and Collaborators:	Faina Kligman, Roger E. Marchant
4. Advisor:	Kandice Kottke-Marchant
5. Departments:	Department of Biomedical Engineering, Department of Clinical Pathology
6. Institutions:	Case Western Reserve Univeristy, Cleveland Clinic Foundation
7. Support:	The authors gratefully acknowledge the financial support provided by NIH Grant 5R01EB002067 and the facilities provided by the Center for Cardiovascular Biomaterials. Graduate training support was provided for C.C.L. from NIH Grant 5T32GM007250 and an American Heart Association predoctoral fellowship.
8. Please choose your academic program:	MD PHD
9. What year are you in the program?	6
10. Body of Abstract (300 words or less)	<p>Statement of Purpose: There is a pressing clinical need for suitable small-diameter vascular prostheses to bypass diseased coronary arteries. A major impediment for use of artificial materials has been the lack of interface blood compatibility. The challenge of tissue engineering a biocompatible blood interface of confluent, healthy endothelial cells (ECs) is that the same matrix proteins (e.g. fibronectin, FN) or FN-derived peptides that bind ECs will also bind platelets and initiate thrombosis. Here, we report a novel biomimetic construct engineered for EC-selective adhesion to vascular graft material; this is accomplished by utilizing a cyclic peptide ligand (CRRETAWAC) with specificity and high affinity for EC integrins, but low affinity for platelet integrins. The EC-selective ligand is presented on a fluorosurfactant polymer (FSP) that allows for simple and durable modification of expanded polytetrafluoroethylene (ePTFE), a clinically relevant vascular graft material.</p> <p>Results: We found that CRRETAWAC peptide has low affinity for platelet binding. IC50 values for CRRETAWAC inhibition of fibrinogen (FG) binding to immobilized αIIb β3 platelet integrin and platelet aggregation inhibition were significantly higher than for GRGDSP peptide, suggesting that specific CRRETAWAC-platelet interaction is very limited. EC attachment to CRRETAWAC FSP was α5 β1 integrin specific; attachment was also CRRETAWAC peptide specific. ECs attached with high efficiency to the CRRETAWAC FSP and grew as rapidly as ECs on FN. Cells demonstrated shear stability on CRRETAWAC FSP with no significant cell loss after 4 h of 38 dynes/cm² applied shear stress. Cells adherent to CRRETAWAC FSP demonstrated production of the antithrombotic mediators PGI₂ and tPA comparable to ECs on FN.</p> <p>Conclusions: Our results demonstrate successful modification of ePTFE vascular graft material with an EC-selective FSP that promotes specific EC attachment, growth, shear stability, and function. This biomimetic construct has the potential to promote rapid endothelialization without platelet adhesion on small-diameter vascular grafts.</p>

LEE, HYON JAE

1. Title	Changes in the NO Signaling Pathway in Response to Chronically Altered Blood Flow
2. Student Presenter:	Hyon Jae Lee
3. Co-workers and Collaborators:	Haiying Zhang, M.D.
4. Advisor:	Steven Fisher, M.D.
5. Departments:	Division of Cardiology
6. Institutions:	Case Western Reserve University School of Medicine (Biomedical Research Building)
7. Support:	Crile Grant (Case Western School of Medicine)
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Nitric oxide (NO) causes smooth muscle relaxation through a cGMP-mediated pathway involving dephosphorylation of myosin by myosin phosphatase (MP). NO, synthesized by various isoforms of nitric oxide synthase (eNOS, iNOS and nNOS), activates soluble guanylyl cyclase (sGC), which converts GTP to cGMP. cGMP-dependent protein kinase (cGKI) activates MP, leading to smooth muscle relaxation.</p> <p>Small arteries and arterioles display greater resistance, and therefore control blood flow. Previous studies have shown that changes in blood flow result in changes in NO/cGMP signaling in small mesenteric arteries.</p> <p>Conditions of high blood flow (HF) and low blood flow (LF) were created by ligating 2nd order small mesenteric arteries of every other 1st order arteries (MA1) branching off the superior mesenteric artery in a rat model. Vessels were collected 1 day to 28 days after surgery, and RNA isolated and reverse transcribed. These HF and LF vessels were studied with real-time PCR to quantify differences in mRNA expression in the proximal NO/cGMP signaling pathway, specifically of eNOS, iNOS, sGC, and cGMP-specific phosphodiesterase (PDE5).</p> <p>Under conditions of chronic HF, and to a lesser extent chronic LF, eNOS and iNOS were rapidly induced and returned to near-normal levels over 28 days. The cGMP-degrading enzyme PDE5 was similarly induced, while the receptor for NO, guanylate cyclase, was variably down-regulated. We propose that this system is behaving as a classic signaling system in a disease state. Increased synthesis of the ligand (NO) mediates acute vasodilatation, balanced by subsequent receptor (sGC) down-regulation and de-sensitization (up-regulation of PDE5) in the target tissue. These results provide a novel mechanism for the dynamic changes in NO signaling, and perhaps nitrate tolerance, in high flow and low flow disease states. This hypothesis will be tested in future functional studies of these vessels, using pharmacological inhibitors or gene deletions to test component of this pathway.</p>

LEI, LEI	
1. Title	Mortality Prediction by Normal Range Creatinine Phosphokinase Cardiac Markers
2. Student Presenter:	Lei Lei
3. Co-workers and Collaborators:	John Mafi
4. Advisor:	Dr. Frank Peacock
5. Departments:	Emergency Department
6. Institutions:	Cleveland Clinic
7. Support:	NIH T35 Grant
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Background: Serum concentration of the MB fraction of creatinine phosphokinase (CK-MB) exceeding the institutional cut point aid clinicians in diagnosing acute myocardial infarction. However, it is unclear if fluctuations below the institutional cut off point are prognostically significant. Our purpose is to assess whether fluctuating CK-MB values that never exceed the institutional cut off point are associated with adverse cardiac events.</p> <p>Methods: We performed a post-hoc analysis using the ItrACS registry of emergency department (ED) patients who were suspected to have acute coronary syndrome (ACS). Patients were included if they had two cardiac markers drawn within six hours of ED presentation, and no marker values exceeded the institutional CK-MB cut point. Adverse cardiac events (ACE) were defined as ED revisit or hospital admission within 30 days, a positive stress test, subsequent myocardial infarction, coronary vascularization, or death. Myocardial ischemia risk was estimated using the acute cardiac ischemia–time insensitive prediction instrument (ACI-TIPI) which predicts cardiac ischemia probability using ECG measurements and other factors such as age, gender, and chief complaint.</p> <p>Results: Of 17,713 patients, 1,311 (7.4%) had two CK-MB assays within six hours of ED presentation. Evaluation using ACI-TIPI showed that decreasing CK-MB values were associated with a lower risk for adverse cardiac events compared to patients with stable CK-MB (mean difference -2.5%, 95CI -5.1% to 0.0%). Patients with increasing CK-MB values were not at an increased risk for ACE compared to patients with stable CK-MB values (mean difference 1.0%, 95CI -3.0% to 5.1). 30 day ACE were lower with a decreasing CK-MB: OR .67; 95% CI .48-.95, and unchanged for an increasing CK-MB: OR .96; 95% CI .57-1.6.</p> <p>Conclusions: An increasing CK-MB below the institutionally defined limit of normal is not associated with an elevated risk of cardiac ischemia and 30 day adverse cardiac events.</p>

LIN, JENNIFER

1. Title	The RNA Binding Protein hnRNP-U Regulates Axon Outgrowth and Associates with the N-Terminus of Ezrin.
2. Student Presenter:	Jennifer Lin
3. Co-workers and Collaborators:	Christy Gray
4. Advisor:	Alfred Malouf
5. Departments:	Department of Pediatrics
6. Institutions:	Case Western Reserve University
7. Support:	NIH NINDS NS 41383 (ATM)
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Background: The long-term objective of this project is to examine mechanisms that regulate axon outgrowth and regeneration that can be used to repair Central Nervous System (CNS) damage caused by traumatic injury, stroke, or neurodegenerative diseases. One of the newest mechanisms of CNS repair involves localized protein synthesis in the growth cone of regenerating nerve axons. Although protein synthesis traditionally has been thought to be restricted to the cell body, recent data have shown that the response to certain guidance molecules requires protein synthesis in the growth cone. While it is known that specialized proteins are needed to bind, transport and target mRNA to the growth cone, it is not known how these mRNA/protein complexes are targeted to growth cones. Data from the Malouf lab has shown that the mRNA binding protein, hnRNP-U, is localized to axon growth cones and that hnRNP-U co-immunoprecipitates with ezrin, a well-known scaffolding protein localized to axon growth cones.</p> <p>Question: The goal of the summer research project is to identify whether the N-terminus of ezrin is responsible for binding to hnRNP-U.</p> <p>Approach: Co-immunoprecipitation experiments were performed using Flag-tagged ezrin proteins expressed in NIH/3T3 cells. Vectors for the expression of full-length (1-586-FLAG) and the N-terminal region of ezrin (1-311-FLAG) were made by Christy Gray, a MSTP student in the Malouf lab. NIH/3T3 cells were homogenized 48 hours after being transfected using Lipofectamine 2000. Western analysis was performed using a rabbit polyclonal antibody against hnRNP-U to determine if hnRNP-U binding is associated with expression of the N-terminal region of ezrin.</p> <p>Results: hnRNP-U co-immunoprecipitated with endogenous as well as overexpressed full-length ezrin (1-586-FLAG) and the N-terminal fragment of ezrin (1-311-FLAG), suggesting that hnRNP-U binds to the N-terminus of ezrin. Additional experiments will be performed to demonstrate whether or not the C-terminus can also mediate ezrin-hnRNP-U interactions.</p>

LO, RUBY

1. Title	Parent Roles in Pediatric Obesity Treatment Programs
2. Student Presenter:	Ruby Lo
3. Co-workers and Collaborators:	
4. Advisor:	Dr. Leslie Heinberg
5. Departments:	Epidemiology & Biostatistics, Division of Public Health
6. Institutions:	Case Western Reserve University, Rainbow Babies and Children's Hospital
7. Support:	T35
8. Please choose your academic program:	MD MS
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>The rapid increase in the prevalence of childhood overweight in the past few decades is of concern because of its many comorbidities, such as diabetes and cardiovascular disease. In response to this trend, the Healthy Kids, Healthy Weight Program at Rainbow Babies and Children's Hospital seeks to provide an early intervention program for obese pediatric patients while collecting clinical data, in hopes of contributing to the research community as well as providing education and support to the broader community.</p> <p>In my study, I looked at what parental factors were associated with more successful program outcomes. Success was defined as achieving positive dietary and physical activity changes, greater reductions in BMI and meeting specific goals set by the physicians and program staff in collaboration with the patients. Examples of parental factors that were reviewed included parental self-efficacy, socioeconomic status, parent's perspective, and maternal depression. Most of the data that was analyzed was collected from questionnaires, including weight and physical activity self-efficacy questionnaires, change assessment scales and family relationship inventories. Measures of program outcomes were in the form of diet and exercise logs, ratings of participant involvement by the program staff, and BMI tracking.</p> <p>The following correlations were found: There was a negative correlation between parent involvement during the program and the number of participant absences. Factors that predicted patient absences and low attendance included being male, African American, lower family income, maternal depression and lower parental exercise self-efficacy. Factors that predicted achieving stated goals were being female and having a higher family income. Having a father with a lower BMI predicted having more minutes of activity recorded per week.</p> <p>Healthy Kids, Healthy Weight is still a young program with ongoing enrollment. Hopefully as more data is collected, the factors that predict success in pediatric obesity treatment programs will be elucidated.</p>

LOMINADZE, GEORGE

1. Title	Proteomic Approach for the Detection of CCSP-2, a Candidate Serum Marker for Colon Neoplasia
2. Student Presenter:	George Lominadze
3. Co-workers and Collaborators:	Kathleen Lundberg, Sanford Markowitz, Mark R. Chance
4. Advisor:	Mark R. Chance
5. Departments:	Case Center for Proteomics, and Ireland Comprehensive Cancer Center
6. Institutions:	Case School of Medicine
7. Support:	Crile Fellowship. American Gastroenterological Association Student Reserach Fellowship
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Cancers of the colon and rectum are the second leading cause of cancer death among adult Americans. At early stages, colon cancer is highly curable. The current "gold standard" for screening is colonoscopy, which is an invasive and uncomfortable test, and only 10% of adults over the age of 50 have ever had a screening colonoscopy. Thus, there is a need for a more comfortable screening test. Recently, Dr. Markowitz's lab identified Colon Cancer Secreted Protein-2 (CCSP-2) as a highly overexpressed protein in human colon cancer tumors, compared to normal mucosa of the same patients. CCSP-2 can be detected by western blotting as a circulating biomarker in the blood of mice with human colon cancer xenografts. In order to develop a colon cancer screening test, in this study we aimed to establish a method to detect CCSP-2 in the human serum using highly sensitive proteomic technology. As a test sample we used normal human serum spiked with recombinant CCSP-2 (19 picomolar). For sample deconvolution, we employed sequential steps of protein precipitation, chaotrope solubilization, liquid isoelectric focusing (LIEF), and gel electrophoresis followed by protein band trypsin digestion and matrix assisted laser desorption ionization mass spectrometry (MALDI-MS) to detect CCSP-2 peptides. We successfully identified seven peptides from CCSP-2 each of which unambiguously identified the protein. Thus we have taken a first step toward establishment of CCSP-2 as a testable serological marker of colon cancer, which could lead to the development of a comfortable and simple cancer screening blood test.</p>

LOO, FLORENCE

1. Title	Identification of Genes Upregulated in Acute Leukemia Cells In Vivo in an Allogeneic Post-Bone Marrow Transplant Immune Environment
2. Student Presenter:	Florence Loo
3. Co-workers and Collaborators:	Johan Jansson, Andrew Campbell, Kris Lambert
4. Advisor:	Craig Mullen
5. Departments:	Pediatric Hematology/Oncology
6. Institutions:	Strong Children's Research Center, University of Rochester
7. Support:	Strong Childrens Research Center
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Background/Hypothesis This work tested the hypothesis that the in vivo acute leukemia cells upregulate genes that enhance leukemia growth after bone marrow transplant (BMT). This subset of upregulated genes may identify gene targets for therapies to decrease the likelihood of leukemia relapse in BMT patients.</p> <p>Methods C1498, a spontaneous arising acute leukemia arising from a C57BL/6 mouse, served as the model for this study. C1498 was recovered from the following environments and gene expression profiles were compared.</p> <p>Environment: Allogeneic Pressure</p> <p>In vitro tissue culture: - Syngeneic C57BL/6 mice not undergoing BMT: None Mice undergoing allogeneic BMT: + Mice undergoing allogeneic BMT & post-transplant leukemia vaccine therapy: ++</p> <p>C1498 leukemia cells and bone marrow were harvested after the development of disease symptoms. Leukemia cells were separated from other bone marrow cells and the total RNA was isolated. Gene expression microarray analysis was performed to identify potential biomarkers for therapy. The data were computed using three separate algorithms: GCRMA, RMA, and MAS 5.0. Upregulated genes were defined as genes demonstrating >4 fold greater change compared to the in vitro control sample. To increase confidence, only genes upregulated in all sample replicates and all three algorithms were considered genes of interest.</p> <p>Conclusion 115 genes upregulated in vivo were identified. 192 genes upregulated in the allogeneic post-BMT immune environment were identified.</p>

MAFI, JOHN

1. Title	Serum Troponin Fluctuations Below Institutional Cut-Points Predict Higher Risk of Adverse Cardiac Events
2. Student Presenter:	John N. Mafi
3. Co-workers and Collaborators:	Dr. Nolan McMullin, Lei Lei, MS-II
4. Advisor:	Dr. Frank Peacock
5. Departments:	Emergency Department
6. Institutions:	The Cleveland Clinic Foundation
7. Support:	NIH T35 Grant
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Introduction: Serum troponins (Tn) are powerful diagnostic markers in assessing acute myocardial infarction. The significance of small Tn fluctuations below the institutional cut-point, however, is not well defined. Our purpose was to evaluate the relationship between Tn fluctuations below the institutional cut-point and adverse cardiac events (ACE).</p> <p>Materials and Methods: We performed a post-hoc analysis of the I*trACS registry which enrolled Emergency Department (ED) patients with suspected acute coronary syndromes (ACS) across the spectrum of risk. We included all patients with two sets of cardiac markers drawn within six hours of presentation, both of which were below the institution's pre-specified upper limit of normal. Fluctuation was defined as either an increase or decrease in Tn (either I or T) exceeding 15% of the initial value. Adverse cardiac events (ACE) were defined as a positive stress test, myocardial infarction, coronary revascularization, or death within 30 days of presentation. Risk of ischemia was also evaluated by the acute coronary ischemia-time insensitive prediction instrument (ACI-TIPI).</p> <p>Results: Of 17,713 patient visits, 2,021 had two Tn results within 6 hours of presentation. Compared to having a stable Tn, patients with a decreasing or increasing Tn ischemia risk per ACI-TIPI that was 7.9% (95CI 3.6-12.2) and 9.7% (95% CI 5.2-14.2) higher, respectively. ACE were higher with any Tn fluctuation: OR 2.25; 95% CI 1.42-3.55 for decreasing Tn, and 3.04; 95% CI 1.94-4.75 if increasing.</p> <p>Conclusions: Small fluctuations in troponin concentration, below the institutionally defined limit of normal, are associated with a significantly increased risk of cardiac ischemia and 30 day adverse cardiac events.</p>

MAGYAR, DARI

1. Title	Outcomes of Female Heart Transplant Recipients Bridged to Transplantation with a Ventricular Assist Device
2. Student Presenter:	Dari Magyar
3. Co-workers and Collaborators:	N.G. Smedira; K. Hoercher; J.L. Navia; T. Mihaljevic; D.O. Taylor; R.C. Starling; G.V. Gonzalez-Stawinski
4. Advisor:	Gonzalo Gonzalez-Stawinski, M.D.
5. Departments:	Thoracic and Cardiovascular Surgery
6. Institutions:	The Cleveland Clinic Foundation
7. Support:	NIH-Heart Lung and Blood Institute
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Background: Studies have demonstrated worse outcomes for females undergoing VAD implantation and heart transplantation when each is considered independently. However, the impact of gender on outcomes of patients BTT with a VAD is ill-defined.</p> <p>Methods: A retrospective chart review of patients BTT with a VAD (n=214) between 1984 and 2003 was undertaken. Patients were divided into two groups based on gender. Short- and long-term outcomes were compared between females (n=30) and males (n=184).</p> <p>Results: Baseline demographics between groups were similar although females were less frequently transplanted across 4 or more HLA antigen mismatches (26.7 vs. 50.5 %, $p < 0.05$), less likely to have a history of cardiac surgery (43.3 vs. 69.6 %, $p < 0.05$), and more likely to have a PRA $>10\%$ (33.3 vs. 13%, $p < 0.05$). When comparing survival, females had a slightly lower 30-day (86.7 vs. 92.9%, $p = 0.348$) and 1-year survival (73.3 vs. 83.2%, $p = 0.265$). Post-transplantation, females were approximately three times more likely to die of infection (13.3 vs. 4.4%, $p = 0.176$) or organ failure (6.7 vs. 2.2%, $p = 0.352$). However, females were less likely to die of cardiovascular disease (0 vs. 5.4 %, $p < 0.05$) or malignancy (0 vs. 3.8%, $p < 0.01$). They were also less likely to develop post-transplant lymphoproliferative disease (0 vs. 2.2%, $p < 0.05$) and moderate/severe transplant vasculopathy at 1 (0 vs. 3.3%, $p < 0.05$) and 7 years (0 vs. 3.3%, $p < 0.05$). When comparing bouts of rejection (ISHLT 3A or $>$) both groups were similar.</p> <p>Conclusion: The gender-based differences in outcomes illuminated in this study raise questions as to the underlying basis for these differences and provide an opportunity for further investigation. A better understanding of the role that gender plays in the clinical course of heart transplant recipients will allow health care professionals to more effectively manage patients and improve outcomes.</p>

MARK, DAVID

1. Title	A Usability Analysis of a Healthy Behaviors Website
2. Student Presenter:	David Mark
3. Co-workers and Collaborators:	Dr. Susan Flocke
4. Advisor:	Dr. Susan Flocke
5. Departments:	Family Medicine
6. Institutions:	Case Western
7. Support:	
8. Please choose your academic program:	MD MPH
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Background: The internet is a powerful tool for conveying health information. However the underserved have been shown to have the most difficulty using the internet. Therefore, a health promotion website was designed for maximum accessibility. The purpose of this study was to conduct a usability analysis of the website among a sample of medically underserved patients with a range of internet experience.</p> <p>Methods: Adult patients seeking care in one of two safety-net family practices were invited to participate in a usability test. A purposeful sampling design was used to ensure representation from both genders, a range of age groups, and different internet experience levels. Usability testing included an interview during which patients performed three tasks using the website. The time and number of clicks needed to complete each task were recorded and compared across internet experience levels. In addition, opinions on the ease of navigation and recommendations for improvement for the website were recorded.</p> <p>Results: Overall 41 participants completed the interview. The majority of participants found the website easy to use and helpful for healthy behavior information. Overall participants with no or minimal internet experience performed as well as those with medium or high levels of internet experience across the three tasks. There was a trend of those with no internet experience to take longer to complete the tasks, however this was significant ($p = .01$) for only 1 of the three tasks. Additionally, there was no significant difference in the number of unnecessary clicks in completing the three tasks.</p> <p>Conclusions: It was found that patients from safety-net practices including those with limited internet experience could successfully navigate the website. Most importantly, this study demonstrated the potential of carefully designed websites to be an effective tool in the primary care setting for communicating health information and supporting healthy behavior changes.</p>

MAUGHAN, BRANDON

1. Title	Influence of nurse and physician workload on intensive care unit outcomes
2. Student Presenter:	Brandon Maughan
3. Co-workers and Collaborators:	
4. Advisor:	Allan Garland, M.D., M.A.
5. Departments:	Department of Medicine
6. Institutions:	Case Western Reserve University School of Medicine; MetroHealth Medical Center
7. Support:	NIH T35 Training Grant
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Background: Prior studies have had conflicting results regarding the impact on nursing workload on clinically relevant outcomes for hospitalized patients. We are not aware of any data on the impact of physician workload on such outcomes. Our goal was to measure the effect of physician and nursing workload on short-term mortality for critically ill patients in an intensive care unit.</p> <p>Methods: Retrospective, observational study performed in a 13 bed medical intensive care unit of an urban teaching hospital. We assessed 2,404 admissions from February 2002 to December 2005. The effects of workload variables on intensive care unit mortality was assessed using multivariable logistic regression adjusted for age, gender, insurance status, comorbid conditions, type and severity of acute illness, neurologic function, and the source of intensive care unit admission. Workload variables, calculated for each calendar day or nursing shift, were intensive care unit census, patient to nurse ratio, and the number of ICU admissions. For each workload variable, the workload relative to individual patients was calculated as the average over her/his entire stay in the ICU. Values are reported as Mean \pm SD; p-values < .05 were considered significant.</p> <p>Results: ICU census was 10.0 \pm1.9; nurse:patient ratio was 1.7 \pm0.2, daily number of intensive care unit admissions was 3.0 \pm1.0. None of the three workload variables were significantly related to ICU mortality (p=0.23 to 0.77).</p> <p>Conclusion: Workload for intensive care unit physicians and nurses, within the range of variation present, did not influence the short-term mortality rate among critically ill medical patients.</p>

MORRISON, JAMIN

1. Title	Calcitonin-gene related peptide receptor regulation in human heart failure
2. Student Presenter:	Jamin Morrison*
3. Co-workers and Collaborators:	Christine S Moravec¥, W.H. Wilson Tang¥, Jeff Southard€, Lee Southard€, Randall C. Starling¥ and Sathyamangla V. Naga Prasad*
4. Advisor:	Sathyamangla V. Naga Prasad and Randall C. Starling
5. Departments:	Departments of Molecular Cardiology* and Cardiovascular Medicine¥
6. Institutions:	Cleveland Clinic Foundation, 9500 Euclid Avenue, Cleveland, OH and €VasoGenix Pharmaceuticals Inc., Lenexa, KS
7. Support:	T35 Short-term Research Training Grant entitled "Research Training in Heart, Lung, Blood & Sleep Disorders," grant number HL082544
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Background: Human alpha-Calcitonin gene-related peptide (CGRP) is a 37 amino-acid neuropeptide that is a potent vasodilator found widely in the nervous and cardiovascular systems. Studies have shown that CGRP treatment results in strong positive inotropic and chronotropic effects on the heart that is independent of beta-adrenergic receptor (beta-AR) stimulation. CGRP binds to the calcitonin receptor-like receptor (CRLR). The CRLR acts as a CGRP receptor only when it is associated with receptor activity modifying protein-1 (RAMP1). Interestingly, association of CRLR with receptor activity modifying protein-3 (RAMP3) causes CRLR to act as a receptor for adrenomedullin. Adrenomedullin is another neuropeptide found widely throughout the body and is upregulated in human heart failure. Since the presence of CRLR in human hearts has not been previously confirmed nor its regulation elucidated, we wanted to test the levels of CGRP receptor complex expression in human hearts.</p> <p>Methods: Cardiac plasma membrane fractions were isolated from non-failing unmatched organ donors without cardiac disease (n=4) and heart failure samples diagnosed with dilated cardiomyopathy (n=6). The plasma membrane fractions were subjected to CGRP radio-ligand binding assay in the absence and presence of receptor agonist, synthetic human alpha-CGRP (VasoGenix Pharmaceuticals Inc., Lenexa, KS).</p> <p>Results: Radio-ligand binding shows that there is a significant increase (38%) in the CGRP receptors (CRLR/RAMP1 complex) in conditions of dilated cardiomyopathy compared to the unmatched non-failing controls (15.25 +/- 1.34 versus 11.05 +/- 1.48 fmol/mg protein, p< 0.02). To determine the mechanism of upregulation, RT-PCR is being carried out on cardiac RNA isolates from the non-failing and failing heart samples on CRLR, RAMP1 and RAMP3.</p> <p>Conclusion: We have demonstrated that CGRP receptors are upregulated in the myocardium of human failing heart. The relative contribution of RAMP1 and RAMP3 will be determined to elucidate the potential mechanisms of CGRP action in human heart failure.</p>

NGUYEN, MIKE

1. Title	Characterization of Atherosclerotic Lesions with Cryoimaging
2. Student Presenter:	Mike Nguyen
3. Co-workers and Collaborators:	Olivier Salvado, Robert Hoffman
4. Advisor:	Jeff Duerk, Jeff Sunshine, Dave Wilson
5. Departments:	Radiology Biomedical Engineering
6. Institutions:	Case Western Reserve University
7. Support:	NIH T35
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>During the process of atherosclerosis, arteries undergo physiological changes that can be observed both grossly and histologically. The first signs are fatty streaks and as the disease progresses a lumen-narrowing plaque may form. Tissue types that have been identified in these diseased arteries include necrotic core, calcification, lipid, fibrosis, thrombus, hemorrhage, intima, media, and adventitia. Standard histological methods are the gold-standard for classifying tissue types. However, these methods are time-consuming and expensive. We hypothesize that the main tissues in atherosclerotic lesions can be accurately identified using cryoimaging. Cryoimaging is a new imaging modality developed by Professor Wilson where block faces of frozen samples are imaged at high resolution with bright and fluorescent lights. We expect specificity and sensitivity to be tissue type-specific. To test this hypothesis, we designed a double-blind study whereby tissue types of diseased common iliac arteries from human cadavers are identified independently from cryoimages and histological sections. We will perform statistical analysis to compute specificity and sensitivity for the tissues listed above, analyze contingency tables to identify the main sources of errors, and compute the mean and standard deviation of signal intensity for each tissue type. Results are pending.</p> <p>Status: Common iliac arteries from 11 cadavers have been procured. Brightfield and autofluorescent cryoimages and histological studies have been performed. The next steps are to identify tissue types from the cryoimages and histological sections and then to run statistical analyses.</p>

NORTON, MICHAEL

1. Title	Exploring the roles of Glu166 and Asn170 in the catalysis of b-lactams by the SHV-1 b-lactamase
2. Student Presenter:	Michael Norton
3. Co-workers and Collaborators:	Chris Bethel
4. Advisor:	Robert Bonomo
5. Departments:	Medicine, Pharmacology, and Molecular Biology and Microbiology
6. Institutions:	Louis Stokes Cleveland VAMC
7. Support:	
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>b-Lactamases are the major mechanism of resistance to b-lactams in Gram negative bacteria. Glu166 is a strictly conserved residue in the omega loop of Ambler Class A b-lactamases and is thought to play an important role during acylation and deacylation of b-lactam antibiotics. Asn170, another conserved amino acid in the omega loop, holds a strategically located water molecule with Glu166 and is also invariant in class A enzymes. Clinical isolates with substitutions at either position have not been found. Our goal was to explore the sequence requirements at Glu166 and Asn170 that are necessary for catalysis in a model class A b-lactamase (SHV-1). Our intention is to understand the essential function of these residues in Class A enzymes.</p> <p>Using site-saturation mutagenesis we engineered the complete set of amino acid substitutions at positions Glu166 and Asn170. Substitutions at Glu166 and Asn170 result in abolishment of resistance to penicillins, as well as a decrease in resistance to cephaloridine and cephalothin. Surprisingly, some of these variant b-lactamases demonstrated increased resistance to ceftriaxone, ceftazidime, and cefotaxime. This is particularly true of the Glu166Tyr and Asn170Pro mutants. We propose a possible mechanism by which these substitutions confer increased cephalosporin resistance. These amino acid substitutions result in conformational shifts involving the SHV-1 active site, creating a more ideal fit for the larger cephalosporins while decreasing its ability to effectively accommodate and deactivate penicillins. It is hoped that further study, including protein modeling, may elucidate the mechanism for this altered resistance profile.</p>

OH, SEONG

1. Title	Validation of Acoustic Pharyngometry using Magnetic Resonance Imaging
2. Student Presenter:	Seong Cheol Oh
3. Co-workers and Collaborators:	Jennifer Frame, Jack Jesberger, Jean Tkach, Ph.D., Susan Redline, M.D., Sanjay R. Patel, M.D.
4. Advisor:	Sanjay R. Patel, M.D.
5. Departments:	Pulmonary/Critical Care and Sleep Medicine
6. Institutions:	University Hospitals Case Medical Center, Case Western Reserve University School of Medicine
7. Support:	Crile Fellowship, NIH HL081385, HL046380
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Obstructive sleep apnea (OSA) is a common disease affecting 2-4% of middle-aged populations characterized by collapse of the oropharynx during sleep [1]. Thus, oropharyngeal size is an important predictor of apnea status. Acoustic pharyngometry is a technique that delivers sound waves through the mouth and utilizes the echoes from the throat to calculate upper airway dimensions. In this project, we attempted to assess the accuracy of acoustic pharyngometry by comparing results to those obtained from MRI in patients with a wide range of airway dimensions.</p> <p>Eight subjects (2 men and 6 women, mean age 45 y, mean BMI 33.7 kg/m²) were studied. Pharyngometry was performed while awake in the sitting and supine positions [2]. MRI was performed with the patient awake and supine in a T scanner. Images of 256x256 pixels in the transverse plane with a slice thickness of 5.0 mm were acquired. The cross-sectional areas (CSA) of the oropharynx were measured by superimposing a polygon drawing tool on the images through ImageTool.</p> <p>Minimum CSA ($r=0.68$), mean CSA ($r=0.61$) and oropharyngeal volume ($r=0.57$) by pharyngometry showed good correlation between seated and supine measurements. However, all 3 measures were significantly smaller when supine (mean differences of 0.37 cm², 0.79 cm², 4.49 cm³ respectively). On the other hand, little to no correlation was found between supine pharyngometry and MRI measurements.</p> <p>These data suggest that there is strong correlation between pharyngometry measured while seated and supine. However, due to a small number of subjects the results are statistically not significant. In addition, there was a substantial decrease in airway dimensions while supine, which helps explain why OSA is most severe in this position. The lack of correlation between pharyngometry and MRI measurements is surprising and suggests further research and refinement of our MRI algorithm is needed.</p> <p>References: 1. Malhotra A., White D.P. Obstructive Sleep Apnoea. Lancet. 2002; 360(9328):237-45. 2. Monahan K., Kirchner H.L., Redline S. Oropharyngeal dimensions in adults: effect of ethnicity, gender, and sleep apnea. Journal of Clinical Sleep Medicine. 2005; 1(3):257-263.</p>

OOMMEN, BRIAN

1. Title	The maculo-ocular reflex of the mouse
2. Student Presenter:	Brian S. Oommen
3. Co-workers and Collaborators:	Robert A. James
4. Advisor:	John S. Stahl
5. Departments:	Neurology
6. Institutions:	University Hospitals of Cleveland, Case Western Reserve University School of Medicine
7. Support:	Crile
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Studying eye movements of the mouse allows investigators to use genetically modified animals to explore links between genes, neural signals, and behavior. While eye movements induced by semicircular canal stimulation have been studied in mice, the maculo-ocular reflexes induced by maintained tilts have not been characterized. We measured the maculo-ocular reflexes of the strain C57BL/6 as well as tottering, a strain exhibiting ataxia due to mutation of the P/Q calcium channel. Methods: Awake mice (4 C57BL/6, 2 tottering) were placed in body orientations spanning 360° about the pitch (nose up or down) and roll (ear up or down) directions. The resting horizontal and vertical angular deviations of one eye were measured using videooculography. Results: In both strains, as the nose was pitched downward, the eye assumed progressively higher and more temporal resting positions. Eye elevation increased linearly as pitch angle varied from -90° to 90°. Beyond this range the eye abruptly returned to a neutral position. Prominent horizontal deviation of the eye was generated by downward pitch but upward pitch had little effect. In response to roll tilts, eye elevation increased linearly with ipsilateral tilt in the range of -90° to 90°, and gradually decreased beyond this range, generating a quasi-sinusoidal curve overall. Averaging over the data gathered at pitch angles from 0° to 90° (nose down), tottering exhibited more temporally and vertically displaced eye positions than C57BL/6 by 7.0° and 9.6°, respectively. Conclusions: The maculo-ocular reflexes of the mouse are similar to those of the rabbit, another afoveate and the one best studied to date. Tottering's larger horizontal and vertical deviations in response to pitch are consistent with an earlier observation that this strain exhibits greater eye elevation at rest.</p>

OSTROWSKI, STEPHEN

1. Title	Statins Reduce the Production of Amyloid Beta through Inhibition of Protein Isoprenylation
2. Student Presenter:	Stephen Ostrowski
3. Co-workers and Collaborators:	Brandy Wilkinson
4. Advisor:	Gary Landreth
5. Departments:	Neurosciences
6. Institutions:	Case Western Reserve University
7. Support:	AG16740
8. Please choose your academic program:	MD PHD
9. What year are you in the program?	6
10. Body of Abstract (300 words or less)	<p>Epidemiological evidence suggests that long term treatment with HMG-CoA reductase inhibitors, or statins, decreases the risk for developing Alzheimer's Disease (AD). However, many studies suggest that the effects of statins on AD cannot be fully explained by reduction of cholesterol. In addition to their cholesterol lowering effects, statins have pleiotropic actions and act to lower the concentrations of isoprenoid intermediates, such as geranylgeranyl pyrophosphate and farnesyl pyrophosphate, which are required for the function of Rho and Rab family proteins. We investigated the effects of these cholesterol independent effects of statins on amyloid precursor protein (APP) processing in cell culture. In our cell culture model, treatment with Simvastatin or Lovastatin abolishes the membrane localization of Rho and Rab family proteins without affecting cellular cholesterol levels. We show that this has two main effects on APP metabolism. First, in H4 neuroglioma cells, treatment with statins or Toxin A (which specifically inhibits the function of Rho family proteins) reduces the levels of C terminal fragments of APP, leading to decreased production of amyloid beta. Secondly, in N2a neuroblastoma cells and to a lesser extent in H4 cells, statins cause delayed maturation and accumulation of APP. This effect was not seen when Rho family proteins were inhibited with Toxin A, suggesting that this occurs through inhibition of Rab-mediated vesicular trafficking. We are investigating the effects that this has on the processing of APP to amyloid beta. In conclusion, we show that statins can inhibit the production of amyloid beta through inhibition of protein isoprenylation. This represents a potential mechanism by which statins may limit AD pathogenesis.</p>

PARK, CHRISTIE

1. Title	Health Literacy and Patient Understanding of Prescription Medication Label Instructions
2. Student Presenter:	Christie Park
3. Co-workers and Collaborators:	Silvia Skripkauskas, BA; Terry C. Davis, PhD (Louisiana State University); Ruth Parker, MD (Emory University)
4. Advisor:	Dr. Michael S. Wolf
5. Departments:	Institute for Healthcare Studies, Division of General Internal Medicine
6. Institutions:	Northwestern University Feinberg School of Medicine
7. Support:	
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>The ability to understand and act on health information (a.k.a. health literacy) has recently been positioned as a patient safety issue warranting attention. We examined whether patients could understand and demonstrate the instructions found on the primary container label of common prescription medications. We conducted a cross-sectional study using in-person, cognitive interviews with literacy assessment (Rapid Estimate of Adult Literacy in Medicine, or REALM) at a Federally Qualified Health Center (FQHC) in Chicago, and a primary care clinic located within a public hospital in Shreveport, Louisiana. In all, 297 patients were recruited (n=67 from Chicago site). Correct understanding of instructions for four common prescription medications, using 14 different instructional formats, was determined by blinded panel review of patients' verbatim responses. Rates of understanding ranged from 64 percent to 93 percent across the labels. Patients reading at the 6th grade level or below (low literacy) were less able to understand label instructions. After controlling for potential confounding demographic, socioeconomic, and health status variables, low (Adjusted Relative Risk 2.18, 95% Confidence Interval 1.29-3.25) and marginal (7th-8th grade; Adjusted Relative Risk 1.87, 95% Confidence Interval 1.15-2.75) health literacy skills were significantly associated with misunderstanding instructions as compared to patients with adequate literacy skills. In a comparison of different formats, patients were better able to comprehend instructions that were 1) explicit to the time of day to be taken, 2) minimized cognitive load through separation of dose, interval, and instruction, and 3) avoided giving numeric information in text (i.e. '2 times' vs. "twice"). While we were unable to investigate adherence practices or adverse events associated with medical error, this research supports an association between limited health literacy with a greater likelihood for misunderstanding prescription medication label instructions. Physicians and pharmacists should be trained to be specific when instructing patients on regimens. Policies should be enacted to standardize label content.</p>

PARK, JANE

1. Title	Examination of the Natural Progression of Intima-Media Thickness in Adolescent Girls
2. Student Presenter:	Jane Park
3. Co-workers and Collaborators:	Christian Binder, MD (1); Michael McNamara MD (1), Michelle Secic (3)
4. Advisor:	Barbara Cromer, MD (2)
5. Departments:	(1) Radiology (2) Pediatrics
6. Institutions:	(1) & (2) MetroHealth Medical Center (3) Secic Statistical Consulting
7. Support:	T35 NIH-NHLBI
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Background: Arterial intima-media thickness (IMT) has been shown to be an important pre-clinical marker of cardiovascular disease. The progression of IMT through adolescence is of interest since the age at which this thickening first presents, the manner of manifestation, and the underlying hormonal mechanisms have not been established. The purpose of this cohort observational study was to describe the natural history of the IMT of 6 subjects from a larger longitudinal study (n=44) and to see if the initial statistically significant decrease over 1.5 years persisted for up to 4 years.</p> <p>Methods: Ostensibly healthy adolescent girls from the larger study were recruited for this follow-up. Of the 21 eligible subjects, 6 participated. Participants had measurements of salient background variables. High frequency, B-mode ultrasound was used to measure IMT from 3 planes of the distal right common carotid artery. Analysis was limited to descriptive techniques.</p> <p>Results: Mean age of the subjects was 16.8 (SD 0.6). Mean BMI was 26.7 (SD 5.5), mean total cholesterol was 144 (SD 19) and mean HDL was 45 (SD 7). Mean systolic BP was 114 (SD 14) and diastolic BP was 64 (SD 5). Mean time since the last visit of the previous study was 26.2 months (SD 2.7), ranging from 23 to 30 months. The mean composite change in IMT from baseline to final visit was -0.03mm, -5.0% (SD 13.8). This finding may be placed within the context of findings from the previous larger study: baseline to 6 months -0.01mm, -1.0% (SD 6.05, p=0.10); baseline to 12 months -0.01mm, -1.5% (SD 7.05, p=0.09); and baseline to 18 months -0.02mm, -4.2% (SD 8.37, p=0.08).</p> <p>Conclusions: This follow-up study shows that the previous statistically significant results are robust over time and the thickness of the common carotid artery appears to decrease through adolescent development. The data also support the idea that hormonal changes during adolescence have a salutary effect on this aspect of cardiovascular health.</p>

PATEL, RAVI

1. Title	3-Dimensional Finite Element Optimization of Drug Delivery from Implantable Time-release Polymer Millirods
2. Student Presenter:	Ravi B. Patel
3. Co-workers and Collaborators:	Brent D. Weinberg, Gerald M. Saidel, Jinming Gao
4. Advisor:	Agata Exner
5. Departments:	Department of Biomedical Engineering (Weinberg, Patel, Saidel) Simmons Comprehensive Cancer Center (Gao) Department of Radiology (Exner)
6. Institutions:	Case Western Reserve University (Weinberg, Patel, Saidel, Exner) University of Texas-Southwestern Medical Center (Gao)
7. Support:	NIH MSTP Program Department of Defense Breast Cancer Research Program Predoctoral Fellowship
8. Please choose your academic program:	MD PHD
9. What year are you in the program?	3
10. Body of Abstract (300 words or less)	<p>To combat tumor recurrence after radiofrequency (RF) ablation, drug-containing polymer implants designed to release chemotherapeutic agents into the ablated region have been developed. However, in vivo studies demonstrated that drug released from implants placed in the center of ablated tumors may not penetrate to risk areas located at the tumor periphery. To design a better treatment strategy, a framework of drug transport and elimination was used to develop a three-dimensional (3-D) finite element method (FEM) model of drug distribution in non-ablated and ablated tumors. Doxorubicin transport parameters established in previous studies were then used with this model to simulate drug transport from implants placed in multiple locations around the periphery of tumors. By varying the extent of ablation, implant drug release profile, the implant placement geometry, a wide variety of possible tumor treatments were designed. For each treatment, drug concentration at each location in the tumor was simulated as a function of time. Because ablated tumors are most likely to recur at the ablation boundary, treatment quality was determined by evaluating the cumulative drug exposure in the outermost 25% of the ablated tumor volume. The doxorubicin distribution simulations found that using multiple implants strategically placed throughout a tumor can maximize drug exposure in the risk areas where tumors are most likely to recur after treatment, providing considerable advantage over using a single implant. This study establishes the viability of using a 3-D FEM model to simulate intratumoral drug delivery from implants after RF ablation and suggests the possibility of using a similar tool to customize a treatment for each patient. Future work will emphasize validating this approach in an animal model.</p>

PRIETO CENTURION, VALENTIN

1. Title	Smallpox Transmission Models
2. Student Presenter:	Valentin Prieto Centurion
3. Co-workers and Collaborators:	
4. Advisor:	Daniel Tisch
5. Departments:	Epidemiology and Biostatistics
6. Institutions:	School of Medicine, CWRU
7. Support:	Crille Fellowship
8. Please choose your academic program:	MD MPH
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Smallpox is a highly contagious viral disease that was officially declared eradicated in 1980. There are current concerns about its re-emergence and recent research efforts have been focused on estimating its impact on contemporary populations. In order to understand smallpox transmission patterns we reviewed historical data from outbreaks dating back to 1872. A systematic review was used to identify papers from the National Library of Medicine, Ovid, Index Medicus and reference lists of included publications. Two authors reviewed selected papers for smallpox outbreaks. 97 relevant papers were identified, containing data from 121 outbreaks. The standard mean basic reproductive rate was 5.49 (SD=5.65) secondary cases per index case before intervention, ranging from 0 to 17 secondary cases per index case. This number was found to vary according to the setting of the outbreak, year and geographical location. Results are interpreted by number of cases in the outbreak, case-fatality rate and % of cases that were successfully vaccinated. It was determined that the transmission of smallpox was highest in a general hospital setting before the diagnosis of smallpox ($R_0=9.32$, $SD=6.40$, Range=1 to 17), outbreaks occurring after 1950 ($R_0=6.26$, $SD=6.67$, Range=0 to 18) and in outbreaks in developing countries ($R_0=5.67$, $SD=6.97$, Range=0 to 12). According to the reviewed literature, early diagnosis and implementation of control measures, such as case-isolation and contact vaccination, were the most important factors in controlling the outbreak. Given the current lack of herd immunity and its unanticipated nature, a rapid epidemic rise can be expected in the case of a smallpox outbreak before the implementation of public health interventions and in regions with crowding and inadequate infrastructure.</p>

PRITCHETT BURGE, ERIKA

1. Title	Assessment of perceived barriers to participation in genetic research by families of young children: Exploration of ethnic differences
2. Student Presenter:	Erika M. Pritchett Burge
3. Co-workers and Collaborators:	
4. Advisor:	Susan Redline
5. Departments:	Pediatrics
6. Institutions:	CWRU School of Medicine
7. Support:	T35 HL080981
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Background and Rationale: Asthma is the most common chronic childhood condition, affecting 10% of children. Poor and minority children are disproportionately affected. With growing availability of new classes of asthma medications, it is becoming necessary to include biological analysis in each child's asthma risk profile. If revolutionary discoveries come from medical research utilizing these analyses, the noted underrepresentation of African Americans and other minorities among research participants will affect the generalizability of research conclusions to these high-risk populations in pediatric asthma.</p> <p>Question: What are the perceived barriers to research participation, specifically genetic/biorepository collection and use, by families of young children? Is there an ethnic or socioeconomic divide?</p> <p>Methods: A culturally sensitive and clinically effective questionnaire to identify potential barriers to genetic research participation by minority families of young children will be accomplished through a combination of literature review, medical and bioethics expert input and focus group feedback.</p> <p>Review and interviews were used to compile a discussion guide. Each of three focus groups will include 6-10 adult primary caregivers of asthmatic children who self-identify as African American, Latino or Caucasian. Participants will also be characterized by socioeconomic status (insurance). Key words and concerns expressed during the focus groups will be used to modify preliminary questionnaire, which will be refined with expert assistance and piloted. The final questionnaire will be given to those who refuse any portion of genetic information collection and future use in the Personalized Asthma Care Team study. Data from completed questionnaires will be analyzed to determine if there are statistically significant differences among races or socioeconomic groups.</p> <p>Results: An extensive literature review was performed, and experts in Bioethics and Health Disparities were interviewed to compile a Focus Group Guide. A protocol was submitted to the UHHS IRB. Due to inability to gain IRB approval in allotted time, recruitment for focus groups was not begun during the summer.</p>

RASTEGAR, JESSICA

1. Title	Distinct Phenotypic Characteristics of Exacerbation-Prone Asthmatics
2. Student Presenter:	Jessica Rastegar
3. Co-workers and Collaborators:	A.L. Innes, MD, K.S. Okamoto, BS, H. Wong, BS
4. Advisor:	J.V. Fahy, MD
5. Departments:	Pulmonary and Critical Care Medicine, Cardiovascular Research Institute, Department of Medicine
6. Institutions:	University of California, San Francisco
7. Support:	R01 HL080414
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Asthma exacerbations are a significant economic and healthcare burden with known precipitants but relatively undefined risk factors. We propose that characteristics other than severity of airflow obstruction can identify asthmatics who are exacerbation-prone from those who are not. 142 asthmatics were enrolled in a case-control study (61 cases; 81 controls) investigating mechanisms of asthma exacerbation. "Exacerbators," or cases, were defined by oral prednisone use for asthma within the last 2 years, whereas "non-exacerbators," or controls, had not experienced an exacerbation requiring prednisone since age 12. Asthmatics on chronic oral prednisone were excluded. Subjects were recruited using community advertising and our research center's asthma recruitment database. Subjects were characterized during their study visits by history and physical examination, pulmonary function testing, and asthma characterization questionnaires. Diagnosis of asthma was based upon methacholine bronchoprovocation or bronchodilator reversibility. We found that recent "oral prednisone use" among asthmatics did indeed identify cases with distinct phenotypic differences from controls. Health care utilization was significantly greater in cases than controls when evaluated by ER visits, hospitalizations, and intubations ($p < 0.05$ by chi square for all analyses). Weekly asthma symptoms and albuterol use were greater in cases than controls ($p < 0.05$ by rank sum). FEV1/FVC was lower in cases ($64.4\% \pm 17.7\%$) than controls ($72.2\% \pm 12.7\%$) ($p=0.003$), but there was no statistically significant difference in FEV1% predicted or PC20. Although there were more women than men in the total cohort, there was no statistically significant difference in gender distribution between cases (66.7% women) and controls (62.3% women). Recruitment of exacerbation-prone asthmatics utilizing "recent oral prednisone use" therefore enables the identification of phenotypically distinct asthmatics. This may serve as a useful strategy for the identification of unique exacerbation-prone asthmatics in future studies of mechanisms of asthma exacerbation.</p>

RYMAN, DAVIS

1. Title	Quantitative trait loci modulating brain amyloid-beta metabolism in a transgenic mouse model of Alzheimer's disease
2. Student Presenter:	Davis Ryman
3. Co-workers and Collaborators:	Yuan Gao, Bruce T. Lamb
4. Advisor:	Bruce T. Lamb
5. Departments:	CWRU School of Medicine, Dept of Genetics CWRU School of Medicine, Dept of Neuroscience Lerner Research Institute, Dept of Neurosciences
6. Institutions:	Lerner Research Institute, Cleveland Clinic Foundation Case Western Reserve University School of Medicine
7. Support:	CWRU MSTP T32 GM07250; NIH Genetics Training Grant T32 GM008613; Glenn/American Federation for Aging Research Scholarship for Research in the Biology of Aging; NIH Grant AG023012; Alzheimer's Association Zenith Award
8. Please choose your academic program:	MD PHD
9. What year are you in the program?	5
10. Body of Abstract (300 words or less)	<p>Alzheimer's disease (AD) is characterized by the presence of senile plaques in the brain formed by aggregation of the amyloid beta (Abeta) peptide, a processed product of the amyloid precursor protein (APP). While several genes directly involved in APP processing have been implicated in rare familial AD syndromes, the study of AD patient populations has demonstrated a very significant degree of unexplained heritability for AD risk, resulting from an unknown number of genetic factors which have proven extremely difficult to identify in human studies. Our lab has developed a unique mouse model system for the study of genetic modifiers of AD pathogenesis, by integrating a full genomic copy of R1.40, a mutant allele of APP known to result in familial human AD, into identical integration sites on the genetic background of four different inbred strains of laboratory mice. Intriguingly, mice from the C57BL/6J and DBA2/J genetic backgrounds carrying the R1.40 APP transgene produce identical levels of unprocessed APP, but demonstrate significant, heritable differences in brain Abeta levels. To identify specific loci responsible for the observed genetic control of Abeta metabolism in this model system, we have performed a whole-genome quantitative trait locus (QTL) mapping experiment on a total of 516 animals from a C57BL/6JxDBA/2J intercross, using a dense set of 909 informative SNP genetic markers. Our studies have identified three genetic loci on mouse chromosomes 1, 2, and 7 showing significant or suggestive associations with brain Abeta levels, several of which contain regions syntenic to previous reports of linkage in human AD.</p>

SANDO, MARK

1. Title	Trauma Patient Urine in the ICU: Is it Dirty?
2. Student Presenter:	Mark J. Sando
3. Co-workers and Collaborators:	Joseph F. Golob, MD, Jeffrey A. Claridge, MD
4. Advisor:	Jeffrey A. Claridge, MD
5. Departments:	Department of Surgery: Division of Trauma, Critical Care, Burns, and Life Flight
6. Institutions:	MetroHealth Medical Center, Case Western Reserve University
7. Support:	National Institute of Child Health and Human Development, Multidisciplinary Clinical Research Career Development Programs Grant K12 RR023264 Fratianne Scholar, Department of Surgery: Division of Trauma, Critical Care, Burns and Metro Life Flight
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>BACKGROUND: Urinary tract infections (UTIs) are the most common nosocomial infection and create economic burden through increased testing, treatment, and morbidity. The purpose of this study was to define the current practice for obtaining urinalysis (UA) and urine cultures (UCx) in trauma patients admitted to the surgical and trauma intensive care unit (STICU), and to evaluate the association of fever and leukocytosis with UTIs.</p> <p>METHODS: An 18-month retrospective cohort analysis was performed on consecutive patients admitted for ≥ 2 days to the STICU at a level I trauma center. Data collected included: demographics, injuries, and the first 14 days of daily maximal temperature (Tmax), leukocyte count, UA, and UCx. Fever and leukocytosis were defined as Tmax ≥ 38.5C and leukocyte count $\geq 12,000/\text{mm}^3$, respectively. Positive UA was defined as a positive urine nitrite and/or a positive urine leukocyte ($\geq 10/\text{HPF}$). UTI was defined as a positive UCx (≥ 105 organisms).</p> <p>RESULTS: 510 patients were evaluated for a total of 3839 patient-days. The mean age was 48.6 ± 0.9 and injury severity score was 19.4 ± 0.5. 72% were males and 91% had blunt injuries. 470 UAs and 407 UCx were obtained. 42 (8%) patients had 60 UTIs. Our practice demonstrated a significant association of obtaining UCx with fever and fever+leukocytosis ($p < 0.0001$), but no association with leukocytosis alone. Our outcomes revealed no association of UTI with fever, leukocytosis, or fever+leukocytosis. In the patients with a UA and UCx done concomitantly, the sensitivity and specificity was 54% and 80%, respectively for a UA predicting UTI (PPV=35% and NPV=90%).</p> <p>CONCLUSIONS: Our practice for obtaining UCx was related to fever and fever+leukocytosis. However, fever and/or leukocytosis were not associated with UTIs in STICU patients. Our study suggests that the paradigm for evaluating UTI needs to be reevaluated in critically ill trauma patients.</p>

SCHENK, AUSTIN

1. Title	CD8 memory T cells initiate Mig production early post-transplant
2. Student Presenter:	Austin Schenk
3. Co-workers and Collaborators:	
4. Advisor:	Robert Fairchild
5. Departments:	Pathology & Immunology
6. Institutions:	Case School of Medicine Cleveland Clinic Foundation
7. Support:	NIH, American Heart Association, CASE MSTP
8. Please choose your academic program:	MD PHD
9. What year are you in the program?	5
10. Body of Abstract (300 words or less)	<p>Organ transplantation saves lives but rarely restores a normal life expectancy, in part because many transplanted organs fail prematurely. Transplanted organs are damaged by surgical trauma, oxygen deprivation, reperfusion injury, and immunity. Memory T cells are one type of adaptive immune cell known to participate in graft injury, but mechanisms of memory T cell functioning are incompletely understood. Previously, our laboratory demonstrated in a murine heterotopic cardiac transplantation model that the T cell chemoattractant Mig (CXCL9) is elevated in allogeneic but not syngeneic cardiac allografts at day 3 post-transplant, and that in vitro culture of CD44^{hi} (but not CD44^{lo}) memory phenotype CD8 T cells with allogeneic (but not syngeneic) endothelial cells results in production of the T cell chemoattractant Mig (CXCL9). We now demonstrate in the murine cardiac transplantation model that adoptive transfer of CD44^{hi} memory CD8 T cells elevates the amount of Mig protein detectable in allografts at day 3 post transplant. This allorecognition event was reduced when β2-microglubulin -/- donor grafts were transplanted into allogeneic recipients, and was undetectable when recipient mice lacked CD8 T cells. Administration of antibodies that inhibit IFN-γ and ICOS reduced intragraft Mig levels but antibody inhibition of CD40L or administration of control IgG had no effect. When recipient mice were depleted of neutrophils prior to allogeneic transplantation, intragraft Mig levels were substantially reduced on the third transplant day. We believe that allorecognition of donor MHC I by circulating CD8 memory T cells early post-transplant initiates intragraft Mig production that optimizes subsequent infiltration by effector T cells. The role for neutrophils in this process emphasizes an important aspect of synergism between innate and adaptive immunity.</p>

SCHULDT, STEPHEN

1. Title	Values exemplified by primary care providers
2. Student Presenter:	Stephen Schuldt
3. Co-workers and Collaborators:	Mary Ruhe; Sharon Weyer
4. Advisor:	Dr. Kurt Stange
5. Departments:	Family Medicine
6. Institutions:	Case
7. Support:	Crile
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Previous efforts to improve primary care practice may have had limited effect because they attempt to reduce variability without taking into account practice values that motivate behavior. Using a comparative case study analysis of 79 primary care practices in Northeast Ohio, a typology of practice values was created. We identified values that guided primary care practice structure, culture, and provision of care, and observed patterns or values within practices. Primary care values can be classified according to Internal or External focus. We found that Internally focused practices defined their values in relation to their own ability to achieve a desired end while Externally focused practices defined their values in relation to the recipients of their care. Internally focused values included Business focus and Service focus. Externally focused values included Population focus and Patient focus. Further, our analysis suggests predominant practice values often shape practices to the point of minimizing the influence of other values. This was noticed in the absence of Patient focus as an influential value in practices dominated by a Business focus, and by the absence of a Business focus as an influential value in practices dominated by Patient focus. The values typology developed here can be used to understand variation in primary care practices and to tailor practice change strategies by linking to existing motivation. Future research should examine the effect of practice values on patient outcomes and on practice-individualized quality improvement interventions.</p>

SHELLY, ALICIA

1. Title	How Coping Skills Associate with Cardiovascular disease
2. Student Presenter:	Alicia D. Shelly
3. Co-workers and Collaborators:	
4. Advisor:	Sonja Harris-Haywood, MD MS and Esa Davis, MD MPH
5. Departments:	Family Medicine
6. Institutions:	Case School of Medicine
7. Support:	NIH
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Context: Stress is an emerging risk factor for obesity and coronary heart disease, not being able to cope with stress may contribute to the development of cardiovascular disease (CVD)</p> <p>Objective: The purpose of this study was to investigate whether obese/overweight people who are not actively trying to lose weight are more likely to have negative coping skills in comparison to average weight adults. In addition, this study investigates whether adults with negative coping skills have more risk factors for cardiovascular disease.</p> <p>Methods: We conducted a cross-sectional study of 200 adults with various weights receiving care at an urban family medicine practice in northeast, Ohio. Data collection consisted of a self-administered questionnaire that assessed demographics, height, weight, health status and coping skills. The “coping skills” items came from two well known scales: Ways of Coping and the COPE questionnaire. The main outcomes were the prevalence of risk factors for cardiovascular disease (CVD) and obese vs. non obese as measured by BMI. A multiple logistic regression was used to assess the relationship of negative coping skills and CVD risk factors and weight. Results: Data is still currently being collected .</p> <p>Conclusion: If the results of our study show that obese adults have negative coping skills and that those with negative coping skills are associated with higher prevalence of cardiovascular risk factors; it may suggests that strategies and screening tools needed to address stress and coping are important in weight management programs and early CVD prevention.</p>

SHENKO, CHRISTINA

1. Title	Characteristics of Eligible Non-participants in a Randomized Controlled Trial on Supportive Care in Advanced Cancer
2. Student Presenter:	Christina A. Shenko
3. Co-workers and Collaborators:	Mary Ellen Lawless
4. Advisor:	Julia H. Rose, Ph.D.
5. Departments:	Department of Medicine, MHMC; Geriatric Research, Education and Clinical Center, VAMC
6. Institutions:	MetroHealth Medical Center, Louis Stokes VA Medical Center
7. Support:	Crile Fellowship; NIH grant: NCI-CA10282-01; VHA grant: IIR 03-255 - 1; ACS grant: ROG-04-090-01
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>BACKGROUND: Given recent concerns regarding unequal access to and utilization of novel medical research [1], patient accrual, recruitment and retention in clinical trials have begun to attract more scholarly attention. However, analysis has focused primarily on enrolled participants, and has failed to investigate those who are eligible for enrollment but refuse participation [2,3,4].</p> <p>METHODS: We analyzed the demographic information from the Aging and Supportive Care in Advanced Cancer (ASC) study, to identify population-level differences between participants (n=335) and non-participants (n=117), who were further stratified as middle-aged (aged 40 to 60) and young-old (aged 61 to 80). We also examined the reasons given by non-participants when asked why they chose not to enroll.</p> <p>RESULTS: Non-participants were significantly ($p < 0.05$) more likely to be young-old (versus middle-aged), to be living without a partner, and to have a yearly income less than \$20,000. There was a trend ($p < 0.10$) of more non-participants being male. Employment status, level of education achieved and self-reported race were not correlated with study participation. Of the 106 non-participants (90.6%) who gave a reason for refusal, 30 (28.3%) felt they did not need the intervention offered, 25 (23.6%) felt the study itself was too burdensome, 17 (16.0%) felt emotionally unable to participate, and the remaining 34 (32.1%) cited various other reasons.</p> <p>CONCLUSIONS: The finding that non-participants were more likely to be older, to have lower incomes and to have less social support at home is a concern, as this study is testing the efficacy of a coping and communication support for the underserved. Almost a quarter of non-participants cited study demands (e.g., interviews) as their reason for refusal. Increased knowledge about non-participants in medical research can be useful both to identify those patients unlikely to utilize the intervention and to achieve higher rates of patient accrual in future investigations.</p> <p>-----</p> <ol style="list-style-type: none"> 1. NIH Revitalization Act. Subtitle B: § 131-133; 1993. 2. Murthy VH, Krumholz HM, Gross CP. Participation in cancer clinical trials: race-, sex-, and age-based disparities. <i>JAMA</i> 2004;291:2720-2726. 3. Northouse LL, Rosset T, Philips L, Mood D, et al. Research with families facing cancer: challenges of accrual and retention. <i>Research in Nursing and Health</i> 2006;29:199-211. 4. Cooley ME, Sarna L, Brown JK, Williams RD. Challenges of recruitment and retention in multisite clinical research. <i>Cancer Nursing</i> 2003;26:376-386.

SHULTZ, DAVID

1. Title	IKKbeta is required for the induction of several IFN-gamma stimulated genes
2. Student Presenter:	David Shultz
3. Co-workers and Collaborators:	Nywana Sizemore and George Stark
4. Advisor:	George Stark
5. Departments:	Pathology, Case Western Reserve University School of Medicine and Molecular Genetics, Cleveland CLinic Foundation
6. Institutions:	Case Western Reserve University School of Medicine and Cleveland Clinic Foundation
7. Support:	
8. Please choose your academic program:	MD PHD
9. What year are you in the program?	5
10. Body of Abstract (300 words or less)	<p>Abstract: Sizemore et al (PNAS, 101(21), 2004) recently identified a subset of ISGs that are not induced in response to interferons (IFNs) in mouse embryonic fibroblast cells (MEFs) doubly null for the expression of IβB kinase α and β (IKKα and IKKβ). Our work has revealed that the IFN-induced transcription of other IKK-dependent ISGs is specifically dependent on IKKβ expression. In a microarray experiment, of 584 ISGs induced in a pool of IKKβ^{-/-} cells stably restored for IKKβ expression, 370 (63%) were not induced in IKKβ^{-/-} cells. Several of these genes have been confirmed by Northern and quantitative PCR analysis. We are currently working to identify the mechanism(s) by which IKKbeta is required for the induction of these genes.</p>

SILVERBERG, AMY

1. Title	Lead Screening: Attitudes and Practices of Cuyahoga County Primary Care Providers
2. Student Presenter:	Amy Silverberg
3. Co-workers and Collaborators:	Leila Jackson, Margaret Pizzi, Matthew Carroll, Terry Allan
4. Advisor:	Dorr Dearborn
5. Departments:	Department of Environmental Health Sciences, Swetland Center for Environmental Health, Department of Epidemiology and Biostatistics
6. Institutions:	Case Western Reserve University School of Medicine, University Hospitals, Cleveland Department of Public Health, Cuyahoga County Board of Health
7. Support:	Greater Cleveland Lead Advisory Council, HUD Healthy Homes grant OHLHH0141-05, QualChoice, CareSource
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Childhood lead exposure remains a serious environmental health problem in the Cleveland area, especially for poor families, because of the age and condition of available housing. While at high levels lead can make exposed individuals obviously sick, the more common lower level exposures close to and even below the CDC's 10 µg/dl level of concern can have more subtle effects, including long-term and potentially permanent cognitive impairment and behavior problems. New cases of children with elevated blood lead levels continue to be diagnosed at an alarming rate in Cuyahoga County while state Medicaid records show that large numbers of children who by law should be screened by their physicians are not being screened. Recognizing that by the time a child tests positive for an elevated blood lead level, some of the damage has already been done, a widely used screening program is still an important part of eliminating childhood lead poisoning since it serves to raise awareness, to alert families and their physicians more quickly to potential problems, and to pinpoint sites for potential remediation. We distributed a survey to 1900 primary care providers in Cuyahoga County to learn more about their attitudes and practices regarding lead screening. The goal of the project is to better understand the barriers faced by physicians and their patients which are preventing large numbers of children from being screened. The surveys are currently being returned, and preliminary data will be analyzed over the next few months.</p>

SIMMONS, DAIMON

1. Title	Cell Surface Marker Response to BCG Infection
2. Student Presenter:	Daimon Simmons
3. Co-workers and Collaborators:	Nicole Pecora
4. Advisor:	Cliff Harding
5. Departments:	Pathology
6. Institutions:	Case Western Reserve University
7. Support:	
8. Please choose your academic program:	MD PHD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>It has previously been shown in vitro that infection of mouse immune cells with Mycobacterium bovis (BCG) results in down-regulation of Class II MHC. Now we examine this phenomenon with an ex vivo model in which expression levels are compared in immune cells from naïve mice and BCG-infected mice through flow cytometry. Levels of MHC-II and TLR-2 both appear to increase globally in some populations of cells upon infection, and infected cells may increase or decrease levels of these proteins depending on which population they belong to. Finally, examination of one of the cell surface markers (CD11B) used to distinguish these different subpopulations, reveals that the levels of expression of these cell surface markers also change in cells infected with BCG. The in vitro experiment shows cells infected with BCG concurrently decrease levels of CD11B and MHC-II.</p>

SPENCE, JEFFREY

1. Title	Holes in the Safety Net: The Near-Poor Slip Right Through
2. Student Presenter:	Jeffrey Spence
3. Co-workers and Collaborators:	
4. Advisor:	Dr. David Litaker
5. Departments:	Division of General Internal Medicine
6. Institutions:	Louis Stokes Cleveland VA Medical Center
7. Support:	Crile Fellowship
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Healthcare resource changes may affect the health outcomes of patients, especially when occurring rapidly and in economically vulnerable communities. This study assessed health care access, utilization, and health status following the closure of four hospitals in Cuyahoga County between 1998 and 2004 and examined whether a disproportionate effect was observed among the most economically disadvantaged residents</p> <p>We examined three waves of data on Cuyahoga County residents (sample sizes: 1495, 1420, and 3410) participating in the Ohio Family Health Survey. Trends on insurance and general health status, the presence of a usual source of care, and health care utilization were correlated with patient demographics and hospital utilization statistics. Respondent income (poor <100% Federal Poverty level [fpl], near-poor 100-200% fpl and not poor >200% fpl) was used in stratified analyses to assess its relationship with health outcomes during the period studied.</p> <p>Although basic demographics across cohorts remained stable, educational attainment, annual income, Medicaid enrollment (12.0% vs. 15.2%) and poverty levels (14.7% vs. 18.3%) all increased over time, suggesting increasing income inequality. The proportion with unmet health care needs and poor health status both increased, especially among the near-poor - the only group to report no increase in having a usual source of care. Hospital admissions dropped initially following the hospital closures, while occupancy rates increased.</p> <p>A short-term decrease in access to care related to hospital closures and a decline in health status among study participants raises questions about the ability of remaining hospitals to meet the needs of county residents. While Medicaid expansion may have affected the availability of usual sources of care and helped to buffer the effects of these closures, the near-poor were not aided by this expansion. Future policy initiatives are needed to specifically target this subset of individuals who are not currently eligible to access safety net services.</p>

TARKOWSKY, STEPHANIE

1. Title	Alzheimer's disease pathology mediated by gonadotropins
2. Student Presenter:	Stephanie Tarkowsky
3. Co-workers and Collaborators:	Gemma Casadesus ¹ , Kate M. Webber ¹ , Christopher W. Gregory ³ , Richard L. Bowen ^{3,5} , Craig S. Atwood ² , George Perry ^{1,4} and Mark A. Smith ¹ .
4. Advisor:	Mark A. Smith
5. Departments:	Pathology
6. Institutions:	¹ Department of Pathology, Case Western Reserve University, Cleveland, Ohio; ² School of Medicine, University of Wisconsin and William S. Middleton Memorial Veterans Administration, Madison, WI; ³ Voyager Pharmaceuticals Corporation, Raleigh, NC; ⁴ College of Sciences, University of Texas at San Antonio, San Antonio, TX. ⁵ Current Address: Raleigh NC
7. Support:	AFAR, Culpepper Fellowship
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Age-related increases in luteinizing hormone (LH) have recently been implicated in the etiology of Alzheimer disease (AD), particularly in mechanisms involving amyloid-β synthesis and deposition. To further explore the potential pathophysiological mechanisms involved in the actions of LH in AD, we used an in vitro model system (SH-SY5Y) to examine the effects of LH on oxidative stress, cell signaling, and tau phosphorylation. Our data demonstrates that LH dose-dependently leads to increases in tau phosphorylation, ERK activation, and increases in the activity of GSK-3β. Importantly, similar doses also lead to redox changes including increased cellular stress as shown by increases in oxidized cellular glutathione (GSH) levels. These results indicate that LH is likely to be pluripotent mediator of the disease since, in addition to modulating amyloid-β-related mechanisms, LH also mediates redox and cytoskeletal imbalances associated with the modulation of endogenous antioxidant systems such as GSH and aberrant tau phosphorylation. Moreover, since high LH levels were associated with ERK phosphorylation and GSK-3β, it is likely that LH may, at least partially, work via cell signaling mechanisms involving mitogenic pathways.</p>

THOMSON, JODI	
1. Title	Paradoxical increase in sulbactam susceptibility among a panel of clavulanate resistant SHV beta-lactamase mutants at Ambler position 244
2. Student Presenter:	Jodi M Thomson
3. Co-workers and Collaborators:	Anne M. Distler, Tarek S. Mansour, Robert A. Bonomo
4. Advisor:	Robert A. Bonomo
5. Departments:	Department of Pharmacology
6. Institutions:	Department of Pharmacology, Case Western Reserve University School of Medicine, Cleveland, Ohio, 44106, Wyeth Research, 401 N. Middletown Road, Pearl River, New York 10965, and Louis Stokes Cleveland Department of Veterans Affairs Medical Center Cleveland, Ohio, 44106
7. Support:	This work was supported by National Institutes of Health 1R01 A1063517-01 and the Veterans Affairs Medical Center Merit Review Program (RAB). JMT was supported in part by NIH T32 GM07250 and the Case Medical Scientist Training Program
8. Please choose your academic program:	MD PHD
9. What year are you in the program?	6
10. Body of Abstract (300 words or less)	<p>Resistance to β-lactamase inhibitors has been steadily growing and threatens the use of β-lactam antibiotics for serious infections. Recently, our lab studied clavulanate resistance as a result of mutations at Ambler position R244 in the class A β-lactamase SHV. After finding significant increases in resistance to clavulanate in our panel of R244 mutants, we were intrigued to notice that all 19 variants exhibited hyper-susceptibility to the sulfone sulbactam. To probe the mechanistic basis for sulfone hyper-susceptibility in R244 variants, we performed steady state kinetics to determine K_I, k_{inact} and k_{cat} values for sulbactam and tazobactam. In addition, Mass spectrometry was performed on SHV-1 and SHV R244S before and after a 15 minute incubation with a 1000:1 sulbactam:enzyme ratio. Interestingly, although K_I values were universally increased in R244S, -Q, and -L, just as we had observed with clavulanate, the ability of the enzymes to turnover sulbactam was drastically reduced (from 13,000 to = 500 per 24 hours). In mass spectrometry studies, a majority of SHV-1 had been regenerated by 15 minutes. In contrast, intact R244S is barely detectable at this time point, with prominent peaks representing 70 and 88 dalton adducts. To further our study of this interesting panel of mutants, we studied novel penem inhibitors and probed their ability to inactivate SHV-1 and the R244 mutants. Compared to clavulanate and the sulfones, turnover of the penem inhibitors by all enzymes was strikingly low (<2 inhibitor molecules per 24 hours). In addition, mass spectrometry experiments indicate that these inhibitors do not exhibit fragmentation within the active site of SHV-1 or R244S as is seen with sulbactam and tazobactam.</p>

TOOGOOD, PAUL

1. Title	A Comparison of Periarticular Tibial Plate Fits on Normal Humans
2. Student Presenter:	Paul Toogood
3. Co-workers and Collaborators:	Goyal, KS; Marcus, RE; Vallier, HA; Haille Sallasse, J.
4. Advisor:	Dr. Daniel Cooperman
5. Departments:	Department of Orthopaedic Surgery; CWRU-SOM
6. Institutions:	CWRU-SOM, University Hospitals of Cleveland, Metrohealth Medical Center; Cleveland Museum of Natural History
7. Support:	CWRU-SOM (Crile Fellowship)
8. Please choose your academic program:	MD MS
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>A variety of surgical plates for fixation of proximal tibial fractures are currently available. A plate whose contours minimize space between itself and the bone and whose axes align with those of weight-bearing is desirable to minimize impingement on surrounding tissue and intimately secure fracture fragments.</p> <p>This study attempted to quantify fit amongst three different, widely available lateral proximal tibial plates (Zimmer Non-locking, Synthes Non-Locking, Synthes Locking) on 100 normal humans to test each plate's ability to fit a random sample and to examine differences amongst the three systems.</p> <p>The study utilized right tibias of 25 white males, 25 white females, 25 black males, and 25 black females made available from the Hamann-Todd Osteological Collection. Each of the plates was secured to each tibia in "best-fit" orientation and measurements taken with a Microscribe G2LX and Rhinoceros software to determine the plate's alignment with the tibial plateau and shaft and the amount of space between the plate and the bone in total, as well as in defined proximal, middle, and distal surfaces of the plate. If the average distance between the plate and tibial surface in the middle and distal regions was within 1mm of each other the plate was said to fit evenly, otherwise the fit was spanned (middle > distal) or impinged (middle < distal). An anatomic fit was defined as an average total distance of less than 1.5mm, plus an even fit, plus a plateau and shaft alignment of less than 2 degrees.</p> <p>Out of 100 tibias, 7 Zimmer Non-Locking, 9 Synthes Non-Locking, and 3 Synthes Locking met the criteria for anatomic fit. This translates into the majority of tibia having large volumes, spanned/impinged fits, or poor alignment. Such findings suggest the importance of objectively defining "anatomic fit", a term applied by most manufacturers of contemporary plating systems.</p>

TORRES, LISA

1. Title	The Effects of Hyperthyroidism on Mg ²⁺ Homeostasis in the Heart
2. Student Presenter:	Lisa Maria Torres
3. Co-workers and Collaborators:	
4. Advisor:	Dr. Andrea M.P. Romani
5. Departments:	Physiology and Biophysics
6. Institutions:	Case Western Reserve University School of Medicine
7. Support:	T35 grant
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Thyroid hormone (T3) hyper-secretion has well-documented effects in humans. At the heart level, hyperthyroid hormone production results in a switch in the myosin heavy chain isoform expression, and an increase in both adrenergic responsiveness and heart contractility via modulation of phospholamban and associated SERCA pump. At the pharmacological level, beta-blocker therapy only provides a partial amelioration of some of these symptoms, thus suggesting that some of the thyroid hormone-induced modifications within the cardiac myocytes are long-lasting and not simply reconducible to beta-adreno-ceptor activity and responsiveness. Possible explanations include inhibition of β-adrenergic cascade inhibitors, upregulation of β-adrenergic stimuli by thyroid hormone, and increase in the expression of the β-adrenergic receptor subtype 1.</p> <p>We tested the hypothesis that an increase in circulating T3 affects cation distribution within cardiac cells and possibly systemically. The data I obtained indicate that male Sprague-Dawley (~300g) rats rendered hyper-thyroid by 3-4 administrations of T3 or T4 presented ~25% increase in total magnesium (Mg²⁺) content within cardiac ventricular myocytes. In contrast, rats rendered hypothyroid presented a ~20% decrease in total Mg²⁺ content. Similar changes were also observed in the serum and liver tissue. The administration of specific β-adrenergic agonists (e.g. isoproterenol) or cell permeant cyclic-AMP analogs (e.g. 8-Cl-cAMP) resulted in a 25% and 35% increase in the amount of Mg²⁺ extruded into the circulation from the hearts of T4 and T3-injected rats, respectively. My next step was to determine Mg²⁺-distribution within cardiac myocytes. One model consisted in isolating cardiac ventricular myocytes from hyperthyroid animals by collagenase-digestion. The second model consisted in reproducing hyper-thyroid conditions in the H9C2 cardiac myocyte cell line. The preliminary results indicated that H9C2 cells needed to be treated for ~96 hours with daily administrations of T3 to present a detectable increase in cellular Mg²⁺ content that was similar to the increase observed in collagenase-dispersed myocytes isolated from hyperthyroid rats.</p>

VARR, BRANDON

1. Title	Prognostic Significance Of Left Atrial Appendage Sludge In Patients With Atrial Fibrillation
2. Student Presenter:	Brandon Varr
3. Co-workers and Collaborators:	Boris Lowe MD
4. Advisor:	Allan Klein MD
5. Departments:	Section of Cardiovascular Imaging, Department of Cardiovascular Medicine
6. Institutions:	Case Western Reserve University, The Cleveland Clinic Foundation
7. Support:	T-35 grant
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>OBJECTIVE: To assess the mortality of patients with atrial fibrillation (AF) and left atrial appendage (LA/AA) sludge.</p> <p>RATIONALE: Patients with AF and LA/AA dense spontaneous echocardiographic contrast (SEC) or thrombus have an increased mortality and risk of cerebral thromboembolism. Thrombus stands as a contraindication to cardioversion, but there are no published studies on the fate of patients with LAA sludge to direct clinical management.</p> <p>METHODS: Patients with AF undergoing transesophageal echocardiographic (TEE) evaluation prior to electrical cardioversion or radiofrequency pulmonary vein isolation were included in the retrospective case-control study. Sludge was defined as optically intense dynamic gelatinous consistency echodensities, without a discrete mass, in the LAA throughout the cardiac cycle. Event rate was all cause mortality.</p> <p>RESULTS: A total of 127 patients with AF undergoing TEE evaluation prior to elective electrical cardioversion or radiofrequency pulmonary vein isolation with LA/AA thrombi, sludge, dense SEC comprised the study groups. Patients with AF, but without these echocardiographic risk factors, served as control patients. Interobserver agreement for the presence of sludge was kappa = 0.92. In the LA/AA, 27 patients (21%) had thrombi, 58 patients (46%) had sludge, and 42 patients (33%) SEC. In patients with LAA sludge, the event rate was 47% (p=0.019). Appendage thrombus was associated with a 59% event rate (p=0.003). This compares with an event rate of 25% in the control group.</p> <p>CONCLUSIONS: Patients with AF and LAA sludge identified by TEE have a high likelihood of death. In the clinical management of these patients, sludge should be considered as evidence against undergoing cardioversion procedures.</p>

VENKATESH, RAVI

1. Title	Endoscopic Demonstration of Third Ventriculostomy in the Preserved Human Cadaver Brain
2. Student Presenter:	Ravi M. Venkatesh
3. Co-workers and Collaborators:	Dr. Sunil Manjila, Dr. Alan R. Cohen
4. Advisor:	Dr. Alan R. Cohen
5. Departments:	Pediatric Neurological Surgery
6. Institutions:	Rainbow Babies & Children's Hospital
7. Support:	T-35 grant
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Endoscopic neurosurgery has gained widespread popularity because it can be performed with minimal disruption of neural structures. Third ventriculostomy has become an effective method of cerebrospinal fluid diversion in non-communicating hydrocephalus. This procedure is now the treatment of choice for acquired aqueductal stenosis. The aim of our study was to develop a cadaver hydrocephalus model to elucidate the trajectory for endoscopic third ventriculostomy and to evaluate the relevant endoscopic anatomy.</p> <p>Ten cadaver heads were embalmed and preserved in ethanol after flush-irrigation through cannulated carotid arteries and jugular veins. The vessels were then injected with siliconated dyes and then dissections were performed. A frontal burr hole was made and a 30° angled endoscope lens was inserted into the frontal horn of each lateral ventricle through the brain parenchyma. Landmarks in the lateral ventricles such as the septum pellucidum, choroid plexus, anterior septal and thalamostriate veins, and the foramen of Monro were identified. The endoscope was passed through the foramen of Monro into the third ventricle, and the third ventricular floor was closely inspected to study the anatomy of the mammillary bodies, infundibular recess, optic chiasm, and optic recess. Additionally, the endoscope was navigated around and in front of the massa intermedia.</p> <p>Using the cadaver models for teaching endoscopic ventricular surgery has been a frustrating experience for both educators and students. Not only are these heads expensive and difficult to procure, transport, and preserve, but recreating the dilated ventricular system of hydrocephalus is also a challenge. The cadaver brains selected for reproducing ventriculomegaly must be fresh and soft. Ventricles are usually small and shrunken in older, firm, fixed or autolysed brain specimens, rendering ventriculoscopic navigation extremely difficult. The author has succeeded in producing a viable model of ventricular cannulation, demonstrating the proper trajectory for skill-training in third ventriculostomy.</p>

WALKER, HOLLIS

1. Title	Propofol-Induced Production of Nitric Oxide and Nitrosylation of PKC-(epsilon) in Diabetic Cardiomyocytes
2. Student Presenter:	Hollis Walker
3. Co-workers and Collaborators:	Peter J. Wickley, B.S., Brad A. Martin, B.S., Paul A. Murray, Ph.D, Derek S. Damron, Ph.D.
4. Advisor:	Dr. Derek Damron
5. Departments:	Center for Anesthesiology Research
6. Institutions:	Cleveland Clinic Foundation
7. Support:	
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Background: Diabetes-induced cardiac dysfunction is characterized by a decrease in myocardial performance independent of vascular disease. Our lab has demonstrated that 1) nitric oxide synthase (NOS) and protein kinase C (PKC) isoforms are up-regulated and 2) propofol decreases myofilament Ca²⁺ sensitivity via a PKC-NOS-dependent pathway in diabetic cardiomyocytes. Moreover, nitric oxide (NO) nitrosylates tyrosine residues on PKC-E, facilitating its translocation from cytosolic to membrane fractions. Our study determined whether propofol stimulates NO production and subsequent nitrosylation of PKC-E in diabetic cardiomyocytes.</p> <p>Methods: Cardiomyocytes were obtained from normal and streptozotocin-induced diabetic rat hearts. NO production was assessed with and without propofol, S-Nitroso-N-acetylpenicillamine (SNAP), and phorbol myristate acetate (PMA) using an ELISA kit. Pretreatment with bisindolylmaleimide I (BIS) was used to assess the role of PKC in NO production. Immunoblots of whole cell lysates following exposure to SNAP and propofol with and without L-NAME and Ebselen assessed tyrosine nitrosylation of PKC-E and the subcellular distribution and translocation of PKC-E.</p> <p>Results: In diabetic hearts, propofol, SNAP and PMA increased NO production by 74±10%, 128±12% and 85±4%, respectively, compared to control. PKC inhibition by BIS attenuated the propofol-induced increase in NO production by 41±11%. Propofol, SNAP and PMA increased nitrosylation of immunoprecipitated PKC-E 118±13%, 201±19%, and 143±11%, respectively. The propofol-induced increase in nitrosylation was attenuated by the NOS inhibitor, L-NAME (89±12%) and the peroxynitrite scavenger, Ebselen (96±9%). PKC-E was primarily in the cytosolic fraction (81±12% of total protein content). Propofol and SNAP caused an increased translocation from 19±9% in controls to 71±17% and 43±13%, respectively, which was attenuated by L-NAME (54±14%) and Ebselen (53±17%).</p> <p>Discussion: Propofol causes a PKC-dependent increase in NO production in diabetic cardiomyocytes. This increase could be partially responsible for the depressed contractile function observed in diabetic hearts. Propofol also increased tyrosine nitrosylation of PKC-E, which contributed to the translocation of PKC-E to the membrane. This nitrosylation potentiates the propofol-induced activation of PKC in diabetic hearts.</p>

WALTHER, NOLAN

1. Title	Abnormalities associated with the loss of the Chromodomain Helicase Binding Protein 4 (CHD4)
2. Student Presenter:	Nolan D. Walther
3. Co-workers and Collaborators:	Elvin Brown, Ph.D. candidate; Jocelyn E. Krebs, Ph.D.
4. Advisor:	Jocelyn E. Krebs, Ph.D.
5. Departments:	Department of Biological Sciences
6. Institutions:	University of Alaska Anchorage
7. Support:	
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>DNA in cells is found in chromatin, the combination of DNA and histone proteins that condenses long DNA molecules into a small nucleus. Chromatin remodeling complexes contain ATP-dependent enzymes that essentially slide histone proteins along the DNA to allow or restrict access to specific DNA sequences. Some nuclear protein complexes contain both histone modification and chromatin remodeling capabilities such as the NURD (nucleosome remodeling and deacetylation) complex. Within the NURD complex is the chromodomain helicase DNA binding protein 4 (CHD4), also known as Mi-2beta. Antibodies to the CHD4 protein known as anti-Mi-2 autoantibodies are commonly found in some patients with skin and muscle disorders such as dermatomyositis, polymyositis, and inclusion body myositis. In addition, CHD4 has been shown to play a role in regeneration of the lens of the eye.</p> <p>We investigated the role CHD4 during eye development by performing gene silencing techniques specific for the CHD4 gene. We injected small amounts of antisense morpholino oligonucleotides into the cytoplasm of <i>Xenopus laevis</i> embryos in order to inhibit translation of the CHD4 protein, and then monitored the development of the resulting CHD4 morphants.</p> <p>Injection of 43 ng of CHD4 antisense morpholino resulted in obvious and severe ocular malformations, a pronounced groove in the forehead between the eyes and cement gland, a noticeably shortened anterior-posterior length, and lack of response upon stimulation. Surprising, injection of 86 ng of CHD4 morpholino did not yield the same level or spectrum of phenotypes, but that may be attributed to the low sample size. Embryos injected with the same amounts of CHD4 inverse morpholino or sterile nanopure water were used as controls along with uninjected embryos, all of which developed normally in these experiments. In summary, it is clear that CHD4 plays an essential role in early development, and the specific activities of CHD4 in the early embryo will be the subject of future studies.</p>

WEINBERG, BRENT

1. Title	Estimating doxorubicin transport properties to improve intratumoral drug delivery
2. Student Presenter:	Brent D. Weinberg
3. Co-workers and Collaborators:	Ravi B. Patel, Gerald M. Saidel, Jinming Gao
4. Advisor:	Agata A. Exner
5. Departments:	Department of Biomedical Engineering (Weinberg, Patel, Saidel) Simmons Comprehensive Cancer Center (Gao) Department of Radiology (Exner)
6. Institutions:	Case Western Reserve University (Weinberg, Patel, Saidel, Exner) University of Texas-Southwestern Medical Center (Gao)
7. Support:	Department of Defense Breast Cancer Research Program Predoctoral Fellowship
8. Please choose your academic program:	MD PHD
9. What year are you in the program?	6
10. Body of Abstract (300 words or less)	<p>Developing an intratumoral drug delivery implant to supplement radiofrequency (RF) ablation requires detailed knowledge of the drug transport properties in tumor tissue. To gain insight into tissue properties governing drug release from these implants and local drug transport, a one-dimensional (1-D), radially-symmetric finite element method (FEM) drug transport model was generated. The model was based on previous work where doxorubicin distribution from implants was measured on days 4 and 8 in non-ablated and ablated rabbit VX2 liver carcinomas. In this model, the implant occupied the center, and was surrounded by non-ablated or ablated tumor and normal liver. Transport was governed by two parameters in each tissue: diffusion, D, and elimination, G. Values for D and G were estimated by coupling the FEM solution with least squares optimization to minimize the sum of square residuals between the model output and experimental data. In non-ablated tumor, D was estimated at $5.0 \times 10^{-11} \text{ m}^2 \text{ s}^{-1}$ (25% slower than normal liver), and G was $5.9 \times 10^{-5} \text{ s}^{-1}$ (94% slower than normal liver). In ablated tumor, diffusion varied as a function of distance from the ablation center. Doxorubicin diffusion near the center was $10.6 \times 10^{-11} \text{ m}^2 \text{ s}^{-1}$, but in the periphery of ablation it decreased to levels seen in normal liver. In contrast, the elimination rate was homogeneous throughout the ablated tumor but varied as a function of time. Before day 4, G was near 0 and increased linearly between days 4 and 8 to $5.7 \times 10^{-5} \text{ s}^{-1}$, a value similar to that of non-ablated tumor. By fostering doxorubicin distribution and reducing elimination, RF ablation opens a window of time in which local drug distribution around an intratumoral implant will be improved. Knowledge of these tissue properties can be used to design better treatments that maximize drug delivery to tumor areas which are most at risk for recurrence.</p>

ZSEBIK, GRETCHEN

1. Title	Low Risk of Meperidine Induced Seizures in Children With Sickle Cell Disease
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6. Institutions:	Rainbow Babies and Children's Hospital
7. Support:	
8. Please choose your academic program:	MD
9. What year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Seizures are a potential serious side effect of meperidine caused by the production of toxic metabolites that require renal elimination. Consequently, meperidine is rarely used to treat pain at most pediatric medical centers. Over the past twelve years, Rainbow Babies & Children’s Hospital has utilized a pain protocol for sickle cell patients, administering meperidine or morphine every two hours at standard doses and weaning by 25% every 24 hours until the patients can be switched to oral analgesics. Our study compared the frequency of seizures among the pediatric sickle cell patients receiving meperidine and morphine over the last seven years to determine if the risk of meperidine induced seizures in this clinical setting is prohibitive. We performed a retrospective, observational study using billing codes to identify sickle cell patients who developed seizures while hospitalized for pain and the medications they were receiving at the time. A chart review was carried out to determine the cause of seizure and to eliminate patients with an underlying seizure disorder. 160 patients with diagnostic codes for sickle cell disease who were billed for either morphine or meperidine were identified over the course of 730 hospital admissions. Over the 730 admissions, the total morphine usage was 7388 hours versus 25,540 hours for meperidine. One seizure occurred with meperidine and one seizure occurred with morphine, but in the setting of eclampsia. The rate of seizures was 0.135 per 1000 hours of morphine exposure and 0.039 per 1000 hours of meperidine exposure. In conclusion, we observed an extremely low rate of seizures in pediatric sickle cell patients receiving meperidine, a rate comparable to that observed in those receiving morphine. In our experience, the risk of meperidine induced seizures was not prohibitive. Therefore, meperidine should remain a therapeutic option for pediatric sickle cell patients experiencing vaso-occlusive pain.</p>

