1. **Title:** A Model to Predict Failure of Uterine Fibroid Embolization

2. **Presenter:** Sara Abbott

3. **Co-workers and Collaborators:** Michael Kattan, PhD

4. **Advisor:**

5. **Departments:** OB/GYN & Women’s Health Institute, Quantitative Health Sciences

6. **Support:** Foundation for Female Health Awareness

7. **Institutions:** Cleveland Clinic

---

**Background:** Uterine fibroid embolization (UFE) is gaining popularity as a treatment for symptomatic uterine fibroids. Compared to hysterectomy, UFE is less invasive, less painful, has a faster recovery, and is uterus-sparing. However, hysterectomy guarantees symptom relief while symptom recurrence following UFE is common. Further specification of the optimal UFE candidate would help reduce non-beneficial procedures.

**Objective:** To develop a statistical model, displayed as a nomogram, to accurately predict the probability of UFE failure given a set of routinely available baseline patient characteristics.

**Methods:** The model will be created using data from the FIBROID Registry, a 3-year, prospective, multi-center cohort of women undergoing UFE for the treatment of symptomatic uterine fibroids. Multivariable analysis of pre-selected predictor variables will be conducted using a Cox proportional hazards model that allows for non-linearity. A bootstrapping technique will be used to internally validate the predictive accuracy of
Finally, the model will be illustrated as a nomogram for easy use as an evidence-based, clinical decision-making tool.

**Results/Conclusions:** This research is currently ongoing and results and conclusions are pending.

---

**Lepow Day Abstract**

1. **Title:** Sarcoidosis: Th1 mediated Epitheloid Granulomatous Inflammation and Macrophage Activation State

2. **Presenter:** Amir Al-Dabagh

3. **Co-workers and Collaborators:** Susamma Abraham, Lisa Ruple

4. **Advisor:** 

5. **Departments:** Pathobiology, Pulmonary

6. **Support:** Dean's Summer Research Award

7. **Institutions:** Cleveland Clinic

8. **Body of Abstract: (300 words or less)** Hypothesis: Th1-mediated epithelioid granulomatous inflammation is dependent on macrophage activation state. Although sarcoidosis is traditionally thought of as a Th1 lymphocyte-dependent disease, there are accumulating data to suggest a significant role for macrophages in determining the outcome of the disease. A gap in our knowledge is the
influence of macrophage activation state on the course of sarcoidosis. In this project, genes involved in Th1-biased granuloma formation are being assessed in order to parse out how macrophage activation state influences formation and resolution of granulomas using a murine model of granulomatous lung disease. In brief, mice were sensitized with either PPD or schistosomal egg antigen then challenged via tail vein injection 14 days later with PPD- or SEA-coated beads, which embolized to the lung leading to pulmonary granuloma formation. After 4-8 days, the mice underwent sacrifice; the lungs from the mice were embedded in OCT and snap-frozen. The lungs were then subjected to laser microdissection in order to isolate granulomas. RNA was extracted from the isolated granulomas, and quality was assessed using the Agilent Bioanalyzer. Thereafter, the RNA was subjected to microarray analysis in the CCF Genomics Core. Differentially expressed genes will be identified by comparing the results from control mice (sensitized but injected with uncoated beads) to both Th1 and Th2 granulomas. The genes of interest will be those involved in macrophage activation or differentiation programs, and will be selected using bioinformatics assistance from the Genomics Core, as well as prespecified mediators of macrophage activation that are also known to be important in sarcoidosis. Identified candidate mediators will be confirmed using a combination of real-time RT-PCR and also immunohistochemistry. Depending on the results, we will thereafter attempt to transition to assess whether human homologues are involved in development of or phenotype of sarcoidosis. We anticipate that understanding macrophage biology as it relates to differentiation into epithelioid cells of granulomas, and
their subsequent resolution will lead to novel therapeutic targets.

10. Please choose your academic program: MD

11. What year are you in the program? 2

12. What was your role in this project? My role was to perform the laser microdissections after the lungs were prepared and purify the RNA before giving it to the CCF Genomics Core. I will also be involved in subsequent parts such as analyzing the microarray, choosing the genes, and possibly transitioning to human homologues.

13. Date: 11/08/2010

Alleyne, Brendan

**Lepow Day Abstract**

| 1. Title: | Harnessing the Osteogenic Potential of Neonatal Rat Dura to Heal Critical Sized Defects |
| 2. Presenter: | Brendan J. Alleyne |
| 3. Co-workers and Collaborators: | Davood Varghai, Christy Gliniak, Erin Miller, Harvey Chim, Walter Sweeney, Gregory Cooper |
| 4. Advisor: | |
| 5. Departments: | Plastic Surgery Research |
| 6. Support: | Crile Fellowship |
| 7. Institutions: | University Hospitals of CWRU and University of Pittsburgh |
| 8. Body of Abstract: (300 words or less) | **Background**

The surgical community has been unable to adequately address the operative repair of the craniofacial skeleton for pediatric patients secondary to trauma, neoplastic processes, or craniofacial malformations. Autogenous bone grafts give unacceptable donor site morbidity while alloplastic bone substitute fails to osseointegrate into the host skeleton; therefore, harnessing the osteogenic potential of neonatal dura could offer a novel therapeutic
approach to the shortcomings of current treatment.

Hypothesis

We hypothesize that dura mater removed from the parietal and occipital regions of neonatal rat pups will induce bone formation in critical sized defects of adult rats. Secondary and tertiary aims of this longitudinal study will be to elucidate the identity and exact proportion of growth factors needed to mimic the ideal osteogenic environment and to inlay a Dermamatrix scaffold mimicking this in vivo.

Methods

In our study we harvested dura from the occipital and parietal bone of fetal, neonatal, juvenile, and adult rats. This dura was transplanted into adult rats with bilateral critical sized defects. At 2, 4, 8 and 12 week time points all animals underwent micro-CT imaging and those exhibiting defect healing underwent qPCR. At the 12 week time point all animals underwent histology.

Results

Both micro-CT images and qPCR data are still being analyzed, however the initial micro-CT images confer decreases in the bone gap distance which correlates with bone formation.

Conclusions

The initial results corroborate the results from the pilot study in that transplanted dura retains its osteogenic capability and younger dura leads to stronger defect healing. The continuing study aims to use microarray to aid in comparison of the gene expression
profiles between regenerating and non-regenerating calvaria to assist in identifying growth factors and cytokines that positively or negatively regulate bone healing. Growth factors and cytokines identified in these molecular analyses will be bio-printed onto human allograft scaffolds.

Support

Support for this project was offered through the Crile Research Fellowship.

Conferences

*This was presented at the May 2010 Ohio Valley of Plastic Surgeons Conference.

*This was presented at the October 2010 American Society of Plastic Surgeons Conference.

*This project has been approved for a three year grant offered through the CranioMaxillofacial Clinical Priority Program and AOCSMF.

### 10. Please choose your academic program:

| MD MS |

| 11. What year are you in the program? |

| 2 |

| 12. What was your role in this project? |

| I was responsible for surgical transplantation and dura isolation, rat pre and post-op therapy which included antibiotic and analgesic injections twice a day (for 45 rats initially), and keeping records of the CT scans. I aided with pres-surgical planning and weekly summaries of events during the lab meetings. I helped create the poster presented at ASPS. |

| 13. Date: |

| 11/09/2010 |

Alleyne, Brendan

### Lepow Day Abstract

| 1. Title: |

| Flexi-seal Tube use for Enteric Fistula Control in Abdominal Wall Reconstruction |
2. Presenter: Brendan J. Alleyne

3. Co-workers and Collaborators: Marc Serret, Christopher Salgado (ChristopherSalgado@med.miami.edu), Allen Livingstone

4. Advisor:

5. Departments: Plastic Surgery Research

6. Support: N/A

7. Institutions: University Hospitals at CWRU and University at Miami Miller School of Medicine

---

**Introduction**

Enteric fistulas can hinder abdominal wall reconstruction efforts when there is a lack of effluent control. If no immediate plan for fistula takedown exists, these patients with superficial enterocutaneous fistulas may require prompt cutaneous reconstruction to reduce their evisceration risk even when fascial competence is not feasible. In this regard, we introduce the use of the Flexi-Seal® Fecal Management System (FMS) for effluent control of enteric fistulas during complex abdominal wall reconstruction.

---

**Methods**

The FMS system was used for enteric fistula effluent control on four patients with an average age of 59, who underwent abdominal wall reconstruction under a single surgeon from July 2007 to November 2009. None of the patients studied had immediate plans for fistula takedown due to their multiple co-morbidities. Abdominal wall reconstruction proceeded by a variety of means ranging...
from skin grafting to local flap reconstruction. Pre-procedural utilization of the FMS device provided effluent control with a low inflation pressure, and was maintained until reconstruction was complete. In some cases, the above allowed for conversion into a controlled stoma. Follow-up duration ranged from 3 to 12 months with a mean of 6 months.

Results

The FMS device facilitated successful abdominal wall reconstruction in all four patients studied regardless of whether skin grafting or local flap reconstruction was used.

Conclusion

The FMS device serves as a valuable tool in aiding in effluent control in complex abdominal wall reconstruction in patients presenting with enterocutaneous fistulas or enteroatmospheric fistulas.

Conferences

This was presented at the May 2010 Ohio Valley of Plastic Surgeons Conference.

This was presented at the June 2010 Abdominal Wall Reconstruction Conference.

Publications

This was accepted for publication in the Journal of Plastic
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<tr>
<td>12. What was your role in this project?</td>
<td>I conducted the background research for the paper as well as authoring the first draft of the manuscript. I assisted in its re-writing throughout the multiple drafts. I additionally presented it at the Abdominal Wall Reconstruction conference in Georgetown, Washington D.C.</td>
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<tr>
<td>13. Date:</td>
<td>11/09/2010</td>
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**Appachi, Swathi**

### Lepow Day Abstract

1. **Title:** Adipogenic Inflammation and Cardiovascular Risk in an Obesity Surgery Cohort

2. **Presenter:** Swathi Appachi

3. **Co-workers and Collaborators:** Karen R Kelly PhD, Philip R. Schauer MD, John P. Kirwan PhD, Stanley Hazen MD, PhD, Manjula Gupta MD

4. **Advisor:**

5. **Departments:** Endocrinology Institute, Department of Pathobiology

6. **Support:** This work was supported by National Institutes of Health, RO1 DK089547-01 NIDDK/NIH.

7. **Institutions:** Cleveland Clinic, Lerner Research Institute

8. **Body of Abstract: (300 words or less)**

   **Background and Rationale:** Identifying specific factors associated with obesity that confer susceptibility for cardiovascular disease (CVD) may help with risk stratification and target treatment strategies in the obese population. Adiponectin, leptin, and TNF-a are
hormones produced by adipose tissue, or adipokines, and are associated with insulin resistance, energy homeostasis, and inflammation. Adipokine levels are also implicated with CVD risk and change in response to obesity surgery.

**Hypothesis:** We hypothesize that bariatric surgery reduces CVD risk by altering the adipokine profile of adipose tissue through the mechanism of weight loss.

**Methods:** 142 patients underwent obesity surgery at the Bariatric Surgery Institute of the Cleveland Clinic. Of these patients, 45 returned for follow up at 6 months. At both timepoints, total cholesterol (TC), high-density lipoprotein cholesterol (HDL), low-density lipoprotein cholesterol (LDL), triglyceride (TG), adiponectin, leptin, and TNF-a measurements were obtained, as was body mass index (BMI). TC/HDL, LDL/HDL and TG/HDL ratios were obtained as these are important clinically to estimate CVD risk. Descriptive statistics of these variables were calculated. Pearson correlation coefficients were determined between all variables to assess the strength of associations between
any two variables.

Results: Prior to surgery, the metabolic activity of fat as represented by adiponectin and adiponectin/TNF-a was associated with CVD risk – specifically with altered triglycerides, HDL, and TC/HDL, LDL/HDL and TG/HDL ratios. Following surgery, BMI decreased by 22%, adiponectin increased by 93%, and leptin decreased by 50%. The change in leptin/adiponectin, which represents the ratio of fat mass to metabolic activity, was associated with favorable changes in triglycerides, HDL, and TC/HDL, LDL/HDL and TG/HDL ratios. Additionally, more favorable changes in BMI, HDL, and leptin/adiponectin were associated with Roux-en-Y surgery (RYGB) as compared to all other types of obesity surgery.

Conclusions: Bariatric surgery, especially RYGB, significantly ameliorates CVD risk by causing weight loss and reduction of adipogenic inflammation represented by improved adiponectin and the leptin/adiponectin ratio.

Note: This work has been submitted to Obesity and is pending review.
11/10/2010

Arslan, Defne

**Lepow Day Abstract**

1. **Title:**
   The Interaction between Cellular and Humoral Immunity in Lung Transplant Recipients

2. **Presenter:**
   Defne Arslan

3. **Co-workers and Collaborators:**
   Jacqueline Chu, Sarah Worley, Lara Danziger-Isakov

4. **Advisor:**

5. **Departments:**
   Pediatric Infectious Diseases

6. **Support:**
   T-32 NIH Training Grant, IDSA Medical Scholars Program Grant

7. **Institutions:**
   Cleveland Clinic Foundation

8. **Body of Abstract: (300 words or less)**

   **Background:** Lung transplant recipients diagnosed with hypogammaglobulinemia (HGG) are at increased risk of bacterial, viral, and fungal infections. Defects in the cellular immune system may also exist in these patients; specifically, altered T cell function may be associated with HGG. Our study aimed to investigate the potential association between IgG levels and T cell function in lung transplant recipients.

   **Methods:** A retrospective chart review was conducted on patients that received lung transplants between January 2008 and January 2010 at a single transplant center. Data included demographics, transplant information, donor and recipient serologies, IVIG/CMVIG, IgG levels, and Immune Function Assay results. The association between ATP and IgG levels was assessed using repeated measures mixed models.
Results: The analysis included 1,980 pairs of ATP-IgG measurements on 170 subjects (1-37 measurements per subject, median of 14). Subjects had a mean age of 56 years at transplant (range of 20-74 years) and included 69% males, with the most common pre-transplant diagnoses consisting of Idiopathic Pulmonary Fibrosis (47%), COPD/Emphysema (22%), and Cystic Fibrosis (10%). The association between ATP levels and IgG was not statistically significant (P=0.40) with a negligible expected increase in ATP associated with even a 100-unit increase in IgG.

Conclusion: Without adjusting for other clinical and demographic factors, there is no evidence that ATP and IgG are associated. Further investigation is needed to assess the impact of such factors as time since transplant, subject age, and immunosuppression levels.

10. Please choose your academic program: MD
11. What year are you in the program? 2
12. What was your role in this project? Project design, data collection, writing
13. Date: 11/10/2010

Au,Yu

**Lepow Day Abstract**

1. Title: Determination of physiological mechanisms for electrical wound therapy
2. Presenter: Gabriel Gabarain, Yu Kan Au
4. Advisor: 
5. Department: APT Center of Excellence, Louis Stokes
**Departments:**
Cleveland VA Medical Center, Department of Orthopedics, Case Western Reserve University, Department of Biomedical Engineering, Case Western Reserve University

**6. Support:**
Department of Veterans Affairs Rehabilitation Research & Development Service, Merit Review award F7129-R

**7. Institutions:**
Louis Stokes Cleveland VA Medical Center, Case Western Reserve University

**8. Body of Abstract: (300 words or less)**
The project objective is to determine the physiological mechanisms for effective electrotherapy in healing of ischemic wounds. The effects of varying electrical stimulation parameters are to be investigated using a chronic wound animal model. The findings are to be evaluated to determine the feasibility of translation of electrotherapy to clinical use by veterans with chronic wounds.

The primary hypothesis is that electrotherapy promotes closure of ischemic wounds through promotion of angiogenesis, primarily through the sustained up-regulation of vascular endothelial growth factor (VEGF).

Evaluation of electrotherapy variables are carried out using the Modular Stimulation System (MSS), a powered surface stimulation device incorporating programmable and stimulation circuitry mounted onto a disposable flexible substrate. The control and stimulation components of the device are reusable and are combined with stimulating electrodes onto the flexible substrate.

In order to establish the effectiveness of ES in the treatment of chronic wounds, a rat(Rattus norvegicus) model is being used to compare the effect of various electrotherapy variable settings on a chronic wound model against a control, represented by the unaided healing of control wounds on the same animal. MSS devices for use in the animal model have electrodes patterned in a standardized shape and layout because the wound geometry and location are controlled. PCR
analysis will be used to determine the expression of targeted wound healing genes including VEGF, TNF-alpha, Fibronectin, and Collagen 3A1.

As of the end of our involvement in the project, experimental challenges were still being addressed. The protocols for animal surgery and post-operative care were updated based on experimental experience in order to minimize infection risk and animal discomfort that may affect the rate of wound healing. Additionally, changes to the MSS and substrate design were made in collaboration with the engineering team. A protocol for making PCR standards and testing the quality of PCR primers was also developed for the measurement of the expression of targeted wound healing genes.

During the fellowship period, significant progress was made in the optimization of the MSS design, in the surgical procedure, and in the post-operative care of the animals. These activities facilitate the progress of the project. Evaluation of physiological mechanisms for effective electrotherapy is in progress.

| 10. Please choose your academic program: | MD |
| 11. What year are you in the program? | 2 |
| 12. What was your role in this project? | Aid in developing experimental protocols and overcoming experimental obstacles |
| 13. Date: | 11/08/2010 |

Azam, Arsalan

**Lepow Day Abstract**

1. **Title:** Evaluation of the Lifespring Nurse Certification Program
2. **Presenter:** Arsalan Azam
3. **Co-workers:**
Introduction:
Lifespring hospitals (LS), a low-cost maternity hospital in Hyderabad, India, has experimented with the use of standardized clinical processes carried out by nurses acting as physician extenders, to engineer cost savings and improve outcomes. In order to improve the performance of its nursing core, who often enter LS with varying degrees of academic preparation, the organization has opted to design an in-house Certified Nurse Program (LCNM), thereby formally certifying its nurses’ preparation and training.

Hypothesis
The LCNM program is hypothesized to improve nurse competency in carrying out core procedures in maternal and child health. While data is still pending, it is expected that nurses will perform key procedures (e.g. taking a maternal history, conducting a delivery, etc.) with greater adherence to Lifespring’s clinical processes (which detail necessary steps involved in such procedures), presumably reducing medical errors and increasing clinical efficiency.

Methodology
Following completion of the training program, nursing performance was evaluated with OSCE-style assessments focused on major procedures the nurses were required to carry out on a frequent basis. The performance of these nurses was tested against a control group of nurses who received the same assessments without the benefit of a training program.

Results
Data is pending as LS has not completed...
### Lepow Day Abstract

| **Title:** | Prophylaxis against thromboembolism initiated in the Emergency department for high-risk medical patients (POTENT): A National Quality Improvement Initiative for Hospitals - The MetroHealth Experience |
| **Presenter:** | Emily Bacon |
| **Co-workers and Collaborators:** | Julie Nichols, RN; Heather Tinsley, RN |
| **Advisor:** | |
| **Departments:** | Emergency Department |
| **Support:** | |
| **Institutions:** | MetroHealth Medical Center |

**Background:** The incidence of venous thromboembolic events (VTE) among hospitalized general medicine patients has been reported to be as high as 15%.

**Objectives:** The primary objective of POTENT is to characterize the impact of pharmacological prophylaxis against VTE in three high-risk cohorts of patients (acute heart failure [CHF], chronic obstructive...
pulmonary disease [COPD], or acute community acquired pneumonia [CAP]) admitted to medical services during hospitalization and for the 30 days following ED care. The objective of this secondary analysis is to characterize and describe the demographics and pharmacologic prophylaxis used for a high risk population of patients admitted to MetroHealth Medical Center.

Methods: POTENT is a multi-center case-control study involving 20 Emergency Departments (ED) in the United States. The medical records of consecutive patients in the three high risk cohorts admitted between 11/03/2009 and 07/29/2010 were reviewed by a trained reviewer using a structured abstraction form and analyzed with respect to VTE prophylaxis, patient demographics and risk factors for VTE. Risk factors included: Family history of deep vein thrombosis /pulmonary embolism (DVT/PE), previous PE, DVT, or other venous stasis/thrombotic disorders; obesity; pregnancy (current or recent); malignancy; estrogen replacement therapy; oral, transdermal, or transcervical contraceptive use; miscarriage or abortion; recent surgery, trauma, or hospitalizations; edema; indwelling venous catheters; immobilization; neurological paralysis; systemic lupus erythematosus; diabetes mellitus (DM); sickle cell disease; hypertension (HTN); coronary artery disease (CAD); smoking; alcoholism; CHF; COPD; asthma; connective tissue diseases; lung fibrosis; sarcoidosis; pulmonary hypertension; and HIV. Data were analyzed using Stata 10-SE. This project was approved by The
Results: Fifty-one patient records were reviewed.

Demographic factors  
N=51
Sex, (% female) 49%
Age (years), median (IQR) 54 (48, 61)

Race (%)  
African American 16 (32)
Caucasian 24 (48)
Hispanic Caucasian 8 (16)
Hispanic Non-Caucasian 0 (0)
Other 2 (4)

The most frequent VTE risk factors, excluding those that were also admitting diagnoses (CHF and COPD) were smoking (35, 68.6%), diabetes mellitus (23, 43%), and obesity (18, 35.3%). The median number of risk factors per patient was 3 (IQR: 2-6). 45 (88.2%) patients received VTE prophylaxis on the day of admission; 31 (74.4%) of patients received either enoxaparin or unfractionated heparin, 7 (13.7%) received mechanical prophylaxis.

Conclusions: Patients admitted from The MetroHealth Medical Center ED for treatment of CHF, COPD and CAP have multiple risk factors for DVT/PE. The use of DVT/PE prophylaxis among these patients is high but there is room for improvement.
11. What year are you in the program? 
1

12. What was your role in this project? 
My role was to review consecutive medical records of patients in the above high risk groups using a structured abstraction form and analyze the resulting data with respect to VTE prophylaxis, patient demographics, and risk factors for VTE using Stata 10-SE.

13. Date: 11/08/2010

Bagheri, Nika 

**Lepow Day Abstract**

1. **Title:** Imaging Human Postmortem Eyes with SLO and OCT

2. **Presenter:** Nika Bagheri

3. **Co-workers and Collaborators:** Brent A. Bell, Vera L. Bonilha

4. **Advisor:**

5. **Departments:** Department of Ophthalmology

6. **Support:** This work was supported by the Foundation Fighting Blindness and Research to Prevent Blindness.

7. **Institutions:** Cole Eye Institute

8. **Body of Abstract:** (300 words or less)

**Introduction:** Confocal Scanning Laser Ophthalmoscope (SLO) and Spectral-domain Optical Coherence Tomography (OCT) provide a comprehensive diagnostic assessment in the clinic. Here we describe the use of SLO and OCT as the initial assessment to both screen ‘normal’ postmortem donor eyes for retinal lesions and to characterize retinal lesions in eyes with suspected pathology prior to histological analysis.

**Methods:** The six human donor eyes described
here were imaged using bright-field macroscopy, SLO, and OCT.

**Results:** One normal appearing eye was found to have a macular hole, and another normal appearing pair was found to have bilateral retinal pigment epithelium detachment centered on the fovea. SLO and OCT further characterized known retinal lesions in age-related macular degeneration and retinitis pigmentosa donor eyes.

**Conclusion:** This is the first time both SLO and OCT are applied in addition to bright-field macroscopy to screen and characterize a range of retinal pathology in human postmortem eyes. The use of combined imaging modalities identified and localized retinal lesions in postmortem donor eyes that would have been overlooked by using bright-field macroscopy alone.

Note: This work has been submitted for publication.

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<tr>
<td>12. What was your role in this project?</td>
<td>Nika Bagheri wrote the paper that has been submitted. Brent A. Bell did the imaging with assistance from Nika Bagheri. Dr. Hollyfield and Dr. Bonilha maintained the donor eye bank of the Foundation Fighting Blindness. All authors conceived of the project.</td>
</tr>
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### Lepow Day Abstract

<table>
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<th>1. Title:</th>
<th>Intensity of Vascular Access Device Use in Critical Care and its Impact on Catheter Associated Bloodstream Infection Rates</th>
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<tr>
<td>2. Presenter:</td>
<td>Mary Banks</td>
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<tr>
<td>3. Co-workers and Collaborators:</td>
<td>Rebekah Benish BS, Cynthia Fatica RN, BSN, CIC, Melissa Triche BA, Nehemiah Smith MHSA, Steven M. Gordon MD, Thomas G. Fraser MD</td>
</tr>
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<td>4. Advisor:</td>
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<td>5. Departments:</td>
<td>Infectious Disease</td>
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<td>7. Institutions:</td>
<td>Cleveland Clinic Foundation</td>
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<td>8. Body of Abstract: (300 words or less)</td>
<td>The presence of a central venous catheter (CVC) is a risk for hospital acquired bloodstream infection (HABSI) in critically ill patients. The rate of HABSI attributable to CVCs is defined as catheter associated bloodstream infections (CLABSI) over CVC days. This rate does not risk adjust for patients whose care requires multiple CVCs and arterial catheter. We performed a pilot study to evaluate the intensity of line use in our critical care units (ICUs) and its potential impact on CLABSI rates. The number of CVCs and arterial lines were counted Monday through Friday for all patients admitted to one of 209 adult ICU beds at the Cleveland Clinic between June 15\textsuperscript{th} and August 5\textsuperscript{th} by 2 of the investigators. Six different ICU groups were observed: cardiovascular and thoracic surgery, cardiac, heart failure, medical, surgical, and neurosciences. Of the 1,636 patients, 428 were not observed to have a CVC. Two hundred and forty seven (15%) were observed to have more than one CVC and these patients were responsible</td>
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for 19% of the total patient days. There were 4,666 traditional line days resulting in a device utilization ratio of 0.786. There were 5,936 actual line days count resulting in a device utilization ratio of 1.272. There were 3,853 arterial line days. Total vascular access days were 9,789 resulting in a device utilization ratio of 1.648.

During the observation period there were 18 CLABSIs. The CLABSI rate was 3.86 per 1,000 traditional device days, 3.03 per 1,000 actual line days, and 1.84 per total vascular access days (p= 0.03 RR0.47[0.25-0.93] for the comparison of traditional vs. total vascular access days).

Our pilot study demonstrated that traditional methodology for tracking device utilization underestimated the intensity of line use in our ICUs. Using total vascular access days as the denominator resulted in a significant difference in CLABSI rates as compared with NHSN definition. Further work is needed to explore the relationship between intensity of lines and the risk of CLABSI and HABSI.

| 10. Please choose your academic program: | MD |
| 11. What year are you in the program? | 2 |
| 12. What was your role in this project? | I counted all line devices for half of the patients in the study per day for the observation period. I also helped compile the data, and write the methods section. |
| 13. Date: | 11/08/2010 |
| Bartley, Matthew |

**Lepow Day Abstract**

1. Title: Development of T cell clones to study MHC-II restricted B-cell receptor-mediated antigen presentation by human B-lymphocytes.

2. Matthew Bartley
Introduction

Understanding MHC-II antigen presentation by human antigen-presenting cells (APC) can provide insights useful for vaccine development. T-cell hybridomas, fusion products of peptide-specific T lymphocyte clones and T-thymoma cell lines, have proven effective in the study of antigen presentation in animal models since the 1970s. More recently, T-cell hybridomas generated from mice transgenic for human HLA-DR has provided a readily renewable T-cell reagent for the study of antigen presentation of human APC. We use these CD4+ T-cell hybridomas to demonstrate that antigen presentation by human B-lymphocytes is dramatically enhanced by uptake through the B cell receptor (BCR).

Materials & Methods

Hybridoma clones were generated by immunization of mice with purified antigen, harvesting of draining lymph nodes, restimulating with antigen, and fusing with immortal thymoma fusion partners. Antigen presentation assays were conducted with purified human B-lymphocytes incubated with antigen and T-cell hybridoma cells.

Results

The hybridomas were generated against goat
antibody. This allows the goat antibody, specific for human BCR, to be taken up as the antigen for processing and presentation specifically by the BCR rather than nonspecific uptake mechanism. Antigen presentation of the goat immunoglobulin specific for the human BCR was enhanced >4 logs compared with nonspecific goat IgG. The BCR specificity of the antigen presentation enhancement was confirmed by addition of rabbit anti-BCR as an inhibitor, as well as heat treatment of goat anti-BCR to disrupt specificity and thereby inhibit the BCR-specific uptake of the immunoglobulin. In addition, presentation by these B-lymphocytes of an antigen that is taken up by nonspecific mechanisms was not enhanced by coinoculation with anti-BCR antibody, demonstrating that BCR-mediated antigen presentation requires BCR-specific uptake, not simply BCR-related activation.

**Discussion**

We have shown that T-cell hybridomas can serve as an effective, specific tool in assays of B-cell receptor mediated antigen presentation. With many practical advantages including the potential to design any combination of HLA-DR restriction and antigen specificity, T-cell hybridoma lines could prove instrumental in the study of BCR-mediated antigen presentation that is required by T helper cell dependent vaccines.

**Future Publication:** Journal of Immunological Methods (pre-submission draft)

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<tr>
<td>12. What was your role in</td>
<td>I was responsible for the majority of laboratory work and am currently working to compose a draft for submission of a</td>
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There is evidence that supports that bariatric surgery can reverse insulin resistance in obese individuals (BMI 30-35). Studies have begun to provide possible mechanisms by which this surgery illicits such effects. Since an accepted mechanism of insulin resistance is direct fatty acid metabolite inhibition of the insulin signaling pathway, a supported theory for bariatric surgery’s effect is that it leads to the upregulation of enzymes, AMPK, and Sirt1, which play specific roles in mitochondrial biogenesis. We have used qPCR and western blot analysis to quantify the RNA and protein levels of AMPKa1, AMPKa2, AMPKg1, and SIRT1 in diabetic (zucker) rats that have undergone Roux-en-Y gastric bypass surgery (RYGB). The RNA and protein levels were compared to a SHAM control group, where the results revealed no significant increase in expression. Despite insignificant results, we remain interested in the role of the AMPK/Sirt1 pathway, and are currently considering different approaches to modify the protocol to get ideal results.
### 11. What year are you in the program?

2

### 12. What was your role in this project?

Helped organize study design and run qPCR analysis of AMPK and SIRT

### 13. Date:

11/09/2010

---

**Batt, Courtney**

## Lepow Day Abstract

<table>
<thead>
<tr>
<th>1. Title:</th>
<th>Spinal Cord Slice Culture: A New Model For Studying Remyelination?</th>
</tr>
</thead>
<tbody>
<tr>
<td>2. Presenter:</td>
<td>Courtney Batt</td>
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<tr>
<td>3. Co-workers and Collaborators:</td>
<td>Anita Zaremba</td>
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<td>4. Advisor:</td>
<td></td>
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<tr>
<td>5. Departments:</td>
<td>Department of Neurosciences</td>
</tr>
<tr>
<td>6. Support:</td>
<td>Myelin Repair Foundation</td>
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<tr>
<td>7. Institutions:</td>
<td>Case Western Reserve University School of Medicine</td>
</tr>
</tbody>
</table>

### 8. Body of Abstract: (300 words or less)

Multiple sclerosis (MS) is an inflammatory disease of CNS that destroys myelin, oligodendrocytes and axons. The hallmark lesions involve demyelination occurring in the white matter. Remyelination occurs but is not complete. Currently, therapies exist to delay progression of the disease, but not to reverse the effects of MS. Therefore, goals for MS therapies include exploring methods to enhance remyelination.

In order to test these therapies, both in vivo and in vitro models must be developed in which the cellular and molecular environment can be manipulated. The current study examines the use of a spinal cord slice culture model with which to explore myelination and remyelination. This preliminary research will pave the way to conduct
future studies that will focus on elucidating other factors that affect oligodendrocyte maturation and remyelination. We hypothesize that these therapies will increase myelination as measured by immunohistochemical staining in this culture system.

The spinal cords of P8 rat pups were dissected and cut at 350 µm on a McIlwain tissue chopper. Slices were plated and maintained in growth media consisting of 50% minimal essential medium (MEM)-25mM Hepes, 25% heat inactivated horse serum, 25% Hank’s balanced salt solution and supplemented with 25.5 mg/ml D glucose, 2mM glutamax and PenStrep at 37°C and 5% CO₂. Sections were fixed and stained with antibodies to MBP, neurofilament, GFAP and various oligodendrocyte lineage markers.

The cytoarchitecture of the spinal cords is maintained in these spinal cord slice cultures. The overall pattern of myelination in the spinal cord slice cultures is consistent with the pattern seen in vivo, and primary motor neurons can be seen clustered in the ventral horn. Staining patterns also indicated that oligodendrocyte lineage cells and astrocytes are present.

We conclude that spinal cord slice cultures would provide a useful model in which to study CNS myelination and remyelination. This model provides a cytoarchitecturally intact ex-vivo system in which axons can be traced to specific motor neurons.

10. Please choose your academic program: MD

11. What year are you in the program? 2

12. What was your role in the project? I performed the literature review and initial culture experiments to determine the viability and efficacy of this model.
### Lepow Day Abstract

| 1. Title: | Characterization of Rnd1 and Rac1 Interactions with the Rho-GTPase Binding Domain (RBD) of the Human Plexin-B1 Receptor Using Disulfide Bond Formation |
| 2. Presenter: | Janine Bernardo |
| 3. Co-workers and Collaborators: | SoonJeung Kim, Prasanta Hota |
| 4. Advisor: | |
| 5. Departments: | Department of Physiology and Biochemistry |
| 6. Support: | I am a medical student at the Lerner College of Medicine. I had support from the faculty and staff, as well as the classes I took this summer |
| 7. Institutions: | Case Western Reserve University |

**8. Body of Abstract: (300 words or less)**

Cell signaling events depend upon the careful interaction of membrane receptors with intracellular signaling molecules to initiate complex and crucial regulatory events. A large number of small GTPase proteins are involved in a diverse array of cellular events including signal transduction, cytoskeletal organization, cell migration, transcription, cell proliferation, and overall cell growth. Plexins are cell surface receptors known to interact directly with small GTPases. Specifically, human Plexin-B1 is known to interact with the small Rho GTPases Rnd1 and Rac1 at the membrane through an intracellular domain known as the RBD (Rho-GTPase Binding Domain). Upon binding, Plexin-B1 functions as a GAP (GTPase Activating Protein), converting a second GTPase, R-Ras, to its inactive, GDP-bound form. The cellular consequences of these interactions result in alteration of cell movement and motility, specifically the loss of cell adhesion to the extracellular matrix. Loss of R-Ras control has also been implicated in a variety of different cancers.
research is lacking on the interface that exists between Plexin-B1 RBD with both Rnd1 and Rac1. The current study looks to examine this interface by cross linking the RBD domain with the small GTPases. This will be accomplished through the creation of RBD, Rnd1, and Rac1 mutants that contain cysteine residues located at or near this interface. These mutants will be capable of undergoing disulfide bond formation through the addition of hydrogen peroxide. Once bound together, NMR analysis will be performed to elucidate the specific binding characteristics and the residues involved in the interaction. Our preliminary data shows that, upon hydrogen peroxide treatment, Plexin-B1 RBDs form dimers through disulfide bonding instead of complexes with Rnd1 or Rac1. In addition, cysteine mutants Rac1 L66C and RBD D103C appear to form a stable complex that can be further analyzed.

| 10. Please choose your academic program: | MD MPH |
| 11. What year are you in the program? | 1 |
| 12. What was your role in this project? | I worked as a summer student in growing and purifying various protein mutants, then testing to see which were capable of disulfide bonding together. I also contributed to lab meetings and events throughout the summer. |
| 13. Date: | 11/01/2010 |

**Bledsoe, Trevor**

**Lepow Day Abstract**

1. **Title:** Radiologic Mimicry of Carotid Body Tumors
2. **Presenter:** Trevor Bledsoe
3. **Co-workers and Collaborators:**
4. **Advisor:**
5. **Departments:** Cleveland Clinic Head and Neck Institute
6. **Support:**
7. **Institutions:** Cleveland Clinic
8. **Body** (This project is not yet complete, so I am only
able to provide background and planned methods at this point, as instructed by Todd Fennimore.)

Background:
Neck masses present a diagnostic challenge because of their deep location that limits clinical examination. In the parapharyngeal space of the lateral neck, the two most common neurogenic tumors are carotid body tumors, or paragangliomas, and sympathetic chain schwannomas, or neurolemmomas. These two types of tumors share many characteristics that make them difficult to differentiate between. Both carotid body tumors and schwannomas often have the similar presentation of being localized at the carotid bifurcation and resulting in the splaying of the carotid bifurcation. Because of these similarities, sympathetic chain schwannomas are often mistaken for carotid body tumors upon preoperative imaging.

Planned Methods:
Diagnostic criteria were developed to more accurately diagnosis carotid body tumors in the parapharyngeal space. These criteria are: 1. Hypervascularity: Flow voids on T2 imaging 2. Carotid fork origin of the mass: presence of tumor right at the fork 3. Carotid fork origin tumor: Greater than 180 degree encasement of the carotid by tumor. These criteria will be applied by a number of neuroradiologists to a selection of cases to determine if the criteria improved diagnostic accuracy.

10. Please choose your academic program: MD

11. What year are you in the program? 2

12. What was your role in this project? I am responsible for preparing a literature review, conducting a chart review, and collaborating with Dr. Manzoor Ahmed in developing diagnostic criteria.

13. Date: 11/09/2010

Bradke, Amanda

Lepow Day Abstract

1. Title: HIV, Health and Access to Care
<table>
<thead>
<tr>
<th>2. Presenter:</th>
<th>Amanda Bradke</th>
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<tbody>
<tr>
<td>3. Co-workers and Collaborators:</td>
<td>Clinical Staff (RN, LISW and MD)</td>
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<td>4. Advisor:</td>
<td></td>
</tr>
<tr>
<td>5. Departments:</td>
<td>Department of Infectious Disease</td>
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<tr>
<td>6. Support:</td>
<td>HRSA GRANT NO.: H97HA08543--01-02 Enhancing Linkages to HIV Primary Care in Jail Settings</td>
</tr>
<tr>
<td>7. Institutions:</td>
<td>MetroHealth</td>
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<tr>
<td>8. Body of Abstract: (300 words or less)</td>
<td>Incarcerated populations have a much higher rate of HIV infection when compared with the general population. This research project aims to determine if there are any predictive or protective factors for HIV infection in the inmate population, and the ability of this population to access care. In order to investigate this question, data has been collected through interviews with both HIV-positive and HIV-negative inmates at the Cuyahoga County Corrections Center. The questionnaire categories covered during these interviews included family and social relationships, living conditions, HIV testing and medical treatment, medical status and health insurance, drug and alcohol use, psychiatric status, criminal justice history, employment status, health and wellbeing, support systems, risk behaviors and demographics. Currently data is also being collected using this same interview tool to evaluate these factors in a non-incarcerated, HIV-positive population, in order to better evaluate and parse out the specific and unique needs of the incarcerated HIV-positive population. Patient data will continue to be collected until 60 clinic participants are reached. One year retrospective and prospective chart reviews will be completed for each participant to verify medications, T cell counts and viral loads. Finally all data collected will be compared in aggregate to the data obtained from the incarcerated population. I hypothesize that the questionnaires will show the incarcerated HIV-positive population has an increased need for assistance in</td>
</tr>
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</table>
obtaining healthcare and other services, as well as greater mental health needs, greater levels of substance abuse and lower levels of social support and increased need for social services in general. It is a hope that the results of this research will aid in elucidating increased, and unique needs of incarcerated populations in regards to HIV testing, access to medical care and linkages to other social services.

10. Please choose your academic program: MD

11. What year are you in the program? 2

12. What was your role in this project? I wrote the IRB, recruited patients and conducted interviews, and will completing chart reviews and analyzing the data in the future.

Date: 11/10/2010

Brandt, Eric

Lepow Day Abstract

1. Title: Full Volumetric 3 Dimensional Coregistration of Coronary Arteries using Cryo- and OCT Imaging

2. Presenter: Eric J. Brandt


4. Advisor:

5. Departments: Department of Biomedical Engineering, Case Western Reserve University

6. Support: NIH T35 Grant

7. Institutions: University Hospitals – Harrington-McLaughlin Heart & Vascular Institute at Case Medical Center

8. Body of Abstract: (300 words or less) Introduction/Plan: Optical coherence tomography (OCT) is a new intracoronary imaging modality that can provide in vivo high-resolution images. The resolution of OCT is approximately 10-15 μm, which permits arterial plaque characterization. Previous techniques to validate plaque characterization abilities
have used the traditional “gold standard” of histology, which has its limitations. These limitations include tissue shrinkage, tissue distortion, loss of tissue during processing and inability to obtain accurate volumetric data, as samples can be obtained only every 1 to 3 mm. New validation techniques must be developed that best measure the abilities of iOCT. One such method is in using a unique cryo-imaging system that combines robotic slicing and automatic image acquisition, with which frozen tissue sections can be visualized at 40 µm increments. This allows for volumetric data to be obtained, while minimizing tissue loss, shrinkage and distortion. The purpose of this study is to prove the ability of cryo-imaging to achieve a full volumetric coregistration with iOCT images.

**Methods:** Coronary vessels were obtained from the Cuyahoga County Coroner’s office from human cadavers within 24 hours of death. Samples were stored at 4 °C prior to OCT imaging. The specimen had a luer placed at the ostium of the coronary artery, was flushed with saline to clear blood from the lumen, and then was imaged with iOCT at 100 µm frame intervals as saline was flushed through the system. The sample was then frozen in OCT gel and stored at -80 °C for cryo-imaging. Samples were cut to 4 cm blocks, per the sample size limit in the cryo-imaging system. The unique cryo-imaging system was then used to acquire images at 40 µm increments. Images were reconstructed using Matlab and Amira software to construct volumetric data sets to
coregister the OCT and cryo-images.

**Results:** The length of the reconstructed vessels obtained using OCT and cryo imaging was compared. Preliminary results have shown that the cryo imaging system is a valid and accurate modality to validate iOCT images.

| 10. Please choose your academic program: | MD |
| 11. What year are you in the program? | 2 |
| 12. What was your role in this project? | My role in the project is in acquiring samples from the coroner office, aiding in preparation of the samples for iOCT imaging by suturing in the luer to the vessel and preparing the experiment space, operating the iOCT machine, preparing the sample for cryo-imaging, coregistration of the obtained images, and some help in post-image processing, which includes using Matlab and Amira programs to prep |

### Lepow Day Abstract

**1. Title:** Analysis of tuberculosis worksite contact investigations in Santa Clara County, CA

**2. Presenter:** Magdalene Brooke, Class of 2012

**3. Co-workers and Collaborators:** Laura Tang, Yilei Hsu, Duy T. Dao, Lorenzo Deveza, Jeremy P. Harris, Shawn R. Lin, Sydney X. Lu, Kerry-Ann Stewart, Stephen R. Vossler

**4. Advisor:**

**5. Departments:** Santa Clara County, California, Department of Tuberculosis Prevention & Control; Stanford University School of Medicine

**6. Support:**

**7. Institutions:** Santa Clara County Public Health Department, Stanford University School of Medicine

**8. Body of Abstract: (300 words or less)**

**SETTING:** Santa Clara County, California; Department of Tuberculosis Prevention & Control

**OBJECTIVES:** To determine the outcomes of general worksite contact investigations for tuberculosis in Santa Clara County (SCC) from 2006-2009, and to identify barriers impeding their completion. To evaluate the importance of
worksite investigations in relation to other TB program activities.

**DESIGN:** Retrospective review of public health charts for all general worksite investigations from 2006-2009 in Santa Clara County.

**RESULTS:** 59 investigations were initiated and 46 carried out. 432 contacts were identified, with an average of 9 contacts identified per worksite investigation. Seventy-seven percent of identified contacts were fully screened for TB disease and infection, and 34% of those evaluated were diagnosed with latent TB infection (LTBI). Eight of these contacts were probable conversions, indicating that workplace transmission took place in these cases (2.4% of evaluated contacts). One case of secondary, active case of TB was found (0.3% of evaluated contacts). Treatment was initiated in 57% of those contacts in which treatment was recommended, and 57% of those treated completed the full treatment course.

**CONCLUSION:** General worksite contact investigations can be an effective means of identifying LTBI and preventing TB transmission in Santa Clara County. Work contacts of TB cases are at lower risk of TB transmission and worksite contact investigations than household contacts, but transmission does occur in the workplace. General worksite investigations should be pursued as a medium priority activity in Santa Clara County.

The report which resulted from this project has been sent to the State of California Department of TB Prevention and Control and is currently being evaluated as to the possibility of publication. This abstract will also be submitted for poster and presentation consideration at one or more of the following 2011 conferences: American Occupational Health Conference, National Association of County and City Health Officials Conference, California TB Controllers Conference, and/or American Public Health Association Conference.

**10. Please choose your academic program:**

| MD |
**11. What year are you in the program?**

| 3 |

**12. What was your role in this project?**

With a great deal of help and guidance from my adviser, Dr. Julie Higashi, I formulated the objectives and intentions of the project. I devised the methods of the project, set up spreadsheets for the data, and carried out the chart review. I also analyzed the data, created the tables and figures, conducted a literary review for context, wrote the summary paper, and designed the poster.

**13. Date:** 11/10/2010

**Brown, Gregory**

### Lepow Day Abstract

<table>
<thead>
<tr>
<th>1. <strong>Title:</strong> Lipopolysaccharide Signaling Without a Nucleus: Kinase Cascades Stimulate Shedding of Proinflammatory IL-1β Rich Microparticles</th>
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<tbody>
<tr>
<td>2. <strong>Presenter:</strong> G. Thomas Brown</td>
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<tr>
<td>3. <strong>Co-workers and Collaborators:</strong></td>
</tr>
<tr>
<td>4. <strong>Advisor:</strong></td>
</tr>
<tr>
<td>5. <strong>Departments:</strong> Cell Biology, Cell Biology Graduate Program, Medical Scientist Training Program</td>
</tr>
<tr>
<td>6. <strong>Support:</strong> NIH Grant 1 P01 HL087018</td>
</tr>
<tr>
<td>7. <strong>Institutions:</strong> Case SOM, Cleveland Clinic</td>
</tr>
</tbody>
</table>

#### Background:

Platelets contain unspliced heteronuclear IL-1β RNA, which is rapidly spliced and translated upon activation. During sepsis and other conditions, platelets may contribute to the proinflammatory response. **Question:** How LPS induces proinflammatory cytokine production in anucleate cells lacking NF-κB is unknown. **Methods:** Purified, isolated human platelets were treated with LPS or buffer alone. We used a combination of small molecule inhibitors, cell-penetrating chimeric peptide inhibitors, and gene-targeted animals to examine the effects of LPS on protein kinase phosphorylation, RNA splicing, protein production, and microparticle shedding. **Results:** LPS induced rapid splicing, translation, and secretion of mature IL-1β after caspase-1 processing. LPS also stimulated microparticle shedding, and secreted IL-1β was
exclusively present in these particles. Microparticles from LPS-stimulated platelets induced VCAM-1 production by cultured human endothelial cells, and blockade of endothelial IL-1β receptor with IL-1 receptor antagonist completely suppressed endothelial activation. Splicing was post-transcriptional as the SR kinase inhibitor TG003 blocked IL-1β RNA production by platelets, but not by monocytes, and was dependent on exogenous CD14 - a property of platelets. We used a combination of small molecule inhibitors, cell-penetrating chimeric peptide inhibitors, and gene-targeted animals to show splicing required MyD88 and TIRAP, and IRAK1/4, AKT and JNK phosphorylation and activation. TRAF6 couples MyD88 to the AKT pathway and, remarkably, a TRAF6 interacting peptide-antennapedia chimera was more effective than LPS in stimulating IL-1β splicing. The TRAF6 chimera did not, however, stimulate microparticle shedding, nor was IL-1β released. Conclusion: LPS-induced kinase cascades are sufficient to alter cellular responses, three signals emanate from platelet TLR4, and that AKT and JNK activation are sufficient to initiate post-transcriptional splicing while another event couples microparticle shedding to TLR4 activation. Platelets contribute to the inflammatory response to LPS through production of microparticles that promote endothelial cell activation.

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<tr>
<th>10. Please choose your academic program:</th>
<th>MD PHD</th>
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<tr>
<td>11. What year are you in the program?</td>
<td>6</td>
</tr>
<tr>
<td>12. What was your role in this project?</td>
<td>As a Medical/Graduate Student, I performed nearly all experiments and procedures. Collaborators provided various reagents and I received technical assistance for platelet isolation and purification.</td>
</tr>
<tr>
<td>13. Date:</td>
<td>11/11/2010</td>
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<tr>
<td>Buller, Leonard</td>
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</table>

**Lepow Day Abstract**

| 1. Title: Predicting Success of Single-Stage Irrigation and Debridement with Polyethylene Exchange for Hip and Knee Prosthetic Joint Infections |
| **2. Presenter:** | Buller, Leonard T. |
| **3. Co-workers and Collaborators:** | Youssef Sabry, Fady, Easton, Robert |
| **4. Advisor:** | |
| **5. Departments:** | Department of Orthopaedic Surgery |
| **6. Support:** | N/A |
| **7. Institutions:** | Cleveland Clinic Orthopaedic & Rheumatologic Institute (ORI) |
| **8. Body of Abstract: (300 words or less)** | **Background:**
Prosthetic joint infections (PJIs) are devastating complications of hip and knee arthroplasties associated with considerable morbidity (1) and economic burden (2). The goal of surgical management of PJIs is the eradication of the infection with restoration of a pain-free, functional joint. Single-stage irrigation and debridement (SSID) with polyethylene exchange is one surgical approach for PJIs. Identifying patients at high risk for treatment failure following SSID with polyethylene exchange will improve preoperative risk assessment and allow for consideration of alternative therapies. Therefore, we propose to create a prediction model for the probability of success of SSID with polyethylene exchange following PJI of the hip and knee.

**Methods:**
All revision hip and knee arthroplasties performed at Cleveland Clinic from 1990 to 2009 will be retrospectively reviewed for cases of SSID with polyethylene exchange. We will collect information regarding each subject’s demographic variables, clinical
presentation variables, microbiological variables, perioperative variables, and medical comorbidity variables. Logistic regression will be used to construct a prediction model for the probability of success of SSID with polyethylene exchange following PJI using these variables. We will create a paper nomogram and online clinical risk calculator, accessible on the World Wide Web, using the coefficients from the regression model.

**Results:**

Greater than 8,000 cases of hip and knee revision arthroplasties have so far been reviewed and data collection is ongoing. By reviewing charts back to 1990, we expect to power our analysis with over 350 cases of PJI treated by SSID with polyethylene exchange.

**Conclusions:**

Having the ability to preoperatively predict the likelihood of success following a SSID with polyethylene exchange may decrease the incidence of progression of acute PJIs to chronic PJIs. Additionally, it may decrease the incidence of multiple surgeries for a single patient for PJI, secondarily reducing healthcare costs.

**References**


2. Bozic KJ, Ries MD. The impact of infection after total hip arthroplasty on hospital and surgeon resource
### Lepow Day Abstract

**1. Title:** Proximal Femoral Angles Can Predict Acetabular Angles in a Large Cohort of Normal Hip Joints.

**2. Presenter:** Buller, Leonard T.

**3. Co-workers and Collaborators:** Monaco, Feno M., Bryan, Jason

**4. Advisor:**

**5. Departments:** Department of Orthopaedic Surgery

**6. Support:** N/A

**7. Institutions:** Cleveland Clinic Orthopaedic & Rheumatologic Institute (ORI)

**8. Body of Abstract: (300 words or less)**

**Background:**
Normal hip mechanics depend upon the dynamic interaction between the acetabulum and femoral head. Studies in pathologic hip joints have suggested a complementary relationship between femoral and acetabular version. The purpose of this study was to determine if a predictable relationship between proximal femoral and acetabular angles exists in normal hip joints.

**Methods:**
The femoral neck version, neck shaft angle, acetabular version, inclination and center edge angle were measured in 230 normal hip joints in 115 adults using previously validated 3D reconstruction software. Using a stepwise regression method, the data was analyzed to determine if a relationship between proximal femoral and acetabular angles exists.

**Results:**
The mean values and standard deviation, in degrees, were: 4.60 (8.33) and 4.64 (8.71) for left and right femoral neck version,
respectively, 128.03 (5.97) and 128.81 (6.87) for left and right neck shaft angle, respectively, 27.31 (5.97) and 27.32 (5.77) for left and right acetabular version, respectively, 54.80 (4.11) and 55.73 (4.74) for left and right acetabular inclination, respectively, and 37.89 (6.90) and 37.39 (7.15) for left and right center edge angle, respectively. The variables femoral neck version, neck shaft angle, age and gender were sufficiently independent of one another to permit their inclusion in a regression model. Stepwise regression analysis resulted in three models to predict left acetabular version, left acetabular center edge angle and right acetabular version.

Conclusions:
This study demonstrates that, using a large cohort (n=230) of normal hip joints, a predictable relationship exists between proximal femoral and acetabular angles. Our model to predict right acetabular version uses femoral neck shaft angle and femoral version as significant terms. These results may further support the hypothesis that a complementary developmental relationship occurs between the femoral head and acetabulum.

| 10. Please choose your academic program: | MD |
| 11. What year are you in the program? | 3 |
| 12. What was your role in this project? | Medical student researcher |
| 13. Date: | 11/03/2010 |

Buller, Leonard

**Lepow Day Abstract**

1. **Title:** Evaluation of a Patient-Specific Acetabular Positioning System for Total Hip Arthroplasty in a Sawbones Model

2. **Presenter:** Buller, Leonard T. and Monaco, Feno M.

3. **Co-workers and Collaborators:** Smith, Travis, Rodriguez, Eric, Bryan, Jason

4. **Advisor:**

5. **Departments:** Department of Orthopaedic Surgery

6. **Support:**

7. **Institutions:** Cleveland Clinic Orthopaedic & Rheumatologic Institute (ORI)

8. **Body of Abstract: (300 words or less)**

**Background:**
Total hip arthroplasty has demonstrated high
clinical success rates (1-3), enabling the majority of patients to resume an active and independent life. However, premature implant failure requiring revision is a limitation, often resulting from poor implant placement (4-6). Currently, implant placement relies on the use of generic instruments that do not take into consideration a patient’s unique anatomy or degree of pathology. This study was conducted to compare the performance of patient-specific total hip arthroplasty instruments to standard surgical instruments.

**Methods:**

Five surgeons each attempted to place two acetabular shells in two separate sawbones hemipelvis using standard instruments at a prescribed abduction angle and version. The five surgeons then examined a preoperative plan created in our surgical simulator and used our patient-specific instruments (PSIs) to place an additional two acetabular shells at the same prescribed angles. The implanted sawbones were CT scanned and digitally imported into software previously validated to make virtual measurements (8). The version and abduction angle of the implant were measured using this software. The absolute difference between the measured angles and the prescribed angles was compared between groups using a Student’s t-test.

**Results:**

The mean difference in degrees from the prescribed version for the standard instrumentation group and PSI group was 13.90 (SD: 16.54) and 2.80 (SD: 2.15), respectively (P=0.0497). The mean difference in degrees from the prescribed abduction angle for the standard instrumentation group and PSI group was 13.33 (SD: 8.96) and 1.2 (SD: 1.23), respectively (P<0.0005).

**Conclusions:**

This study demonstrated that the use of PSIs yields a statistically significant improvement in acetabular component placement when compared to the use of standard surgical instruments by multiple surgeons. This
may lead to the creation of surgeon friendly products that improve the accuracy and precision of component placement, enhance patient outcomes and decrease health care costs.

References:

Please choose your academic program:  

<p>| MD |</p>
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<thead>
<tr>
<th>Question</th>
<th>Answer</th>
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<tbody>
<tr>
<td>11. What year are you in the program?</td>
<td>3</td>
</tr>
<tr>
<td>12. What was your role in this project?</td>
<td>Feno Monaco and I were medical student researchers on this project.</td>
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<tr>
<td>13. Date:</td>
<td>11/09/2010</td>
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**Lepow Day Abstract**

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<tbody>
<tr>
<td>1. Title:</td>
<td>Working the Web: Using online design to make Pharmacology Phresh</td>
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<tr>
<td>2. Presenter:</td>
<td>Rhett Butler</td>
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<tr>
<td>3. Co-workers and Collaborators:</td>
<td>Marvin Neiman, Amy Wilson-Delfosse, Peggy Kim</td>
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<td>4. Advisor:</td>
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<tr>
<td>5. Departments:</td>
<td>CWRU School of Medicine Office of Curricular Affairs</td>
</tr>
<tr>
<td>7. Institutions:</td>
<td>Case Western Reserve University; Cleveland, OH</td>
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</table>
| 8. Body of Abstract: (300 words or less) | **Background**  

The Case Western Reserve University School of Medicine curriculum includes a supplemental online pharmacology curriculum that runs concurrently with the regular curriculum to introduce first-year students to pharmacology principles during block 2 and 3. This voluntary online pharmacology curriculum (Pharmweb) correlates with higher test scores, but utilization is among medical students is low.  

**Hypothesis**

We hypothesize that, by improving the look and feel of the modules as well as improving access to the modules and the quiz questions associated with them, we can promote adoption and appreciation of this voluntary curriculum, and pharmacology in general.

**Methods**
The pharmweb quiz questions were integrated with weekly voluntary MCQs and the modules redesigned with a cleaner, more accessible, user interface. Additionally, links to the modules were included in the MCQ stems. We then compared the use of pharmweb modules by the graduating class of 2014, who used the updated design, compared to the classes of 2011/2012 who used the older design by comparing the number of pageviews. We also compared survey results to gauge the sentiment of the students towards the pharmacology curriculum.

**Results**

This project is currently being implemented and no objective data has been interpreted.

**Conclusions**

We expect that a usable, more accessible design will result in greater utilization and appreciation for the pharmweb modules, but without interpreted data, a conclusion is impossible to construct yet.

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<th>10. Please choose your academic program:</th>
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<tr>
<td>11. What year are you in the program?</td>
<td>2</td>
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<tr>
<td>12. What was your role in this project?</td>
<td>I developed and implemented the changes to the eCurriculum system. I will also be analyzing the data once the project is complete.</td>
</tr>
<tr>
<td>13. Date:</td>
<td>11/09/2010</td>
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Carruthers, Kadir

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<th><strong>Lepow Day Abstract</strong></th>
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<tr>
<td>1. Title:</td>
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<td>2. Presenter:</td>
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<td>3. Co-workers and Collaborators:</td>
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Skeletal muscle loss induced by cachexia is directly responsible for at least 20% of cancer fatalities. Cachexia is characterized as an overall state of ill health accompanied by a loss of lean body mass (LBM), fat mass, weakness, and fatigue. Impaired respiratory muscle function in cachexic patients in addition to immune defects frequently leads to pneumonia as a cause of death. Little is known about the impact of tumor production on systemic bone metabolism.

The principal aim of our research was to demonstrate the effects of cancer cachexia on bone mineral density (BMD) and LBM. We utilized a mouse model of cancer cachexia using Lewis lung carcinoma (LLC) cells to induce tumor growth in C57BL/6 mice. We hypothesized that over a period of 21 days, LBM and BMD would be reduced in LLC animals, with a proportionally greater decrease in LBM relative to BMD. To accomplish this, mice were injected with either LLC cancer cells (n=6) or with cell culture medium alone (controls, n=4). We assessed body composition by PIXIImus scan (dual energy x-ray absorptiometry for small animals) immediately following injection and again 21 days later. Wholebody bone mineral density and % fat and lean mass were determined from these scans for each animal at each time point. We found no significant difference in LBM between the 2 groups at either time point (86%). We did find that the tumor mice had lower BMD compared to the control mice at the 21 day time point (from 0.60 grams/cm² to 0.054 grams/cm², 10%). Based on these findings, we conclude that this methodology is sufficient to study the impact of tumor growth on bone metabolism but not for the development of cachexia (loss of LBM). Additional work is required to demonstrate loss of LBM in this...
system, including increasing the number of cancer cells injected and extending the period of observation.

| 10. Please choose your academic program: | MD |
| 11. What year are you in the program? | 2 |
| 12. What was your role in this project? | My specific role in the project was to weigh and assess both the tumor and control mice each day for the 21 day period. In addition, I assisted with body composition and bone density determination by DXA. Furthermore, I aided with sample collection for microCT and histology. |
| 13. Date: | 11/10/2010 |

**Lepow Day Abstract**

**1. Title:** Downstream Coronary Effects of Drug Eluting Stents: Unintended Therapeutic Target?

**2. Presenter:** George Cater

**3. Co-workers and Collaborators:** Ganesh Devendra, Mehdi Shishehbor M.D., Steven Nissen M.D., Stephen Ellis M.D., Richard Krasuski, M.D.

**4. Advisor:**

**5. Departments:** Cardiovascular Medicine

**6. Support:** American Heart Association Student Scholarship in Cardiovascular Disease and Stroke

**7. Institutions:** Cleveland Clinic Foundation

**8. Body of Abstract: (300 words or less)**

**BACKGROUND:**

Drug eluting stents (DES) target local endothelial trauma and prevent in-stent restenosis. The antiproliferative agents used in DES have been shown to attenuate atherosclerosis, however downstream effects of DES have not been previously examined. To study this we compared downstream lesion development in patients receiving either DES or bare-metal stents (BMS).

**METHODS:**

A large single-center interventional database was utilized to identify patients undergoing initial PCI with
implantation of a single stent in a proximal coronary artery with no initial downstream disease who returned for subsequent intervention. In these 463 patients, a non-intervened control vessel was also identified. Endpoint was defined as the angiographic identification of a de-novo stenosis in the downstream vessel within 12 month sof initial PCI.

RESULTS:
Among the 342 BMS patients and 121 DES patients, 68 lesions were identified in the target vessels compared to 32 lesions in the control (p<0.001). There was lesser likelihood of lesions downstream to DES (13% vs. 32%, p= 0.005). No difference in downstream lesions was seen in the respective control vessels (8% vs. 16%, p=0.20). Using a multivariable hazards model, only use of DES predicted freedom from downstream stenosis (HR 0.38, 95% CI 0.18-0.72, p=0.02).

CONCLUSIONS:
Patients receiving DES are less likely to develop downstream lesions compared to BMS, suggesting downstream drug delivery. Control vessels were not affected suggesting limited systemic delivery. The use of a stent for paracrine drug delivery deserves further study.

| 10. Please choose your academic program: | MD |
| 11. What year are you in the program? | 3 |
| 12. What was your role in this project? | Study Design, Data Collection, Statistical Analysis, Conclusions |
| 13. Date: | 11/01/2010 |

Chang, Bianca

Lepow Day Abstract

1. Title: The Effect of Combined Epidural-General Anesthesia and Postoperative Bupivacaine Epidural Analgesia on Natural Killer Cells and Interleukin-2 in Patients Undergoing Non-Small Cell Lung Cancer Resection

2. Presenter: Bianca W. Chang
3. Co-workers and Collaborators: Maria Bauer; Gregory Plautz; David Mason; Andrea Kurz

4. Advisor: 

5. Departments: Department of Outcomes Research and General Anesthesiology

6. Support: T-32 NIH Training Grant

7. Institutions: Cleveland Clinic, Cleveland, Ohio

8. Body of Abstract: (300 words or less)

**Introduction:** Natural killer (NK) cells play an important role in cancer surveillance and tumor cell lysis. Interleukin (IL)-2 has been known to have beneficial effects on the immune response, and may be associated with tumor reduction via the stimulation, proliferation, and activation of NK cells. Surgical stress has been associated with perioperative immunological changes, and particular anesthetics may further diminish NK cell activity while promoting tumor growth and metastasis. In order to counteract these negative effects on NK cells, researchers have added regional anesthesia to the intraoperative anesthetic strategy, which has been proposed to reduce overall anesthetic and opioid consumption, ameliorate surgical stress, facilitate pain control, and preserve NK cell function.

**Hypothesis:** We hypothesized that the addition of intraoperative epidural analgesia to general anesthesia, followed by epidural bupivacaine without opioids during and after resective surgery for non-small cell lung cancer (NSCLC), ameliorates a postoperative reduction of circulating NK cells and improves postoperative plasma IL-2 concentrations when compared to the use of general anesthesia only followed by opioid-based analgesia.

**Methods:** Patients meeting the inclusion criteria were randomized to either Postoperative Epidural Analgesia (PEA) only or Intraoperative Epidural Analgesia (IEA). The PEA group received, after thoractomy closure, a bolus of 6-9mL of 0.1% bupivacaine plus 2 mcg/mL of fentanyl, followed by infusion of the
same solution at 6-9 mL/hr, maintained throughout the postoperative period; the IEA group received, before thoractomy incision, a bolus to 6-9 mL of 0.25% bupivacaine followed by the infusion of 0.2% bupivacaine at 6-9 mL/hr throughout the postoperative period. Blood samples obtained before anesthesia induction and 24 hours post-operatively were used for peripheral blood mononuclear cell (PBMC) isolation, flow-cytometry, and cytokine analysis. Laboratory data was analyzed using repeated-measure ANOVA.

**Results:** Nineteen patients in the PEA group and eighteen patients in the IEA group were included in the statistical analysis. Flow-cytometry analysis revealed that, while both groups had comparable percentages of NK cells preoperatively, twenty-four hours post-operatively the percentage of NK cells decreased significantly compared to baseline in the PEA group, but remained stable in the IEA group. When IL-2 levels were evaluated, preoperative plasma concentrations were significantly lower in both groups compared to healthy subjects; these levels remained low regardless of treatment.

**Conclusions:** Intraoperative epidural administration of bupivacaine followed by postoperative infusion of 0.2% bupivacaine prevented the decrease in NK cells that was observed in patients who did not receive an intraoperative bolus of bupivacaine and had a postoperative infusion of a lower concentration of local anesthetic with fentanyl. Additionally, patients with NSCLC have very low or undetectable levels of baseline IL-2, a finding which may guide treatment.

| 10. Please choose your academic program: | MD |
| 11. What year are you in the program? | 2 |
| 12. What was your role in this project? | I was responsible for processing fresh blood samples for PBMC and serum isolation. From there, I stained and fixed PBMCs for flow-cytometry and performed ELISAs on the serum looking for particular cytokines. Additionally, I was involved in the writing |
and editing of a couple papers, one written for a conference, and one for a journal publication.

13. Date: 11/10/2010

Chauhan, Vishal

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<tr>
<th>Lepow Day Abstract</th>
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<tbody>
<tr>
<td><strong>1. Title:</strong> Gene transfection of primary retinal pigment epithelial cells using compacted DNA nanoparticles is dose dependent</td>
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<tr>
<td><strong>2. Presenter:</strong> Vishal Chauhan</td>
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<tr>
<td><strong>3. Co-workers and Collaborators:</strong> Kichiro Okano</td>
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<tr>
<td><strong>4. Advisor:</strong></td>
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<tr>
<td><strong>5. Departments:</strong> Departments of Ophthalmology and Pharmacology</td>
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<tr>
<td><strong>6. Support:</strong></td>
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<td><strong>7. Institutions:</strong> Case Western Reserve University, Cleveland, OH 44106</td>
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**Purpose:**
To study the efficiency of gene transfer using compacted DNA nanoparticles in primary retinal pigment epithelial (RPE) cells.

**Materials & Methods:**
Primary RPE cells were isolated from mice eye as previously published (Sonoda et al., Nature Protocol, 2009). The eyes of WT mice (C57BL/6) were enucleated and placed into serum free media. The eyes then underwent a dissolution process with 2% dispase in general media. Afterwards, the cornea and lens were removed using sterile surgical technique and the RPE cells were isolated and plated onto a 12 well plate. At time points 15 and 30 days post isolation, the cells were lysed and RT-PCR was conducted to amplify RPE cell specific genes (Rpe65, Lrat) and retina specific gene (Rho). At 15 days post isolation, cells were transfected with luciferase in vectors of naked DNA, lipofectamine, and compacted DNA nanoparticles. Two days after transfection, a luciferase assay was conducted to measure the efficiency of gene transfer.

**Results:**
Isolated primary RPE cells showed a positive signal for *Lrat* and *Rpe65* at the 15 day timepoint and a positive signal for *Lrat* at the 30 day time point. The signal for *Rho* was negative at 15 and 30-day time points. This confirms that the isolated cells are indeed RPE cells and have no contamination with photoreceptor cells. Transfection of primary RPE cells with compacted luciferase DNA nanoparticles showed a dose-dependent relationship. In addition, transfection efficiencies of luciferase with lipofectamine was comparable to that of low dose compacted DNA nanoparticles.

**Conclusions:**

Transfection of primary RPE cells with compacted DNA nanoparticles has a dose dependent relationship and shows comparable efficiencies to that have lipofectamine. These characteristics along with their documented ability to transfect non-dividing cells, shows them to be good agents for transfection in-vivo retinal gene therapy.

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### Lepow Day Abstract

1. **Title:** Confronting death: Home-based hospice experiences in preclinical medical education
2. **Presenter:** Cindy Chen
3. **Co-workers and Collaborators:**
4. **Advisor:** Beth McLaughlin, M.D.
5. **Departments:** Family Medicine and Palliative Care
6. **Support:**
7. **Institutions:** Case Western Reserve University School of Medicine, University Hospitals Case Medical Center
8. **Body of Abstract: (300 words or less)**

Many medical school graduates feel that their medical school curriculum has inadequately prepared them for
taking care of patients at the end of life. This study addresses whether a longitudinal home-based hospice elective for preclinical medical students resulted in a better understanding of the interdisciplinary nature of hospice and palliative care and greater comfort in communicating with patients and family members about chronic illness and death. In addition to those objectives, the elective sought to foster more positive attitudes about end-of-life care and increase medical knowledge of palliative and end-of-life care. Ultimately, the goal of the elective was to help preclinical medical students build knowledge and skills that would better prepare them for taking care of patients, especially those who are terminally ill, during the clerkship years and beyond. First year medical students were matched with a hospice patient living at home and worked one-to-one with the hospice nurse overseeing the patient’s care. Students had opportunities to interact with the patient’s family and the rest of the healthcare team, such as the physician, social worker, nurse’s aide, and spiritual care provider. Students also attended meetings involving the entire healthcare team. Prior to entering patient homes, students attended a group training session to learn about the goals of the hospice elective and received an introduction to hospice. Data was collected through focus groups at the beginning, middle, and end of the elective period. During each focus group, elective participants completed a questionnaire and discussed their experiences while being audiotaped. In the findings to date, students cited the vital importance of communication among healthcare team members in order to resolve disagreements regarding a patient’s care and effectively manage the multiple aspects of care. Students also mentioned that communication between the healthcare team and the patient was crucial in order to meet both parties’ goals for the patient’s health and wellbeing.

10. Please choose your academic program: MD

11. What year are you in? 2
| 1. Title:  | Assessment and Functional Activation of Sonic Hedgehog Pathway in GBM Stem Cells |
| 2. Presenter: | Yunwei Chen |
| 3. Co-workers and Collaborators: | Amber Kerstetter, Alex Polinkovsky |
| 4. Advisor: | |
| 5. Departments: | Neurological Surgery & Department of Neurosciences |
| 6. Support: | The investigator provided the background knowledge and resources necessary for the fellow to understand not only the minute details of the specific assays, but also the aims of the research project as a whole. He created an atmosphere in which the fellow was comfortable asking questions about the research material and also about the utilized methods. Throughout the summer the investigator took time to have one-on-one meetings with the fellow, asking his opinions on the project and to make sure that he was enjoying his day to day experience. |
| 7. Institutions: | University Hospitals & Case Western Reserve University School of Medicine |

**Body of Abstract: (300 words or less)**

The goal of this research project is to assess the function and significance of the Sonic Hedgehog (SHh) signaling pathway in Glioblastoma Multiforme (GBM) derived cancer stem cells. GBM account for over half of all primary brain tumors and overall prognosis has not improved in three decades despite maximal surgery, radiation and cytotoxic chemotherapy. Cancer stem cells, such as those found in GBMs, may account for this treatment resistance. The SHh signaling pathway serves a critical role in the normal development of the central nervous system and is linked to cellular proliferation and angiogenesis. Recently, mutations in the SHh pathway have been linked to the pathogenesis of medulloblastomas, another CNS neoplasm. Further characterization of the SHh pathway and its role in glioma stem cells may ultimately allow for a better understanding of GBM pathogenesis and...
possible non-cytotoxic personalized targeted treatment for patients suffering from this disease. Our hypothesis is that the SHh pathway will be functionally important in GBM stem cells. We will test this hypothesis by assessing the expression of SHh family genes in GBM-derived glioma stem cells by RT-PCR and assessing the effects of specific SHh pathway agonists and antagonists on neurosphere initiation and proliferation in GBM derived stem cells.

10. Please choose your academic program: MD
11. What year are you in the program? 2
12. What was your role in this project? The fellow assisted with tissue culture in the harvesting and isolation of brain tumor stem cells from freshly resected brain tissue. The fellow also set up and analyzed proliferation and limiting dilution assays to assess the functional activation/inhibition of neurosphere formation in the presence of various drugs. This is a measurement of “self-renewal.” Immunohistochemistry and cellular imaging were also performed.
13. Date: 11/10/2010

Cho, Deborah

Lepow Day Abstract

1. Title: The Morality of Mammography
2. Presenter: Deborah Cho
3. Co-workers and Collaborators: 
4. Advisor: 
5. Departments: Case Western Reserve University School of Medicine, Department of Bioethics
6. Support: Dean’s Summer Research Award, Case Western Reserve University School of Medicine
7. Institutions: Case Western Reserve University School of Medicine, Department of Bioethics; The Hastings Center
8. Body of Abstract: (300 words or less) Background: In November of 2009, the United States Preventive Services Task Force (USPSTF) released recommendations for breast cancer screening that differed from the prevailing American Cancer Society (ACS) recommendations. These recommendations dictate both physician and patient decisions, as well as states’ mandates for insurance coverage. The ethical imperative to continually
reassess the morality of actions requires that these recommendations and the rationale behind them be continually improved to serve the intended purpose of benefiting the population.

Hypothesis: Recommendations by both the ACS and USPSTF will reflect the inherent values of those making the decisions, i.e. board members, and may not reflect the values of the American patient population.

Methods: Through examination of the current ACS and USPSTF recommendations on mammography, guideline construction will be analyzed. Publications that examine the issue from public health, medical, patient-centered, political, and ethical perspectives will be reviewed.

Results: The ACS and USPSTF both apply the values of the physicians and other public health professionals involved in their organizations to the formation of breast cancer screening guidelines. Physicians, public health professionals, and patients have different values that ought to be respected by these recommendations. It is extremely difficult to determine who ought to construct recommendations, so constant reevaluation of recommendations and their authors is necessary.

Conclusions: In the United States, physicians are taught to practice as if resources are infinite and that the ultimate good is to cure patients of disease. Physicians believe that they are capable of applying patient values and goals to healthcare, but are not officially trained to do so. Physicians ought to be trained in this field early on in their medical education. More research ought to be done to answer the question: What are medical students taught to value?

10. Please choose your academic program: MD
11. What year are you in the program? 2
12. What was your role in this project? Conducted independent research at The Hastings Center, gave a presentation at the beginning at the end of my time at the center. Received input and assistance from staff at The Hastings Center and from staff at CWRU SOM, Bioethics department.
13. Date: 11/10/2010

Cizek, Stephanie

Lepow Day Abstract

1. Title: Professionalism education in the Western Reserve2 curriculum: making a difference vs. finding a deviance
2. Presenter: Stephanie Cizek
3. Co-workers and Collaborators: Elizabeth McKinley, Kathy Cole-Kelly, Klara Papp
Background and Rationale: Professionalism is an important and challenging area of learning that includes a complex set of skills often considered difficult to define and assess. Research shows that medical student lapses in professionalism correlate with later state medical board referrals. Professionalism errors by physicians are associated with a range of serious consequences. We propose a new paradigm for professionalism learning based on the premise that all medical students are novices in coping with stressors, conflicting demands, and ethical dilemmas that face physicians. Rather than focus on those who falter, we frame professionalism as a complex, adaptive challenge and ongoing area of quality improvement for all.

Hypothesis: The five-component WR2 professionalism curriculum will result in 1) increased positive professionalism behaviors among students, 2) improvement in student satisfaction with small group function, and 3) a reduction in professionalism lapses.

Methods: A post-test comparison group design will compare perceptions and behaviors of students in the classes of 2013 (comparison group) and 2014 (intervention group) after each class’s first year of medical school. The five components of the intervention include: a) 360-degree evaluations, b) student self-reflection and development of personal improvement plans, c) small group discussions of personal narratives and professionalism scenarios, d) a professionalism portfolio competency, and e) a system for early reporting of professionalism concerns. Results will be analyzed using the Mann-Whitney Test for non-parametric ordinal data and t-Tests for parametric ratio or interval data.

Results and Conclusions: Four components of the intervention have been implemented. The early concerns form is in discussion. After some initial concern about 360-degree feedback, student buy-in is positive.
Preliminary analysis of data from the comparison group survey suggests that students support professionalism education, but feel only a few “problematic” students need it. Faculty and staff support has been critical for successful program implementation.

| 10. Please choose your academic program: | MD |
| 11. What year are you in the program? | 2 |
| 12. What was your role in this project? | First author. Completed needs assessment, developed study design and student survey, submitted IRB proposal, and assisted with development and implementation of curriculum interventions. |
| 13. Date: | 11/10/2010 |

Cover, Michael

**Lepow Day Abstract**

1. Title: Development of a Porcine Model for Acute Infected Wounds
2. Presenter: Michael Cover
3. Co-workers and Collaborators: Jonathan Macknin, MD; Kath Bogie, DPhil
4. Advisor: 
5. Departments: Department of Orthopaedics
6. Support: 
7. Institutions: Case Western Reserve University

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<th>8. Body of Abstract: (300 words or less)</th>
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<td>Background: The countless blast-induced wounds sustained during the Operation Enduring Freedom/Operation Iraqi Freedom (OIF/OEF) conflicts have generated an increasing need for interventions that can both accelerate healing and ameliorate infections. Such interventions would also positively impact civilian trauma management. Military blast injuries have a high rate of bacterial colonization that delays healing and can cause cross-contamination. Blast wound bacteriology includes Staphylococcus aureus, Pseudomonas aeruginosa, and increasingly drug resistant bacteria strains. Electrical stimulation has been shown to reduce acute wound infection by inhibiting growth of several bacterial strains relevant to acute traumatic wounds.</td>
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Methods: In order to evaluate a novel electrical stimulation
device, a suitable animal model must first be developed and characterized. Yorkshire pigs were selected because their wound healing is highly concordant with human healing. Female 40kg Yorkshire pigs are placed under general anesthesia and 6 full-thickness wounds created on their dorsum; 3 are inoculated with Pseudomonas aeruginosa at the time of initial surgery. The effects of infection over a clinically relevant time frame of 14 days are evaluated using a multivariate quantitative methodology. Tissue biopsies and wound culture swabs are collected at 7 time points post-injury. Evaluations include bacterial load and quantitative real-time PCR assessment of genes pertinent to wound healing.

Results:
Infectious disease data gathered from the current study characterized bacterial infection associated with acute wounds. Real-time PCR data provided a quantitative baseline for expression of five genes pertinent to the healing process.

Discussion:
This study created a well-characterized model of acute infected wounds, which will be used as the basis for further testing of a novel electrical stimulation device by our laboratory. The model will directly impact society by facilitating pre-clinical evaluation of novel devices and techniques to reduce infectious complications and shorten healing time in acute infected wounds.

10. Please choose your academic program: MD
11. What year are you in the program? 2
12. What was your role in this project? Collection, purification, and RT-PCR analysis of tissue samples for development of a porcine acute infected wound model.
13. Date: 11/09/2010

Cronin, Thomas

Lepow Day Abstract
1. Title: Effect of Fiber Orientation Distribution Function Reconstruction on Probabilistic Tractography
2. Presenter: Thomas Cronin
3. Co-workers: Dr. Ken Sakaie, Dr. Mark Lowe, Dr. Michael Phillips, Dr. Robert
A head to head comparison of the effects of choice of reconstruction function on multifiber tractography results has not been previously performed. Multifiber tractography has the potential for producing detailed maps of the white matter architecture in the brain, which can then be used to study structural connectivity and the causes and effects of neurological disease. We perform an apples-to-apples comparison of how modeling fiber orientations with either spherical deconvolution or persistent angular structure impacts tractography in healthy controls and multiple sclerosis patients. We find qualitative differences between the tracks, significant differences in the tracking efficiency, and significant differences in the track consistency.

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<th>De Silva, Gayan</th>
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**Lepow Day Abstract**

1. **Title:** THE ROLE OF KLF4 IN TUMOR ANGIOGENESIS
2. **Presenter:** Gayan De Silva
3. **Co-workers and Collaborators:** Dr. Anne Hamik, Ejike Anih, Dr. Mukesh K. Jain
4. **Advisor:**
5. **Departments:** Case Cardiovascular Research Institute
6. **Support:** NIH T-35 Training Grant
7. **Institutions:** Case Western Reserve University School of Medicine - University Hospitals
8. **Body of Abstract: (300 words or less)** Diseases of the vascular endothelium and
Processes associated with inappropriate vascularization are responsible for numerous diseases, including those associated with pathological inflammation (i.e., atherosclerosis) and tumor growth resulting from uncontrolled vascularization. Elucidating the cellular mechanisms that underlie these disease processes is a growing area of research, and one that will contribute to the basis of treating these diseases.

Kruppel-like factors (KLFs), a family of zinc-finger proteins, play an integral role in the regulation of cellular growth and differentiation. Constituting an abundant class of DNA binding proteins and transcription factors, the functionality of the zinc-finger protein arises from the assembly of cysteine (C) and histidine (H) amino acid residues around the namesake zinc ion. Previous research has demonstrated that the KLFs KLF2 and KLF4 play an integral role in maintenance of a non-inflammatory, anti-coagulant, vasoactive endothelium. Furthermore, there is nascent evidence to suggest that these KLFs modulate the angiogenic pathway.

Preliminary data performed in the Jain lab demonstrates that mice with transgenic overexpression of endothelial KLF-4 overexpression have significantly decreased tumor (subcutaneous melanoma) growth as compared to control mice. In fact, the structural phenotype of the tumors in the transgenic animals is reminiscent of those seen with dll4 blockade: small tumors with enhanced, but dysfunctional, vascularity. This data would seem to suggest that KLF-4 is a mediator of angiogenesis in a separate, but equally important mechanism as VEGF and Notch.

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<tr>
<td>11. What year are you in the program?</td>
<td>2</td>
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<tr>
<td>12. What was your role in this project?</td>
<td>My role in the project was to carry out the objectives laid out in my prior research proposal. I carried out all of the experiments by myself, and reported directly to Dr. Anne Hamik, as we discussed possible interpretations of the data, and created new</td>
</tr>
</tbody>
</table>
Experimental avenues to push forward the objectives of the project.

13. Date: 11/10/2010

Decker, Ilka

Lepow Day Abstract

1. Title: High levels of Zinc Protoporphyrin Identify Iron Metabolic Abnormalities in Pulmonary Arterial Hypertension

2. Presenter: Ilka Decker


4. Advisor: 

5. Departments: Pathobiology; Pulmonary, Allergy and Critical Care Medicine; Clinical Pathology; Pediatrics and Medicine

6. Support: HL 60917; Howard Hughes Medical Institute Medical Research Fellows Program [57006972, ID]

7. Institutions: Lerner Research Institute, Cleveland Clinic; Respiratory Institute, Cleveland Clinic; Pathology and Laboratory Medicine Institute, Cleveland Clinic; Taussig Cancer Institute, Cleveland Clinic; Columbia University College of Physicians and Surgeons

8. Body of Abstract: (300 words or less)

Zinc is inserted to protoporphyrin (Zn-pp) when there is inefficient iron incorporation into heme. Recent studies reveal that iron influences the development of pulmonary arterial hypertension (PAH) secondary to hypoxia or hematologic disorders. Based on the relationship between iron and secondary forms of PAH, we hypothesized that the pathophysiology of primary or idiopathic PAH (IPAH) may also be influenced by alterations in iron metabolism. To test this hypothesis, we measured sensitive markers for iron metabolism such as Zn-pp, ferritin, transferrin receptor and parameters of red blood cell numbers and morphology. Despite similarly normal red cell counts, hemoglobin and other measures of iron metabolism, Zn-pp levels of IPAH patients were ~2-fold higher than asthmatic and or healthy individuals,
and were closely related to measures of disease severity. The red cell distribution width (RDW) was also higher in IPAH than control samples, and was strongly related to Zn-pp levels. In an expanded cohort that included primary PAH patients with the familial form of the disease (FPAH), the elevation of RDW was validated and found to be related to clinical parameters of severity, such as pulmonary artery pressures and 6 minute walk distances. The findings identify that primary forms of PAH have alteration in hemoprotein synthesis that is quantitatively related to disease severity parameters, which support a role for occult abnormalities of iron metabolism in the pathophysiology of pulmonary hypertension.

The results of this research were submitted in an abstract to the 2011 annual American Thoracic Society meeting and I am currently in the process of writing a manuscript.
Introduction: Mounting evidence has shown that premature adrenarche (PA) is associated with greater risk of metabolic disease and is associated with hyperinsulinism, dyslipidemia, and obesity in girls. Retinol binding protein-4 (RBP-4), an adipokine secreted by adipose tissue and the liver, has been shown to correlate with obesity, insulin resistance (IR) and cardiovascular risk factors. The purpose of this study was to determine if RBP-4 correlates with comorbidities in this group and if RBP-4 is a marker of IR in prepubertal children with PA.

Methods: Study subjects were prepubertal children between ages 5 – 9 years. 18 children with PA (5 boys, 13 girls) and 20 age-matched control subjects (13 boys, 7 girls) participated in the study. Height, weight, blood pressure and waist circumference were measured and BMI and BMI z-score were calculated. Baseline lipids, hormones, and RBP-4 levels were drawn. RBP-4 ELISA assays (ALPCO) were performed in duplicate. Insulin resistance was assessed by 2 hr oral glucose tolerance test (OGTT) derived measures including SIM, WBIS, and HOMA-IR. Data was analyzed by simple t-test, analysis of variance and Pearson correlations.

Results: There was no significant difference in RBP-4 levels between PA children (15.6 ± 3.9mg/L) and controls (14.7 ± 6.0 mg/L). There was no significant correlation of RBP4 with markers of IR (FGIR, WBIS, SIM, HOMA) in whole group analyses. RBP-4 correlated with triglycerides (TGs) in whole group analysis (P = 0.0046), and with triglycerides (P = 0.003) and HDL cholesterol (P = 0.070) when the entire group was adjusted for BMI-z score.

Conclusion: RBP-4 did not correlate with markers of IR; however, RBP-4 did correlate with TGs and inversely (trend) with HDL cholesterol in this prepubertal study group. It remains unclear if RBP4 is a useful early clinical marker of IR or metabolic abnormalities in prepubertal children with PA.
note that the above report contains confidential information as the results from these studies are not yet published. In addition, I helped recruit young women aged 13 to 21 years for our related study in a

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**Desai, Ravi**

**Lepow Day Abstract**

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<tr>
<th>1. Title:</th>
<th>Right Ventricular Function after Mitral Valve Surgery with or without Concomitant Tricuspid Valve Procedure</th>
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<tbody>
<tr>
<td>2. Presenter:</td>
<td>Ravi Desai, BE</td>
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<tr>
<td>3. Co-workers and Collaborators:</td>
<td>Lina M. Vargas Abello, MD, Edward R. Nowicki, MD, MS, Jeevanantham Rajeswaran, MSc, Allan L. Klein, MD, Eugene H. Blackstone, MD, Gösta B. Pettersson, MD, PhD</td>
</tr>
<tr>
<td>4. Advisor:</td>
<td></td>
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<tr>
<td>5. Departments:</td>
<td>Cardiothoracic Surgery, Cardiovascular Medicine, Quantitative Health Sciences</td>
</tr>
<tr>
<td>6. Support:</td>
<td>AATS Summer Fellowship</td>
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<tr>
<td>7. Institutions:</td>
<td>Cleveland Clinic</td>
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</table>
| 8. Body of Abstract: (300 words or less) | Background: Functional tricuspid valve regurgitation (TR) accompanying mitral valve disease is associated with right ventricular (RV) dysfunction. Our objectives were to study RV function after mitral valve surgery with or without a concomitant tricuspid valve (TV) procedure. 

Methods: From 2001 to 2007, 1,833 patients with degenerative mitral valve disease, structurally normal TV, and no coronary artery disease underwent surgery. RV function (myocardial performance index [MPI] and tricuspid annular planesystolic excursion [TAPSE]) were measured before and after surgery on transthoracic echocardiograms for 100 randomly selected patients from each of the TR grades 0, 1+, and 2+, and for all 93 with 3+/4+, 393 patients in total. Sixty-seven had a concomitant TV procedure. Separate multivariable longitudinal (repeated-measures) modeling and regression analyses were used to evaluate the temporal trend of RV function. |
Results: A TV procedure effectively reduced TR to levels comparable to patients with no TV procedure (Figure, left). RV dysfunction increased early after surgery in the no-TV-procedure group, but then improved to levels just above normal (0.4 for MPI; Figure, right). In contrast, RV function improved substantially in the TV-procedure group, reaching levels similar to those of the no-TV-procedure group within a few months after surgery. TAPSE behaved similarly to MPI.

Conclusion: Mitral valve surgery induced mild immediate RV dysfunction, which improved overtime but never fully reached preoperative level. Patients with severe TR and RV dysfunction undergoing a concomitant TV procedure showed improved RV function immediately after surgery and eventually recovered RV function comparable to that in the no-TV-procedure patients. Fixing severe TR improves RV function.

10. Please choose your academic program: MD
11. What year are you in the program? 3
12. What was your role in this
### Lepow Day Abstract

| 1. Title: | An Assessment of Chronic Cerebrospinal Venous Insufficiency by Tissue Analysis of the Cerebrospinal Veins |
| 2. Presenter: | Claudiu Diaconu |
| 3. Co-workers and Collaborators: | Robert J. Fox, MD; Alex Rae-Grant, MD; Soo Hyun (Ester) Kim, MD, MPH; Irene Katzman, MD, MS; Mei Lu, MD, PhD; Michael D. Phillips, MD; Susan Staugaitis, MD, PhD; Jennifer McBride, PhD; Elizabeth Fisher, PhD; Jar-Chi Lee, MS |
| 4. Advisor: | |
| 5. Departments: | CCF Mellen Center |
| 7. Institutions: | Neurological Institute |

#### Background

Chronic cerebrospinal venous insufficiency (CCSVI) is a new controversial and potentially paradigm-shifting theory for the cause of multiple sclerosis (MS). Venous reflux, resulting from congenital stenoses, has been found in the veins draining the brain and spinal cord of some MS patients. Backflow of toxins into the central nervous system is presumed responsible for MS plaques. A recent Italian study reported 100% sensitivity and specificity for CCSVI in MS [1], and showed that endovascular treatment of the stenoses improved clinical function [2]; however, subsequent studies from other groups have not been so definitive. Nonetheless, the CCSVI theory spurred much interest in the MS community, urging further research. We aim to determine whether CCSVI is truly associated with MS. If it is, we expect to visualize stenoses and inflammatory changes in the vessel walls. We will also assess for actual reflux with MRV and ultrasound [1-3].

#### Methods

Ten MS cadavers will be compared to 10 non-MS, age-matched controls. The neck veins, harvested soon after death, will be injected with silicone fluid that cures in situ to create a luminal cast of the vessels, which will be removed from the body, photographed, and sent to the lab for pathological and histological analysis [4]. The luminal casts will be inspected for stenoses/abnormalities. We will
perform Ultrasound and MRV of the cerebrospinal veins on 90 MS and 80 control patients.

Results
So far, we have ultrasound data for 2 MS patients, one of which met criteria. None of the normal “practice” volunteers have met criteria to date. We have harvested veins from one MS body donor, but pathological analysis is pending.

Conclusion
The importance of the results are obvious: patients are currently seeking to have their neck veins checked, and some are even traveling abroad to have their veins “opened”, a procedure that is not without risks. Notably, our study is first to look at the tissue pathology of the veins; CCSVI has only been studied via imaging.

References:

Future Publications:
An abstract regarding the technical aspects of the ultrasound involved in assessing CCSVI has already been submitted to the American Academy of Neurology (AAN), and a poster will also result from this abstract.
AAN was also specifically interested in the tissue analysis aspect of the project and asked for another “breaking-news” abstract to be submitted in January or
February.

We are also preparing a presentation on the exact procedure involved in the injection of silicone and harvesting of veins.

Data from the entire project will be sent for publication sometime in the second half of 2011.

10. Please choose your academic program: MD

11. What year are you in the program? 4

12. What was your role in this project? The project has 3 main components: Ultrasound, MRV and Anatomical analysis. I helped with the IRB application on all 3 components, and I will also be involved with all 3 aspects of the project. However, my main focus will be on the anatomical aspect of the project. So far, I have practiced and developed the protocol for injecting and harvesting the veins from cadavers. I also helped to create the

13. Date: 11/12/2010

Dong, Huan

Lepow Day Abstract

1. Title: Percutaneous manipulation and fixation as a viable alternative to open reduction internal fixation of calcaneal fractures in a high-risk population

2. Presenter: Huan Dong

3. Co-workers and Collaborators:

4. Advisor:

5. Departments: Department of Orthopaedics

6. Support: none

7. Institutions: MetroHealth

8. Body of Abstract: (300 words or less) Intra-articular fractures of the calcaneus are devastating injuries that have long been associated with chronic pain and poor outcomes. Strong prognostic indicators of poor outcome include increased age at injury (>50 years), high BMI, labor-intensive profession, smoking, diabetes, open fractures, and decreased Bohler angle. Workers’ compensation status may also be associated with worse outcomes.

Much debate has existed over the appropriate treatment of intra-articular calcaneal fractures. Currently, open reduction and internal fixation (ORIF) has gained prominence over non-surgical treatment of displaced articular
In comparative studies, ORIF is associated with better function and pain outcomes as well as average long-term economic savings of $19,000 per patient.

However, ORIF is not appropriate for all patients. The extensile lateral approach carries risks of wound dehiscence, infection, and other complications that do not occur with closed treatment. We assessed the validity of percutaneous manipulation and fixation (PMF) of calcaneal fractures as an acceptable alternative to both ORIF and non-surgical treatment in smokers, diabetics, and patients with open fracture patterns who are at demonstrably higher risk for wound healing and infection complications in a retrospective cohort study of N = 70 calcaneal fracture patients managed by a single practitioner at a Level 1 trauma center from 2001-2008. Data analysis in progress.

### Lepow Day Abstract

1. **Title:** Heapatic Steatosis and Insulin Resistance, Cause or Effect?
2. **Presenter:** Nkiruka Ezewajiaku
3. **Co-workers and Collaborators:** Anna Wentz, Mary Weber, Peter Crawford
4. **Advisor:**
5. **Departments:** Department of Medicine
6. **Support:** Crile
7. **Institutions:** Washington University School of Medicine, St Louis

### Body of Abstract: (300 words or less)

Insulin resistance has been identified to be associated with type II diabetes mellitus, cardiovascular disease, hypertension, dyslipidemia and many other public health concerns. Recent data indicate that an independent predictor, and therefore potentially causal influence, of insulin resistance is
increased hepatic storage of triglyceride (hepatic steatosis). However, select physiological states, including starvation and maintenance on a very low-carbohydrate, high-fat (ketogenic) diet, are also associated with hepatic steatosis, but the effect of these states on glucose tolerance and insulin responsiveness is unknown.

This raises the hypothesis that insulin resistance is not caused by stored hepatic triglyceride, but is promoted by a lipid profile that is associated with only carbohydrate-rich states of caloric excess that promote hepatic steatosis. Experiments involved the use of magnetic resonance spectroscopy to measure hepatic lipid content on mice fed standard chow, ketogenic diet, and western diet. The major difference between the western and ketogenic diet was a reduced glucose content in the ketogenic diet. Using spectrophometric assays, the effects of these different diets on glucose tolerance and insulin resistance were determined. Finally, the effects of these diets on hepatic gene expression of key metabolic enzymes were measured using qPCR.

From this experiments we discovered that the western diet and ketogenic diet had increased hepatic triglyceride content when compared to the chow diet. However hepatic metabolic enzyme mRNA quantification showed increased expression levels of lipid synthesis enzymes in the western diet and lipid oxidation enzymes in the ketogenic diet. Glucose tolerance test also detected impaired glucose tolerance and insulin sensitivity in the western diet compared to ketogenic diet.

| 10. Please choose your academic program: | MD |
| 11. What year are you in the program? | 1 |
| 12. What was your role in this project? | My role in this research involved implementing the experiments stated above. From these experiments, I was responsible for acquiring data and analyzing the results obtained |
**Pursuit of the Horizon: Analysis of a Medical Immersion Program for Urban Teens**

**Kevin Fang**

### Co-workers and Collaborators
Sarah Nickolich, Joseph Helpern

**Advisor:**

**Departments:**
Office of Curricular Affairs

**Support:**
Mount Sinai Foundation, Office of Curricular Affairs, Committee of Student Representatives

**Institutions:**
Case Western Reserve University School of Medicine

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### Background

In 2008, 53.7% of Cleveland Public School students graduated on-time, rising from 33.3% in 1999. A high school dropout is expected to live 9.2 years less than a high school graduate, relating to poor health literacy, increased incidence of chronic disease and lack of health insurance. This study seeks to determine whether a medical school immersion program (called Horizons) leads to improvements in academic achievement among participants as compared to non-participant peers. Outcome measures included self-efficacy, academic interest, knowledge of the medical field and performance on Ohio Graduation Tests. Self-efficacy is a better predictor of science achievement than gender, ethnicity or parental background, and has been shown, along with academic interest, to correlate with academic achievement among urban teens.

### Methods

Sixteen sophomore students from a Cleveland public school were selected by application. Nine completed the program, which was held over seven weeks at the Case Western Reserve University School of Medicine. Each participant was assigned undergraduate and medical student mentors, who facilitated small-group learning sessions focused on type 2 diabetes mellitus. Participants also created public service announcements (http://www.youtube.com/horizonscwru).

A nine-person matched comparison group was established from non-applicant peers. Data from pre/post-program surveys on self-efficacy, academic interest and knowledge of the medical field were analyzed by chi-square tests. Pre/post-program
scores on Ohio Graduation Tests were analyzed by paired-difference and independent two-sample t-tests.

**Results:**
The study is on-going and results are unavailable at this time.

**Conclusion:**
We hope to show that Horizons positively impacts the academic achievement of local teens and that Horizons can serve as a model for similar programs at other medical schools, specifically those in urban areas.

**10. Please choose your academic program:**
MD

**11. What year are you in the program?**
2

**12. What was your role in this project?**
Co-creator of the Horizons program in December 2009. Coordinator of the 2010 Horizons program, which included mentor and physician volunteer recruitment, room reservations, acquisition of funding and communication with mc2STEM high school. Co-writer of several aspects of the curriculum including the IQ-style case, surface anatomy lesson and public service announcement.

**13. Date:**
11/10/2010

Feng, Taoyuan

**Lepow Day Abstract**

1. **Title:**
Developing PINCH-ILK-Parvin-Targeted Drugs for Potential Therapy of Heart Attacks

2. **Presenter:**
Taoyuan Robert Feng

3. **Co-workers and Collaborators:**
Koichi Fukuda, Mingyue Zheng, Hualiang Jiang

4. **Advisor:**

5. **Departments:**
Structural Biology Program, Department of Molecular Cardiology

6. **Support:**

7. **Institutions:**
Lerner Research Institute

8. **Body of Abstract: (300 words or less)**
The PINCH-ILK-parvin (PIP) complex is an essential heterotrimeric complex in modulating integrin-actin dynamics through an integrin-PIP-actin linkage, which affects a variety of cell adhesion-dependent processes such as cell spreading and migration that are important in development. More recently, the PIP complex has been found to be abnormally up-regulated in human failing hearts and in mouse models with acute myocardial
infarction. However, its precise role in this condition is uncertain. Since the high resolution 3D structures of PINCH-ILK and ILK-parvin have been determined, the discovery of a compound that interferes with the PIP complex at a cellular level has become possible and may lead to an effective therapy for heart attacks. Thus, our team aims to develop a drug that effectively binds to and disrupts the PINCH-ILK-parvin interaction by attacking the PINCH-ILK and ILK-parvin interfaces. To achieve this goal, we take a computational approach combined with nuclear magnetic resonance analyses to screen for potential compounds. Preliminary structure-based computational studies have identified several lead compounds that bind to the CH2 domain of α-parvin, which may disrupt the interaction with the pseudokinase domain of ILK. The binding dynamics of these compounds have been studied using 2D HSQC NMR to determine the strongest binders. Further elucidation of the binding affinity of these compounds and their refinement into high-affinity binders using chemical modification and fragment-based development is planned. The discovery of such high-affinity compounds will be important in gaining understanding of the PIP complex and its role in myocardial infarctions, and could ultimately lead to the treatment of acute myocardial infarction as well as other disease states in which the PIP complex is involved.

| 10. Please choose your academic program: | MD MS |
| 11. What year are you in the program? | 1 |
| 12. What was your role in this project? | I worked on this project during the year 1 summer research program at the CCLCM. I performed the NMR studies on the initial compounds obtained through computational screening. I also analyzed these spectra through comparison and through preliminary binding affinity studies to determine the best candidates for further refinement using fragment-based development. |
| 13. Date: | 11/10/2010 |
| Fisher, William |
## Lepow Day Abstract

<table>
<thead>
<tr>
<th>1. Title:</th>
<th>Comparative anatomy of the pineal region, with and without 2D/3D reconstruction, using 1.5 Tesla and 4Tesla MR scanning</th>
</tr>
</thead>
<tbody>
<tr>
<td>2. Presenter:</td>
<td>William Fisher</td>
</tr>
<tr>
<td>4. Advisor:</td>
<td></td>
</tr>
<tr>
<td>5. Departments:</td>
<td>Neurosurgery</td>
</tr>
<tr>
<td>6. Support:</td>
<td></td>
</tr>
<tr>
<td>7. Institutions:</td>
<td>UH</td>
</tr>
</tbody>
</table>

### Introduction:
In recent years, MR imaging has been utilized at higher and higher field strengths due to the theoretical linear increase in signal to noise ratio as magnetic field strength increases. This benefit has been heavily utilized by the functional MRI community because of the increased blood oxygen level dependent effect at higher field strength especially. Not as much work has been done with field strengths of 4 T in structural MRI, however. The authors set out to first utilize high field strength MRI to show the detailed anatomy around the pineal region of the brain including the galenic venous system, which are otherwise not so clearly visualized in lower field strength MR imaging.

### Study design:
The authors have performed 4 Tesla MR image acquisitions of human brain to compare the pineal region anatomy with those obtained by 1.5 Tesla MR scanner. Five healthy adult volunteers were studied employing a 4Tesla scanner and the images compared with those acquired from 1.5 Tesla MR scanner. A protocol was designed to help identify the complex neurovascular structures of the pineal region and the basal cisterns-quadrigeminal and ambient. A T2 fast- spin-echo (FSE) scan and 2 high spin gradient echo time of flight (TOF) scans with tracking spatial resolution pulses positioned for arterial or venous blood flow were performed at 2 mm thru plane and .57X.51mm in plane. These images were then subjected to processing and read thereafter by two independent radiologists to obviate the inter-observer variability. Statistical analysis was then performed to determine if 4T images allowed better visualization of
key neurovascular structures in the pineal region than 1.5 T images

10. Please choose your academic program: MD

11. What year are you in the program? 2

12. What was your role in this project? research coordinator and analyst

13. Date: 11/09/2010

Gabarain, Gabriel

**Lepow Day Abstract**

1. **Title:** Determination of physiological mechanisms for electrical wound therapy

2. **Presenter:** Gabriel Gabarain and Yu Kan Au

3. **Co-workers and Collaborators:** Jonathan Macnin, Bruce Kinley, Danli Lin, Dan Howe, Jeremy Dunning, Christian Zorman, Bradley Boggs, Kristi Henzel

4. **Advisor:**

5. **Departments:** APT Center of Excellence, Louis Stokes Cleveland VA Medical Center, Department of Orthopedics, Case Western Reserve University, Department of Biomedical Engineering, Case Western Reserve University

6. **Support:** Department of Veterans Affairs Rehabilitation Research & Development Service, Merit Review award F7129-R

7. **Institutions:** Louis Stokes Cleveland VA Medical Center, Case Western Reserve University

8. **Body of Abstract: (300 words or less)**

   The project objective is to determine the physiological mechanisms for effective electrotherapy in healing of ischemic wounds. The effects of varying electrical stimulation parameters are to be investigated using a chronic wound animal model. The findings are to be evaluated to determine the feasibility of translation of electrotherapy to clinical use by veterans with chronic wounds.

   The primary hypothesis is that electrotherapy promotes closure of ischemic wounds through promotion of angiogenesis, primarily through the sustained up-regulation of vascular endothelial growth factor (VEGF).

   Evaluation of electrotherapy variables are carried out using the Modular Stimulation System (MSS), a powered surface stimulation device incorporating
programmable and stimulation circuitry mounted onto a disposable flexible substrate. The control and stimulation components of the device are reusable and are combined with stimulating electrodes onto the flexible substrate.

In order to establish the effectiveness of ES in the treatment of chronic wounds, a rat (Rattus norvegicus) model is being used to compare the effect of various electrotherapy variable settings on a chronic wound model against a control, represented by the unaided healing of control wounds on the same animal. MSS devices for use in the animal model have electrodes patterned in a standardized shape and layout because the wound geometry and location are controlled. PCR analysis will be used to determine the expression of targeted wound healing genes including VEGF, TNF-alpha, Fibronectin, and Collagen 3A1.

As of the end of our involvement in the project, experimental challenges were still being addressed. The protocols for animal surgery and post-operative care were updated based on experimental experience in order to minimize infection risk and animal discomfort that may affect the rate of wound healing. Additionally, changes to the MSS and substrate design were made in collaboration with the engineering team. A protocol for making PCR standards and testing the quality of PCR primers was also developed for the measurement of the expression of targeted wound healing genes. During the fellowship period significant progress was made in the optimization of the MSS design, in the surgical procedure and in the post-operative care of the animals. These activities will facilitate the progress of the project. Evaluation of physiological mechanisms for effective electrotherapy is in progress.

10. Please choose your academic program: MD MS

11. What year are you in the program? 2

12. What was

1. Surgically created standardized wounds based on a chronic
**your role in this project?**

ischemic wound model. 2. Applied and secured the flexible, electrotherapy wound care devices over the standardized chronic wounds and performed weekly changes. 3. Monitored and provided supportive care for experimental animals. Formulated, mixed and administered pre- and post-operative analgesia and antibiotics. 4. Gathered and record

**13. Date:** 11/08/2010

**Gala, Raj**

### Lepow Day Abstract

<table>
<thead>
<tr>
<th>1. Title:</th>
<th>Effect of low oxygen tension and growth factors on postexpansion chondrogenesis</th>
</tr>
</thead>
<tbody>
<tr>
<td>2. Presenter:</td>
<td>Raj Gala</td>
</tr>
<tr>
<td>3. Co-workers and Collaborators:</td>
<td>Havalee Henry</td>
</tr>
<tr>
<td>4. Advisor:</td>
<td></td>
</tr>
<tr>
<td>5. Departments:</td>
<td>Department of Orthopaedics</td>
</tr>
<tr>
<td>6. Support:</td>
<td>NIH Grant 2R01DE015322</td>
</tr>
<tr>
<td>7. Institutions:</td>
<td>Case Western, BRB301A</td>
</tr>
</tbody>
</table>

**8. Body of Abstract: (300 words or less)**

**Background**

Cartilage remains a very difficult tissue to repair. Previous work has shown that low oxygen tension during expansion periods improves the chondrogenesis of articular chondrocytes. In addition, certain growth factors have also been shown to promote the chondrocyte phenotype and result in greater amounts and better quality of cartilage production in vitro.

**Goal and hypothesis**

The goal of this project is to produce a sufficient number of chondrocytes that make effective cartilage that can eventually be used for cartilage repair. It is hypothesized that low oxygen tension, along with a combination of growth factors will result in chondrocytes of higher chondrogenic potential.

**Methods**

Chondrocytes obtained previously were thawed and plated in different situations. The different growth solutions were: 10% FBS, 5% FBS, 5% FBS with FGF-2, or 5% FBS with FGF-18. In addition, each was also plated in either 21% (normal) or 10% (low) oxygen tension. The plating efficiency was measured for each condition immediately after thawing. After one week of expansion,
the cells were re-cultured and the plating efficiency was measured again. Cell counts were obtained after one week and after two weeks.

Results

The cells expanded in low oxygen tension along with FGF-18 had the highest cell counts after week 1 and week 2. Overall, the cells that were plated in low oxygen tension had a higher plating efficiency than cells plated in normal oxygen tension. The addition of the growth factors seemed to have no effect on the plating efficiency, but did result in an increase in doubling times (growth of the cells).

Conclusion

Oxygen tension has an effect on how well cells stick to the plate, with a lower oxygen tension resulting in a higher plating efficiency. FGF-18 shows the most potential for increasing doubling times, without having an effect on plating efficiency. Together they may best promote the chondrocyte phenotype.

| 10. Please choose your academic program: | MD |
| 11. What year are you in the program? | 2 |
| 12. What was your role in this project? | Performance of studies and/or experiments, Experimental design, Interpretation of data. I designed the experimental plan. I did all the cell culturing, all the cell counting, and all the data analysis. |
| 13. Date: | 11/09/2010 |

Gebhart, Jeremy

Lepow Day Abstract

1. Title: Predictive Anthropometric Measurements for Humeral Head Curvature
2. Presenter: Jeremy Gebhart
3. Co-workers and Collaborators: 
4. Advisor: 
5. Departments: Orthopaedics - Sports Health
6. Support: Crile Fellowship
7. Institutions: Cleveland Clinic Foundation
Background: To achieve proper conformity to the native articulating surface in shoulder replacements and in osteochondral allograft transplantation for the treatment of osseous defects to the humeral head, it is essential that the curvature of the humeral head of the allograft tissue match that of the native tissue. The purpose of this study was to investigate the value of various anthropometric measurements for predicting humeral head curvature.

Methods: 122 (64 female, 58 male; 61 right extremity, 61 left extremity) cadaveric humeri were obtained from the Hamann-Todd Human Osteological Collection. Specimens ranged from 20 to 35 years of age at the time of death (28.4 ± 4.2, mean ± SD). Specimens from this collection include height and weight as collected at the time of death. All humeri were scanned with a 3-dimensional laser scanner that has been shown to be accurate to within 0.005 inches (NextEngine, Santa Monica, California, USA). Linear measurements were made by choosing points on the three-dimensional scan and according to the recording standards for skeletal remains. Measurements included maximum length of humerus and epicondylar breadth. Humeral head curvature was determined by a custom computational...
code to fit a sphere to the articulating surface of the humerus.

Results: The coefficient of determination was determined for gender, age, height, weight, maximum humeral length, and epicondylar breadth. Patient height ($R^2 = 0.64$), epicondylar breadth ($R^2 = 0.69$), and gender ($R^2 = 0.62$) were most correlated with humeral head curvature.

Conclusion: If only a single measurement can be used to size the humeral curvature, patient height will give approximately the same accuracy as epicondylar breadth, and can more easily be obtained.
Background: Knee osteoarthritis (OA) is a major source of morbidity in the aging population with a prevalence of over 16% in people 45 and older. The Osteoarthritis Initiative (OAI) is a multi-center, four-year observational study focusing on OA incidence and progression. Using this cohort to gain insight into different patterns of progression would be valuable in guiding clinical treatment.

Objective: Our goal was to analyze patient-reported and performance measure outcomes from the OAI in order to characterize patterns of change in symptomatic OA. We hypothesized that we could demonstrate different patterns of progression, and that use of both patient-reported and performance measures would improve grouping of patients.

Methods: Patient-reported outcome measures included were the Knee Osteoarthritis Outcome Score (KOOS) subscores of function / sports & recreation (FSR), quality of life, knee pain and knee symptoms. Performance measures included were 20-m walk pace and repeated chair stand pace. Analysis was completed in three steps. First, annual changes in outcome measures at baseline and years 1 – 3 were modeled using linear regression. Second, the slopes of the linear regressions for all outcome measures were subjected to factor analysis. Third, patients were grouped using the outcome measures that best correlated with each factor via k-means cluster analysis.

Results: Factor analysis yielded two factors that correlated best with KOOS FSR and Chair Stand Pace and together accounted for 65% of the variability present in the outcome measures. Cluster analysis with these two variables yielded 7 total clusters. The resulting clusters fell into 3 broad groups of KOOS FSR change: two clusters improved, two clusters worsened and three clusters showed little-to-no change. Clusters with similar patterns of KOOS FSR change showed differences in trends for chair stand pace.
Conclusions: Our data show that patients can be successfully grouped in terms of patterns of osteoarthritis progression, and that both patient-reported outcome and performance measures must be considered when categorizing symptomatic progression of OA. Interestingly, some patients may have an improvement in patient-reported outcome while experiencing worsening of functional performance, and vice versa. Future analysis of demographics, patient characteristics and imaging will hopefully allow development of models to predict which pattern of symptomatic progression individual patients will experience. Such information would be invaluable in guiding clinical decision-making for patients with osteoarthritis.
dysfunction over time is not known.

**Methods**

Patients with a normal ejection fraction undergoing two echocardiograms, with a contemporary diastolic assessment, at least one year apart were included in the study. Clinical data was extracted from an electronic medical record using ICD9 codes and linked to echocardiographic measurements. Patients were categorized into diastolic class and class change over time. The primary outcome was the incidence of clinically diagnosed heart failure >6 months after the first echocardiogram. Logistic regression and neural network analysis was performed using NeuralTools, (Palisade Co., NY).

**Results**

Clinical and Echocardiographic data was available on 450 diabetic patients and 58 controls. The average age was 68 +/- 13 years, 57% were male. At baseline 2% had AF, 11% had HTN and 10% had CHF. Diastolic class worsened in 33% of diabetic patients compared to 16% of controls, p = 0.006. Incidence of the primary endpoint occurred in 45 (10%) patients. Abnormal diastolic function was
Associated with an incidence of heart failure of 12% versus 3.6% in controls, 95% CI 3 to 13, p = 0.047. A relationship between change in diastolic class over time and incidence of new heart failure was seen (Fig 1.) Logistic regression and neural network analysis indicated that age, presence of atrial fibrillation at baseline and diastolic class at baseline contributed to the incidence of heart failure.

**Conclusion**

Diabetic patients had a greater progression of diastolic function than controls. Abnormal diastolic function at baseline was associated with a higher incidence of heart failure. Progression of diastolic function was associated a stepwise incidence of clinical presentations with heart failure.

| 10. Please choose your academic program: | MD |
| 11. What year are you in the program? | 2 |
| 12. What was your role in this project? | Gathered data and made the poster. |
| 13. Date: | 11/11/2010 |

**Goodnough, Robert**

**Lepow Day Abstract**

1. **Title:** The Role of Macrophages in Vaccine Immunity against H. Pylori in Mice
2. **Presenter:** Robert Goodnough
3. **Co-workers and Collaborators:** Nayer Bagheri, PhD, Annette Wong, Hiroyuki Inoshita, MD, Lawrence Henry Goodnough
H. Pylori is a causative agent of peptic ulcer disease and gastric cancer. Vaccine prevention of infection can overcome the problems of antibiotic resistance, cost and logistics of treatment, and risk of re-infection. Integral to the pursuit of a feasible human vaccine is an understanding of the immune mechanism of a vaccine response, which in animal models has been shown to be mediated by CD4+ T cells, with the ultimate mechanism remaining elusive. The goal of this project was to explore the possible role of macrophages as the ultimate effector cell in vaccine immunity against H. pylori. Using conditional macrophage knock out “MAFIA” mice, we put forth the hypothesis that mice which had been immunized against H. pylori and then macrophage depleted before challenge with H. pylori would show greater colonization after a two week period than mice which had been immunized and challenged without macrophage depletion. A third control group of mice were not immunized but were challenged with H. Pylori. Each group consisted of five mice. Mice were immunized intranasally, using 100 micrograms of H. Pylori lysate along with 5 micrograms cholera toxin as adjuvant. Mice were macrophage depleted using the chemical dimerizer AP20187 daily for five days prior to challenge, with maintenance dosing every other day until sacrifice. Challenge was via oral gavage with 2x10^6 CFU of live H. pylori and 2 weeks later mice were sacrificed and stomach sections were homogenized for quantitative culture on blood agar plates. Frozen sections were also taken of each mouse stomach and spleen. Technical difficulties resulted in bacteria failing to grow; however the frozen stomach tissues have been sent to a collaborator for q-PCR quantification of H. pylori. Results: Pending Conclusions: pending.
### Lepow Day Abstract

1. **Title:** Effect of ciprofloxacin/dexamethasone versus ciprofloxacin/hydrocortisone on lipopolysaccharide induced experimental otitis media

2. **Presenter:** Amar Gupta

3. **Co-workers and Collaborators:** Charles Pudrith, Dusan Martin, G Michael Wall, Timothy Jung

4. **Advisor:**

5. **Departments:** Otolaryngology - Head and Neck Surgery

6. **Support:** Dean's Summer Research Award

7. **Institutions:** Loma Linda University School of Medicine

8. **Body of Abstract:** (300 words or less)

Otitis media is a general term used to describe any inflammatory process of the middle ear cleft. It is a prevalent condition in the pediatric population and the large majority of children suffer from at least one episode. While antibiotics have widely been used in the management of this condition, the addition of corticosteroids to older treatment protocols is now being investigated. In this study, topical ciprofloxacin with dexamethasone was compared to topical ciprofloxacin with hydrocortisone in the treatment of lipopolysaccharide induced otitis media with effusion in chinchillas. Otitis media with effusion was induced in 5 groups of chinchillas (n=61) by injecting 0.3 mL (1 mg/mL) of *Salmonella enteric* lipopolysaccharide into the superior bullae of each test animal. Each group was treated with 0.2 mL of test article at -2, 24, 48, and 72 hours relative to the lipopolysaccharide injection at 0 hours. Group 1 was treated with vehicle control. Groups 2-5 received 0.3% ciprofloxacin with either 0.1% dexamethasone (Group 2), 1% dexamethasone (Group 3), 0.1% hydrocortisone (Group 4), or 1% hydrocortisone (Group 5). The outcome of each treatment was measured at 120 hours post...
lipopolysaccharide injection by the amount of middle ear fluid present and by mucosal thickness. None of the test articles reduced middle ear effusion volume significantly (at either concentration) when compared to each other or to vehicle control. Ciprofloxacin 0.3% with dexamethasone 1% significantly reduced the mucosal thickness compared to the control group. The other test articles, however, did not reduce mucosal thickness in a statistically significant manner when compared to each other or to control. Further study is needed in both laboratory and clinical venues to quantify and compare the effects of these and additional corticosteroids in the treatment of otitis media.

10. Please choose your academic program: MD
11. What year are you in the program? 2
12. What was your role in this project? My role was to help carry out the animal experiments and help with writing of the manuscript.
13. Date: 11/09/2010

Gupta, Amar

Lepow Day Abstract
1. Title: Evaluating the Safety and Effectiveness of Percutaneous Acetabuloplasty
2. Presenter: Amar C. Gupta
3. Co-workers and Collaborators: 
4. Advisor: 
5. Departments: Neurointerventional Radiology
6. Support: Dean’s Summer Research Award
7. Institutions: Massachusetts General Hospital
8. Body of Abstract: (300 words or less) Purpose: To evaluate the safety and effectiveness of percutaneous acetabuloplasty in treating the pain and disability related to metastatic lesions of the acetabulum.
**Materials and Methods:** This IRB approved retrospective study examined 11 patients who underwent percutaneous acetabuloplasty in our hospital from April 2007 to June 2010. All patients gave informed consent prior to the procedure, and all records were HIPAA compliant. Chart review was performed to collect patient demographics and to assess pre- and post-treatment patient performance on the Visual-Analog Scale (VAS), Functional Mobility Scale (FMS), and Analgesic Scale (AS). Paired testing comparing the pre- and post-treatment scores for each patient was performed using the Wilcoxon signed rank test.

**Results:** There was a statistically significant decrease in patient VAS score (p=0.001) and FMS score (p=0.03) after treatment. There was no change in median AS scores pre- and post-treatment, although paired testing revealed a trend toward reduced analgesic use post-operatively (p=0.06). There was no clinically significant complication in this series.

**Conclusion:** Percutaneous acetabuloplasty appears to be safe and effective for improving the pain and decreased
mobility secondary to metastatic lesions of the acetabulum.

10. Please choose your academic program: MD

11. What year are you in the program? 2

12. What was your role in this project? Collected, organized, and analyzed data on percutaneous acetabuloplasty procedures performed in the Neurointerventional Department. Wrote the entirety of the paper including the abstract and all figures. Dr. Albert Yoo edited all work.

13. Date: 11/08/2010

Hahn, Elizabeth

Lepow Day Abstract

1. Title: Multi-Modality Brain Monitoring to Test for Parameters of Cerebral Vasospasm in SAH

2. Presenter: Elizabeth Hahn

3. Co-workers and Collaborators:

4. Advisor:

5. Departments: Neurosurgery

6. Support:

7. Institutions: Cleveland Clinic Foundation

8. Body of Abstract: (300 words or less)

Background

Control of intracranial pressure (ICP) and cerebral perfusion pressure (CPP) is the basis for traumatic brain injury (TBI) and subarachnoid hemorrhage (SAH) management. This and other recent studies, have shed doubt on the efficacy of this conventional ICP- and CCP- guided neurocritical care. There is evidence demonstrating the advantages in reducing mortality through the use of online brain tissue oxygen (PtiO2) monitoring.

Method

During surgery of intracranial aneurysms, monitoring of PtiO2 was performed using a polarographic microcatheter (Licox), which was placed in the vascular territory of the artery harboring the aneurysm. This information was used in a retrospective observational study to compare clinical
outcomes with trends in PtiO2 and other physiological parameters including cardiac output (CO), ICP and CPP.

Findings

Results are still being analyzed and cultivated, but preliminary understanding suggests that trends in PtiO2 and MAP (calculated from CPP) can predict ischemic episodes. Number and duration of ischemic episodes have been correlated with worsened clinical outputs and increased mortality rates.

Conclusions

As results are still being cultivated, it is difficult to formulate a significant conclusion. However, preliminary data suggests that patients respond with varying sensitivity in PtiO2 fluctuation to conventional ICP- and CPP-guided therapy. Additionally, data suggests that clinical outcomes are highly correlated to PtiO2 levels. This indicates that improving predictive ability about patients' sensitivity will ultimately reduce mortality and morbidity rates.

Lepow Day Abstract

1. Title: Immunological Biomarkers for Protection against TB disease
2. Presenter: Drisana Henry
3. Co-workers and Collaborators: Jayne Sutherland, Patrick Owiafe, Leopold Tientcheu Djomkam, Joseph Mendy, Adama Bojang, Marie Gomez, Sainabou Njie, Awa Mendy, Pa Kinteh, Oley Faal, Dr. Ifedayo Adetifa and the clinical TB team
4. Advisor:
5. Departments: Tuberculosis Immunology Laboratory and Tuberculosis Clinic
6. Support: Medical Research Council (UK), Grand Challenges in Global Health Program of Bill and Melinda Gates Foundation (BMGF)
7. Institutions: Medical Research Council (MRC), The Gambia, West Africa
8. Body of Abstract: (300) Background and rationale for doing the study:
Tuberculosis (TB), primarily caused by the bacteria *Mycobacterium tuberculosis* (MTB), is a major health concern and approximately 1/3 of the world’s population currently has a TB. Remarkably, only 3-5% of people who come in contact with TB-infected individuals develop active TB disease. The purpose of this study was to investigate the immunological biomarkers that confer resistance to the development of TB post-exposure.

Question or hypothesis that you addressed: Since there exist no reliable biomarkers for protective immunity against developing active TB disease, this study focused on identifying these biomarkers. Identification of these biomarkers will make it possible for individuals with latent infection to be accurately identified and treated before developing active disease. They will also aid in predicting responses of individuals to different TB treatment regimens and will be critical in the formulation and evaluation of novel TB vaccines.

Methods used to pursue this question/hypothesis: This study was comprised of two distinct components—clinical and laboratory. The clinical component consisted of visits to local villages to collect information and blood samples of (active) TB-infected patients and their household members. Patients and their families were followed for a period of two years in order to determine the incidence of secondary TB infection in household contacts. In addition to field studies, many patients and their families traveled to the MRC’s TB Clinic to receive examinations and treatment for TB infection. In the laboratory, samples were compared between household contacts that developed TB and those that did not. Techniques used to analyze these groups included Flow Cytometry, HLA Assays, Peripheral Blood Mononuclear Cells (PBMC) separation, RNA extraction, and whole blood assays (ELISA). These tests allowed us to determine the genetic links and immunological determinants of TB susceptibility.

Results: This study is currently in progress and results are not yet available. If they become available prior to the presentation of this research, they will be included.

Conclusions: Clinical and laboratory techniques were used to investigate the immunological biomarkers that serve as protective factors against developing active TB disease after exposure. Immunological profiles will allow susceptible individuals to be identified early and latent infection to be diagnosed and treated prior to developing active TB disease. Findings from this study will be used for numerous purposes such as TB vaccine and
mycobacterial drug development and will help to improve health in the developing world.

10. Please choose your academic program: MD

11. What year are you in the program? 2

12. What was your role in this project? I was involved in both the clinical and laboratory components of this research. I traveled with the clinical team to field sites. At these sites, I administered PPD TB skin tests, drew blood from patients, and filled out questionnaires. I also assisted the staff with patients at MRC's TB Clinic. In the laboratory, I primarily performed RNA extractions, HLA assays, and PBMC separation and analysis.

13. Date: 11/10/2010

Hirschtritt, Matthew

**Lepow Day Abstract**

1. **Title:** Electrocardiographic Profile Associated with Combined Lithium and Divalproex Sodium in Children and Adolescents with Bipolar Affective Disorder

2. **Presenter:** Matthew Hirschtritt, BA

3. **Co-workers and Collaborators:** Janine Arruda, MD; Jeannine Schuman, MD; Benjamin D Otto, BA; Amy S Nowacki, PhD; Christine A Demeter, MA; Brieana Rowles, MA; Robert L Findling, MD

4. **Advisor:**

5. **Departments:** Cleveland Clinic Lerner College of Medicine of Case Western Reserve University, Department of Pediatric Cardiology, Cleveland Clinic Foundation; Department of Psychiatry, Case Western Reserve University/University Hospitals Case Medical Center, Departments of Education and Quantitative Health Sciences, Lerner Research Institute, Cleveland Clinic

6. **Support:** Supported by NIH Heart, Lung and Blood Institute Grant: Ruth L. Kirschstein National Research Service Award Short-Term Institutional Research Training Grants (T35). The clinical trials on which these data are based were primarily supported by a Clinical Research Center Grant from the Stanley Medical Research Institute. Study medication was supplied in part by Abbott Laboratories.

7. **Institutions:** Cleveland Clinic, University Hospitals Cleveland, Case Western Reserve University

8. **Body of Abstract: (300 words or less)**

**Objective:** The primary goal of this study was to describe and explore changes in electrocardiographic (ECG) parameters among youths with a bipolar disorder (BPD) who were taking lithium (Li) and/or divalproex sodium (DVPX). This post-hoc data analysis uses data from a single, multistage trial to investigate changes in specific
ECG parameters during short-term combined and monotherapeutic use of Li and DVPX. **Method:** Youths, ages 5-17 years, were enrolled in an open-label trial of combined Li and DVPX for up to 20 weeks (stage 1), followed by a double-blind, randomized trial of Li or DVPX monotherapy for up to 76 weeks for participants who had achieved remission during combined use of Li and DVPX (stage 2). ECG parameters identified as being affected by these agents in the literature were extracted from standard 12-lead ECG tracings for subjects who had completed $\geq 8$ weeks treatment to analyze changes during each stage. **Results:** Eighty-seven subjects completed $\geq 8$ weeks of stage 1 and 23 completed $\geq 8$ weeks of stage 2 (Li+placebo, n=13; DVPX+placebo, n=10). Preliminary analyses reveal that combined Li and DVPX therapy (stage 1) was associated with a significant increase in the PR duration (mean difference [MD] $\pm$ standard deviation [SD]=4.4 $\pm$ 16.5 msec; $p=.016$) and QTc (MD $\pm$ SD=7.5$\pm$32.6 msec). There were no significant differences in ECG parameters from end of stage 1 to end of stage 2, for either the Li or DVPX arm. **Conclusion:** Combined and monotherapeutic use of Li and DVPX therapy was associated with statistically significant but clinically negligible changes in ECG parameters; however, subsequent monotherapeutic use of Li or DVPX was not associated with any significant changes in any of these parameters. Limited sample size in both arms of phase 2 may obscure possible changes in parameters because of
**Rationale:** Apolipoprotein A1 (apoA1) is the major HDL protein which mediates removal of cholesterol from peripheral tissues in a process called reverse cholesterol transport (RCT). However, apoA1 undergoes oxidative modification by the leukocyte enzyme myeloperoxidase (MPO) that renders it dysfunctional. Recombinant human apoA1 (in which four tryptophan residues were replaced by phenylalanine), called the 4WF isoform, is resistant to loss of function by MPO treatment *in vitro*.

**Hypothesis:** We hypothesize that the 4WF transgenic mice will be superior to wild type human-apoA1 transgenic mice in mediating RCT under inflammatory conditions.

**Methods:** Bone marrow macrophages are cholesterol loaded and labeled with acetylated LDL and \[^{3}H\]-cholesterol. Macrophages and MPO are resuspended in matrigel and injected subcutaneously into transgenic mice expressing either human apoA1 or the 4WF isoform. The mice
will then be injected subcutaneously with hydrogen peroxide. RCT will be assessed through measurement of plasma and fecal \[^{3}\text{H}\]-cholesterol radioactivity.

**Results:** Our *in vitro* studies show that apoAI can be modified in the MPO-containing matrigel plug when exogenous hydrogen peroxide (MPO co-substrate) is added. Macrophages remained viable in the matrigel even when incubated with high molar concentrations of hydrogen peroxide. Using transgenic mice expressing human apoA1, we have shown that mice injected with a suspension of matrigel, foam cells, and MPO led to impaired RCT when compared with controls injected similarly except without the MPO. We have also shown in apoA1 knock-out mice that s.c. injection with human apoA1 results in greater RCT to the plasma compared with injection using saline. We are currently genotyping transgenic mice expressing 4WF apoA1, and we hope to match these mice to mice expressing human apoA1 at similar expression levels.

**Conclusion:** We hope to determine that oxidative resistant 4WF apoAI is superior to wild type apoA1 in an *in vivo* model, thereby making “good cholesterol” *even better.*

| 10. Please choose your academic program: | MD |
| 11. What year are you in the program? | 3 |
| 12. What was your role in this project? | I am building and creating the in vivo model with the guidance of my research advisor, Dr. Smith. Once our model is completed, I will be testing our hypothesis using the in vivo model which I helped to create. If I am successful and am able to achieve my goals within this year of research, I will be the first author of any resulting publications. |
| 13. Date: | 11/09/2010 |

Huo, Siya

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**Lepow Day Abstract**

1. **Title:** Enhanced Depth Imaging Optical Coherence Tomography (EDI OCT) Evaluation of Choroidal Thickness

2. **Presenter:** Siya Huo
Background/Rationale: The choroid, found between the retina and sclera, serves as the major vascular supply of the outer retina that helps support its metabolic demand. However, due to its posterior location, clinical imaging of this layer has remained difficult. Recently, a technique dubbed Enhanced Depth Imaging (EDI) Optical Coherence Tomography (OCT) using already existing Spectral Domain OCT (SD-OCT) technology was described. This technique produces fast, non-invasive, in vivo, cross-sectional imaging of the choroid in which the entire thickness of the structure can be visualized and measured. Preliminary studies have already correlated changes in choroidal thickness on EDI OCT to a variety of pathologies, indicating the clinical and scientific promise of this imaging technique.

Objective: EDI OCT imaging published in the literature has only been performed on a single SD-OCT model (Heidelberg Spectralis), and no follow-up studies have been done using any of the other commercially available SD-OCT devices. We therefore proposing a study to compare choroidal thickness measurements amongst three SD-OCT models, including the Heidelberg Spectralis, Topcon 2000, and RTVue Optovue.

Methods: Sixty-six (66) eyes of 59 patients, with a variety of retinal diseases were imaged using EDI OCT on at least two of the three SD-OCT devices listed above. Choroidal thickness was measured as the distance from the retinal pigment epithelium (RPE) to the choroidal-scleral junction. Manual measurements were taken directly below the fovea as well as 2mm both nasally and temporally. Measurements from each device were statistically compared to each other using the paired student-t test.

Results: Twenty-five (25) males (42.4%) and 34 females (57.6%) with a mean age of 72.7 years were included in the analysis. Choroidal thickness was greatest
at the fovea (217.0 ± 101.1 um), slightly thinner temporally (195.4 ± 72.5 um), and thinnest nasally (155.7 ± 77.9) on all three devices. In general, choroidal thickness measurements did not differ significantly among the devices, except between the Topcon 2000 and RTV Optovue at both the subfoveal (mean difference 2.39 ± 7.90 um, p=0.03) and nasal (mean difference -3.67 ± 7.50 um, p=0.0005) locations.

Conclusions: Our data suggests that choroidal thickness measurements obtained by EDI OCT using various SD-OCT devices generally are comparable and do not differ significantly from each other.

Lepow Day Abstract

1. Title: Characterization of nontypeable Streptococcus pneumoniae isolates from 1994-2008
2. Presenter: Jessica Ing
4. Advisor: 
5. Departments: Pediatric Infectious Disease
6. Support: 
7. Institutions: Texas Children's Hospital
8. Body of Abstract: (300 words or less) Streptococcus pneumoniae is a major cause of bacteremia, meningitis, pneumonia, sinusitis, and acute otitis media in children. Although optochin sensitivity, bile solubility, and Quellung testing are the standard in identifying and differentiating pneumococci, there are many reports of nontypeable pneumococci that do not meet one or more of these criteria. Our objective was to characterize 53 isolates previously described at Texas Children’s Hospital between 1994 and 2008 with updated antisera for the Quellung test, optochin sensitivity, and molecular
typing methods. Amplification of *ply* and *psaA* genes was done, as well as multilocus sequence typing (MLST) to determine sequence types, serotypes, and to construct phylogenetic trees. Of the 53 isolates, 38 were optochin sensitive, *psaA* and *ply* positive, and could be eventually serotyped by Quellung testing after multiple passages. Twenty of these were identifiable as serotype 6 with an antisera pool that was recently added. Three isolates were optochin sensitive, *psaA* and *ply* positive, were not serotypeable, but had MLST profiles with singular sequence types and thus could be identified as true pneumococci. Fifteen isolates were optochin resistant. Three of these were still *psaA* and *ply* positive, not serotypeable despite multiple passaging, and could not be identified by MLST. However, phylogenetic trees based on sequences from these strains clustered them with genuine, serotypeable pneumococci rather than nontypeable strains. Characterization of the remaining strains remained inconclusive. The results indicate that although there have been improvements in identification methods through the years, there still exist unresolved issues in the classification of pneumococci despite the use of genotypic and phenotypic methods in combination. Furthermore, we found that strains identified as nontypeable or atypical by traditional methods can still occasionally be genotypically classified and identified.

| 10. Please choose your academic program: | MD |
| 11. What year are you in the program? | 2 |
| 12. What was your role in this project? | I completed the majority of the laboratory research. I had some assistance from the lab tech, Linda Lamberth as well as the micro lab at Texas Childrens Hospital, and was advised and mentored by Kristina Hulten, Edward Mason, and Sheldon Kaplan. |
| 13. Date: | 11/10/2010 |

Lepow Day Abstract

1. Title: Effect of iron on the progression of nonalcoholic fatty liver disease
2. Presenter: Jeffrey Jacobs
3. Co-workers and Collaborators: Jeffrey Jacobs
Nonalcoholic fatty liver disease (NAFLD) is the most common cause of chronic liver disease in the United States. NAFLD is strongly associated with obesity and insulin resistance, and is estimated to affect more than 30% of the population. NAFLD describes hepatic steatosis in people who have consumed less than 20 grams of ethanol per week. NAFLD also includes non-alcoholic steatohepatitis (NASH), which includes hepatocyte injury and hepatic inflammation and is a more severe form of disease. The disease progression is described by the two hit hypothesis: first the liver accumulates fat due to insulin resistance, which is followed by a second hit of oxidative stress, possibly partially caused by excess iron deposition. Excess iron deposition in the liver can lead to the production of reactive oxygen species, which can then cause lipid peroxidation and cellular damage. The excess iron and cellular damage can activate Kupffer cells and lead to an inflammatory process which can lead to further liver damage and activation of hepatic stellate cells, required for fibrinogenesis. This pathological accumulation of iron can, over time, cause liver dysfunction and even cirrhosis and hepatocellular carcinoma. Less well known is the role iron accumulation plays in other chronic liver diseases such as hepatitis C and NAFLD. Our hypothesis is that hepcidin mediated iron retention leads to lipid peroxidation, apoptosis, and stellate cell activation. We are investigating...
The effects of iron on non-alcoholic fatty liver disease. To test this we are performing immunohistochemistry studies to determine if iron retention has these effects on liver cells. We will be staining with antibodies to ferroportin and CD68 to determine the level of iron retention. The level of apoptosis in relation to the amount of iron deposition will be evaluated using TUNEL staining. Double staining for iron and 4-HNE, which is indicative of lipid peroxidation and thus oxidative stress, will help establish the amount of lipid peroxidation relative to iron deposition. To test the amount of hepatic stellate cell activation, which is implicated in fibrinogenesis, double staining for iron and α-smooth muscle actin, a marker for stellate cell activation, are being performed.
can be effective. We conducted this study to determine the incidence and character of neurological trauma among urban, rural non-Amish, and Amish children to better target prevention programs in our region.

Methods: With IRB approval 1481 patients admitted to our institution with head, neck, or spine injuries between 1/1/97 and 5/31/10 were extracted from the Rainbow Trauma Registry. Adequate information for analysis was available for 1355 patients who were then categorized based on three designations - Amish/Non-Amish, Rural/Urban, and Mechanism of Injury. We compared these groups using a Z-test for two proportions, $\chi^2$-test for goodness-of-fit, and T-tests for unequal samples.

Results: The Z-test revealed that Amish patients make up a significantly greater proportion of our patient pool than expected. Chi-square comparisons showed that the distribution of injury mechanism varied significantly between Amish and Non-Amish patients ($p < 0.001$), primarily due to the Animal mechanism, but not between Amish, and non-Amish rural ($p > 0.05$). No significant differences in average age were found between Amish and non-Amish patients, either overall or within categories of mechanism of injury.

Conclusion: Amish children have a higher incidence of neurological trauma than their non-Amish peers. The primary mechanistic difference between the two groups is the number of Amish children experiencing animal-related trauma. This seems to be due to the increased exposure of Amish children to animals, as they share a similar level of risk for this type of injury as rural non-Amish children.

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<th>10. Please choose your academic program:</th>
<th>MD MS</th>
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<tr>
<td>11. What year are you in the program?</td>
<td>2</td>
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</table>
What was your role in this project?

My role was to gather and collate the data from computerized and paper-format medical charts and consult sheets, perform statistical analysis on the collected data, and be the primary writer on the paper that was based on our results.

Date: 11/09/2010

**Lepow Day Abstract**

<table>
<thead>
<tr>
<th>1. Title:</th>
<th>Characterizing Colon Cancer Secreted Protein-1 (CCSP-1): A novel Secreted Protein Highly Induced in Human Colon Neoplasia</th>
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<tr>
<td>2. Presenter:</td>
<td>Yunnan Jiang</td>
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<tr>
<td>3. Co-workers and Collaborators:</td>
<td>Stephen P. Fink</td>
</tr>
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<td>4. Advisor:</td>
<td></td>
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<tr>
<td>5. Departments:</td>
<td>Cleveland Clinic Lerner College of Medicine, Department of Medicine and Ireland Comprehensive Cancer Center</td>
</tr>
<tr>
<td>6. Support:</td>
<td>Joseph S. Silber student summer fellowship, American Cancer Society</td>
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<tr>
<td>7. Institutions:</td>
<td>Case Western Reserve University</td>
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Cancers of colon and rectum are the second leading cause of both cancer incidence and death in adults in the United States. Screening for colorectal cancer (CRC) is a highly effective intervention that reduces cancer-specific mortality by detecting cancer at an early stage when surgical curing rate is high. Colon Cancer Secreted Protein-1 (CCSP-1) is a novel candidate biomarker of human colon neoplasia whose expression is upregulated 54-fold in colon cancer, the function of which is unknown. CCSP1 might be a novel, positively regulated target of Wnt signaling. Through the use of both CCSP1-inducible as well as CCSP1 knocked out cell lines previously constructed in the Markowitz laboratory, the aim of this study is to test whether CCSP-1 protein overexpression in colorectal cancers promotes the motility of cancer cells by interacting with cytoskeleton. In CCSP1-induced cells, phalloidin staining for actin expression showed increased formation of actin cables 48 hours after the induction of CCSP-1. Wound healing (scratch) assay showed increased cell migration when CCSP-1 expression was induced. In the knock-out cell line, phalloidin staining for actin showed reduced formation of lamellipodia. Wound healing assay showed reduced cell migration in the knockout cell lines. However, Western
analysis failed to detect changes in the expression and phosphorylation of Rho 16, 24, 48 hr after CCSP-1 expression was induced by tetracycline treatment. We did not find sufficient evidence supporting an effect of CCSP-1 on cell migration or cytoskeleton.

References

10. Please choose your academic program: MD
11. What year are you in the program? 2
12. What was your role in this project? Summer research fellow
13. Date: 11/10/2010

Kanters, Arielle

Lepow Day Abstract
1. Title: Incidence of Inguinal Hernia Recurrence in Adolescents after High Ligation of Sac
2. Presenter: Arielle Kanters
3. Co-workers and Collaborators: Christopher Campbell, Todd Ponsky, MD
4. Advisor:
5. Departments: Division of Pediatric Surgery
6. Support:
7. Institutions: Rainbow Babies & Children's Hospital

8. Body of Abstract: (300 words or less) Introduction: The current approach to treating indirect hernia repair differs between pediatric and adult surgeons. Most pediatric surgeons attempt a high ligation of sac, whereas adult surgeons use mesh to close off areas of muscle weakness. While there are definitive treatments for pediatric patients and adult patients, there is some
discrepancy as to how hernias in the adolescent population (patients between the ages of 11 to 18) should be treated. The argument has been made that adolescents should be treated with high ligation of sac as this will result in low rates of hernia recurrence.

**Study Design:** This retrospective study considers recurrence of inguinal hernias in the adolescent population a minimum of 2 years after surgery. One hundred and fifteen patients between the ages of 11 and 18, who underwent high ligation of sac for indirect hernia repair, were contacted to determine postoperative complications. A 6-question survey was conducted over the phone. It assessed pain, numbness and bulging associated with the surgical repair. Suspected and confirmed recurrences were also evaluated.

**Results:** Of the 50 responses collected thus far, 2 patients (4%) reported pain at the surgery site, no patients reported numbness at surgery site, and 3 patients (6%) reported a bulge in the groin on the same side as the hernia repair. Overall there were 3 reports (6%) of suspected hernia recurrence on the same side, and 1 report (2%) of confirmed hernia recurrence.

**Conclusions:** Initial results suggest there is a confirmed hernia recurrence of 2% following high ligation of sac in adolescents. Given the limited adolescent sample population, involvement of additional medical institutions is necessary before we can compare with other studies. As of right now, we do not have high enough power to compare to adult studies that consider recurrence after mesh repair.

| 10. Please choose your academic program: | MD MS |
| 11. What year are you in the program? | 2 |
| 12. What was your role in this project? | I was responsible for determining eligible participants, contacting participants, and collecting and analyzing data. Once the data collection is completed, I will also be responsible for writing the |
**Lepow Day Abstract**

1. **Title:** Expert-led discussion and self-tracked health behavior change for the promotion of well-being and burnout prevention in first-year medical students in a problem-based learning curriculum: a pilot elective

2. **Presenter:** Rachel Katz

3. **Co-workers and Collaborators:** Erik Yannone (research assistant)

4. **Advisor:**

5. **Departments:** Psychiatry

6. **Support:**


7. **Institutions:** University Hospitals, Case Western Reserve School of Medicine

8. **Body of Abstract: (300 words or less)**

   **BACKGROUND**

   The American medical student population shows a higher percentage of depression, distress, burnout and suicide ideation than their age-matched peers. Medical students who experience burnout are more likely to report unprofessional behavior and less altruistic values. Burnout can be the product of long-term distress and low quality of life, and we believe students can acquire the tools to constructively deal with stress and anxiety, thereby preventing or helping with burnout. We are developing a unique elective to help Case Western first-year medical students combat burnout through expert-led discussion and self-tracked health behavior change, providing skills and coping mechanisms to carry throughout their medical careers.

   **METHODS**
Experts in physical and mental health, and medical professionals will lead eight 1.5-hour meetings, each with a different theme. Each meeting will begin with a thirty-minute presentation from the experts, followed by interactive discussion among panelists and participants. The first three meetings will focus on three aspects of personal health care, after which each participant will choose one in which to make a positive health behavior change, which they will track with a partner through the rest of the elective. Two evaluative tools, the Maslach Burnout Inventory and the Medical Education Quality of Life Questionnaire, will be administered before and after the elective, as well as to a control group of volunteers from the same class, at the same time interval. Data sets will be compared before and after the elective in individual groups as well as to each other for changes in levels of burnout and quality-of-life.

RESULTS
Results will be collected at the beginning and end of the 8-week elective, which will take place between March and May 2010.

CONCLUSIONS
None at this time.

| 10. Please choose your academic program: | MD |
| 11. What year are you in the program? | 2 |
| 12. What was your role in this project? | I have designed the study, performed the literature review, will be running the eight sessions, will be collecting the data and writing the majority of the paper when the data is collected. |
| 13. Date: | 11/09/2010 |

Kent, Jillian

Lepow Day Abstract

1. Title: Effect of Time to Intervention on the Outcome of Image Guided Percutaneous Thrombectomy in the setting of Clotted Surgical Dialysis Access Sites
2. Presenter: Jillian Kent
3. Co-workers Sonali Mehandru, MD; Abdus Sattar, PhD
<table>
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<tr>
<th><strong>4. Advisor:</strong></th>
<th>Dept. of Radiology; Dept. of Biostatistics &amp; Epidemiology</th>
</tr>
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<tr>
<td><strong>5. Departments:</strong></td>
<td>No funding was set aside for this project. I was awarded a stipend of $3530 as part of the NIH T35 training grant.</td>
</tr>
<tr>
<td><strong>6. Support:</strong></td>
<td>University Hospitals/Case Medical Center; Metrohealth Medical Center</td>
</tr>
<tr>
<td><strong>7. Institutions:</strong></td>
<td>University Hospitals/Case Medical Center; Metrohealth Medical Center</td>
</tr>
</tbody>
</table>

**8. Body of Abstract: (300 words or less)**

**TITLE:** Effect of time to intervention on the outcome of image guided percutaneous thrombectomy in the setting of clotted surgical dialysis access sites.

**AUTHORS (LAST NAME, FIRST NAME):** Mehandru, Sonali; Kent, Jillian; Sattar, Abdus; Prologo, John D.

**INSTITUTIONS (ALL):** Radiology, University Hospitals Case Medical Center, Cleveland, OH, United States.

**KEYWORDS:** hemodialysis vascular access, Thrombectomy.

**ABSTRACT BODY:**

Background/Rationale
Vascular access dysfunction remains the leading cause of hospitalization in dialysis dependent patients, and most surgical access sites are ultimately lost due to thrombotic events that cannot be resolved. The optimal time window for intervention in the setting of an occluded surgical access has yet to be defined.

Hypothesis
It is our hypothesis that the patient’s need for emergent dialysis should govern the triage of thrombectomy procedures performed in interventional radiology, and that the “sooner is better” assumption is unfounded.

Materials and Methods
Records from patients who underwent percutaneous thrombectomy of occluded surgical hemodialysis access sites in interventional radiology during 2007-2010 were retrospectively reviewed from two institutions, University Hospitals/Case Medical Center and Metrohealth Medical Center. At both institutions, the initial request for thrombectomy of a clotted surgical access was documented by electronic order entry. The time of procedure was documented on PACS, and the outcome of the procedure described
in the official report. Elapsed time was taken as a continuous value in the model. A binary value (0,1) was assigned to each procedure outcome representing either unsuccessful or successful restoration of flow. The outcomes were analyzed using a multivariable logistic regression model accounting for elapsed time to procedure, age, gender, and surgical access type (graft or fistula).

Results

377 procedures were performed on 363 access sites (348 synthetic grafts and 29 fistulae). 290 were performed within 24 hours of the initial request and 87 after. The success rates for thrombectomies performed were 95.9% for grafts and 75.8% for fistulae (94.4% overall). An unadjusted analysis indicated no statistically significant relationship (5% level) between elapsed time to procedure and binary outcome value. After fitting the multivariable logistic regression model, access type (graft v. fistula) was the only significant (p<0.001) predictor of success outcome.

Conclusion

Our results suggest that time to procedure following surgical dialysis access thrombosis does not effect outcome in the setting of percutaneous image guided thrombectomies performed in interventional radiology. The only significant predictor of outcome is type of surgical access.

10. Please choose your academic program: MD

11. What year are you in the program? 2

12. What was your role in this project? I coordinated the Metrohealth Medical Center division of the study with the help of Dr. John D. Prologo, Interventional Radiology attending at UH. With the help of Dr. Prologo, I developed the MHMC IRB proposal based off of a previously submitted proposal to UH drafted by S. Mehandru and J.D. Prologo. Most importantly, I was the sole person responsible for data collection at MHMC.

13. Date: 11/10/2010

Khwarg, Juewon

Lepow Day Abstract

1. Title: Detecting Diabetic Retinopathy in at-risk populations using the PanOptic Ophthalmoscope (DRPOO) - evaluating the accuracy of non-mydriatic direct ophthalmoscopy by non-specialists versus analysis of dilated fundus photos

2. Presenter: Juewon Khwarg

3. Co-workers and Collaborators: Suber Huang, MD, MBA

4. Advisor: 

5. Departments: UH Ophthalmology
Diabetic retinopathy (DR) is currently the leading cause of blindness among working age adults, despite the fact that vision loss is preventable with early detection and therapy. Studies have shown that at least half of diabetic patients do not get the recommended annual screenings from ophthalmologists, perhaps due to lack of money or time. Meanwhile, DR screening modalities used in the majority of primary care practices have been shown to have low sensitivity and specificity. Recently, a new ophthalmoscope, called the PanOptic, has been developed that allows vastly expanded visualization of the retina in an undilated eye. If it is found that a non-ophthalmologist using the PanOptic can detect DR with an accuracy comparable to an ophthalmologist’s exam, it can offer a low-cost, easily adoptable and widely available alternative for assessing the risk of vision loss in diabetic patients.

The objective of this study is to assess the accuracy of DR detection with the PanOptic when used by three groups: primary care physicians, medical students and undergraduate students. Each study patient will have both eyes examined by a primary care physician, a medical student and an undergraduate student using the PanOptic. Then, the patient will have a dilated fundus photograph taken of each eye. A retina specialist will analyze these images, and their findings will serve as a gold standard. The findings of the different examiners will be compared to the findings of the retina specialist to assess for sensitivity and specificity in the detection of DR.

The study population will consist of diabetic, uninsured patients, as they are at highest risk of having previously undetected DR.

The study is currently being run through a series of monthly free clinics, and study completion is anticipated in 2012.
Please choose your academic program: MD

What year are you in the program? 2

As a co-principal investigator, I was responsible for writing the protocol and all study related documents, as well as obtaining IRB approval. I will also be responsible for the recruitment of patients, running the study, and assisting in data analysis.

Date: 11/09/2010
Kim, Hidong

**Lepow Day Abstract**

1. Title: Comparison of Frailty Scores in Geriatric Outpatients as Assessed by Two Different Models of Frailty
2. Presenter: Hidong Kim
3. Co-workers and Collaborators: Hidong Kim, Patricia Higgins, Thomas Hornick
4. Advisor:
5. Departments: Geriatric Research Education and Clinical Center
6. Support: Dean's Summer Research Award
7. Institutions: Case Western Reserve University School of Medicine, Frances Payne Bolton School of Nursing, Louis Stokes Cleveland Veterans Affairs Medical Center

8. Body of Abstract: (300 words or less)

Aims: Frailty among older patients is associated with higher risks of morbidity and mortality. A challenge for healthcare providers is assessing whether or not a patient is frail, as there is no universally accepted definition or set of criteria for frailty. In this study, geriatric outpatients were evaluated for frailty by two different current models of frailty.

Intervention and Methods: Older adults arriving for previously scheduled appointments at the Louis Stokes Cleveland VA Medical Center Geriatrics Clinic were evaluated for frailty by the Fried and Gill frailty models. Each subject was evaluated by both models. The evaluations consisted of questionnaires and physical performance tests.

Data analyses: SPSS 15 was used for statistical analyses.

Results: A total of 60 male veterans were evaluated. The convenience sample was 62%
African American. Mean age = 82.9 (range = 64-93), MMSE = 24.5 (range = 8-30), BMI = 26.0 (range 14.9- 50.9). Frailty classifications by model: Fried = 71% moderate or severe; Gill = 35% moderate or severe. Nine subjects were determined to be frail by each of the Fried and Gill models of frailty. Only 3 subjects, however, were determined to be frail by both the Fried and Gill models of frailty. Among subjects who were determined to be frail by the Fried model, grip strength was the single criterion most correlated with frailty. For subjects determined to be robust, the concordance between the Fried and Gill models was higher than for subjects determined to be frail.

Conclusion: The findings show little concordance between the Fried and Gill models of frailty in identifying frail subjects compared with identifying robust subjects. Such disparities likely result from different criteria used to evaluate frailty in each model. For example, the Fried frailty model employs physical activity questionnaires and physical performance tests, while the Gill frailty model consists only of physical performance tests. Our results indicate that the determination of frailty is highly dependent on the frailty model used in the evaluation. Results of frailty evaluations by the Fried model also suggest that grip strength is the best single criterion for determining frailty.

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<tr>
<td>11. What year are you in the program?</td>
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<tr>
<td>12. What was your role in this project?</td>
<td>Interviewed subjects, tested subjects, analyzed data.</td>
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<td>13. Date:</td>
<td>11/10/2010</td>
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LaSota, Emily

**Lepow Day Abstract**

1. **Title:** Comparative Effectiveness Analysis Of Treatment Options for Pituitary Microadenomas in Acromegaly
2. **Presenter:** Emily A. LaSota
3. **Co-workers and** Nicholas F. Marko, MD, Amir Hamrahian, MD, Robert J. Weil, MD
<table>
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<th>Collaborators:</th>
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<td>4. Advisor:</td>
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<tr>
<td>5. Departments:</td>
<td>The Brain Tumor and Neuro-Oncology Center, Department of Neurosurgery</td>
</tr>
<tr>
<td>6. Support:</td>
<td>Crile Fellowship</td>
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<td>7. Institutions:</td>
<td>Cleveland Clinic, Cleveland, OH</td>
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### 8. Body of Abstract: (300 words or less)

Acromegaly is a syndrome of excess growth hormone, most often caused by a GH-secreting pituitary adenoma, that results in organ overgrowth and physical deformity. Untreated, acromegaly reduces life expectancy by approximately 10 years, with death commonly resulting from cardiovascular, cerebrovascular, metabolic, and respiratory comorbidities. Since there is no uniform standard of care for acromegaly, alternate management strategies requiring variable durations of therapy are often employed before achieving biochemical control. This comparative effectiveness research (CER) study aimed to integrate efficacy data with cost and quality of life data in order to more completely inform clinical decisions regarding alternate treatment modalities when treating patients with acromegaly (resulting from GH-secreting pituitary microadenomas). Strategies examined included surgery, radiotherapy, stereotactic radiosurgery (SRS), and pharmacotherapy using somatostatin analogues (SA) [lanreotide, octreotide] or growth hormone receptor antagonists [pegvisomant]. A management decision tree was constructed based on current treatment recommendations and data; from this, five unique strategies, each consisting of 4 potential steps, were selected for further analysis (with subsequent steps only necessary if the previous modality had failed to achieve control). Efficacy was determined by assembling the currently available data on the ability of treatments to obtain biochemical control. Cost estimations for drugs were determined by Average Wholesale Price, while procedural costs were obtained from the Healthcare Cost and Utility Project. Quality of Life (QoL) data were obtained from independent studies utilizing the AcroQoL...
questionnaire. Individual reatment modalities were ranked in each of the three domains, according to highest rate of success, lowest cost, and highest QoL; scores in all three domains, weighted equally, were combined to determine the most effective treatment options and to formulate the best potential approach to treating acromegaly. Surgery proved most effective, exhibiting highest efficacy, lowest cost, and highest QoL. The remaining therapies followed (in order of effectiveness): pegvisomant, SA, and SRS.

10. Please choose your academic program:
   MD

11. What year are you in the program?
   2

12. What was your role in this project?
   Expanding on an idea from my advisor, Dr. Marko, I collected and assembled all data, wrote the paper, and helped with revisions.

13. Date: 11/10/2010

Lee, David

**Lepow Day Abstract**

1. **Title:** Development of bronchial OCT imaging to identify premalignant changes in the pulmonary epithelium

2. **Presenter:** David W. Lee

3. **Co-workers and Collaborators:**

4. **Advisor:** Jeffrey Kern, M.D. and Zhilin Hu, Ph.D

5. **Departments:** Pulmonary Medicine & Biomedical Engineering (respectively)

6. **Support:** T-32 grant

7. **Institutions:** University Hospitals & CWRU (respectively)

8. **Body of Abstract:** (300 words or less)
   Optical coherence tomography (OCT) is a real-time imaging procedure that provides high-resolution, cross-sectional, subsurface imaging of tissue by measuring backscattered infrared light. OCT uses low-power wavelengths of light that range from 600 nm to 2000 nm, where most tissue components have low absorption. When these wavelengths of light interact with tissue surfaces, they scatter and form an image based on the difference in optical properties of the tissue. The time delay and intensity of the back-scatter light are measured to form OCT images. OCT imaging is used to diagnose lesions in the retina, gastrointestinal tract, and cardiovascular system. However, applications for OCT imaging in studying pulmonary tissue are still in development.
   We developed novel OCT probes and tested the probes on bronchiole tissue samples, supplied by the Department of Pulmonary Medicine. After collecting OCT images from healthy bronchiole tissue samples, we identified key histological features on healthy tissue, such as the epithelial lining, the basement membrane, and the lamina propria.
membrane, and cartilage. Next, we looked at bronchiole tissue samples with premalignant and malignant changes, and identified key histological features on these tissue samples. Afterwards, we directly compared the OCT images obtained from the tissue samples to pathologic findings of the respective human lung resections, which were supplied by the Department of Pathology. We scored the OCT images as normal or abnormal, and the diagnosis was verified by pathologic sampling. We have started to establish an OCT image database defining the characteristics of normal, metaplasia, dysplasia, carcinoma in situ, and invasive carcinoma. Currently, we do not have a large collection of samples and images. However, we can distinguish normal lung tissue from pathological lung tissue. We will continue to construct an OCT image database. The success of this project will lead to a clinical trial to detect early or premalignant pulmonary epithelial lesions.

10. Please choose your academic program: MD

11. What year are you in the program? 2

12. What was your role in this project? I helped prepare the tissues for taking images, operated the probe, took images, and cleaned the images.

13. Date: 02/03/2010

Lee, Tamara

Lepow Day Abstract

1. Title: Continuous intravenous infusion of fentanyl suggests improved safety over morphine in preterm infants undergoing laser therapy in retinopathy of prematurity

2. Presenter: Tamara Lee

3. Co-workers and Collaborators: Faruk H. Orge MD; Michele Walsh MD; Kimberly Gordon RN; Jeffrey N. Bloom MD

4. Advisor: 

5. Departments: Ophthalmology

6. Support: 

7. Institutions: Case Western Reserve, University Hospitals Rainbow Babies & Children’s Hospital

8. Body of Abstract: (300 words or less) Purpose: Currently, there is no consensus regarding the optimal mode of anesthesia for retinopathy of prematurity (ROP) laser treatment. Studies have established that general anesthesia with intubation confers significant risk in preterm neonates, and that opioid analgesia with benzodiazepine sedation is ideal when the NICU is equipped for such surgical procedures. While small retrospective studies have looked at the safety and efficacy of morphine (n=130), ketamine (n=11), and remifentanil (n=6), no studies have looked at fentanyl for ROP laser surgery. Methods: This is an observational, non-randomized, retrospective study of 33 consecutive preterm neonates undergoing laser treatment of ROP in the NICU. Eighteen
patients received morphine and 15 patients received fentanyl. In both groups, midazolam was used on a case-by-case basis. All data were documented at 5 minute intervals for all surgeries.

**Results:** Mean gestational age was 24.7 and 24.0, and mean birth weight was 637.3 and 631.3 in the morphine and fentanyl groups, respectively. Change in ventilation status was noted in 41.18% of patients in the morphine group and 20.00% of patients in the fentanyl group. Temperature instability (outside of 36.5-37.4° range) was noted in 5.56% of patients in the morphine group and no patients in the fentanyl group. Apneic, bradycardic, and desaturation events were respectively 5.15, 1.53, and 1.68 times more common in the morphine group.

**Discussion:** Our data suggests continuous fentanyl infusion is safer compared to morphine for preterm infants undergoing ROP laser therapy in the NICU setting.

**Conclusions:** Compared with morphine, fentanyl sedation for ROP laser treatment results in fewer complications.

| 10. Please choose your academic program: | MD |
| 11. What year are you in the program? | 3 |
| 12. What was your role in this project? | I wrote and submitted an IRB application, with help from my advisor and the clinical research coordinator. I conducted a chart review for clinical information specific to my project. I conducted all statistical analyses using JMP statistical software. I prepared this abstract and I am currently writing a manuscript. I submitted this abstract to AAPOS national conference with Dr. Orge's guidance. |
| 13. Date: | 11/11/2010 |

**Lepow Day Abstract**

1. Title: Direct regulation of Human CD4+ T Cell Activation by Mycobacterium tuberculosis Components
2. Presenter: Daniel Linfesty
3. Co-workers and Collaborators: Qing Li, Xuedong Ding Liao, Roxana Rojas and Henry Boom
4. Advisor:
5. Departments: Division of Infectious Disease
6. Support: NIH/NIAID RO1 A127243 and NIH/NHLBI RO1HL055967
7. Institutions: Case Western Reserve University

8. Body of Abstract: (300 words or less) 

**Introduction:** Mycobacterium tuberculosis (Mtβ), the causative agent of tuberculosis (TB) is one of the leading causes of death among adults worldwide. Mtβ is an intracellular pathogen that infects antigen-presenting cells (APC). Control of Mtβ infection is achieved by cooperation between infected APC and T cells. Activation of aß TCR+ CD4+ T cells has a
central role in protection. *Mtb* is known to regulate CD4+ T cell activation indirectly through manipulation of APC function. However, mycobacterial molecules traffic from the infected APC to the extracellular compartment where they may interact directly with T cells. Our group has recently identified two types of *Mtb* molecules with direct effects on human CD4+ T cells, i.e. glycolipids and lipoproteins. The goal of the present study was to identify other mycobacterial molecules with direct regulatory effects on CD4+ T cell activation.

**Methods:** In this study purified *Mtb* subcellular fractions and purified cell wall associated molecules were screened for inhibition or upregulation of TCR triggered CD4+ T cell activation. To prevent indirect effects mediated by APCs, cells from the human CD4+ T cell line, Jurkat, were stimulated with α-CD3 (10µg/ml) and α-CD28 (1µg/ml) antibodies in presence of different concentrations of *Mtb* components. IL-2, a marker of T cell activation, was measured in culture supernatants by ELISA. IL-2 levels in cultures from untreated or *Mtb* component- treated T cells were compared.

**Results:** Among 14 *Mtb* components screened, cell wall associated-arabinogalactan, was found to have inhibitory effect on anti-CD3 triggered IL-2 secretion from Jurkat cells. Arabinogalactan inhibited IL-2 secretion in a dose-dependent manner, triggering 46% inhibition (CI 95% = 40-52%) at 12.5 µg/ml and 88% inhibition (CI 95% = 74-103%) at 100 µg/ml.

**Conclusions:** In addition to evading the immune system through manipulation APC function, our results support the hypothesis that *Mtb* reduces protective immune responses through direct inhibition of CD4+ T cell activation. A better understanding of this new mechanism of immune regulation by *Mtb* may lead to new targets for more effective TB vaccines and treatments.

| 10. Please choose your academic program: | MD |
| 11. What year are you in the program? | 2 |
| 12. What was your role in this project? | Set up screening process including finding conditions for screen, finding optimal conditions for T cell stimulation and resuspending Mtb components. Run experiments, collect and organize data. Analyze Data and produce graphs. |
| 13. Date: | 11/12/2010 |

**Liu, Jane**

**Lepow Day Abstract**

| 1. Title: | Vein Graft Patency in Lower Extremity Arterial Bypass |
| 2. Presenter: | Jane Liu |
| 3. Co-workers and Collaborators: | Marilou Bastan, M.D., Timur Sarac, M.D. |
4. Advisor: 

5. Departments: Vascular Surgery

6. Support: 


7. Institutions: Cleveland Clinic Foundation

8. Body of Abstract: (300 words or less)

   Background: Vascular disease of the lower extremity is a disabling and painful condition that affects up to 10% of American adults (1). Patients at risk include those with diabetes, hypertension, hyperlipidemia, and smokers (2). Up to 25% of patients will require re-vascularization (1), and vein bypass grafts connecting pre-occlusion and post-occlusion arteries are indicated in patients with claudication, limb ischemia, and/or tissue necrosis (3). The latest study examining the causes of bypass failure was conducted in 1991 (4), and more recent studies have looked at isolated features such as vein grafting technique and early detection (5,6). Our study is an updated comprehensive look at the factors contributing to graft patency rates following revascularization.

   Methods: 640 patients at Cleveland Clinic Foundation underwent lower extremity arterial bypasses between the years 1996 and 2009. We looked at pre-operative and post-operative factors such as co-morbidities and medications, as well as intra-operative details such as vein graft size, orientation, placement, composition, anticoagulant use, doppler, and arteriogram use. Vein grafts were followed and assessed for primary patency,
primary assisted patency, and secondary patency, as well as limb salvage and location of graft failure. Results will be analyzed with Kaplan-Meier methods as patients were lost to follow-up or deceased.

Discussion: Vein bypass procedures are time-consuming, costly, and invasive procedures. In order to optimize outcome, we must examine the factors that improve the long-term patency of the grafts. Our study offers an in-depth, up-to-date look at the factors involved in bypass procedures. These results will help determine the progress in vein bypass procedures in recent years, contribute to understanding of re-vascularization outcomes, and help guide clinical decision-making for future procedures.

10. Please choose your academic program: 
   MD

11. What year are you in the program? 
   2

12. What was your role in this project? 
   I am compiling data from the charts, writing the paper, and modifying the study methods as I work through the chart review.

13. Date: 
   11/10/2010

Magnetta, Michael

Lepow Day Abstract

1. Title: Performance Limits of a Microfabricated Artificial Lung

2. Presenter: Michael Magnetta

3. Co-workers and Collaborators: Abigail Vinson

4. Advisor:

5. Departments: APT Center

6. Support: T32

7. Institutions: VA Medical Center

8. Body of Abstract: (300 words or less) 
   The human lung provides a maximum O₂ and CO₂ flux of 2-6 L/min. Current artificial lungs are capable of providing only 250-400 ml/min of flux with an efficiency of 0.01 – 0.02 ml/(s.cm³). This limits their effectiveness [1]. This insufficiency is due to a relatively decreased surface area, smaller surface-area-to-volume ratio, and greater
wall thickness of artificial lungs [1]. Advances in the micromachining of silicone [2] have made it possible to create efficient artificial lungs with feature sizes similar to that of the human lung theoretically capable of providing scalability through increased efficiency.

This project characterized a micromachined artificial lung device made of polydimethylsiloxane by quantitatively measuring the oxygenation of animal blood passed through the device. It was hypothesized that this microfabricated artificial lung would have a greater efficiency than conventional artificial lungs. Modeling and fabrication techniques [3] were utilized to design and construct a silicone artificial lung prototype that was both efficient and scalable. The device consisted of synthetic blood capillaries (20 mm diameter) separated from airflow channels by a thin (15 mm) silicon membrane.

The device was tested by pumping deoxygenated blood through the device, where it was allowed to undergo gas exchange with room air. Blood flow rates ranging from 0.3-1.5 mL/min were tested for efficiency. The blood’s pH, O₂, CO₂, and metabolic characteristics were measured and recorded prior to entering and directly after leaving the device with an iSTAT Clinical Portable Analyzer. The efficiency of the tested device ranged from 0.15-0.40 mL/(s.cm³) with increasing rates of blood flow resulting in better O₂ transfer efficiency. The device tested had greater O₂ gas transfer properties than that of devices currently in use. Future work will include further design iterations to further optimize oxygen exchange, reduce clotting and to improve device scaling (to 2-4 L/min flux) to accommodate in vivo oxygen demands.

10. Please choose your academic program: MD

11. What year are you in the program? 2

12. What was your role in this project? I was a co researcher on this project with Abbie Vinson and participated in device manufacture and testing.

13. Date: 11/09/2010

Mani, Preethi

**Lepow Day Abstract**

1. **Title:** Favorable Shifts in LDL Particle Size after Treatment with Pioglitazone are Associated with Less Progression of Coronary Atherosclerosis in Patients with Type 2 Diabetes

2. **Presenter:** Preethi Mani


4. **Advisor:**

5. **Departments:** Cardiovascular Medicine

6. **Support:** Research partially supported by T32 grant from CCF Department of Cardiovascular Medicine

7. **Institutions:** Cleveland Clinic Foundation

**Background:** While conventional lipid parameters are known to correlate with progression of coronary atherosclerosis, the impact of measures of LDL particle size and concentration are unknown. It has been accepted that small LDL particles are more highly atherogenic than large LDL particles, but the effect of LDL particle size modification on progression of coronary atherosclerosis has not been studied.

**Methods:** PERISCOPE evaluated plaque progression with intravascular ultrasound in 360 diabetic patients treated with pioglitazone or glimepiride. The relationship between changes in LDL particle size and number determined by NMR spectroscopy and plaque burden was also characterized and was correlated with...
Results: Pioglitazone was associated with increases in large LDL particle number (+61.2±4.4 v +15.7±4.2%, p<0.001) and mean LDL particle size (3.6±0.2 v 0.7±0.2%, p<0.001) and decreases in small LDL particle (-37.5±3.9 v -2.8±3.7%, p<0.001) and total LDL particle number (-15.1±1.8% v -1.5±1.7%, p<0.001). Progression of percent atheroma volume (PAV) was associated with increases in small LDL particles (r=0.18, p<0.001) and the total number of LDL particles (r=0.12, p=0.03). Increases in large LDL particle number(r=-0.17, p=0.002) and mean LDL particle size (r=-0.21, p<0.001) were associated with less disease progression. Substantial regression was associated with a greater increase in LDL particle size compared with progression (3.3±0.4% v 1.7±0.4%, p=0.006). The highest tertile of increase in large LDL number(p=0.02) and mean LDL size (p<0.001) and decrease in small LDL number (p<0.001) were each associated with plaque regression. In patients with intensive lowering of LDL-C <=70 mg/dL, a greater increase in mean LDL particle size remained associated with less progression of PAV (-0.89±0.48% vs. 1.01±0.44%, p=0.004). Furthermore, in patients whose LDL-C decreased, greater progression of PAV was observed when the number of large LDL particles decreased (0.69±0.30 vs. -0.13±0.29%, p=0.05) and number of small LDL particles increased (0.85±0.43 vs. 0.09±0.24%, p=0.12). Multivariable analysis revealed that the change in LDL mean particle size independently predicted disease progression (p=0.003).

Conclusion: Measures of LDL particle size and number predict plaque progression in diabetic patients, even in patients whose LDL-C appears to be well controlled. These measures may highlight patients who require intensive risk modification strategies beyond control of LDL-C.

Publication expected from project:
Mani P, Uno K, Thornton J, Kupfer S, Perez A, Tuzcu EM,
Hazen SL, Nissen SE, and Nicholls SJ
"Favorable Impact on LDL Particle Size in Response to Treatment with Pioglitazone is Associated with Less Progression of Coronary Atherosclerosis in Patients with Type 2 Diabetes" (in progress)
Poster presentations:
Uno K, Mani P, Thornton J, Kupfer S, Perez A, Tuzcu EM, Hazen SL, Nissen SE, and Nicholls SJ "Favorable Impact on LDL Particle Size in Response to Treatment with Pioglitazone is Associated with Less Progression of Coronary Atherosclerosis in Patients with Type 2 Diabetes" CCF, Cleveland Clinic Lerner Research Institute Research Day, 10/2010 (Winner, Best Poster Award)

10. Please choose your academic program:
   MD

11. What year are you in the program?
   3

12. What was your role in this project?
   I began this project, which utilized data collected in PERISCOPE trial coordinated by Dr. Nicholls' lab. I was able to analyze and interpret the results of the statistical analysis and formulate it into a manuscript that is being finalized for submission to a high impact cardiovascular journal (I will be first author on this paper).

13. Date:
   11/15/2010

Mao, Frances

Lepow Day Abstract

1. Title:
   Intra-operative glucose levels and its association with developing post-operative surgical site infections following spine surgeries

2. Presenter:
   Frances Mao

3. Co-workers and Collaborators:

4. Advisor:

5. Departments:
   Cleveland Clinic Center for Spine Health, Neurological Institute

6. Support:

7. Institutions:
   Cleveland Clinic Lerner College of Medicine

8. Body of Abstract: (300 words or less)
   Purpose: Post-operative wound infections following major surgical procedures continue to be a significant source of morbidity and mortality in the United States. Current recommendations from ICU and cardiac surgery management indicate that
aggressive management of intra-operative glucose levels result in lower rates of surgical site infections. This study is a retrospective cohort analysis to determine the incidence of surgical site infections following elevated intra-operative glucose levels during spine surgeries.

Methods: Peri-operative glucose levels and infection control surveillance data were analyzed for 2208 patients who underwent cervical, thoracic, or lumbar spine surgical procedures at the Cleveland Clinic Center for Spine Health between March 2005 and March 2010.

Results: Out of 2208 patients, 112 (5.1%) developed a surgical site infection during the 30 day post-operative period. Non-infected patients had a mean intra-operative glucose level of 132.11 mg/dl (95% CI 130.72 – 133.5) compared to infected patients with a mean intra-operative glucose level of 130.95 mg/dl (95% CI 126.03 – 135.87 mg/dl). An independent two sample t-test found no significant difference in mean intra-operative glucose level between these two groups (p = 0.6523). Univariate logistic regression revealed a risk ratio per unit glucose of 1.00116 (95% CI 0.9953 – 1.0075, p = 0.7081). Chi-square analysis found no association between high glucose level (>110 mg/dl) and surgical site infection (chi square = 0.232, p = 0.6304). Follow-up analyses will be repeated to account for diabetes status.

Conclusions: We did not find a significant association between elevated intra-operative glucose levels and a higher incidence of post-operative surgical site infection. Our results add to previous case-control studies exploring the same association in neurosurgery. Because the causes of surgical site infection are multi-factorial, the role of other peri-operative variables in decreasing SSI incidence should be explored.
11. What year are you in the program?
2

12. What was your role in this project?
I was the primary person that worked on proposal writing and data collection. My adviser conceived the idea, and after discussion with him, I wrote and submitted the IRB application and it was approved by the Cleveland Clinic IRB Office in May 2009. I gathered the data from the relevant databases and plan on analyzing data with statisticians in the Neurological Institute.

13. Date: 11/10/2010

Marmor, Rebecca

Lepow Day Abstract

1. Title: Double mastectomy: Motivations and concerns of women with breast cancer
2. Presenter: Rebecca A. Marmor
3. Co-workers and Collaborators: Sean Brugman (Co-worker); Dr. Robert Shenk (Collaborator); Dr. Hooman Soltanian (Collaborator)
4. Advisor: 
5. Departments: Genetics
6. Support: Departmental Funds
7. Institutions: University Hospitals Case Medical Center

Purpose: Despite the fact that overall survival after breast conserving therapy is equivalent to bilateral mastectomy, recent studies have demonstrated an increase in contralateral prophylactic mastectomy (CPM) amongst breast cancer patients with unilateral disease. The purpose of this study is to identify patient-reported factors which influence the decision to undergo CPM.

Methods: Under an IRB approved protocol, women who were treated at University Hospitals Case Medical Center with CPM for unilateral breast cancer were invited to participate in this qualitative study. To date, open-ended interviews have been conducted with 11 women, with an expected sample size of 24 women. Interviews were audio-taped, transcribed verbatim, and analyzed to identify underlying themes related to the patients’ decision for CPM.

Preliminary Results: Data analysis suggest that patients’ decisions are influenced primarily by the 5 factors: 1) past history of breast-related health
issues: 2) fear of cancer recurrence; 3) perception of bilateral mastectomy as the optimal treatment for breast cancer; 4) desire to achieve a good cosmetic outcome; and 5) information gathered outside of the context of their physicians’ offices. Surgeons’ recommendations were not an important factor influencing patients’ decisions. Decisions to undergo CPM are often made before the patients meet with their breast surgeons to discuss treatment options;

Preliminary Conclusion: Results from this study provide information that can be used by breast surgeons to better advise patients about treatment options. As some women appear to use non-medical sources to make CPM decision, further analyses will focus on how to best provide patients with the information they need to make their surgical treatment decisions.

10. Please choose your academic program: MD
11. What year are you in the program? 3
12. What was your role in this project? Co-Principal Investigator
13. Date: 11/09/2010

Masters, Frank

Lepow Day Abstract

1. Title: Differential frequency of mEPSCs in semilunar granule cells and granule cells suggests that semilunar granule cells may contribute to epileptic pathology
2. Presenter: Frank Masters
3. Co-workers and Collaborators: Ben Strowbridge
4. Advisor: 
5. Departments: Neuroscience
6. Support: Crile Grant
7. Institutions: Case Western Reserve University School of Medicine
8. Body of Abstract: (300 words or less) Epileptic seizures that originate in the hippocampus likely are the result of a pathophysiological reorganization
of synapses within the dentate gyrus, however there is much controversy surrounding exactly how this process occurs. Previous work by Williams and Larimer, et al., 2007 suggests that the larger dendritic expanse and excitatory electrophysiology of semilunar granule cells (SGCs) as compared to granule cells (GCs) may predispose these cells to epileptic behavior in the dentate gyrus. The present study focuses on the synaptic connections between innermolecular layer interneurons (INs), GCs, and SGCs to discern whether their spontaneous activity and synaptic connections contribute to the intrinsic and morphological differences between SGCs and GCs. After using differential interference contrast microscopy and two-photon fluorescence to characterize these cells in rat hippocampal slices, we employed voltage-clamp recordings to evaluate the spontaneous excitatory and inhibitory inputs each of these cell types receives. Bath applied TTX blocked spontaneous spike-evoked postsynaptic currents (PSCs) and revealed the underlying miniature synaptic events. Granule cells exhibited significantly lower miniature PSC frequency than other cell types, but with little change in overall excitatory amplitude. The lower frequency of miniature excitatory PSCs in GCs,
compared with SGCs, is in disagreement with the large
dendritic arborization of SGCs. In addition, we found a
pronounced decrease after TTX in the amplitude and
frequency of IN spontaneous inhibitory PSCs which
indicate that these neurons receive inhibition from other
areas of the dentate gyrus. The experimental evidence in
our study that SGCs receive more excitatory connections
than GCs in the dentate gyrus suggests that SGCs may be
an epileptogenic target for synaptic reorganization in
epileptic pathology.

10. Please choose your academic program: MD
11. What year are you in the program? 2
12. What was your role in this project? Experimental planning, work, and data analysis
13. Date: 11/11/2010

Mehringer, Jamie

Lepow Day Abstract
1. Title: Assessing Pediatric Primary Care Needs in the Sacred Valley of Peru: Toward a sustainable medical alliance
2. Presenter: Jamie Mehringer
3. Co-workers and Collaborators: Satoko Kanahara, Yvonne Chasser, Marcella Luercio, Elena Wagner, Alida Gertz, MD, MPH, Ning-Tsu Kuo, PhD, PharmD, Sangeeta Krishna, MD
4. Advisor: 
5. Departments: Cleveland Clinic Foundation, Department of Pediatrics
6. Support: 
7. Institutions: Case Western Reserve University School of Medicine, Cleveland Clinic Lerner College of Medicine
8. Body of Abstract: (300 words or less) Background: The Sacred Valley is one of the poorest districts in Peru. Located in a remote area of the Andes Mountains, the district has a high burden of infant
mortality and child malnutrition. A group of medical professionals and students from the U.S. have collaborated with the communities of the Sacred Valley to assist in delivering ambulatory healthcare through annual, month-long medical missions.

**Objective:** Our objectives were to: 1) assess the pediatric medical needs in the communities of the Sacred Valley, Peru, and 2) assist local healthcare workers in providing appropriate healthcare and health education to patients.

**Design/Methods:** IRB approval was obtained from the Cleveland Clinic, and a letter of support was obtained from the local government and medical director within the Sacred Valley region, in order to collect and subsequently report on aggregate patient data collected during medical visits. The medical campaign was advertised to patients through posters and radio announcements in the months prior to our arrival. Patients of all ages were seen in an ambulatory setting in medical camps organized in 11 villages from June 1-24, 2010. Demographic and basic medical data were collected at registration and de-identified pediatric data subsets were analyzed.

**Results:** Five hundred and seventy pediatric patients were seen, of which 60% were female and 40% were male. According to the WHO growth standards for children below 5 years of age, 30.1% and 36.4% were found to be below the 10th percentile for weight and height, respectively. The most common categories of chief complaints were: gastrointestinal (37.4%), respiratory (21.9%), ophthalmologic (15.1%), and dermatologic (10%). Two hundred and ninety-three (51.4%) patients were given albendazole for treatment of suspected or confirmed intestinal parasitic infection, and 196 (34.4%) were given multivitamins.

**Conclusions:** Malnutrition is a serious concern for children living in resource-limited mountain villages in Peru. The high prevalence of parasitic infection is likely a contributing factor. Future work will focus on continued collaboration with the
community to secure safe and clean water sources as well as education on nutrition, water sanitation, and early child development.

10. Please choose your academic program: MD

11. What year are you in the program? 2

12. What was your role in this project? My role in this project included collection, entry, and analysis of data.

13. Date: 11/18/2010

Michelson, Andrew

Lepow Day Abstract

1. Title: Clinical significance of Topoisomerase II Expression in Acute Myeloid Leukemia

2. Presenter: Andrew Michelson

3. Co-workers and Collaborators: Erik Koegle, Dr. Ram Ganapathi

4. Advisor:

5. Departments: Department of Translational Hematology and Oncology Research

6. Support: Dr. Marukh Ganapathi

7. Institutions: Taussig Cancer Institute, Cleveland Clinic

Background: Firstline treatment for acute myeloid leukemia (AML) routinely involves the usechemotherapeutic agents that preferentially target topoisomerase II (Topo II)as a means of inhibiting tumor cell proliferation and improving clinical outcomes. The goal of this study was to determine whether the relative expressionof Topo II isozymes alpha and beta contain prognostic significance for patients with AML. Methods: Bone marrowaspirate or purified RNA from 268 patients was obtained from the South WesternOncology Group (SWOG) and used for quantitative Real-Time PCR analysis. The foldexpression of Topo II alpha and beta were calculated using beta-2-microglobulin(B2MG) as an endogenous control and compared to Kasumi, an AML cell culturemodel. Results: Of the 268 patient samples analyzed, 29 had levels of Topol alpha, beta, or B2MG that were undetectable (Threshold cycle >40). In the remaining 239 evaluablepatients, the average-relative expression of Topo II alpha and beta was 0.4-times (range ± SD: 0.0063-7.27±0.96)and 0.95-times (range ± SD: 0.15-2.65 ±1.18) that found in the Kasumi AML model,respectively. Thirty-nine patients expressed higher levels of Topo II beta thanalpha, while the remaining 200 patients expressed higher amounts of Topo llalpha than beta (range alpha/beta: 0.36-2.65). The correlation with clinical outcomes of Topo II.
II expression for the coded patient information is now pending analysis from the statistical center at the SWOG. **Conclusions:** AML patients express marked differences in the relative expression of both Topo II alpha and beta. The results following statistical analysis from the SWOG will help determine whether the relative expression of Topo II alpha, beta, or their ratio is associated with prognostic significance or treatment-response in patients with AML.

10. Please choose your academic program: MD

11. What year are you in the program? 1

12. What was your role in this project? I created the experimental design, chose positive controls, synthesized the patient products required for qRT-PCR, isolated RNA from bone marrow aspirate and ran sample qRT-PCR experiments to verify data. I also performed some data analysis and quality control measures.

13. Date: 11/09/2010

Miller, Philip

**Lepow Day Abstract**

1. **Title:** Disclosure of Positive HIV Status and Sources of Emotional Support in Namakkal, Tamil Nadu, India

2. **Presenter:** Philip Miller and Dora Horovitz

3. **Co-workers and Collaborators:** Dr. N.M. Samuel

4. **Advisor:**

5. **Departments:** CWRU - School of Medicine

6. **Support:** We received a grant from CWRU, and a great deal of help, translation and advice from Dr. N.M. Samuel and the staff of the C.A.R.E Health Center in Namakkal, India.

7. **Institutions:** Case Western Reserve University, CARE Health Center

8. **Body of Abstract: (300 words or less)** This project sought to determine the feasibility of conducting a survey of people living with HIV/AIDS (PLWHA) at the C.A.R.E. (Concern for AIDS Research and Education) Health Center in Namakkal, India. Namakkal is a rural village in a district with disproportionately high HIV prevalence relative to the rest of the country. The researchers developed a 13-question survey to gather information about client demographics, perceptions of stigma, HIV status disclosure, and sources of emotional support. The survey and informed consent document were written in English and translated into Tamil. 43 HIV positive adult clients of the C.A.R.E. Center currently taking Anti-Retroviral Therapy, 40 women and 3 men, participated in the study. The majority of participants were over the age of 35, and the average length of known infection was 6.9 years.

As this was a feasibility study, the primary focus was on assessing the effectiveness of the study design for this setting rather than on data analysis. During the course of the study several problems were identified with the survey, and with its
administration. The Western-style survey format seemed problematic for many of the participants, who may not have been previously exposed to this type of questionnaire. Further training should have been provided by the researchers for the C.A.R.E. Center staff members on how to best administer the survey. Some of the questions in the survey were unclear and/or culturally inappropriate. Due to these factors much of the data collected was invalid. Other problems encountered included: Difficulty obtaining study approval from two regulating bodies in different countries, language barriers between the researchers, research assistants and study participants, and difficulty communicating and coordinating with project collaborators abroad. Though cross-cultural research is difficult under the best of circumstances, other student researchers can learn from these mistakes and avoid similar pitfalls.

10. Please choose your academic program: MD

11. What year are you in the program? 2

12. What was your role in this project? Dora and I identified advisers and the research site, conducted background research, developed the survey, obtained CWRU IRB and CARE Foundation Ethics Committee approval, traveled to Namakkal, oversaw administration of the survey, and compiled and analyzed the data together.

13. Date: 11/08/2010

Mitchell, Keisha

**Lepow Day Abstract**

1. Title: Low Dose Prostaglandin E1 as a Treatment for Ductus Arteriosus-Dependent Congenital Heart Anomalies

2. Presenter: Keisha Mitchell

3. Co-workers and Collaborators: Lourdes Prieto, MD, Chris Belotti, MD, Shanna Botos, CPNP

4. Advisor:

5. Departments: Pediatric Cardiology


7. Institutions: Cleveland Clinic Foundation

8. Body of Abstract: (300 words or less) Newborns dependent on a patent ductus arteriosus (PDA) to maintain pulmonary or systemic circulation are placed on prostaglandin (PG) E1 at doses varying from 0.015 to 0.05 ug/kg/min. Limited published data suggests that
the lower dose is as effective with decreased side effects. Since May 2009, the pediatric cardiology at CCF has treated all newborns prenatally diagnosed, or diagnosed shortly after birth with PDA-dependant CHD, with low dose PG (0.015 ug/kg/min). At this dose the incidence of apnea is exceedingly low, and neonates do not typically require elective intubation. The initial data shows that patients on low dose PG have a lower incidence of ventilation related complications, less hypotension, and decreased need for volume resuscitation and inotropes. Using data from clinical records on EPIC, patients were matched based on diagnosis, weight, surgery performed, and other medical complications. A control patient (high dose PGE1) before the protocol (i.e. before May 2009) was matched with a recent patient (low dose PGE1) and their clinical courses were compared. This included days of intubation, apneas, transport BP or airway complications, days in the hospital, etc. It was found that there was a significant difference in the clinical courses/outcomes between low dose and high dose PGE1 patients. At this point, the study is in the initial phase of statistical analysis.

| 10. Please choose your academic program: | MD |
| 11. What year are you in the program? | 2 |
| 12. What was your role in this project? | Collected and analyzed data Matched high dose (control) patients and patients from the new protocol (low dose). |
| 13. Date: | 11/09/2010 |

Moh, Calvin

**Lepow Day Abstract**

1. **Title:** The Effects of Chronic Mannitol Infusions through the Carotid Artery in Wild-type Mice

2. **Presenter:** Calvin Moh

3. **Co-workers and Collaborators:** Sandy Richardson

4. **Advisor:**

5. **Departments:** Pathology

6. **Support:**
### Alzheimer's Disease

Alzheimer's disease is a severe, tragic condition of the elderly. Currently, there is no cure for the disease, and a better understanding of the mechanism behind this process is necessary to achieve a cure. We propose that opening and closing of the blood-brain barrier can lead to brain pathology and expedite the development of Alzheimer's disease. To better understand this mechanism, we investigated the effects of daily mannitol infusions through the carotid artery in wild-type mice. Carotid artery lines were surgically installed in 12 wild-type mice. 6 of the mice were assigned to a saline control group, while the other 6 mice were assigned to a mannitol experimental group. Once a day, these mice were infused with either saline or 25% mannitol in saline solvent for 21 days. Each day, the weight of the mouse before infusion and the amount and type of fluid infused were recorded. After 21 days, the mice were placed in a T maze behavioral experiment and the results were analyzed. Once the data was collected, mice were sacrificed and perfused, and paraffin sections of the mice brains were extracted for immunohistochemistry. We did not find a significant difference in behavior between mannitol treated and control mice. Immunohistochemistry showed increased gliosis in mannitol treated mice versus control mice. In the future, we propose higher concentrations of mannitol infusions and selection of a more aggressive breed of experimental mice.

### Homocysteine and Cardiovascular Disease

Cardiovascular disease is a leading cause of morbidity and mortality, and plasma homocysteine levels are an independent risk factor for cardiovascular and other diseases. While the mechanisms by which homocysteine acts are not entirely clear, it is known that one of these mechanisms involves covalent modification of proteins through the formation of disulfide linkages with cysteine residues in the protein, in a similar fashion to the formation of disulfide bonds with cysteine residues within proteins.
and between proteins. This study is part of an ongoing effort to identify the specific proteins involved in homocysteinylation, so that links between homocysteine and cardiovascular disease can be elucidated. We treated 50-1,000 ug of purified recombinant proteins with 500 uM 35S-labeled homocysteine at 37°C for 5 hours. Following incubation, proteins were resolved by reducing and non-reducing SDS-PAGE to demonstrate the presence or absence of disulfide linkages between the protein and 35S-labeled homocysteine, and the radioactivity of washed protein was measured to quantitatively assess reaction product. Albumin was used as a positive control, as its tendency to be homocysteinylated has been well characterized in prior studies. The first protein studied was STAT3, a transcription factor involved in cytokine signaling and the inflammatory response. Results from this study were largely inconclusive due to limitations resulting from insufficient protein availability. However, when human a-thrombin was homocysteinylated, a small amount of homocysteinylation was detectable, corresponding to 0.20 moles of homocysteine disulfide linkages per mole of thrombin. Thrombin is a terminal enzyme in the coagulation cascade and plays a role in thrombotic events such as acute myocardial infarction and deep vein thrombosis. This is a promising result, and we believe that future studies with STAT3, thrombin, and other proteins will clarify the role of homocysteine in the pathogenesis of cardiovascular disease.

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<tr>
<th>10. Please choose your academic program:</th>
<th>MD</th>
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<tr>
<td>11. What year are you in the program?</td>
<td>2</td>
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<tr>
<td>12. What was your role in this project?</td>
<td>All experiments involving STAT3, and initial studies with thrombin, were performed by me. Experimental design and production of starting materials were performed partly by me, with assistance from Armend Axhemi and Patricia DiBello. Latest results with thrombin are courtesy of Caroline Gallo, and overall guidance was provided by Donald Jacobsen.</td>
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<tr>
<td>13. Date:</td>
<td>11/08/2010</td>
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Montgomery, Brian

**Lepow Day Abstract**

1. **Title:** Hybrid simulation of pelvic examination: A comparison study looking at two approaches to giving medical students needed experience.

2. **Presenter:** Brian Montgomery

3. **Co-workers and Collaborators:** Michael D. Smith, M.D., F.A.C.E.P.

4. **Advisor:**

5. **Departments:**

6. **Support:**

   1. Pugh CM, Obadina ET, Aidoo KA. Fear of causing harm: use of mannequin-based simulation to decrease student anxiety prior to interacting with female teaching associates. Teach Learn Med. 2009 Apr-Jun;21(2):116-20. 2. Powell HS, Bridge J, Eskesen S, Estrada F, Lay M. Medical students’ self-reported experiences performing pelvic, breast, and male genital examinations and the
Problem: A large percentage of medical students are uncomfortable with performing the pelvic exam\(^1\). One of the only predictors of confidence in performing a female pelvic exam is the number of pelvic exams a student has performed\(^2\). The problem is there are fewer and fewer opportunities for medical students to get the practice and experience they need. This is partially due to the appropriate cessation of allowing medical students to perform pelvic exams on unconsented anesthetized female patients\(^3\). It also has to do with an overall shying away by physicians and patients from allowing medical students to perform procedures.

Objectives: The objectives of the project are to increase students’ perceived level of comfort with performing the pelvic exam, students’ competency with the pelvic exam, and the students’ ability to make real patients comfortable during a pelvic exam.

Description of Project: Fourth-year medical students doing an acting internship through MetroHealth’s ED were randomly divided into two groups and given a survey assessing their comfort level with the pelvic exam. The students were then asked to perform one pelvic exam on either a plastic pelvic trainer or on the hybrid simulation (plastic pelvic trainer plus a standardized patient). The scenario of both the task trainer and hybrid simulation was a routine pelvic exam on a patient with no pathology and the actress behaved as if she wasn’t experiencing any significant pain or discomfort. While performing the exam the students were assessed on their skills by faculty using a checklist. The students then filled out another comfort level survey. At the end of their rotation, the students were observed performing a pelvic exam on a real patient in the ED. The students did another comfort level survey.
Faculty used a competency checklist to assess student’ skills and real patients filled out comfort level surveys after receiving the pelvic exam. 

**Findings to Date:** All the data has been collected and is being compiled into a spreadsheet for statistical analysis.

**10. Please choose your academic program:** MD

**11. What year are you in the program?** 2

**12. What was your role in this project?** I helped develop our study question and project through Scholars Collaboration in Teaching and Learning (SCTL). I took a significant amount of time to do a thorough literature search and find and modify the survey tools and competency checklist that were used in the study. I helped run every data gathering session involving the acting intern students.

**13. Date:** 11/09/2010

Moradzadeh, Nathaniel

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**Lepow Day Abstract**

1. **Title:** The Impact of Blood Pressure Control toward the Outcome of Heart Transplant Recipients

2. **Presenter:** Nathaniel Moradzadeh

3. **Co-workers and Collaborators:** Jon Kobashigawa, Ariel Moradzadeh, Matthew Kawano

4. **Advisor:**

5. **Departments:** Heart Institute

6. **Support:**

7. **Institutions:** Cedar-Sinai Medical Center

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**Purpose:** Hypertension is a known risk factor for patients with cardiovascular disease. It is not known to have the same impact in patients postheart transplant. The immunosuppressive medications such as calcineurin inhibitors increase blood pressure (BP) and cause kidney injury, which can further complicate the hypertensive state. BP measurements in the heart transplant clinics may not be reliable as patients are told to hold their medication to obtain trough levels. Subsequently, this causes patients’ BP to rise when they are seen in clinic. Therefore, we sought to determine the association between the number of BP medications and outcomes after heart transplantation. We further assessed whether
there was a protective effect from any single BP medication as has been reported for ACE inhibitors in heart transplant patients.

**Methods:** We evaluated 558 patients transplanted between 1994 and 2008. Patients were divided into groups based on the number of BP medications taken for > 6 months within the first 2 years post heart transplant. Control patients on 0 BP medications were selected for 2-year conditional survival. Assessed 5-year subsequent outcomes included survival, freedom from cardiac allograft vasculopathy (CAV, stenosis > or = 30%), and freedom from non-fatal major adverse cardiac events (NF-MACE, MI, heart failure, PTCA, pacemaker, stroke, new peripheral vascular disease). BP medications were divided into several categories, including beta blockers, calcium channel blockers, ACE Inhibitors, and angiotensin II receptor blockers.

**Results:** Patients with 3 BP medications exhibited a trend toward lower survival compared to patients with 0 BP medications (70% vs. 82%, p=0.06) and 1 (70% vs. 82%, p=0.07) or 2 (70% vs. 85%, p=0.06) BP medications. Subsequent freedom from CAV and NF-MACE were similar between all groups. Over half of the patients maintained the antihypertensive medication for the subsequent 5-year follow up. There was no difference in outcome for the use of any particular class of BP medication in terms of long term outcomes. Specifically, ACE inhibitors did not reduce angiographic CAV as intimated in previous reports.

**Conclusions:** 3 or more BP medications are associated with poor outcome post heart transplant. This suggests that more refractory hypertension may relate to lower survival.

| 10. Please choose your academic program: | MD |
| 11. What year are you in the program? | 2 |
| 12. What was your role in this study? | I helped come up with the study idea and collected all the data. I assisted in the analyzing of the data and with writing the report. |
**Lepow Day Abstract**

<table>
<thead>
<tr>
<th>1. Title:</th>
<th>Systematic Approach to Detection of Signaling Pathway Aberrations in Small Cell Lung Cancer (SCLC)</th>
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<tbody>
<tr>
<td>2. Presenter:</td>
<td>James Morrow</td>
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<tr>
<td>3. Co-workers and Collaborators:</td>
<td>Amy Kluge</td>
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<tr>
<td>4. Advisor:</td>
<td></td>
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<tr>
<td>5. Departments:</td>
<td>University Hospitals Department of Hematology/Oncology Developmental Therapeutics Program Case Comprehensive Cancer Center</td>
</tr>
<tr>
<td>6. Support:</td>
<td>NIH 5K23 CA109348-05</td>
</tr>
<tr>
<td>7. Institutions:</td>
<td>University Hospitals Case Medical Center</td>
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**Introduction:**

Lung cancer accounts for 28% of all cancer deaths, more than any other form of cancer. According to the American Cancer Society Facts & Figures, estimated 222,520 new cases of lung cancer will occur in 2010. Small cell lung cancer (SCLC) will account for 14% of these cases (1). The majority of patients with SCLC present with distant metastases. Although initial response to systemic therapy is common, the 1-year survival is less than 50% and nearly all patients will die from their cancer. From these statistics, it is clear that more effective treatments are necessary for this disease. To develop effective novel therapies, a sound understanding of SCLC biology is required. The goals of this project were to assess small cell lung cancer cell lines and human tissue samples for somatic oncogene mutations and also for signaling pathway activation through analysis of protein phosphorylation status.

**Methods:**

To achieve these goals, we plan to analyze 12-14 samples using the OncoCarta™ Panel v1.0 available through Sequenom and titanium-oxide column exchange followed by LC-MS/MS, respectively.

**Results:**

Due to various administrative setbacks no data is currently available from this project. It is our hope that the data derived from these experiments may show commonalities between SCLC samples and allow for the development of more rational therapeutic strategies in the future treatment of this disease.

Despite intense interest in the role of oxidative stress in the pathogenesis of NASH, the pathways that contribute to oxidative damage in vivo are poorly understood. Our aims were to assess whether specific oxidation pathways are differentially activated in NASH and hepatic steatosis using novel mass spectrometry-based technology in combination with murine models. **Methods:** C57BL/6 wild-type mice were fed either a high fat (HFAT) diet, a model of obesity and hepatic steatosis, a methionine and choline-deficient (MCD) diet, a model of severe NASH, or a control (CTL) diet (n=5 in each group). After 7 weeks, plasma, adipose (epididymal) and liver tissue were collected. Levels of structurally specific oxidized amino acids (oxAA) that provide molecular fingerprints of the pathways responsible for their generation were measured using high-performance stable isotope dilution liquid chromatography-tandem mass spectrometry. Measured oxAAs included chlorotyrosine (Cl-Tyr), bromotyrosine (Br-Tyr), nitrotyrosine (NO2-Tyr), meta-tyrosine (m-Tyr), and ortho-tyrosine (o-Tyr). **Results:** Of the oxAAs measured, Cl-Tyr and Br-Tyr, products of myeloperoxidase (MPO)- and eosinophil peroxidase (EPO)-catalyzed oxidation, respectively, were found to be markedly elevated in livers of mice with MCD-
induced NASH compared to animals with hepatic steatosis fed HFAT diet or mice receiving CTL diet (Cl-Tyr: 65.7 vs. 14.8 vs. 14.2 umol/molTyr, p<0.01; Br-Tyr: 57.2 vs. 18.8 vs. 18.3 umol/molTyr, p<0.001). Levels of NO2-Tyr, a specific molecular fingerprint for protein modification by NO-derived oxidants, were significantly elevated in adipose tissue of mice fed HFAT compared to CTL diet (276.3 vs. 147.8, p=0.04), but unchanged in liver and plasma. Finally, levels of m-Tyr and o-Tyr, products of protein oxidation by metal-catalyzed hydroxyl radical-like species, were unchanged in both HFAT- and MCD-fed animals compared to controls. **Conclusions:** These findings demonstrate significant tissue-specific increases in levels of specific molecular footprints of distinct oxidative pathways during the development of hepatic steatosis and NASH. This data supports the hypothesis that NO-derived oxidants are involved in adipose tissue oxidative stress associated with obesity and hepatic steatosis, while MPO- and EPO-derived oxidants are involved in liver damage and disease progression to NASH stages. This concept has important implications for the development of novel treatment strategies for patients with this condition.

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**Navarro, Laura**

**Lepow Day Abstract**

1. **Title:** Arginase 2 deficiency results in spontaneous steatohepatitis and fibrosis
2. **Presenter:** Laura A. Navarro
3. **Co-workers and Collaborators:** Michael P. Berk, Sudakshina Ghosh, Serpil C. Erzurum, and Ariel E. Feldstein
4. **Advisor:**
5. **Departments:** Cell Biology
6. **Support:**
7. **Institutions:** Lerner Research Institute, Cleveland Clinic Lerner College of Medicine, Cleveland Clinic
8. **Body of Abstract: (300 words or less)**

**Background:** Innate immuneactivation is central to the development of obesity-related hepatic steatosisand insulin resistance. Arginase 2 competes with inducible
nitric oxidesynthase (iNOS) for its substrate and an imbalance between these two enzymes plays a crucial role in regulating immune responses and macrophage activation. Our aim was to study the effects of arginase 2 deficiency in the development of the metabolic complications of obesity. **Methods:** Male C57BL/6 wild-type (WT) and arginase 2-knockout (Arg2/-) mice were fed a high fat (HFAT) diet, or a control (CTL) diet (n=5 in each group). After 7 weeks, plasma, adipose and liver tissue were collected. Steatosis, inflammation, and fibrosis were assessed by serum ALT values, liver histopathology, Oil-Red-O (ORO), F4/80 and Sirius red staining. Metabolic and inflammatory mediators and markers of stellate cell (HSC) activation were measured by RT-PCR and commercially available kits. **Results:** Arg2/- mice on the CTL diet were heavier than their WT counterparts at the time of sacrifice (34.3 vs. 28.2 g, p<0.01). However, fasting serum assays of metabolic mediators revealed no differences between Arg2/- and WT mice. Unexpectedly, CTL-fed Arg2/- mice showed profound changes in liver characterized by marked hepatomegaly and steatohepatitis, a phenotype similar to human nonalcoholic steatohepatitis (NASH). Histological and ORO examination demonstrated significant lipid deposition. This was associated with increased expression of genes involved in lipogenesis, including SREBP1c and ACC. Liver injury and inflammation was present with elevated serum ALT levels (110 vs. 34.6 U/L, p<0.05) and pronounced increase in mRNA expression levels of inflammatory markers. Liver tissue of Arg2/- mice showed marked infiltration of F4/80 positive cells. Liver fibrosis and HSC activation were also evident in the Arg2/- CTL-fed mice as assayed by Sirius red and RT-PCR of a-SMA, COL1A1, and TGF-β. Finally, these changes were more pronounced when the Arg2/- mice were stressed by the HFAT diet. **Discussion:** This study suggests that arginase 2 is an important regulator of innate immune responses in the liver, lipogenesis, and liver injury. These findings have important implications for the pathogenesis of NASH and potential development of novel treatment strategies for patients with this condition.
11. What year are you in the program? 3

12. What was your role in this project? I have been involved in every aspect of this project, drafting of the research plan, animal work, tissue characterization, data interpretation. This is my main research project for my research year at CCLCM.

13. Date: 11/10/2010

Navarro, Laura

Lepow Day Abstract

1. Title: VTE Prophylaxis in a Children's Hospital: Practices and Opportunities for Improvement

2. Presenter: Laura A. Navarro

3. Co-workers and Collaborators: Kate Gowans

4. Advisor:

5. Departments: Pediatric Hematology/Oncology

6. Support:

7. Institutions: Cleveland Clinic Children's Hospital

Evidence-based data regarding treatment of venous thromboembolism (VTE) in pediatric patients is scant, extrapolated from adult studies, and comprised of consensus guidelines. Despite the rising incidence of VTE in pediatric patients, no data exists for VTE risk assessment and prophylaxis in hospitalized children. In December 2008, Cleveland Clinic Children’s Hospital instituted the Pediatric Anticoagulation Management Program (PACMP), an initiative aimed at standardizing prophylaxis, diagnosis and treatment of thromboembolic events. The PACMP applies to admitted patients age =16 or <16 with weight >70 kg or BMI >30. Patients satisfying these criteria should be risk-assessed and placed on VTE prophylaxis as recommended.

This observational study was designed to examine behaviors surrounding VTE risk assessment and prophylaxis in a tertiary children’s hospital.

Methods: Distribution of risk assessment categories was extracted from the electronic medical records (EMRs) of patients age <18 years admitted to the Children’s Hospital during the three-month period (March-May 2009) immediately following PACMP implementation.

Results and Discussion: Of 1349 admissions, 489 were
risk-assessed at admission, for a compliance rate of 36%. Of those assessed, 24 patients were assessed as “low risk,” 13 as “moderate risk,” 3 as “high risk,” and 512 as “age<18” (it is possible for a patient to be assessed more than once per admission). Of patients assessed as “age <18,” 47 were age ≥16 and 12 were <16 with weight >70 kg or BMI >30. According to the guidelines, these patients are potentially at increased risk of VTE. All patients who fell into this increased risk category were assessed as follows: 59 as “age <18,” 10 as “low risk,” 6 as “moderate risk,” 3 as “high risk;” 144 (64%) were not assessed at all.

**Conclusion:** Implementation of guidelines for VTE prophylaxis has resulted in greater awareness of this topic at our institution. Expectedly, compliance is not optimal; a resident survey indicates that this part of the admission orders is just forgotten, and most residents do not feel qualified to assess VTE risk. This study has identified opportunities for improvement in our institutional practices, particularly with regard to order entry in the EMR and educational initiatives.

10. Please choose your academic program: MD

11. What year are you in the program? 3

12. What was your role in this project? I wrote the IRB for this project, did all of the statistical analysis and data interpretation. This was my research project for my clinical research summer between years 1 and 2 at CCLCM.

13. Date: 11/11/2010

Niles, Philip

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**Lepow Day Abstract**

1. **Title:** Utilization of Laparoscopic Splenectomy: An Analysis from the National Surgical Quality Improvement Program Database

2. **Presenter:** Philip Niles

3. **Co-workers and Collaborators:** Vikram Attaluri MD, Louisa Chiu MD, Eric Hixson PhD/MBA, Haris Kwaja MD, Steven Rosenblatt MD, J. Michael Henderson MD, Allan Siperstein MD

4. **Advisor:**

5. **Departments:** Institute of Surgery

6. **Support:**

7. **Institutions:** Cleveland Clinic Foundation

8. **Body of Abstract:** (300 words or less) **Introduction:** Laparoscopic splenectomy is the widely-accepted standard of care for both benign and malignant disorders requiring the removal of a normal-
sized spleen. With advancements in laparoscopic techniques, the indications for laparoscopic splenectomy have broadened. To determine if clinical practice nationwide reflects the published superiority of the laparoscopic over the open approach, we compared the utilization of laparoscopic versus open splenectomy by analyzing the National Surgical Quality Improvement Program (NSQIP) dataset.

**Methods:** The NSQIP participant user file from 2005 through 2008 was used for data analysis. Pre-operative risk factors, intra-operative events, and post-operative complications were compared between the two groups. A multivariate model was constructed to evaluate the association between laparoscopic surgery, open surgery, and pre-operative risk factors with morbidity, mortality and length of stay (LOS). ICD-9 codes were used to organize patients into five subgroups, (I) benign splenic diagnosis (ITP, spherocytosis), (II) malignancy associated with spleen, (III) splenic lacerations (iatrogenic), (IV) splenomegaly, and (V) miscellaneous diagnosis.

**Results:** CPT codes identified 2,167 patients, 48% underwent laparoscopic (1045 patients) and 52% underwent open (1122 patients) splenectomy from 2005 through 2008. There was no significant change in ratio of laparoscopic to open splenectomies as time progressed. Laparoscopic surgery was significantly (p<0.05) associated with younger age (51.6 yo vs 56.9 yo), higher BMI (28.3 vs 26.9) and female sex (55.6% vs 47.1%). In addition, laparoscopic patients were significantly (p<0.05) less likely to have a history of COPD (3.5% vs 6.1%), renal failure (0.5% vs 1.4%), have ascites (0.8% vs 4.5%), be functionally dependent on others (0.9% vs 7.0%), and be less likely to be emergency operative cases (1.9% vs 26.5%).

Overall morbidity was 20.6% (446/2167) with a 28.9% rate in open procedures and 11.7% rate in laparoscopic. Overall mortality was 3.7% (81/2167) with a 5.3% rate in open procedures and 2.1% in laparoscopic. With multivariate analysis, laparoscopic surgery was not
significantly associated with lower mortality rate but was significantly associated with lower morbidity and shorter LOS. (p<0.05)

Excluding emergency cases, subgroup analysis by ICD-9 codes revealed that laparoscopic surgery was used more often for group I (627 vs 277) and less for group III (4 vs 132). Laparoscopy was associated with lower morbidity for group I (benign splenic disease) and group V (miscellaneous) but this was not a significant relationship for group II (malignancy) and for group IV (splenomegaly). There were too few laparoscopic cases in group III (spleenic injury) for meaningful analysis. Laparoscopy was associated with shorter LOS in all groups except III.

**Conclusion:** Despite literature proposing the superiority of laparoscopic over open splenectomy, less than half of the splenectomies identified in the NSQIP database underwent laparoscopic resection. While laparoscopic patients in this dataset are less likely to have certain risk factors such as COPD, we have shown through multivariate analysis that there is a significantly less morbidity and LOS associated the laparoscopic approaches especially for those with benign splenic disease.

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**Lepow Day Abstract**

1. **Title:** Utilization of Laparoscopic Splenectomy: An Analysis from the National Surgical Quality Improvement Program Database  
2. **Presenter:** Philip Niles  
3. **Co-workers and Collaborators:** Vikram Attaluri MD, Louisa Chiu MD, Eric Hixson PhD/MBA, Haris Kwaja MD, Steven Rosenblatt MD, J. Michael Henderson MD, Allan Siperstein MD  
4. **Advisor:**
Introduction: Laparoscopic splenectomy is the widely-accepted standard of care for both benign and malignant disorders requiring the removal of a normal-sized spleen. With advancements in laparoscopic techniques, the indications for laparoscopic splenectomy have broadened. To determine if clinical practice nationwide reflects the published superiority of the laparoscopic over the open approach, we compared the utilization of laparoscopic versus open splenectomy by analyzing the National Surgical Quality Improvement Program (NSQIP) dataset.

Methods: The NSQIP participant user file from 2005 through 2008 was used for data analysis. Pre-operative risk factors, intra-operative events, and post-operative complications were compared between the two groups. A multivariate model was constructed to evaluate the association between laparoscopic surgery, open surgery, and pre-operative risk factors with morbidity, mortality, and length of stay (LOS). ICD-9 codes were used to organize patients into five subgroups, (I) benign splenic diagnosis (ITP, spherocytosis), (II) malignancy associated with spleen, (III) splenic lacerations (iatrogenic), (IV) splenomegaly, and (V) miscellaneous diagnosis.

Results: CPT codes identified 2,167 patients, 48% underwent laparoscopic (1045 patients) and 52% underwent open (1122 patients) splenectomy from 2005 through 2008. There was no significant change in ratio of laparoscopic to open splenectomies as time progressed. Laparoscopic surgery was significantly (p<0.05) associated with younger age (51.6yo vs 56.9yo), higher BMI (28.3 vs 26.9) and female sex (55.6% vs 47.1%). In addition, laparoscopic patients were significantly (p<0.05) less likely to have a history of COPD (3.5% vs 6.1%), renal failure (0.5% vs 1.4%), have ascites (0.8% vs 4.5%), be functionally dependent on others (0.9% vs 7.0%), and be less likely to
be emergency operative cases (1.9% vs 26.5%).

Overall morbidity was 20.6% (446/2167) with a 28.9% rate of in open procedures and 11.7% rate in laparoscopic. Overall mortality was 3.7% (81/2167) with a 5.3% rate in open procedures and 2.1% in laparoscopic. With multivariate analysis, laparoscopic surgery was not significantly associated with lower mortality rate but was significantly associated with lower morbidity and shorter LOS. (p<0.05)

Excluding emergency cases, subgroup analysis by ICD-9 codes revealed that laparoscopic surgery was used more often for group I (627 vs 277) and less for group III (4 vs 132). Laparoscopy was associated with lower morbidity for group I (benign splenic disease) and group V (miscellaneous) but this was not a significant relationship for group II (malignancy) and for group IV (splenomegaly). There were too few laparoscopic cases in group III (splenic injury) for meaningful analysis. Laparoscopy was associated with shorter LOS in all groups except III.

**Conclusion:** Despite literature proposing the superiority of laparoscopic over open splenectomy, less than half of the splenectomies identified in the NSQIP database underwent laparoscopic resection. While laparoscopic patients in this dataset are less likely to have certain risk factors such as COPD, we have shown through multivariate analysis that there is a significantly less morbidity and LOS associated the laparoscopic approach especially for those with benign splenic disease.

| 10. Please choose your academic program: | MD |
| 11. What year are you in the program? | 3 |
| 12. What was your role in this project? | I was involved in several aspects of our group’s research projects on the National Surgical Quality Improvement Program database. I created several variables and performed much of the data analysis used in our study. |
| 13. Date: | 11/10/2010 |
| Niles, Philip | |
| 1. Title: | Making Supply Meet Demand in Kidney Transplantation |
| 2. Presenter: | Philip Niles |
| 3. Co-workers and Collaborators: | Dr. J.B. Silvers, Chair of Department of Banking and Finance, CWRU Weatherhead School of Management |
| 4. Advisor: | |
| 5. Departments: | Department of Banking and Finance |
| 7. Institutions: | Weatherhead School of Management |

**8. Body of Abstract: (300 words or less)**

**Introduction:** In 1984, the National Organ Transplant Act was passed, prohibiting the offer of "valuable considerations" to a potential organ donor. This 26-year-old policy remains unchanged today. The number of people on the kidney transplant waiting list has grown each year since data was first collected in 1988. In 2010, the kidney transplant waiting list will exceed 100,000 people, and the people on the waiting list will exceed those who receive donations by a factor of over 8:1. Kidney shortage leads to thousands of deaths each year and negative health consequences for the tens-of-thousands receiving dialysis. Attempts to decrease the kidney shortage have failed. We examine the ethical and public health consequences of relaxing the "valuable considerations" clause of the National Organ Transplant Act.

**Methods:** Literature review, data-analysis of United Network for Organ Sharing database, cost-benefit analysis

**Results:** The number of people on the kidney transplant waiting list increased by 3,859 people per year from 1998 to 2008, and has accelerated to an increase of 5,579 people from 2006 to 2007 and an increase of 7,833 people from 2007 to 2008. The rate of kidney transplants to members of the waiting list has increased at a rate of 593
transplants annually and has remained relatively constant. In 2008, there were 78,611 people on the kidney transplant waiting list, 16,406 kidney transplants performed with waiting list recipients, and 5,094 deaths of members of the kidney transplant waiting list. In a preliminary data analysis, we found that ending the kidney transplant shortage would be equivalent to saving approximately 125,000 lives.

Conclusion: The National Organ Transplant Act of 1984 merits reexamination. Relaxing the "valuable considerations" prohibition to organ transplant donors warrants social and ethical reconsideration since the number of lives lost due to organ unavailability has changed since the law’s proposal.

Lepow Day Abstract

1. Title: Making Supply Meet Demand in Kidney Transplantation
2. Presenter: Philip Niles
3. Co-workers and Collaborators: Dr. J.B. Silvers, Chair of Department of Banking and Finance, CWRU Weatherhead School of Management
4. Advisor:
5. Departments: Banking and Finance
6. Support: Weatherhead School of Management
7. Institutions: Weatherhead School of Management

8. Body of Abstract: (300 words or less)

9. Date: 11/10/2010

Niles, Philip

12. What was your role in this project? Project design, conception, research. First author.
**Lepow Day Abstract**

1. **Title:** Evaluation of 3D Digital Imaging for Reliable Wound Healing Measurement

2. **Presenter:** Jennifer Mika Nishimura

3. **Co-workers and Collaborators:** Alex J Davis

4. **Advisor:**

5. **Departments:** The Spinal Cord Injury (SCI) Center

6. **Support:** VISN 10 Research Initiative Program

7. **Institutions:** Louis Stokes Cleveland Department of Veterans Affairs Medical Center (LSCDVAMC)

8. **Body of Abstract:** (300 words or less)

**Background:** Digital imaging in wound assessment is becoming widespread in clinical practice. 3D digital imaging can provide volumetric values, important for wound assessment in clinical practice and as a standard outcome measure for assessment of new therapeutic interventions.

**Hypothesis:** The primary hypotheses are: 1) Repeated 3D imaging of chronic wounds provides a reliable and objective measure of wound size changes. 2) The stereophotogrammetric LifeViz™ 3D system (Quantificare Inc., San Mateo, CA) is acceptable in clinical wound measurement practice.

**Methods:** A pilot clinical study of 50 chronic wounds is being carried out on the inpatient SCI Unit of the LSCDVAMC. 15-25 patients with spinal cord injury (SCI) and at least one chronic pressure ulcer are being recruited. Initial evaluation of wounds includes assessment using the Pressure Ulcer Scale for Healing (PUSH) tool. Wound etiology, location, duration, and patient demographics were also recorded. 3D digital wound images were captured using the LifeViz™ camera weekly over a six week period by four nurses; two expert wound care and ostomy registered nurses (WOCNs) and two non-expert registered nurse (RN) observers. The expert WOCN observers also obtained standard clinical linear and volumetric measurements. Using the DermaPix® software, two observers independently analyzed the images to obtain 3D measurements. A 17-item questionnaire will be administered to the nurse observers to assess acceptability of the LifeViz™ 3D system in clinical practice. Data analysis will include discriminate analysis and regression models. All covariates, such as wound type, location and size will be included using a generalized linear model.

**Results:** This study is still in progress. Eight veterans have been enrolled to date. Ten wounds have been assessed using the 3D LifeViz™ system. Variations observed between wounds and observers will be analyzed using upon completion of the study using methods described in the section above.

**Conclusion:** N/A.
12. **What was your role in this project?**  
My role included setup of the DermaPix® software database and image analysis using the DermaPix® software to obtain 3D measurements.

13. **Date:**  
11/09/2010

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### Lepow Day Abstract

**1. Title:** Control of 5-HT1A receptor signaling by a chimeric, light activated G protein-coupled receptor  
**2. Presenter:** Eugene Oh  
**3. Co-workers and Collaborators:** Takashi Maejima, Chen Liu, Evan Deneris  
**4. Advisor:**  
**5. Departments:** Neurosciences  
**6. Support:** NIH National Research Service Award F30 MH084371; Medical Scientist Training Program Training Grant 2T32 GM007250-29; Neurosciences Training Grant 5T32 AG000271-07  
**7. Institutions:** School of Medicine  

**8. Body of Abstract: (300 words or less)**  
Understanding serotonergic (5-HT) signaling is critical for understanding human physiology, behavior, and neuropsychiatric disease. 5-HT mediates its actions via ionotropic and metabotropic 5-HT receptors. The 5-HT1A receptor is a metabotropic G protein-coupled receptor linked to the Gi/o signaling pathway and has been specifically implicated in the pathogenesis of depression and anxiety. To understand and precisely control 5-HT1A signaling, we created a light-activated G protein-coupled receptor that targets into 5-HT1A receptor domains and substitutes for endogenous 5-HT1A receptors. To induce 5-HT1A-like targeting, vertebrate rhodopsin was tagged with the C-terminal domain (CT) of 5-HT1A (Rh-CT5-HT1A). Rh-CT5-HT1A activates G protein-coupled inward rectifying K+ channels in response to light and causes membrane hyperpolarization in hippocampal neurons, similar to the agonist-induced responses of the 5-HT1A receptor. The intracellular distribution of Rh-CT5-HT1A resembles that of the 5-HT1A receptor; Rh-CT5-HT1A localizes to somatodendritic sites and is efficiently trafficked to distal dendritic processes. Additionally, neuronal expression of Rh-CT5-HT1A, but not Rh, decreases 5-HT1A agonist sensitivity, suggesting that Rh-CT5-HT1A and 5-HT1A receptors compete to interact with the same trafficking machinery. Finally, Rh-CT5-HT1A is able to rescue 5-HT1A signaling of 5-HT1A KO mice in cultured neurons and in slices of the dorsal raphe showing that Rh-CT5-HT1A is able to functionally compensate for native 5-HT1A. Thus, as an optogenetic tool, Rh-CT5-HT1A has the potential to directly correlate *in vivo* 5-HT1A signaling with 5-HT neuron activity and behavior in both normal animals and animal models of neuropsychiatric disease.

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10. **Please choose your academic program:** MD PHD

11. **What year are you in the program?**  
8

12. **What was your role in this project?**  
First author; designed and conducted most experiments.
### Title:
Posterior Fossa Tumors in a Pediatric Population: a Retrospective Chart Review.

### Presenter:
Darren Palathinkal

### Co-workers and Collaborators:

### Advisor:

### Departments:
Pediatric Neurosurgery

### Support:

### Institutions:
Rainbow Babies and Children's Hospital

### Body of Abstract: (300 words or less)

Objective: The goal of this study was to describe the characteristics of posterior fossa tumors in a pediatric patient population. Characteristics that were recorded included tumor type, location, duration of diagnostic delay, age at diagnosis and signs and symptoms.

Methods: We retrospectively analyzed 85 children who were treated for posterior fossa tumors at Rainbow Babies and Children’s Hospital between January 1994 and January 2010, excluding brainstem gliomas. Patients were categorized and compared by tumor type, tumor grade and diagnostic delay. Diagnostic delay was divided into = one month delay, one to = 6 months delay and = 6 months delay.

Results: Diagnoses included astrocytoma (n=36), medulloblastoma (n=22), ependymoma (n=15) and other tumors (n=12). Mean age at diagnosis was 7.6 ± 0.6 years. Mean diagnostic delay was 20.0 ± 3.6 weeks. Patients presented with a variety (>30) signs and symptoms, some not typically associated with posterior fossa tumors. High grade tumors presented at a significantly younger age than low grade tumors (p = 0.001), yet did not differ in diagnostic delay (p = 0.330). High grade tumors present with more vomiting (p = 0.014) and possibly nausea (p = 0.051), while low grade tumors presented with more headache (p = 0.047), even thought they had similar percentages of hydrocephalus (p=0.600). High grade tumors are more likely to be found in the 4th ventricle than low grade tumors (p = <0.001). Patient age (p =0.182) and tumor grade (p = 0.960) did not differ among the diagnostic delay groups. Patients with shorter diagnostic delay present with possibly more vomiting (p = 0.084) and those with longer delay presented with a higher percentage of headache (p=0.019).

Conclusion: Physicians should be sensitized to the large variety of signs and symptoms that accompany posterior fossa tumors. High grade tumors present at a younger age and with more vomiting, likely because of their location. Diagnostic delay is not dependent on patient age or tumor grade. Patients that have a shorter delay in diagnosis may differ in presentation compared to patients that have a longer delay in diagnosis and warrants future further investigation.
Purpose: To determine if post-operative intravitreal triamcinoloneacetonide administration as a conjugate to epiretinal membrane removal surgery improves visual outcomes.

Methods: Visual acuity and intraocular pressure were measured at 0, 1, 3, and 12 months of twenty-two eyes of 22 patients who underwent a pars plana vitrectomy either with or without post-operative intravitreal triamcinolone.

Results: Differences in visual acuity and IOP were not statistically significant at any of the timepoints measured between patients who were administered intravitreal triamcinoloneacetonide versus those who were not treated. Visual outcomes improved over time regardless of whether triamcinolone was administered or not.

Conclusions: The study did not show that post-operative administration of triamcinolone acetonide would lead to better visual outcomes versus those patients who were not treated.
Lepow Day Abstract

1. Title: The Intergenerational Cycle of Teen Motherhood: A Narrative Explanatory Model
2. Presenter: Jessica L. Pippen
3. Co-workers and Collaborators: Katherine Blumoff, M.D; Naila Bitar, M.D.
4. Advisor: 
5. Departments: Pediatrics
6. Support: 
7. Institutions: Rainbow Babies and Childrens’ Hospital

8. Body of Abstract: (300 words or less)

Background:
Teenage pregnancy is still of national concern, given its individual, familial and social impacts. Although the national rate of teenage pregnancy experienced a significant decline from 1991 to 2005, it has been experiencing slight increases since 2006. Research shows that teenage pregnancy puts adolescent mothers at risk for living in poverty, limited educational opportunity, and sexually transmitted infections. Furthermore, data also shows that children born to adolescent mothers are more likely to become adolescent parents themselves, the intergenerational cycle of teenage pregnancy. There are multiple epidemiologic and correlative explanations for this phenomenon – for example, the daughters and sisters of teen mothers have been shown to state a younger ideal age at first parenting – but we believe this to be one of the only studies attempting to elucidate this phenomenon from a narrative perspective.

Methods:
Participants were recruited on the basis of gender, current age and age at the birth of their first child. To qualify, participants had to be mothers who were currently 18 years or older and who had their first child when they were less than 20 years old. They were interviewed using
an open-ended 13 question instrument covering themes of demographics, timing of childbirth, paternal and maternal grandparental involvement, parenting self-efficacy and approval of teenage parenting and sexual activity. Participants were recruited at the Rainbow Babies and Children’s Pediatric Practice and interviewed in a private office at the clinic.

**Results and Conclusions:**
Aggregate interview data were analyzed using a grounded-theory anthropological approach and a narrative explanatory model was generated. Multiple themes emerged in our qualitative data analysis. Participants saw themselves as part of a cycle of teen parenthood that runs through multiple generations. Participants had significant early childcare experience and motherhood. The maternal grandmother plays a key role in co-parenting with participants when they were too young to fully parent. This assistance is also seen in grandparental generations and is both a help to the young mother and a perpetuation of the cycle of teen motherhood roles with respect to their siblings as a result of their own young mothers – imparting comfort with parenting roles at a younger than traditional age. This cycle continues to be perpetuated due to acceptance of cross-generational parenting within the represented population.

| 10. Please choose your academic program: | MD |
| 11. What year are you in the program? | 2 |
| 12. What was your role in this project? | I interviewed participants, transcribed voice recordings, coded transcripts for data analysis and assisted in developing the explanatory model. |
| 13. Date: | 11/10/2010 |

**Poku, Kwaku**

**Lepow Day Abstract**

1. **Title:** Validating the Human Langendorff Model: A Comparative Analysis of Ventricular Fibrillation Dynamics During In-vivo Intraoperative Mapping vs. Ex-vivo Langendorff Mapping

2. **Presenter:** Kwaku Poku

3. **Co-workers and Collaborators:** Krishnakumar Nair, Stephane Massé, Talha Farid, Karthikeyan Umapathy, Gopal Sivagangabalan, Sheila Watkins, John Asta, Elias Sevaptidis, Elnaz Shokrollahi, John Floras, Kumaraswamy Nanthakumar

4. **Advisor:**
5. Departments: Division of Cardiology

6. Support: Case Western Reserve University School of Medicine Dean’s Summer Research Award

7. Institutions: University Health Network - Toronto General Hospital, University of Toronto

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**Body of Abstract: (300 words or less)**

**INTRODUCTION:** There is a paucity of studies validating the human Langendorff model during human ventricular fibrillation (VF).

**OBJECTIVES:** We aimed to compare both closed chest and open chest VF with VF induced in the isolated human heart (IHH) Langendorff model.

**METHODS:** We compared characteristics of closed chest in-vivo VF induced at defibrillation threshold testing (DFT), open chest in-vivo VF mapped intra-operatively and VF induced in isolated human hearts (IHH) in 4 patients with ischemic cardiomyopathy. VF from DFT was compared to VF electrograms from the endocardial balloon in IHHs using the half power scale distribution width extracted from continuous wavelet transform (CWT), and by comparing VF mean cycle length. Moreover, we compared early VF in 3 intraoperatively mapped left ventricular cardiomyopathic patients, with early ex-vivo VF in 3 explanted IHH in a Langendorff system using two metrics: dominant frequency (DF) assessed by the Welsh Periodogram and the number of phase singularities (lasting >480ms).

**RESULTS:** Wavelet analysis (P=0.9) and VF mean cycle length (CL) was similar between the Langendorff and the DFT groups (224.86± 36.15, 225.2±62.7ms, P=0.98) indicating that wave characteristics and activation rate of VF was comparable between the 2 models. Intraoperative DF was slower but comparable to the Langendorff DF over the endocardium (4.62±0.69, 5.0±0.82Hz, P=0.55) and over the epicardium (4.55±0.87, 5.25±0.86Hz, P=0.38). Endocardial phase singularity number (9.67, 13, P=0.87) was comparable between in-vivo and ex-vivo VF as was epicardial phase singularity number (27.3, 24, P=0.63).

**CONCLUSIONS:** VF in the human Langendorff was not significantly different from in-vivo human models suggesting that the human Langendorff approximates in-vivo VF well and may acceptably serve as a model for human VF study.

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**Please choose your academic program:** MD

**What year are you in the program?** 2

**What was your role in this project?** Summer Research Student. Developed tools used to do research. Wrote and edited a third of manuscript. Edited abstract. Created an image for the manuscript.

**Date:** 11/10/2010

**Poloskey, Stacey**
BACKGROUND AND HYPOTHESIS: Vascular occlusion is a well established complication of sickle cell disease (SCD). Abundant evidence suggests that hypercoagulability contributes to vaso-occlusion in part due to increased platelet reactivity. However, the mechanisms underlying this observation are largely unknown. Microparticles (MPs) are small membrane-derived vesicles that “bud” off cells and elevated levels of red blood cell-derived MPs (RMPs) are detected in the circulation of patients with SCD. Previous studies demonstrate that endothelial cell-derived MPs sensitize platelets to activation through interaction via a CD36-phosphatidylserine (PS) dependent mechanism. We therefore hypothesize that RMPs also interact with platelets via a CD36-PS dependent mechanism and that this interaction results in enhanced platelet activation. We further hypothesize that there are elevated levels of circulating MPs in patients with SCD that are correlated to increased platelet reactivity.

METHODS: Calcein-stained platelets were incubated with PKH26-stained RMPs. We used flow cytometry to identify a platelet population positive for PKH26, suggesting a physical interaction with RMPs. To evaluate the mechanism of interaction, platelets were pre-incubated with anti-CD36 antibody or RMPs with annexin V, and the effect on platelet acquisition of PKH26 positivity was assessed. In addition, blood samples were collected from patients with SCD and MPs were counted by flow cytometry. Platelet reactivity was evaluated using aggregrometry.

RESULTS AND CONCLUSIONS: Thirty-five to forty percent of platelets incubated with RMPs acquired PKH26 positivity with an increase in mean platelet PKH26 fluorescence from 5.0 to 19.5 (p = 0.03). There was no
In patients with SCD, there was a linear relationship between MP concentration and platelet aggregation ($r^2 = -0.93, p = 0.03$). Results suggest a physical interaction between platelets and RMPs. Additional studies are needed to conclusively determine the mechanism and effect of this interaction.

10. Please choose your academic program: MD

11. What year are you in the program? 4

12. What was your role in this project? I participated in this project full time for one year. I was involved in all aspects including grant application, writing of an IRB protocol, hypothesis generation, study design, experimental techniques, and analysis and interpretation of data. I presented our findings in poster format at the end of year meeting for Howard Hughes Research Training Fellowship recipients.

13. Date: 11/09/2010

**Rahim, Shiraz**

### Lepow Day Abstract

1. **Title:** Clomiphene Citrate in Unexplained Infertility

2. **Presenter:** Shiraz Rahim

3. **Co-workers and Collaborators:** Dr. Nichole Barker and Dr. William Hurd

4. **Advisor:**

5. **Departments:** Department of Obstetrics and Gynecology, Division of Reproductive Endocrinology and Infertility

6. **Support:** This project was not funded by an outside source. The researchers state no conflicts of interest that may affect the results of this research.

7. **Institutions:** University Hospitals Case Medical Center

8. **Body of Abstract: (300 words or less)**

   **Background and rationale:** Clomiphene citrate (CC) is an estrogen antagonist given to ovulatory women in conjunction with intrauterine insemination to induce ovulation and treat unexplained infertility. The efficacy of the standard starting 50 to 100mg/day dose has not been evaluated. Because these doses might exert an anti-estrogenic thinning effect on endometrium whose thickness is known to correlate positively with successful embryo implantation, some physicians use 25mg/day doses.

   **Hypothesis:** It is hypothesized that a 25mg/day dose of CC given to ovulatory women with infertility will
result in a larger pregnancy rate compared to higher doses of 50 or 100mg. **Methods:** This retrospective cohort study is a chart review of women presenting with = 1 year of infertility. Data on prescribed CC dose will be compared with clinical pregnancy and miscarriage rates in cohorts of 25mg (n=100), 50mg (n=104), or 100mg (n=95) CC starting doses. Effects of confounding factors like endometrial thickness and supplemental progesterone administration used to increase endometrial thickness will also be assessed. **Results:** Chi-squared analysis of CC doses and clinical pregnancy rates showed p-values of .3681, .3833, and .8231 when comparing 25 vs 50mg, 25 vs 100mg, 50 vs 100mg doses respectively. Analysis of patients receiving progesterone and pregnancy rates found p-values of .433, .387, .4028 for doses of 25, 50, and 100mg CC respectively. Analysis of women with endometrial lining greater than 8mm and pregnancy rates found p-values of .740, .0091, and .729 for doses of 25, 50, and 100mg CC respectively. **Conclusions:** The data show no statistically significant difference between pregnancy rates after 25, 50, or 100mg doses of CC. Similarly, there is no difference between pregnancy rates with a given dose in women receiving supplemental progesterone or with endometrial linings greater than 8mm. Small sample sizes suggest the need for further studies with more data.

**Lepow Day Abstract**

1. **Title:** Curcumin as a Growth Suppressive Agent for Cisplatin Resistant HNSCC Cell Lines
2. **Presenter:** Hani Rayess
Cisplatin is a platinum based chemotherapeutic drug that is widely used in the treatment of Head and neck squamous cell cancer (HNSCC). An increasing number of head and neck cancers are resistant to Cisplatin therapy. This resistance has been linked to cancer stem cells which express the cell surface marker Cd44. Curcumin is a chemotherapeutic agent that down regulates NfKb signaling and can potentially be used to treat cisplatin resistant tumor cells. The aim of my experiments was to use FACs analysis to elucidate the mechanism of action of cisplatin and curcumin on the tumor cells.

Methods:
HNSCC cells were plated on 15 cm plates. After serum starvation for 24 hours cells were treated with cisplatin 20 µmol/L for 5 hours, liposomal (curcumin 100 µmol/L) for 8 hours or cisplatin and liposome. Combination treatment consisted of addition of cisplatin 3 hours after curcumin. Untreated cells and cells treated with liposome alone were used as control groups. Each experiment was done in duplicate. FACs analysis was performed on the cells to determine the effect the drugs had on the cancer cells.

Results
Cells treated with cisplatin showed a significant decrease in cell count compared to control cells. Cells treated with curcumin also showed a significant decrease. The decrease in cell count for cisplatin and curcumin was greater than either of the drug individually. FACs analysis was also used to give us an insight into the mechanisms of action of these drugs. Cells treated with cisplatin had 100% arrest in S phase and only 1.91% of cells committed apoptosis. Whereas cells treated with curcumin only had 52% of their cells in S phase and 12.35% of cells had committed apoptosis. Cells that were
treated with both drugs had 53% of their cells in S phase and an apoptotic percentage of 15.16%.

Conclusion:
These results illustrate that cisplatin and curcumin are acting through 2 different mechanisms to inhibit cell growth, therefore curcumin could potentially be used as an adjuvant therapy for cisplatin resistant tumors. Further experiments that need to be performed include isolating the Cd44 high cells using FACs then treating these cells with cisplatin to induce cisplatin resistance. The sensitivity of the cisplatin resistant cancer stem cells to curcumin can then be assessed.

10. Please choose your academic program: MD
11. What year are you in the program? 2
12. What was your role in this project? My role in this project was to take care of the cells, administer the treatment, harvest cells, and participate in the analysis of the data.
13. Date: 11/10/2010

Roman, Carly

**Lepow Day Abstract**

1. **Title:** Melanoma in Hispanics in North Carolina between 1998-2007
2. **Presenter:**
3. **Co-workers and Collaborators:** Dr. Aida Lugo-Somolinos, Carly Roman
4. **Advisor:**
5. **Departments:** Dermatology
6. **Support:** none.
7. **Institutions:** University of North Carolina- Chapel Hill

8. **Body of Abstract:** (300 words or less) Melanoma is the most lethal form of skin cancer, accounting for about 75% of all skin cancer deaths. The incidence of melanoma in Hispanics is on the rise and the Hispanic patients presenting with melanoma are typically at a more advanced stage when compared to Non-Hispanic White patients. This delay in diagnosing melanoma in the Hispanic population can be attributed to a low index of suspicion in both the medical community and the patient population. Our purpose was to examine the incidence rates and location of invasive melanoma in
Hispanics and compare these rates to Non-Hispanics Whites living in North Carolina over a ten-year period (1998-2007). We would like to gain a better understanding of melanoma in this population in order to tailor educational materials to Hispanics and their health care providers. All data regarding cases of invasive melanoma were obtained through the North Carolina Central Cancer Registry. The incidence rate is higher in females than in males in the Hispanic population, which is opposite from the NHW population. A greater proportion of Hispanic females were diagnosed with melanoma compared to the proportion of NHW females. The most common location of invasive melanoma in Hispanics is the Leg/Hip region, which is statistically significant compared to NHW’s (P < 0.05). Between 1998-2007, there were no cases of invasive melanoma diagnosed in Hispanics in the neck/scalp region in North Carolina, but there were 1065 cases diagnosed in this region in the Non-Hispanic population. There is a significant difference between the two populations (P< 0.05). In conclusion, we did find that there is a statistical difference between the percentage of melanoma cases which occurs among females of the Hispanic vs. NHW’s; a greater proportion of Hispanic females are diagnosed with melanoma than the proportion of NHW females. We also determined that the most common area of invasive melanoma in Hispanics is the leg/hip region, which is statistically greater than the NHW population. This data should be compared to the national SEER data to determine consistency and to develop a greater understanding of the patterns of melanoma in the Hispanic population.

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<td>12. What was your role in this project?</td>
<td>My role in the project included: writing the IRB, contacting and organizing data from the Central Cancer Registry, data analysis and writing the final paper.</td>
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<td>11/10/2010</td>
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<td>Rome,Marcie</td>
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### Lepow Day Abstract

1. **Title:** Illuminating the provider practices associated with high rates of inappropriate antibiotic prescribing.

2. **Presenter:** Marcie Rome

3. **Co-workers and Collaborators:** Amy Irwin, RN DNP

4. **Advisor:**

5. **Departments:** Department of Medicine – Division of Infectious Diseases

6. **Support:** Dean’s Summer Research Award, Case Western Reserve University School of Medicine

7. **Institutions:** Denver Health Medical Center, Denver, CO

8. **Body of Abstract:** (300 words or less)

   In the outpatient setting, antibiotics are frequently prescribed to treat viral conditions for which they will have no effect. These inappropriate antibiotic prescriptions lead to increased levels of antibiotic resistance and an increase in drug-related adverse events. What is the extent of this problem, and what provider practices are at its core? Records of patient visits containing ICD-9 codes of infections for which antibiotics are commonly prescribed were collected and a manual review was conducted. Variables gathered included information about whether or not an antibiotic prescription was given, what antibiotic was prescribed, duration of therapy, and the occurrence of adverse events (defined as unresolved infection, hospitalization, ED visit, or Grade 3 or 4 serum abnormality) in the 30-day post-visit period. Preliminary data for the bronchitis cases showed higher than expected prescription rates, so these cases were chosen for the in depth analysis of prescribing patterns. A total of 80 bronchitis cases were reviewed. Patients received an antibiotic prescription at 55 of those visits, or 68.8% of the time. Of the 14 Adverse Events associated with a bronchitis diagnosis, 13 of them occurred in patients given an antibiotic prescription. Prescribing patterns for bronchitis differed by clinic, provider type, and patient age. Physicians and NPs prescribed antibiotics for 63.5% and 69.2% of their patients, respectively, while PAs prescribed antibiotics for 86.7% of patients. The highest prescription rates (66.7%, 73.0%, 72.7%, and 75%) were seen for patients above age 40 and below age 18, while patients between the ages of 18 and 40 were prescribed antibiotics only 50% of the time. When prescriptions were broken down by patient and provider gender, the highest rate of prescriptions was seen in female providers prescribing for male patients (92.9%). Next came female providers prescribing for female patients (68.3%), followed by male providers prescribing for male patients (56.3%) and female patients (55.6%). These results demonstrate that current antibiotic prescribing patterns in the outpatient setting leave significant room for improvement and carry with them serious sequelae. Uncovering the practices that underlie these prescriptions will identify opportunities for targeted intervention.

10. **Please choose your academic program:** MD

11. **What year are you in the program?** 2

12. **What was your role in this project?** My roles included chart review, data collection, data analysis, and abstract authorship.
Osteoarthritis is characterized by non-immune related articular cartilage loss resulting in painful joint inflammation. Diagnostic radiographic imaging can demonstrate loss of joint space width (JSW), which can be measured using data from the Osteoarthritis Initiative (OAI). While studies have investigated the relationship between arthroscopic meniscectomy and JSW, none have compared patients with matched controls. We hypothesize that JSW significantly decreases in meniscectomy patients versus matched controls over a one-year period. A retrospective cohort study was conducted using records from the OAI public use data sets. Details about the OAI and study design are publicly accessible at http://oai.epi-ucsf.org/datarelease/About.asp. Knees were treated as independent subjects. The OAI cohort was queried for subjects who underwent meniscectomy after study enrollment. Exclusion criteria included surgery prior to enrollment or non-meniscectomy surgery post-enrollment. Twenty-five meniscectomy knees were identified and 75 controls were selected using the same exclusion criteria as above while matching for subcohort, gender, study site, age, knee side, and year. Bilateral posteroanterior fixed-flexion radiographs using a positioning frame to maintain consistency were obtained at all visits. Minimum JSW (mJSW) was measured using the method of Duryea et al. Baseline characteristics and change in mJSW were analyzed with a two-sample, two-tailed T-test assuming equal variances and a two-sample, one-tailed T-test using unequal variances, respectively. Baseline characteristics,
including BMI and time interval between X-rays, were not significantly different between meniscectomy and control groups. mJSW decrease (mean (mm) ± s.d.) was 0.842 ± 1.133 in meniscectomy patients and 0.211 ± 0.824 in controls, which was a significant difference (p= 0.007). Utilizing radiographic JSW measurements led us to the conclusion that meniscectomy leads to JSW narrowing much earlier than previously suggested. This may be due immediate loss of joint space due to loss of the interposed meniscus or due to rapid degeneration of articular cartilage in response to increased tibiofemoral contact stress. Partial meniscectomy could also cause dysfunction in the remaining meniscus, possibly resulting in extrusion or flattening, which then manifests as JSW narrowing. Future investigation of change in cartilage volume and meniscus status on MR imaging may further explain the cause of this joint space loss.

10. Please choose your academic program: MD MS

11. What year are you in the program? 2

12. What was your role in this project? I queried the OAI cohort for eligible patients and controls, selecting and applying the exclusion criteria. These patients and controls were categorized and matched based on certain criteria. Bilateral posteroanterior fixed flexion radiographs using the Synaflexer positioning frame to maintain consistent knee flexion were obtained in each subject at baseline and each yearly follow-up visit. Mini

13. Date: 11/09/2010

Sadhu, Anita

Lepow Day Abstract

1. Title: Light Stimulation as a Method for Recovery of Respiration
2. Presenter: Anita Sadhu
4. Advisor:
5. Departments: Department of Neurosciences
6. Support: This project was supported by the Dean’s Summer Research Award 2010
7. Institutions: Case Western Reserve University
8. Body of Abstract: (300 Hypothesis:}
Light-induced excitation of neurons transfected with Channel Rhodopsin-2 can enable restoration of diaphragmatic contraction rhythm in rats with a C2 spinal hemisection.

Respiration impairment is a grim physiological consequence of cervical spinal cord injury. The diaphragm, the primary muscle of inspiration, is under both autonomic and voluntary control by the central nervous system. Without proper neuronal stimulation, individuals must rely on accessory muscles of respiration, resulting in reduced respiratory efficiency, inability to cough (and therefore increased risk of respiratory infection), and respiratory acidosis due to hypoventilation. In addition, individuals may have to use mechanical ventilation to assist in breathing, especially while asleep.

The phrenic nucleus, responsible for motor innervation of the abdominal diaphragm, is located at the C3-C5 spinal cord levels. The driving force for frequency and rhythm of respiration comes from the medullary pre-Botzinger complex and rostral ventral respiratory group. Spinal cord injury at or above this level impairs or severs communication between the phrenic nerves and control centers, rendering the skeletal muscle of the diaphragm incapable of motor function. Because the diaphragm is the primary muscle of inspiration, significant impairment of breathing follows a spinal cord injury of this nature.

This project is part of an ongoing exploration of the role of Channel Rhodopsin-2 as an aid in nerve firing in the absence of physiological stimulation. Channel Rhodopsin-2 (ChR2) is a fluorescing algal protein, currently a popular neuroscientific tool for light-induced nerve stimulation. Using specific viral vectors, the gene for ChR2 can be transfected into the nucleus of a neuron and subsequently transcribed by the cell’s genomic machinery. When exposed to light of a specific frequency, these transfected neurons can be induced to fire an
action potential even in the absence of signaling from supraspinal control centers. The hopeful achievement is full synchrony of the two sides of the diaphragm even after termination of the stimulation interval.

10. Please choose your academic program: MD

11. What year are you in the program? 2

12. What was your role in this project? Research assistant - I assisted in dissections of spinal cords, tissue sectioning, and visualization.

13. Date: 11/08/2010

Sears, Nathaniel

### Lepow Day Abstract

1. **Title:** Caspase-8 mediated cleavage of IRF-3 is necessary for its proteasomal degradation

2. **Presenter:** Nathaniel Sears

3. **Co-workers and Collaborators:** Saurabh Chattopadhyay, George Stark, Ganes Sen

4. **Advisor:**

5. **Departments:** Molecular Genetics

6. **Support:** PO1 CA 062220

7. **Institutions:** The Cleveland Clinic Foundation, Lerner Research Institute

#### Background

Interferon regulatory factor (IRF)-3 is essential for induction of antiviral genes. IRF-3 plays a critical role in initiating apoptosis via a transcription-independent mechanism through activation of caspase-8 through RIG-I (spell out abbreviation). IRF3 is downregulated by proteasomal degradation to attenuate inflammation. In this study we explored whether caspase-8 is involved in proteolytic processing of the activated IRF-3.

#### Methods

N-terminal IRF-3 degradation was analyzed by Western blot in P2.1 cells, an HT1080 derived cell line low in IRF3, using lentiviral expression of IRF3-Flag. We monitored IRF-3 degradation in HT1800 cells after RIG-I or Toll-like receptor 3 (TLR3) activation with and without selective caspase inhibition. We compared IRF3
degradation in ARPE-19 cells which lack caspase 8 before and after transfection of caspase-8. The degradation of WT-IRF3 was compared to an IRF3 mutant containing point mutation in the cleavage site. Ubiquitination was compared between WT and mutant IRF3 by immunoprecipitation of HA-Ub.

**Results**

Caspase-8 mediated N-terminal cleavage of IRF-3 and was necessary for its proteasomal degradation. Prevention of this event by inhibition or genetic absence of caspase-8, or by mutation of the caspase-8 cleavage motif within IRF-3 abolished its proteolytic processing, ubiquinination, and proteasomal degradation.

**Conclusion**

We have defined a novel role for caspase-8 in the cellular viral response. It is possible that viral dsRNA can initiate two different antiviral responses, depending on the level of caspase-8 expression. If caspase-8 is present, a type-I interferon response is initiated which is then attenuated by IRF3 degradation, followed by programmed cell death. If caspase-8 is not present, a sustained type-I interferon response is initiated, not followed by IRF3 degradation and apoptosis. This finding may explain why viral infections have a tropism for certain tissues despite the ability to infect cells ubiquitously. This knowledge could lead to improved therapies against viral infection.

| 10. Please choose your academic program: | MD |
| 11. What year are you in the program? | 5 |
| 12. What was your role in this project? | primary researcher |
| 13. Date: | 11/10/2010 |

Shalman, Dov

**Lepow Day Abstract**

1. **Title:** Is visceral pain a helpful construct in characterizing pelvic pain
2. Presenter: Dov Shalman
3. Co-workers and Collaborators: Sangeeta Senapati, Caroline Edelmann, Kristen Pozolo
4. Advisor: 
5. Departments: Obstetrics and Gynecology,
6. Support: CWRU Summer Research Fellowship
7. Institutions: NorthShore University HealthSystem, Evanston, IL 60201

Goal: Characterize differences between visceral and non-visceral presentations of chronic female abdominal and pelvic pain

Method: This was a retrospective study of all female patients aged 18-55 presenting to a tertiary gynecological pain clinic between October 2004 and April 2008 with the complaint of pelvic and/or abdominal pain. Data was collected from the clinic’s intake questionnaire packet including medical history, the Medical Outcomes Trust’s Short-Form Health Survey (SF-12), McGill Pain Inventory, and the Coping Strategies Questionnaire (CSQ) catastrophizing subscale. Two research assistants independently abstracted subjects’ symptoms, previous conditions, and quality of life measures. An electronic chart review was then conducted by two physicians specializing in pelvic pain, to categorize each patient’s pain as either visceral or non-visceral. Group comparisons were performed using t-tests and X² test of proportions.

Findings: 214 women were identified with abdominal or pelvic pain, 55% of whom were defined as having visceral pain. Duration of pain was higher among visceral pain patients, but not statistically significant. A higher proportion of women with visceral pain had concurrent diagnoses of endometriosis. Higher affective pain ratings and reports of catastrophizing thoughts were associated with visceral pain. Quality of life as determined by the Mental Component Summary of the SF-12 was worse in visceral pain patients, but Physical Component Summary scores did not differ significantly. Self-reported depression was higher among visceral pain patients, while self-reported anxiety did not differ among visceral pain patients.

Results: Our study suggests that visceral pain is likely a relevant category for subclassifying pelvic pain as visceral pain.
is associated with higher morbidity in patients than non-visceral pelvic pain. Most notably the emotional component of the pain experience appears worse in visceral pain patients. Future studies are needed in order to identify validated criteria for diagnosing visceral pain which may lead to earlier prevention of chronic symptomatology.

10. Please choose your academic program: MD

11. What year are you in the program? 2

12. What was your role in this project? Data analysis and writing the paper.

13. Date: 11/11/2010

Shaw, Laura

**Lepow Day Abstract**

1. Title: Preparations for a multifactorial study of healing in pressure ulcer patients

2. Presenter: Laura Shaw

3. Co-workers and Collaborators: Arielle Schindler

4. Advisor: 

5. Departments: 


7. Institutions: Louis Stokes VAMC

8. Body of Abstract: (300 words or less) Patients with spinal cord injuries face unique challenges upon hospitalization that can result in further deterioration of health status. Chief among these, perhaps, is the development of pressure ulcers. Long periods of inactivity result in sustained pressure to weight-supporting parts of the body than compresses muscle and diverts blood flow, the end result of which is mechanical stress and necrosis.
While there are many ways to incur a pressure injury, there are also a number of variables that are known to influence the efficacy of the healing process. Though several studies have been done to assess the role of these factors in both development and healing of these wounds, few look at the whole course of healing, but instead focus on a few factors at a particular stage, leaving scientists unable to define clear linkages between one factor and another.

As such, the objective of the study we would have done was to determine which risk factors are associated with the development of pressure ulcers in patients with spinal cord injuries from pre- to post-hospitalization, including demographic data, the equipment used in care, medications, secondary complications, nutritional status, environmental factors, non-medical therapies, and pre-existing conditions. It is thought that several could contribute through either direct physical stresses or through functional impairments of the healing process.

Data collection was to be accomplished via a retrospective chart review of the medical records of 150-250 individuals admitted to the VA SCI unit between 2006 and 2009 who either arrived with ulcers or developed them during their stays. Pre- and post-admission time points would be examined to generate data that would later be analyzed for statistically significant correlations. Preliminary data sorting and preparation for collection occurred over the summer with the bulk of the gathering was to occur throughout the remainder of the year.

10. Please choose your academic program:
   MD

11. What year are you in the program?
   2

12. What was your role in this project?
   Data collection template design

13. Date:
   11/10/2010

Sinha, Preetha

Lepow Day Abstract

1. Title: The Role of TNFa Signalling in the Neuroprotective Effect of EPO in the Developing Brain

2. Presenter: Preetha Sinha

3. Co-workers and Collaborators: Elizabeth Shick, Mark Eden
4. Advisor: 
5. Departments: Department of Neurosurgery 
6. Support: NINDS R01 NS060765 to SR 
7. Institutions: Case Western Reserve University School of Medicine 

8. Body of Abstract: (300 words or less) 

TNFα (tumor necrosis factor) is an inflammatory cytokine synthesized in transmembrane (tm) and soluble (sol) forms by microglia, astrocytes and certain neuronal populations. Its receptors, TNFR1 and TNFR2, differ in expression profiles, ligand affinity, and downstream signaling. Where TNFR1 can be found in most cell types and shows a preference for solTNF, TNFR2 is typically localized to immune cells and preferentially binds tmTNF. Several studies have shown erythropoietin (EPO) to protect CNS neurons against inflammatory and hypoxic-ischemic injury. Furthermore, this neuroprotection has been shown to involve TNFR1. We sought to investigate whether transient systemic hypoxia-ischemia (TSHI) modulates TNFα signaling via changes in TNFR1 or TNFR2 gene expression. Our experimental methodology involved treating pregnant mice with a prenatal insult consisting of 60 minutes of TSHI on embryological day 18, followed by collection of cortical samples from sham- and HI-treated pups on embryological day 19, and post-natal days 0, 2, and 5. RNA samples were isolated using aTRizol reagent protocol, and cDNA samples were prepared using the First Strand Synthesis kit. Relative TNFR1 and TNFR2 levels were assessed using the iCyclerQPCR system, with target gene expression normalized against the 18s reference gene. Preliminary results suggest that there is little difference in either TNFR1 or TNFR2 expression following TSHI in comparison to sham treatment. There does, however, appear to be more TNFR1 than TNFR2 expression at every time point and condition. These results indicate that receptor transcription is not likely to be the rate-limiting step in the signaling pathway. It is possible that receptor internalization or degradation may play a more significant role. TNFR1 and TNFR2 expression may be altered more significantly following activation of inflammation via lipopolysaccharide treatment, and in the future, we hope to test this hypothesis.

10. Please choose your academic program: MD
11. What year are you in the program? 2

12. What was your role in this project? My role in the project involved isolating RNA from previously collected cortical samples, synthesizing cDNA from the RNA isolates, and using iCycler system to quantify TNFR1 and TNFR2 gene expression as described in the abstract above.

13. Date: 11/10/2010

Soo Hoo, Jennifer

Lepow Day Abstract

1. Title: The effectiveness of a NT-pro BNP based bio-marker strategy as a substitute to stress testing and in predicting short and intermediate term cardiovascular events

2. Presenter: Jennifer Soo Hoo

3. Co-workers and Collaborators: Anish Aneja

4. Advisor:

5. Departments: Department of Cardiology

6. Support: Support grant from MetroHealth Heart and Vascular Center. CTSC grant application is pending.

7. Institutions: MetroHealth Heart and Vascular Center, Case Western Reserve University

8. Body of Abstract: (300 words or less) Chest pain represents the second most common reason for ED evaluation. The most commonly utilized strategy for risk-stratification of chest pain patients presenting to the ED and suspected of unstable angina is the TIMI score. Furthermore, patients who fall under the intermediate risk group based upon a TIMI score of 2-4 pose the biggest diagnostic dilemma in the ED. These patients are usually further risk stratified by stress testing, a logistically challenging and expensive procedure. The use of biomarkers, especially serum natriuretic peptides has recently been espoused for their prognostic value in patients with suspected cardiac chest pain. Despite several studies highlighting their excellent prognostic value in patients with chest pain, their niche in clinical practice remains to be defined. We believe that in intermediate chest pain patients, a NT-pro BNP biomarker-based strategy will be as effective as a stress-testing strategy in predicting short and intermediate term cardiovascular events. The proposed study is a prospective observational study of patients presenting to
the ED with chest pain, deemed at intermediate risk by the TIMI criteria, and eligible for stress testing. These patients in the study will have an estimation of biomarkers including NT-pro BNP, ischemia modified albumin, myeloperoxidase, and high sensitivity C-reactive protein. The investigators will be blinded to the results of these biomarkers until study conclusion (6 months after enrollment), when they will be analyzed. Using statistical models, the predictive value of biomarker elevation will be compared to stress tests positive for inducible myocardial ischemia, which is the primary endpoint of the study. We believe that if a multiple biomarker-based strategy for the diagnosis and prognosis of cardiac chest pains is proven equivalent to traditional stress testing based strategy, it could help change the traditional outlook towards the diagnosis of chest pain and potentially save considerable time and resources.

10. Please choose your academic program: MD

11. What year are you in the program? 2

12. What was your role in this project? I helped screen potential subjects and enroll and consent patients. I also created the RedCap database to put all patients information in. I am currently continuing to help enter new patients data into the system every week.

13. Date: 11/09/2010

Stringham, Alexandria

**Lepow Day Abstract**

1. Title: Misconcepts Impairing Self-management in Asthma Patients

2. Presenter: Alexandria Stringham

3. Co-workers and Collaborators: Laurence Cook, M IV

4. Advisor:

5. Departments: Emergency Medicine

6. Support: T-32 Grant

7. Institutions: MetroHealth, Cleveland, OH

8. Body of Abstract: (300 words or less) **Background:** Asthma is a complex disease for patients to understand partly because of its intermittent nature instead of the more classic constant presence of a
chronic disease. However, patient’s understanding is critical to effective self-management of asthma.

**Hypotheses:** We tested the hypotheses that patients have misconceptions about the pathophysiology of asthma that lead to increased ED visits and worse self-management, but conversely there is information that if understood, allows patients to make better self-management decisions.

**Methods:** Over 200 patients in the MetroHealth ED, who self-reported asthma, were interviewed regardless of the reason for their visit. The interviews consisted of three questionnaires that employed a mix of true/false, multiple choice and open response formats. The first questionnaire was universal asthma management question set. Dr. Cydulka and Laurence Cook designed the second questionnaire, which tested pathophysiologic knowledge of asthma. Patients were also asked to demonstrate how they used an inhaler and asked to identify their own asthma triggers. The third questionnaire gathered background information such as insurance status and what asthma medications patients took.

The data will be analyzed from two different approaches. True/false answers will be compiled into a numerical score to compare with the universal asthma management question set. A correlation will be looked for between knowledge and management. The opened ended questions will be read to look for common threads in patient’s disease models, be they right or wrong. Any frequent components in these models could lend themselves to better or worse management of asthma as a chronic disease. Eventually the hope is to correct these misconceptions in a clinical setting to improve patient self-care.

**Results and Conclusions:** Metro Health IRB took the collected surveys for a data audit and has not yet returned them.
12. What was your role in this project?
Collected majority of the surveys, will be helping analyze the data once the surveys are back from a data audit.

13. Date: 11/09/2010

Lepow Day Abstract

1. Title: Use of ElectroFluidGraph in volume analysis of normovolemic African American patients
2. Presenter: Asha Talati
3. Co-workers and Collaborators: Lori Fiessinger, Tertius Tuy
4. Advisor:
5. Departments: Emergency Medicine Research Department
6. Support: Support for this project was provided by the NIH T32 grant provided through Case Western Reserve University School of Medicine.
7. Institutions: Cleveland Clinic Foundation - Main Campus

The ElectroFluidGraph is an FDA approved device used to measure whole body hydration state via bioimpedance vector analysis (BIVA) technology in a rapid, non-invasive, bed-side manner. BIVA utilizes the body’s capacitance and resistance to a low voltage current to generate an impedance vector and phase angle, which estimate tissue hydration and soft tissue mass, respectively. Several studies have suggested that the convenience and accuracy of BIVA makes it potentially useful in assessing volume status in patients with conditions like heart or renal failure. However, BIVA is currently standardized to Caucasian populations, decreasing its utility amongst the diverse populations in the U.S. This study seeks to provide a range of expected BIVA values and generate 95%, 75%, and 50% tolerance ellipses for African American patients. A convenience sample of self-identified African American or Caucasian patients between the ages of 18 to 80 at baseline health with no limitation to six-month survival were enrolled. Patients were assessed for a 72 hour history of volume anomalies including history of bleeding, diarrhea, vomiting and orthostatic vital signs. BIVA was completed on all enrolled patients and patient chartswer
retrospectively reviewed for conditions suspected to cause volume anomalies. Currently 54 patients have been enrolled in the study and results are pending analysis. Approximately 100 more patients are required in the study to generate enough power to comment on significance. Analysis of gathered data will include use of collected capacitance and resistance measures to generate appropriate tolerance ellipses. All values will be compared to patterns amongst Caucasian patients. Existing literature review has led us to predict that tolerance ellipses of African American patients will differ from those of Caucasian patients through a smaller phase angle and right shift of the impedance vector due to an average higher soft tissue mass.

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<td>12. What was your role in this project?</td>
<td>Project and protocol design, IRB submission and correspondence, patient enrollment, database maintenance, analysis of data.</td>
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Thimmappa, Vikrum

**Lepow Day Abstract**

1. Title: Fine Motor Dysfunctions in Medically Managed Parkinson’s Disease Patients
2. Presenter: Vikrum Thimmappa
3. Co-workers and Collaborators: Stacey Gorniak
4. Advisor:  
5. Departments: Biomedical Engineering
6. Support: Crile Grant
7. Institutions: Cleveland Clinic

8. Body of Abstract: (300 words or less) Previous studies of manual dexterity in Parkinson’s disease (PD) patients have focused on relatively simple one-hand and two-hand tasks that do not necessarily translate to regular activities of daily living (ADLs). In particular, studies that have included bimanual actions have not examined the effects of
rotating an object as part of the manipulation component of the task. We have developed an experimental paradigm that implements a rotational component within the task while grasping forces and torques are captured. The aim of this project was to assess the fine motor control of PD patients while ‘on’ and ‘off’ antiparkinsonian medication to understand the specific effects of PD on fine motor control and the effectiveness of medication on improving function. Medically managed PD (MMPD) patients were recruited to participate in this study. Patients in the MMPD group were tested on and off medication in two separate sessions. Consistent with studies of young healthy control subjects, MMPD patients took longer to perform rotation tasks and to put objects together, as opposed to performing non-rotation tasks and separating two objects (p < 0.001). Additionally, MMPD exhibited similar delays in load force application as compared to the young control subjects. In contrast, MMPD had higher overall slip safety margins when performing each of the tasks as compared to young control subjects. A longer delay in grip force application was noted in the MMPD group during the off medication testing session (p < 0.001). Based on these results, medication status did not significantly alter many features of fine motor control in this patient population. Further studies are planned to explore medication effects of fine motor control on MMPD patients.

10. Please choose your academic program: MD
11. What year are you in the program? 2
12. What was your role in this project? I performed the data analysis and worked through the protocol for testing patients.
13. Date: 11/10/2010

Lepow Day Abstract

1. Title: The Role of Kruppel-like Factor 2 in Transformed Human Brain Microvascular Endothelial Cells
The function of microvascular endothelial cells in the central nervous system is quite unique in that they form the especially selective blood brain barrier. Kruppel-like factor 2 (KLF2), an intracellular transcription factor, is highly expressed in peripheral endothelial cells and has been shown to be critical to the regulation of cellular function and development. A large amount of in vitro work has demonstrated KLF2 to be a critical anti-inflammatory, anti-thrombotic, and vasodilatory factor in peripheral endothelial cells. In light of KLF2’s important role in peripheral endothelial cell function and the overall importance of brain endothelial cells in cerebrovascular disease we hypothesize that KFL2 may be a key regulator of brain microvascular endothelial function and cerebrovascular homeostasis. We assessed the affect of overexpression of KLF2on endothelial cell permeability using transwell assays hypothesizing that cells overexpressing K2 would be less permeable. For overexpression experiments, endothelial cells were infected with adenovirus expressing KLF2 or with EV, a control adenovirus. After coating the transwell insert with collagen and seeding brain microvascular endothelial cells overexpressed in KLF2 into a well, a 2,000-kD fluorescent labeled dextran solution was added to the seeded insert. VEGF, was added to half the EV and K2infected inserts, and the fluid was collected from the bottom chamber at 5different time points. The collected fluid samples were analyzed on a microplate fluorometer (at excitation and emission wavelengths of 485 nm and530 nm, respectively) for relative fluorescence density as compared with the control group. Our results
were consistent with our hypothesis; at time points greater than 5 minutes (30 minutes, 1 hr, 2hr, 4hr) permeability increased significantly in the control group treated with VEGF compared to the nontreated control group, in the study group permeability did not increase after stimulation with VEGF suggesting KLF2 is protective (keeps tight junctions tight).

| 10. Please choose your academic program: | MD |
| 11. What year are you in the program? | 2 |
| 12. What was your role in this project? | I was responsible for some of the cell culture, background PCR trials, each step of the Transwell assay procedure, as well as the formulation of the project results. |
| 13. Date: | 11/10/2010 |

Lepow Day Abstract

1. Title: Platelets and Biomarkers in Stable CAD and STEMI: An EDUCATE Substudy
2. Presenter: Krystyna Traudt
3. Co-workers and Collaborators: 
4. Advisor: 
5. Departments: UHMC Division of Cardiovascular Medicine
6. Support: NIH T35 Grant
7. Institutions: Case Cardiovascular Research Institute; UH Harrington-McLaughlin Heart & Vascular Institute

8. Body of Abstract: (300 words or less) Interest in the use of serum biomarkers as detectable indicators of disease activity in stable and acute coronary syndromes has grown considerably in recent years, as early and continued monitoring of these biomarkers in patients with coronary artery disease (CAD) and myocardial infarction (MI) may provide clinically important information regarding efficacy of therapy as well as prognosis. As thrombotic activity and platelet activation play critical roles in the development of acute coronary syndromes, assessment of platelet surface marker expression in CAD and MI has emerged as a prominent area of research in the investigation of potential new serum biomarkers. Recent studies profiling
platelet mRNA in patients with CAD and ST-elevation MI (STEMI) have demonstrated significantly increased transcription of platelet surface marker CD69 in STEMI patients as compared to healthy controls and stable CAD. Additionally, studies of platelet CD36 expression in patients experiencing restenosis following revascularization procedures have demonstrated the possible role of CD36 in development of stable coronary artery disease.

Based on these preliminary studies, platelet surface markers CD36 and CD69 show potential as clinically useful serum biomarkers in assessment of disease activity and prognosis in stable CAD and acute STEMI. In this investigation, it is hypothesized that statistically significant variation in platelet surface expression of CD36 and CD69 will be seen in patients with acute coronary syndromes as compared to stable coronary disease and healthy controls. Study populations include patients undergoing percutaneous coronary intervention for stable coronary artery disease or acute STEMI, as well as healthy controls. Whole blood and washed activated platelets from patients within these study populations is assessed using flow cytometry assays to detect levels of platelet surface CD36 and CD69 expression 12-18 hours following revascularization. At the current time, data has been collected for healthy controls and patients with stable CAD, though recent IRB approval for data collection on STEMI patients will now permit investigation of platelet activity in this study population as well. Given the established feasibility of the protocol based on data collection in healthy and CAD populations, future goals for this study include expansion of the study population to incorporate additional CAD as well as STEMI patients, which is anticipated to take place over the course of the next year.
12. What was your role in this project?

I obtained blood samples from consented patients in the CICU the morning and independently ran the entire protocol in the lab during the day, including making necessary calculations and alterations to the protocol during the initial days of the protocol to standardize the protocol prior to patient data collection.

13. Date: 11/10/2010

Trotter, Ashley

Lepow Day Abstract

1. Title: MECHANISMS OF PROBIOTIC REGULATION OF INTESTINAL PERMEABILITY IN EXPERIMENTAL CROHN’S DISEASE (CD)

2. Presenter: Ashley Trotter

3. Co-workers and Collaborators: Daniele Corridoni, Luca Pastorelli, Dai Ishikawa, Benedetta Mattioli, Marcello Chieppa, Fabio Cominelli

4. Advisor: 

5. Departments: Digestive Health Research Center and Department of Medicine and Pathology


7. Institutions: Case Western Reserve University

8. Body of Abstract: (300 words or less)

We previously showed that the probiotic mixture, VSL#3, prevents the onset of chronic intestinal inflammation in SAMP/YitFc (SAMP) mice, and this effect was associated with stimulation of epithelial-derived TNF-α. The aim of this study was to mechanistically determine the effects of VSL #3 on the epithelial barrier function in preventing SAMP ileitis. Epithelial permeability was evaluated by measuring transepithelial electrical resistance on ex-vivo cultured full-thickness ileum from pre-inflamed (4 weeks) and older SAMP with established disease (>20 weeks), and age-matched AKR controls at T0 and after 1 h exposure to VSL #3 conditioned media (CM), TNF-α (10ng.ml), or CM+ anti-TNF. Supernatants were collected and measured for TNF-α protein by ELISA. Ileal tight junction (TJ) proteins were assessed by qRT-PCR and confocal microscopy. TNFRI and TNFRII mRNA transcripts were measured in freshly isolated intestinal epithelial cells from pre-inflamed SAMP and AKR mice by qRT-PCR. SAMP ilea exhibited an increase in epithelial permeability following exposure to VSL #3 or TNF-α.
compared to AKR control mice. Culture with VSL#3 CM or TNF-a resulted in decreased ileal paracellular permeability in young, but not old, SAMP compared to vehicle (P<0.05), while in addition of anti-TNF-a abrogated the effects of VSL#3 CM (P<0.05). Modulation of the TJ proteins, claudin-2 and occludin, was observed with a significant decrease in claudin-2 and increase in occludin (P<0.05), following stimulation with VSL#3 CM or TNF-a. TNF-a protein levels were increased in supernatants of SAMP ilea incubated with VSL#3 CM compared to vehicle (P<0.05), while mRNA expression of IEC-derived TNFRI and TNFRII were decreased in SAMP versus AKR mice (P<0.05). Our data demonstrates that the previously established efficacy of VSL#3 in preventing SAMP ileitis is due to improvement of epithelial barrier function through a TNF-a dependant mechanism and modulation of TJ proteins, claudin-2 and occludin.

10. Please choose your academic program: MD

11. What year are you in the program? 2

12. What was your role in this project? For this project I did several things. I first helped to maintain the mice used for these and other experiments, by weighing and feeding them according to a certain schedule. I also sacrificed and took tissue samples for pathology and staining. I was able to prepare samples for transepithelial electrical resistance testing. Lastly, I performed an ELISA for the project.

13. Date: 10/22/2010

Tsai, Jennifer

**Lepow Day Abstract**

1. Title: Review of Outcomes following Allogeneic and Autologous Stem Cell Transplantation for Philadelphia Chromosome Positive Acute Lymphocytic Leukemia at UCSF Medical Center

2. Presenter: Jennifer Tsai

3. Co-workers and Collaborators: 

4. Advisor: 

5. Departments: Hematology/Oncology Faculty Practice

6. Support: 

7. Institutions: University of California, San Francisco Medical Center
**Introduction:** The Philadelphia Chromosome translocation ([Ph], t(9;22)(q34;q11)) is the most frequent cytogenetic abnormality detected in adult ALL, representing approximately 25% of cases. Ph+ patients are traditionally a high-risk subset, with allogeneic hematopoietic stem cell transplantation considered the best chance for cure. The role of autologous transplantation (AHCT) in treating these patients remains controversial. More recently, tyrosine kinase inhibitors (TKIs) have shown promise in treating Ph+ ALL. We retrospectively analyzed adult ALL patients who underwent HCT, to compare outcomes from allogeneic and autologous transplantation and TKI use.

**Patients and Methods:** 121 patients diagnosed with ALL underwent first blood or marrow transplantation at UCSF between 1986 and 2009. 42 patients were Ph positive. Bcr-abl status was confirmed with cytogenetic and molecular methods. Patients received autologous or allogeneic transplant based on donor availability. Patients were conditioned with regimens of total body irradiation (TBI), etoposide, and cyclophosphamide; or fludarabine with busulfan. Patients undergoing allogeneic HCT were given graft-versus-host-disease (GVHD) prophylaxis, and all patients received infectious disease prophylaxis.

**Results:** The median disease-free survival (DFS) overall was 1.59 years for patients receiving AHCT and 1.7 years for allogeneic HCT. The 5-year probability of DFS was 38% for autologous transplants, and 44% for
allogeneic transplants. In the same interval, treatment-related mortality was 9% and 36%, respectively. In the subset of Ph+ patients, 5-year probability of DFS was 58% and 40%, respectively, with no significant difference detected. DFS with TKI use was 70% in the autologous group (n = 10), and 58% in the allogeneic group (n = 17), compared to those who did not receive TKI therapy (0% in the autologous group, n = 3; 20% in the allogeneic group, n = 12).

Conclusion: Our data generally support previously reported data on DFS after HCT. Traditionally, there is a trade-off between TRM in allogeneic transplantation versus relapse in autologous transplantation. The addition of TKI therapy in the treatment of Ph+ patients can tip this balance, decreasing disease recurrence in the autologous setting without the attendant TRM of allogeneic transplantation. We did not find a statistical difference between these treatment modalities, suggesting that outcomes are comparable. Randomized trials and comparison of outcomes regarding transplantation versus chemotherapy are further required to characterize the potential benefits offered by this strategy. In addition, treatment to yield long-term disease-free survival clearly must be developed for Philadelphia chromosome negative patients.

| 10. Please choose your academic program: | MD |
| 11. What year are you in the program? | 2 |
| 12. What was I reviewed charts, gathered the data, analyzed the data, and |
### Lepow Day Abstract

<table>
<thead>
<tr>
<th>1. Title:</th>
<th>Evaluation of Stethoscopes as Vectors of Clostridium difficile and Methicillin-Resistant Staphylococcus aureus (MRSA)</th>
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<tbody>
<tr>
<td>2. Presenter:</td>
<td>Ravy Vajravelu</td>
</tr>
<tr>
<td>3. Co-workers and Collaborators:</td>
<td>Dubert M. Guerrero, MD; Lucy Jury, CNP; Brett S. Sitzlar</td>
</tr>
<tr>
<td>4. Advisor:</td>
<td></td>
</tr>
<tr>
<td>5. Departments:</td>
<td>Infectious Diseases and Infection Control</td>
</tr>
<tr>
<td>6. Support:</td>
<td>No financial support was received for this project either by the presenter of the advisor.</td>
</tr>
<tr>
<td>7. Institutions:</td>
<td>Cleveland Veterans Affairs Medical Center</td>
</tr>
</tbody>
</table>

#### Body of Abstract: (300 words or less)

**Background:** Several studies have demonstrated that stethoscopes may become contaminated with health-care associated pathogens, but the importance of stethoscopes in their transmission is unclear.

**Question:** What is the efficiency of stethoscope transmission of *C. difficile* and MRSA in laboratory and hospital settings?

**Methods:** In the laboratory, nontoxigenic *C. difficile* spores were inoculated onto skin and MRSA onto pigskin. Stethoscope transfer was assessed by placing the diaphragm over the inoculation site, then imprinting onto selective agar. Inpatients with *C. difficile* infection (CDI) or MRSA nares colonization, the chest and abdomen were auscultated, and the stethoscope was imprinted onto selective agar. For comparison, transfer of pathogens from skin by sterile gloves was assessed. The point-prevalence contamination of the stethoscopes of healthcare workers at a VA Medical Center were anonymously collected and the diaphragm was imprinted onto selective agar.

**Results:** In the laboratory, stethoscopes were as efficient as gloved hands for transfer of MRSA, but less efficient for transfer of *C. difficile* (figure).

**Figure:**

http://filer.case.edu/rkv9/Pictures/Vajravelu_abstract_figure.jpg
Figure. Comparison of stethoscope and hand acquisition of \textit{C. difficile} and MRSA from skin surfaces. **: \( P < 0.001 \), *: \( P = 0.01 \), CFU: Colony-forming unit.

Forty-nine total patients were studied, including 24 patients with CDI and 25 with MRSA nares colonization. In comparison to hand imprints of the chest and abdomen of CDI patients, stethoscope imprints were significantly less likely to be positive for \textit{C. difficile} (29\% versus 13\%; \( P = 0.02 \)). For MRSA colonized patients, there was no significant difference in the frequency of positive hand and stethoscope imprints (30\% versus 21\%; \( P = 0.08 \)) (table 1).

\begin{table}
\centering
\caption{Stethoscope and hand contamination after patient examination}
\begin{tabular}{lcc}
\hline
 & \textit{C. difficile} (\% \( n = 24 \)) & MRSA (\% \( n = 25 \)) \\
\hline
Stethoscope imprint & 3/24 (13) & 5/24 (21) \\
Stethoscope gauze & 4/22 (18) & 11/25 (44) \\
Chest/abdomen gloveprint & 7/24 (29) & 7/23 (30) \\
Groin gloveprint & 10/24 (42) & … \\
Arm/hand gloveprint & 4/24 (17) & … \\
\textit{P}: Stethoscope imprint vs. chest/ab. gloveprint & 0.02 & 0.08 \\
\hline
\end{tabular}
\end{table}

Of 50 stethoscopes cultured in the point-prevalence survey of healthcare worker stethoscopes, 1 (2\%) was positive for \textit{C. difficile} and 2 (4\%) were positive for MRSA (table 2).

\begin{table}
\centering
\caption{Point-prevalence survey of healthcare worker stethoscope diaphragms}
\begin{tabular}{lcc}
\hline
 & \textit{C. difficile} (\%) & MRSA (\%) \\
\hline
Attending MD’s & 4 & 0 (0) & 0 (0) \\
\hline
\end{tabular}
\end{table}
<table>
<thead>
<tr>
<th></th>
<th>Residents</th>
<th>1 (7)</th>
<th>1 (4)</th>
</tr>
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<tbody>
<tr>
<td>Medical students</td>
<td>6</td>
<td>0 (0)</td>
<td>1 (17)</td>
</tr>
<tr>
<td>Nurses</td>
<td>14</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Respiratory therapists</td>
<td>1</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Total</td>
<td>50</td>
<td>1 (2)</td>
<td>2 (4)</td>
</tr>
</tbody>
</table>

Note. 2 of 11 stethoscopes additionally cultured by broth enrichment were positive for *C. difficile*.

**Conclusions:** Stethoscopes often become contaminated with MRSA or *C. difficile* after examination of patients harboring these pathogens. In the laboratory, stethoscopes transferred *C. difficile* less efficiently than gloved hands but transferred MRSA at the same rate. The results of this study indicate that stethoscopes are readily contaminated through routine examination and have the potential to transfer pathogens.

**Lepow Day Abstract**

1. **Title:** Complications and Reoperations Following Arterial Switch
2. **Presenter:** Patrick Vargo
3. **Co-workers and Collaborators:** Constantine Mavroudis MD, Robert D. Stewart MD, Carl L. Backer MD, Harish Rudra MD, Marshall L. Jacobs MD
4. **Advisor:**
5. **Departments:** Cleveland Clinic Children’s Hospital, Department of Congenital
| 6. Support: |  
| --- | --- |
| 7. Institutions: | Children’s Memorial Hospital, Northwestern University Feinberg School of Medicine, Case Western Reserve University School of Medicine |

<table>
<thead>
<tr>
<th>8. Body of Abstract: (300 words or less)</th>
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<tr>
<td><strong>Introduction:</strong> The arterial switch operation has been the principal treatment for transposition of the great arteries and its variants for the last 25 years. Early mortality has decreased significantly over time, but long-term complications include pulmonary artery stenosis, coronary artery obstruction, neoaortic valvar insufficiency, arrhythmia, and aortic arch obstruction. The purpose of this study is to review an experience with late reoperations following the arterial switch operation (ASO) and to introduce reparative solutions adapted from previous techniques.</td>
</tr>
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</table>

**Methods:** A retrospective study was performed on 23 patients who underwent late reoperations after ASO between 1983 and 2010. Eighteen previously uncharacterized patients stemmed from a concomitantly reported cohort of 258 ASO patients and 5 others came from distant referrals. Published journal articles were identified through PubMed literature search and the authors selected 72 papers for analysis.
**Results:** Twenty-seven reoperations on 23 patients were performed for lesions relating to coronary insufficiency (9 procedures, n = 7), neoaortic root problems (12 procedures, n = 10), and right ventricular outflow tract obstruction (6 procedures, n = 6). There were two deaths among the group of patients that underwent reoperation.

**Conclusion:** ASO remains the treatment of choice for TGA and its variants. Modifications can be made to the arterial switch operation in an effort to meet the challenges presented by late complications. While the incidence of late reintervention is low, a subset of patients will require operations that extend the principles of myocardial revascularization, left ventricular outflow tract reconstruction, and relief of pulmonary stenosis.

<table>
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<th>10. Please choose your academic program:</th>
<th>MD</th>
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<tbody>
<tr>
<td>11. What year are you in the program?</td>
<td>2</td>
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<tr>
<td>12. What was your role in this project?</td>
<td>I reviewed, selected, and analyzed 72 articles from the current literature on arterial switch operation (ASO) for Transposition of the Great Arteries (TGA). In addition, I reviewed the charts of patients who underwent ASO for TGA, or reoperation for complications, at the Cleveland Clinic Children's Hospital. I collected data and organized it into tabular format, and I contributed to its analysis.</td>
</tr>
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</table>
**Lepow Day Abstract**

<table>
<thead>
<tr>
<th>1. Title:</th>
<th>Effects of TGF-β1 Loaded Gelatin Microspheres on Chondrogenic Differentiation of Human Mesenchymal Stem Cells</th>
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<tbody>
<tr>
<td>2. Presenter:</td>
<td>Eran Vieregge</td>
</tr>
<tr>
<td>3. Co-workers and Collaborators:</td>
<td>Loran Solorio, Chirag Dhami</td>
</tr>
<tr>
<td>4. Advisor:</td>
<td></td>
</tr>
<tr>
<td>5. Departments:</td>
<td>Department of Biomedical Engineering</td>
</tr>
<tr>
<td>6. Support:</td>
<td>The project is supported in part by the Ellison Medical Foundation</td>
</tr>
<tr>
<td>7. Institutions:</td>
<td>Case Western Reserve University</td>
</tr>
<tr>
<td>8. Body of Abstract: (300 words or less)</td>
<td><strong>Background:</strong> Damage to articular cartilage through processes including trauma and osteoarthritis results in permanent impairment of joint function due to the lack of physiologic mechanisms for cartilage repair. The ultimate goal of this work is to develop an implantable substitute for damaged cartilage using autologous human mesenchymal stem cells (hMSC). Addition of gelatin microspheres containing TGF-β1 to standard hMSC pellet culture may provide enhanced chondrogenesis through provision of a uniformly distributed source of chondrogenic growth factor with enhanced capacity for growth factor diffusion to cells located within central regions of the pellet. <strong>Hypothesis:</strong> The question addressed by the current work is whether differentiation of hyaline cartilage may be achieved by the incorporation of TGF-β1 loaded gelatin microspheres into hMSC pellets. <strong>Methods:</strong> Gelatin microspheres were manufactured using previously established protocols, then loaded with TGF-β1 by soaking overnight. MSC harvested from the iliac crest of human donors were expanded in culture and then combined with TGF-β1 loaded microspheres to produce a uniform solution. This mixture was loaded into polypropylene plates and centrifuged to form microsphere-incorporated cell pellets. The control consisted of hMSC pellets without microspheres grown in medium supplemented with TGF-β1.</td>
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</table>
β1. Media for the microsphere-incorporated pellets was not supplemented with exogenous growth factor, with incorporated microspheres serving as the source of growth factor through continuous release. Pellets were harvested at 1 and 2 week time points and chondrogenesis was evaluated using histologic staining for type II collagen and glycosaminoglycans (GAG) and biochemical assays for DNA and GAG content.

**Results:** Results indicate that hMSC pellets cultured with incorporated microspheres containing TGF-β1 achieved chondrogenesis at levels approaching those grown using standard pellet culture techniques with exogenous growth factor supplementation.

**Conclusions:** In conclusion, the current work demonstrates a new system for chondrogenic differentiation of hMSC in pellet culture. This system may result in increased uniformity of matrix deposition, which could improve mechanical properties of cartilage grown *in vitro* for future applications *in vivo*.

| 10. Please choose your academic program: | MD |
| 11. What year are you in the program? | 2 |
| 12. What was your role in this project? | My role was to assist in cell expansion and culture, microsphere synthesis, and growth factor release studies. I also took part in biochemical assays and ELISA. My role in the project is intended to continue to the next phase of the project, which will include in vivo implantation of cartilage constructs. |
| 13. Date: | 11/09/2010 |

**Lepow Day Abstract**

| 1. Title: | Performance Limits of a Microfabricated Artificial Lung |
| 2. Presenter: | Michael Magnetta and Abigail Vinson |
| 3. Co-workers and Collaborators: | |
| 4. Advisor: | |
| 5. Departments: | Advanced Platform Technology (APT) Center |
| 6. Support: | T35 |
| 7. Institutions: | Louis Stokes Cleveland VA Medical Center |
| 8. Body of | Lung diseases affect more than 35 million Americans |
Abstract: (300 words or less)

and are responsible for more than 350,000 deaths every year in the U.S. alone. Artificial lungs have been developed to alleviate lung disease; however, the performance of these devices is significantly lower than that of their natural counterpart. The human lung provides a maximum gas exchange rate for O₂ and CO₂ of 2-6 L/min, but current artificial lungs are only capable of a maximum gas exchange rate of 250-400 ml/min (efficiency of 0.01 – 0.02 ml/s/cm³), which limits their effectiveness. This insufficiency is due to decreased surface area, reduced surface-area-to-volume ratio, and greater wall thickness of artificial lungs. This project characterized an micromachined polydimethylsiloxane artificial lung device by quantitatively measuring the oxygenation of animal blood passed through the device. It was hypothesized that the tested device, with feature sizes close to that of the human lung, would have greater efficiency (gas exchange rate per blood volume) than conventional artificial lungs. Proven modeling and fabrication techniques were utilized to design and construct a polydimethylsiloxane artificial lung prototype. The device consisted of synthetic capillaries (20 μm diameter) separated from airflow channels by a thin (15 μm) silicone membrane. The device’s capabilities were tested by pumping deoxygenated blood through one side of the device while air flowed through the other side. Blood flow rates ranging from 0.3-1.5 mL/min were tested. The blood’s oxygen and carbon dioxide levels were measured and recorded prior to entering and directly after leaving the device with the iSTAT Clinical Portable Analyzer. The efficiency of the tested device ranged from 0.15-0.40 mL/s/cm³. Increased rates of blood flow resulted in increased efficiency. The device’s oxygen transfer efficiency was greater than that of artificial lung devices currently in use. Future work will include further design iterations to optimize oxygen exchange, reduce clotting, and increase device capacity to accommodate in vivo oxygen demands.

10. Please choose your academic program:  MD

11. What year are you in the program?  2

12. What was your role in this project?  I was a co-researcher on this project with Michael Magnetta. I participated in device fabrication, design of experimental procedures, and collected data during experiments.
**Title:** HEXIM1: a direct player in heart wall thickness

**Presenter:** Connie Wang

**Co-workers and Collaborators:** Monica Montano, Yong Qui Doughman

**Advisor:**

**Departments:** Department of Pediatrics

**Support:**

**Institutions:** UH Rainbow Babies and Children's Hospital

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**Body of Abstract:** (300 words or less)

Previous studies determined that transcription factor Hexamethylene-bis-acetamide-inducible protein 1 (HEXIM1) is a tumor suppressor and cyclin-dependent kinase inhibitor that is critical for cardiovascular development. Mice embryos that carried an insertional mutation in the HEXIM1 gene have abnormal coronary patterning and thin ventricular walls. These mice hearts showed reduction in VEGF, known to affect angioblast invasion and myocardial proliferation, and FGF9 expression. Our hypothesis from these data was that HEXIM1 plays critical roles in coronary vessel development and myocardial growth.

For the current study, we made an adult mouse model, where HEXIM1 is overexpressed only in cardiomyocytes. The HEXIM1 overexpressing mouse heart was heavier (higher wet heart weight to body weight ratio, n=3) and appeared to have bigger with thicker walled hearts compared to the control by qualitative histological observations. Whole mount analysis showed that the HEXIM1 overexpressing animals had enlarged atria with blood filled chambers. The preliminary results of the in vivo MRI analyses revealed that the hearts were bigger with a decreased heart rate and an increased ejection fraction. There was no obvious increase in wall thickness. We are currently analyzing gene expression and vascular density in the HEXIM1 overexpressing hearts. Our studies will help us determine
whether the HEXIM1 overexpressing heart resembles more of an athletic than a pathological heart.

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<tr>
<th>10. Please choose your academic program:</th>
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<tr>
<td>11. What year are you in the program?</td>
<td>2</td>
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<tr>
<td>12. What was your role in this project?</td>
<td>Data analysis and collection</td>
</tr>
<tr>
<td>13. Date:</td>
<td>11/09/2010</td>
</tr>
</tbody>
</table>

Welsh, Adrienne

**Lepow Day Abstract**

1. **Title:** Not just "noise": low-concentration patch test reaction is associated with future development of hand dermatitis in healthcare workers

2. **Presenter:** Adrienne Welsh

3. **Co-workers and Collaborators:** Michael Kashon, Health Effects Laboratory Division, National Institute for Occupational Safety and Health

4. **Advisor:**

5. **Departments:** Dermatology

6. **Support:** Dean's Summer Research Award

7. **Institutions:** University Hospitals

8. **Body of Abstract: (300 words or less)**

Irritant hand dermatitis is a common problem in healthcare workers who are exposed to frequent hand hygiene and prolonged use of occlusive gloves. A predictive test for individuals at increased risk for future development of irritant hand dermatitis would be useful as it would provide an opportunity for prevention. We studied the patch test results, TEWL measurements, and personal history of atopic dermatitis of 113 healthcare workers who washed their hands frequently to determine whether environmental factors or individual irritancy threshold might be predictive of the development of irritant dermatitis. We found that patch testing with low concentrations of sodium lauryl sulfate (SLS), sodium hydroxide (NaOH), or benzalkonium chloride (BAK) were all associated with the development of hand dermatitis by clinical exam during the six month study interval (p < 0.05). A history of atopic dermatitis was associated with positive responses to low concentration patch testing with benzalkonium chloride (p = 0.0154) but not with the development of dermatitis. The fact that low concentration irritant patch testing was associated with developing dermatitis suggests a possible genetic
predisposition rather than solely environmental risk factors. Atopic dermatitis was associated with patch test response to low concentrations of BAK but not to TEWL or patch tests with SLS and NaOH. This suggests that genes predisposing to atopic dermatitis account for only a portion of the irritant hand dermatitis risk.

10. Please choose your academic program: MD

11. What year are you in the program? 2

12. What was your role in this project? I entered the data into spreadsheet form, helped determine the results of statistical analysis, and wrote up the data and results into a paper for publication.

13. Date: 11/09/2010

Whitehair, Victoria

Lepow Day Abstract

1. Title: The Short-term Effects of TENS and t-NMES on Pain-Free Range of Motion of the Post-Stroke Shoulder

2. Presenter: Victoria Cooper Whitehair

3. Co-workers and Collaborators: Timothy Beutler, Richard Wilson, MD

4. Advisor:

5. Departments: Department of Physical Medicine and Rehabilitation

6. Support: I received a Dean’s Summer Research Stipend through Case Western Reserve University. Research costs were covered by an NIH K24 grant that my advisor holds.

7. Institutions: MetroHealth Medical Center

8. Body of Abstract: (300 words or less) Background: Electrical stimulation is commonly used to reduce shoulder pain in stroke patients with hemiplegia. While the ability of Transcutaneous Electrical Stimulation (TENS) and Neuromuscular Electrical Stimulation (NMES) to decrease shoulder pain has been shown, a comparison of their effect on pain-free range of motion (ROM) has not been evaluated.

Hypothesis: We hypothesized that exposure to both transcutaneous-NMES and TENS would be associated with a greater angle of external rotation and abduction compared to no stimulation and that t-NMES would lead to greater ROM than TENS.

Methods: The pain-free ROM of five subjects was assessed by measuring angles of shoulder external...
rotation and abduction. For each of the two movements, each subject received each of the three conditions (TENS, t-NMES, and no stimulation) three times in randomized order. A trained professional performed the stimulation, while ROM was measured by a blinded assessor.

Results: Data analysis was done using mean values for each of the conditions and repeated measure ANOVA. External rotation ROM angle means and standard deviations (in parentheses) were as follows: No stimulation: 62.9 (13.9), TENS: 60.6 (13.6), NMES: 62.9 (11.9) (F=1.01, p=0.406). Abduction ROM angle means (and SD) were as follows: No stimulation: 92.0 (19.2), TENS: 89.0 (24.9), NMES: 90.5 (22.2) (F=0.499, p=0.625).

Conclusions: The null hypothesis that the three treatments are equal cannot be rejected for either movement. While recognizing the small sample size, none of the differences seen in the data were clinically important. This lack of a clinically important difference between the treatments could affect the use of these treatments so we have decided to expand the study to include five additional subjects. This second phase is now in progress and is expected to be completed in the next few months, after which we may submit this to either a conference or a journal.
| 4. Advisor: |  |
| 5. Departments: | Department of Pediatrics, Division of Neonatology |
| 6. Support: | No financial support for the project has currently been obtained. |
| 7. Institutions: | Rainbow Babies and Children's Hospital and MacDonald Women’s Hospital |
| 8. Body of Abstract: (300 words or less) | **Background:** The Apgar score is used universally to clinically assess newborn infants in the first minutes of life. The Apgar’s application to preterm infants remains uncertain. Prior studies in premature infants have identified interobserver variability in the total Apgar score only.  
**Hypothesis:** Our first hypothesis is that interobserver agreement in scoring decreases with decreasing gestational age. Additionally, we hypothesize that agreement increases with decreasing respiratory support. Our third hypothesis is that agreement is decreased for muscle tone and reflex irritability.  
**Methods:** Informed, parental consent was obtained to film infants following birth. These videos were used to construct an online survey including 30 second clips of a term infant, a preterm infant on CPAP and an intubated preterm infant at 1, 5, and 10 minutes of life. Participants were asked to score each clip. The survey was preliminarily administered to 26 Neonatal Resuscitation Program certified physicians, nurse practitioners, and respiratory therapists at Rainbow Babies.  
**Results:** For the term infant, 100% agreement was seen among participants in all components of Apgar except appearance. 88.5% of participants assigned both an appearance score of 1 and a total score of 9. For all preterm scenarios, total Apgars varied by 4-5 points with the most frequent representing 25-53.85% of scores assigned. Score variation was seen in all components except heart rate. The most consistent variation was seen in the grimace and respiratory effort with participants assigning the full range of scores (0-2) in 5/6 preterm scenarios.  
**Conclusions:** This preliminary data is promising as it shows an increase in variation in Apgar scores in preterm infants as compared to term infants, particularly in the respiratory effort and grimace components. We hope our upcoming nationwide survey will provide more conclusive, higher power data on the effect of prematurity and increasing respiratory support on agreement in Apgar scoring. |
| 10. Please choose your academic program: | MD |
| 11. What year are you in the program? | 2 |
| 12. What was your role in this project? | My role during most of the summer was helping to locate and tape suitable infants (both term infants and premature infants born before 28 weeks gestation) in order to generate clips for the survey. I also participated in survey development and testing as well as preliminary data analysis this fall (our final survey has not yet been submitted). |
| 13. Date: | 11/10/2010 |
| Wong, Clarissa |  |

**Lepow Day Abstract**

| 1. Title: | Improving Attitudes towards Geriatric Medicine: How a House Calls Curriculum Can Make a Difference |
### 2. Presenter:
Clarissa Wong, Opeoluwa Eleyinafe

### 3. Co-workers and Collaborators:
Kimberly Churbock

### 4. Advisor:

### 5. Departments:
Family Medicine, Geriatric Medicine

### 6. Support:

### 7. Institutions:
Case Western Reserve School of Medicine, University Hospitals

<table>
<thead>
<tr>
<th>8. Body of Abstract: (300 words or less)</th>
</tr>
</thead>
<tbody>
<tr>
<td>It is well known that the population of older adults in the United States is growing to unprecedented numbers. Because comprehensively caring for the elderly requires a unique skillset, these older adults may be facing a health care workforce that is too limited to meet their health needs. The goal of the Project CaRE Elective is to have first year medical students recognize and explore the complexity of the health care for older adults in a homebound or nursing home facility setting. Our study examines how a multi-component Geriatric House Calls Curriculum affects medical students’ attitudes towards elderly patients, which in turn may have an impact on the paths they choose to follow in their careers. The hope is that with this exposure and exploration, students will re-shape their attitudes towards elderly patients. Perhaps with these widened horizons, the students will have an open mind about or become even more interested in caring for elderly patients in whichever field they choose. In this curriculum, students are each paired up with an elderly patient. They attend class meetings followed by individual home visits to interact with their patient. Topics and activities covered include polypharmacy, nutrition, comprehensive history taking and physical examination, geriatrics in medical specialties, and home safety assessments. Pre- and post-intervention surveys and focus groups will reflect the changes in the students’ attitudes toward geriatric medicine compared to their peers who did not participate in the elective. The pilot course will run from November 2010-February 2011. Data will be collected during that time.</td>
</tr>
</tbody>
</table>

### 10. Please choose your academic program:
MD

### 11. What year are you in the program?
2

### 12. What was your role in this project?
As participants in The Scholars Collaboration in Teaching and Learning Program, Ope and I designed this research project from
We worked off of our mentor's (Dr. Wanda Cruz-Knight's) original proposal for the curriculum to fully design and implement the educational intervention in our study.

### 13. Date:
11/09/2010

**Lepow Day Abstract**

<table>
<thead>
<tr>
<th>1. <strong>Title:</strong></th>
<th>Development of WHO Education Materials on Infertility Management for Health Care Providers and Patients in Targeted Countries</th>
</tr>
</thead>
<tbody>
<tr>
<td>2. <strong>Presenter:</strong></td>
<td>Qiaqia C. Wu</td>
</tr>
<tr>
<td>3. <strong>Co-workers and Collaborators:</strong></td>
<td></td>
</tr>
<tr>
<td>4. <strong>Advisor:</strong></td>
<td></td>
</tr>
<tr>
<td>5. <strong>Departments:</strong></td>
<td>Reproductive Health and Research (RHR)</td>
</tr>
<tr>
<td>6. <strong>Support:</strong></td>
<td>Dean’s Scholarship</td>
</tr>
<tr>
<td>7. <strong>Institutions:</strong></td>
<td>World Health Organization (WHO)</td>
</tr>
</tbody>
</table>

8. **Body of Abstract: (300 words or less)**

Worldwide, the inability to bear children is a tragedy for many couples, who may experience tremendous social, economic, and psychological consequences. More than 9% of the world suffers from infertility, medically defined as the inability to conceive a child after 2 consecutive years of trying, whether in a couple that has never conceived before (primary infertility) or in a couple that has previously conceived (secondary infertility). Primary infertility rates are rising in high-income countries where the cause is attributed mainly to the rise in the average maternal age at first conception. Secondary infertility rates are particularly high in low-income countries where infertility is more commonly a result of sexually transmitted infections, unsafe abortions, and post-partum complications. Additional causes of infertility in low-income countries may disproportionately include the patient’s or health care provider’s lack of understanding of reproduction. Educational materials targeting specific countries must therefore take these various elements into consideration. My project at WHO involved the development of evidence-based tools to facilitate infertility diagnosis and management in low-income countries. The project fell under the broader RHR
departmental goal of updating their manuals for the infertile couple (1993) and the infertile man (2000). For my project, I reviewed more than 30 recent papers on male and female factor infertility to produce an update of draft infertility guidelines. My update has mostly redefined the recommendations for management at the community-care and primary-care levels. The community care portion was additionally expanded to serve as groundwork for the development of a patient-education tool similar to other WHO tools. These and further developments of the guidelines and the tool will assist the department of RHR in its aim to strengthen the capacity of countries to enable people to protect their own health and to have access to sound sexual and reproductive health care when needed.

10. Please choose your academic program: MD
11. What year are you in the program? 2
12. What was your role in this project? researcher, draft editor
13. Date: 11/10/2010

Lepow Day Abstract

1. Title: Primary Central Nervous System Lymphoma: The Cleveland Clinic Experience
2. Presenter: Hao Xie, Ph.D.
3. Co-workers and Collaborators: David M. Peereboom, M.D.
4. Advisor:
5. Departments: Cleveland Clinic Lerner College of Medicine of Case Western Reserve University and Brain Tumor/Neuro-Oncology Center, Taussig Cancer Center
6. Support:
7. Institutions: Cleveland Clinic, Cleveland, OH
8. Body of Abstract: (300 words or less) BACKGROUND. Primary central nervous system lymphoma (PCNSL) is an extranodal non-Hodgkin’s lymphoma involving the entire central nervous system. In the past two decades, high-dose methotrexate has
become an essential component of first-line chemotherapy for PCNSL. However, the rarity of PCNSL and the difficulty in conducting large trials limit the evaluation of the efficacy of various treatment options.

METHODS. This was a retrospective study including 153 patients with PCNSL at Cleveland Clinic between 1986 and 2010. With primarily descriptive statistics, it summarized the Cleveland Clinic experience with respect to presentation, treatment, and outcome of patients with PCNSL.

RESULTS. One hundred and fifty three patients diagnosed with PCNSL had a median age of 61 and Karnofsky performance score (KPS) of 70. Cognitive/behavioral changes (45.1%) and ataxia (34.0%) were the most common clinical presentations. Diagnosis of PCNSL was made mainly by stereotaxic brain biopsy (79.7%). The progression-free survival was 35.7 months; the overall survival was 25.8 months. Treatment regimen was mainly methotrexate-based chemotherapy or a combination of methotrexate-based chemotherapy and delayed whole brain radiation therapy. The overall survival of patients treated with the former was 61.3 months; the overall survival of patients treated with the latter was 74.1 months. Age and KPS were identified as the only prognostic indicators from Cox proportional hazard model. Patients were categorized into three groups according to these prognostic factors. Patients with KPS higher than 70 usually had a favorable outcome compared with lower KPS. This especially held true for patients younger than 60, whose overall median survival was 98.0 months.

CONCLUSIONS. The Cleveland Clinic management of patients with PCNSL demonstrated the excellent overall survival, especially for patients with KPS higher than 70 at diagnosis. The methotrexate-based therapy resulted in successful and durable disease control, which allows us to better understand our practice and make further improvement.
10. Please choose your academic program: MD

11. What year are you in the program? 2

12. What was your role in this project? concept and design, collection and assembly of data, data analysis and interpretation, manuscript writing.

13. Date: 11/09/2010

Xu, Duo

### Lepow Day Abstract

| 1. Title: | Continuity of the photoreceptor inner/outer segments and visual acuity in anti-VEGF therapy for exudative AMD |
| 2. Presenter: | David Xu |
| 4. Advisor: | |
| 5. Departments: | Department of Ophthalmology |
| 6. Support: | None |
| 7. Institutions: | Cole Eye Institute, Cleveland Clinic Health System |

**8. Body of Abstract: (300 words or less)**

The retinal photoreceptor inner/outer segments (IS/OS) contain the cone and rod photoreceptors critical to visual perception and has been shown to correlate with visual outcome in a number of retinal diseases. We assessed the continuity of the IS/OS and thickness of the photoreceptor layer in patients with exudative age-related macular degeneration (AMD) to elucidate the correlation of photoreceptor health to visual outcome. A total of 99 eyes of 99 patients undergoing anti-vascular endothelial growth factor (anti-VEGF) monotherapy for exudative AMD were enrolled in this retrospective case series study. Anti-VEGF therapy was administered to patients on an as-needed basis guided by ophthalmic examination, visual acuity, and spectral domain optical coherence tomography (SD-OCT) findings. SD-OCT scans were morphologically analyzed and correlated with clinical measures of Snellen visual acuity, anti-VEGF injection history, and patient demographics. The mean ± SD age was 80.7 ± 9.1 years. Patients underwent a mean of 11.2 ± 8.8 injections over 25.0 ± 17.6 months. At conversion to exudative disease, patients had a mean VA of .572 ± .379 (logarithm of the minimum angle of resolution [logMAR], 20/75 Snellen equivalent). At the time of study, patients had a mean VA of .487 ± .349 (logMAR, 20/60 Snellen equivalent). Age (p=.0390), photoreceptor thickness (p=.0323), baseline BCVA (p=.0046), and BCVA at time of study (p=.0001) were significantly different between patients with continuous and non-continuous IS/OS segment. More discontinuous IS/OS segment grading was associated with advanced age (p=.0390), thinner photoreceptor layer thickness (p=.0323), and worse baseline (p=.0046) and final (p=.0001) visual acuity. Advanced age (p=.0018) and decreased photoreceptor layer thickness (p=.0359) was correlated with worse final BCVA. In conclusion, continuity of the photoreceptor IS/OS segment and increased photoreceptor thickness seen in SD-OCT are protective of visual acuity in patients undergoing anti-VEGF therapy for exudative AMD.
Lepow Day Abstract

1. Title: Transcatheter Heart Valve with Variable Geometric Configuration: In Vitro Evaluation
2. Presenter: Ernest Young
3. Co-workers and Collaborators: Ji-Feng Chen, Owen Dong, Alex Massiello
4. Advisor:
5. Departments: Biomedical Engineering
6. Support: This work was supported by the T-35 NHLBI Training Grant HL082544.
7. Institutions: Lerner Research Institute, Cleveland Clinic Foundation

8. Body of Abstract: (300 words or less)

Background
Clinically the current transcatheter aortic valve (TAV) technology has shown a propensity for paravalvular leak and studies have correlated this to increased calcification at the implantation site and with non-ideal geometry of the stented valve. The present study attempted to evaluate the hydrodynamics of different geometric configurations, in particular the intravalvular considerations.

Methods
Three TAVs were made in order to create a respective size 26 mm TAV. Hydrodynamics were assessed using a pulseduplicator. The geometries tested consisted of the nominal, elliptical, triangular and under-sized shapes; along with half-constriction where only a portion of the stent was constrained. The TAVs were assessed for effective orifice area (EOA), transvalvular pressure gradient (TVG) and regurgitant fraction.

Results:
The nominal sized TAV had a larger gradient (6.2 ± 0.3 mm Hg) than all configurations (p < 0.002) except the under-sized valves. EOA of the nominal sized TAV (1.7 ± 0.1 cm²) was smaller than
triangular and half-elliptical (p < 0.002). Full-elliptical and the under-sized tests had EOAs smaller than the nominal (p < 0.002). Nominal shape had smaller regurgitation (6.7 ± 1.4 %) than all configurations (p < 0.002) except for the half undersized (4.0 ± 0.7, p<0.002) with no statistically significant difference from the full undersized (6.8 ± 1.3, p = 0.724). Results for all combinations and values are outlined in Table 1.

Table 1: Mean and standard deviation values for TVG, effective orifice area (EOA), and Regurgitant fraction.

<table>
<thead>
<tr>
<th>Configuration</th>
<th>TVG (mm Hg)</th>
<th>EOA (cm²)</th>
<th>Regurgitant Fraction (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perimount**</td>
<td>3.0 ± 0.1</td>
<td>2.3 ± 0.0</td>
<td>8.0 ± 0.5</td>
</tr>
<tr>
<td>Nominal</td>
<td>6.1 ± 0.3</td>
<td>1.6 ± 0.1</td>
<td>6.7 ± 1.3</td>
</tr>
<tr>
<td>Half Triangle Commissures in Corner</td>
<td>4.9 ± 0.3*</td>
<td>1.8 ± 0.1*</td>
<td>11.0 ± 2.2*</td>
</tr>
<tr>
<td>Full Triangle Commissures in Corner</td>
<td>6.0 ± 0.8</td>
<td>1.7 ± 0.1*</td>
<td>12.7 ± 1.7*</td>
</tr>
<tr>
<td>Half Triangle Commissures in Middle</td>
<td>5.4 ± 0.3*</td>
<td>1.7 ± 0.1*</td>
<td>10.2 ± 2.6*</td>
</tr>
<tr>
<td>Full Triangle Commissures in Middle</td>
<td>5.4 ± 0.3*</td>
<td>1.8 ± 0.0*</td>
<td>11.8 ± 2.9*</td>
</tr>
<tr>
<td>Half Oval</td>
<td>5.5 ± 0.5*</td>
<td>1.8 ± 0.1*</td>
<td>10.0 ± 1.9*</td>
</tr>
<tr>
<td>Full Oval</td>
<td>5.5 ± 0.3*</td>
<td>1.7 ± 0.1*</td>
<td>11.9 ± 3.3*</td>
</tr>
<tr>
<td>Half Undersized</td>
<td>15.5 ± 0.6*</td>
<td>1.0 ± 0.0*</td>
<td>4.0 ± 0.7*</td>
</tr>
<tr>
<td>Full Undersized</td>
<td>16.0 ± 0.9*</td>
<td>1.0 ± 0.0*</td>
<td>6.8 ± 1.3</td>
</tr>
</tbody>
</table>

*These values were statistically significant when compared to nominal

**The control values are for one valve. HTCC: Half Triangle with commissures at the corners, HTCM: Half triangle with commissures at the midpoint between the corners, FTCC: Full triangle with commissures at the corners, FTCM: Full triangle with commissures at the midpoint between the corners.

Conclusions
The variable geometries that the TAV underwent in this study showed significant differences from the nominal geometry with respect to TVG, EOA and regurgitant fraction. In particular, many of these non-ideal configurations demonstrated an increased intravalvular regurgitation.

10. Please choose your academic program:
   MD

11. What year are you in the program?
   2

12. What was your role in this project?
   Original idea and lead project manager of experiment. Organized materials collection, funding, and distribution of work. Was involved in setting up the test procedure, experimental equipment and then running the experiment and collecting and analyzing the data. Also wrote draft of research findings.

13. Date:
   11/09/2010

Zhou, Hannah

**Lepow Day Abstract**

1. Title: Lgr5 expression in adult murine cells
2. Presenter: Hannah Y. Zhou
3. Co-workers and Collaborators: Kumar Sukhdeo and Monica Venere
4. Advisor: 
5. Departments: Department of Stem Cell Biology and Regenerative Medicine
6. Support: Crile Summer Research Fellowship
7. Institutions: Lerner Research Institute, Cleveland Clinic Foundation, Cleveland, OH 44195

8. Body of Abstract: (300 words or less)
   Stem cells comprise a subpopulation of the body’s cells that have unique properties of self-renewal and capacity for differentiation into multiple lineages with disparate functions. One protein that has been shown to be expressed in certain stem cell populations is leucine-rich repeating-containing G-protein coupled receptor 5 (Lgr5), a Wnt target gene that is important in development. Lgr5 has been reported to be expressed in a restricted population of proliferating stem cells of the stomach, small intestine, colon and hair follicles. Since Wnt signaling is essential for multiple adult tissue stem cells, we hypothesized that Lgr5 expression may identify the stem cell compartment in additional organs. To investigate this possibility we undertook a systematic histologic analysis of 8-12 week old C57BL/6 mice containing a knock-in reporter construct expressing enhanced Green
Fluorescent Protein (eGFP) under the control of the native Lgr5 promoter (Lgr5-EGFP-IRESCreER). Therefore, eGFP expression indicated Lgr5-expressing cells. Transgenic and wild-type (control) C57BL/6 mice were fixed by perfusion with paraformaldehyde and the organs were removed and embedded in Optimal Cutting Temperature medium. Seven micrometer-thick sections were made with a Leica CM1950 cryostat and stained with Hoechst and anti-GFP antibody. We documented eGFP expression in the defined population of the retina, which may represent retinal stem cells. In addition, Sertoli cells of the testes were eGPF-positive, which indicates Lgr5 may not be restricted to stem cells. Future experiments will explore the remaining tissues of the mice to identify additional Lgr5-expressing cells. By crossing Lgr5-EGFP-IRESCreER mice to another strain harboring an inducible Rosa26-LacZ allele, we will perform lineage tracing experiments to confirm whether Lgr5 is being expressed by stem cells. In summary, Lgr5 has the potential to be a marker for stem cells from many tissues, which may prove useful in identifying and extracting stem cells for research and treating degenerative diseases.

| 10. Please choose your academic program: | MD |
| 11. What year are you in the program? | 2 |
| 12. What was your role in this project? | Primary researcher and analyst |
| 13. Date: | 11/10/2010 |

**Zhu, Han**

**Lepow Day Abstract**

1. **Title:** Kruppel-like Factor 15 Regulates Skeletal Muscle Metabolism
2. **Presenter:** Han Zhu
4. **Advisor:**
5. **Departments:** Harrington-McLaughlin Heart & Vascular Institute, CWRU Dept of Medicine (HZ, SMH, PA, DJ, YL, DAP); CWRU Department of Pharmacology (CH, JK, MR); CWRU Dept of Physiology (TN); University of Missouri Kansas City, School of Nursing (MB); Deakin University, Melbourne, Australia (AR)
6. **Support:** AFAR/MSTAR (HZ), NIH HL086614 (SMH), NIH HL084154 (MKJ)
7. **Institutions:** Case Western Reserve University School of Medicine
**Background/rationale:** Skeletal muscle displays remarkable phenotypic plasticity and can adapt its metabolism to accommodate changes in physical activity and nutrient supply. The precise molecular mechanisms that govern this plasticity remain poorly understood.

**Question/hypothesis:** *Klf15* is robustly expressed in skeletal muscle; however, its role in this tissue is unknown. We hypothesized that *Klf15* is an important regulator of skeletal muscle metabolism and function *in vivo*.

**Methods:** We characterized skeletal muscle metabolism/function in *Klf15*−/− mice using physiologic (exercise capacity, indirect calorimetry, isolated muscle force-generation) and biochemical (mitochondrial physiology, ß-oxidation) assays. Using gain/loss-of-function approaches in mice and cell-culture, we delineated *Klf15* targets that mediate its metabolic effects. We dissected the molecular mechanism by which KLF15 induces target genes using transcriptional reporter assays and ChIP.

**Results:** *Klf15* is expressed in adult murine skeletal muscle and induced with fasting, exercise, and by ß2-agonists. Concordantly, *KLF15* is induced in skeletal muscles of human subjects after a single bout of bicycle exercise. *Klf15*−/− mice have impaired endurance exercise capacity, lower oxygen consumption, and fatigability of isolated skeletal muscle. *Klf15*−/− mice have elevated plasma triglyceride but reduced intramuscular triglyceride, consistent with a defect in lipid partitioning. Isolated mitochondria from *Klf15*−/− muscle have impaired ß-oxidation exclusively in the subsarcolemmal mitochondrial fraction, where decreased function of the carnitine-acylcarnitine translocase (*Slc25a20*) is rate-limiting. In accordance with these physiologic and biochemical defects, *Klf15*−/− soleus muscle has decreased expression of multiple genes essential for lipid utilization (e.g. *Fatp1*, *Slc25a20*, *Acox1*), many of which are known targets of PPARδ. Mechanistic studies show that a subset of these genes are direct targets of KLF15 and that PPARδ-mediated transcriptional responses are KLF15-dependent *in vivo.*
**Conclusions:** KLF15 is a critical regulator of skeletal muscle metabolism *in vivo*. These findings have important implications for nuclear receptor signaling, exercise physiology and pathophysiology of metabolic diseases.

<table>
<thead>
<tr>
<th>10. Please choose your academic program:</th>
<th>MD</th>
</tr>
</thead>
<tbody>
<tr>
<td>11. What year are you in the program?</td>
<td>2</td>
</tr>
<tr>
<td>12. What was your role in this project?</td>
<td>I have been working on this project for one year continuously under the mentorship of Drs. Haldar and Jain. I have been involved in almost every aspect of this project, from planning and carrying out many of the mouse experiments, cellular experiments, generating a transgenic mouse and molecular/biochemical analyses. I will be co-author on at least 2 manuscripts based on this work.</td>
</tr>
<tr>
<td>13. Date:</td>
<td>11/09/2010</td>
</tr>
</tbody>
</table>