

ABBAS, ATHEIR

1. Title:	Exploring the physiologic role of 5-HT _{2A/2C} – PSD-95 PDZ domain-mediated interactions
2. Student Presenter:	Atheir Abbas
3. Co-Workers and Collaborators	
4. Advisor	Bryan L. Roth
5. Departments	Biochemistry
6. Institutions	CWRU
7. Support	
8. Please choose your academic program:	MD PHD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Postsynaptic Density 95 (PSD-95), a neuronal MAGUK, is composed of 3 N-terminal PDZ domains and C-terminal SH3 and GK domains, all of which are involved in mediating protein-protein interactions. Immunofluorescent visualization of PSD-95 knockout brain with appropriate receptor-specific antibodies reveals an apparent reduction in 5-HT_{2A} receptor expression along with an almost complete absence of 5-HT_{2C} receptors in regions that would normally express PSD-95. Initial autoradiographic analysis using [¹²⁵I]DOI, a selective 5-HT_{2A/2C} agonist; as well as saturation binding experiments (using homogenates of micro-dissected brain regions of interest like cortex, striatum, and hippocampus) with [³H]ketanserin directed at the 5-HT_{2A} receptor, have confirmed these findings. Initial experiments using saturation binding experiments ([³H]mesulergine) confirm the large reduction in 5-HT_{2C} receptor expression in PSD-95 knockouts.</p> <p>The net effect of PSD-95 is to increase 5-HT_{2A/2C} receptor expression (and possibly modulate function), but whether or not this is an effect specifically of the 5-HT_{2A/2C}-PSD-95 interaction, or an indirect effect due to the disruption of some other interaction, is difficult to establish. In order to better address this problem, I have generated PDZ domain mutants exhibiting high affinity for PDZ ligand motifs. These mutants will be further characterized in vitro, and their potential usefulness in vitro and in vivo will be explored.</p> <p>Finally, we will continue further characterization of the effect of PSD-95 knockout on 5-HT_{2A/2C} receptor function will follow, beginning with an assessment of PSD-95's impact on Gq-coupled signaling by GTP[⁻³⁵S] binding in fresh frozen brain tissue. This will determine if the functional effects parallel the effects on receptor expression. The data thus far provide some of the first in vivo evidence that PSD-95 can indeed modulate the function of its partners, in this case, by affecting 5-HT_{2A} and 5-HT_{2C} receptor expression levels.</p>

ALKHAROUF, NAWAL

1. Title:	Analysis of Changes in Gene Expression Induced by Fusion of Dendritic Cells and Melanoma Cells
2. Student Presenter:	Nawal W. Alkharouf
3. Co-Workers and Collaborators	Gregory Plautz, M.D.
4. Advisor	Gregory Plautz, M.D.
5. Departments	Center for Surgery Research, Surgery Division
6. Institutions	Cleveland Clinic Foundation; Case School of Medicine
7. Support	Crile Fellowship; NIH-NCI RO1 CA91981
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>T cell-mediated cancer immunotherapy depends on adequate sensitization to tumor antigens. We have used electrofusion of dendritic cells (DC) with tumor cells (TC) to generate heterokaryons (DC-TC), which continuously express tumor antigens yet possess the antigen processing and co-stimulatory functions of DC. In preclinical models, DC-TC fusion cell vaccines mediate cure of established tumors but the effects of fusion on gene expression are unknown. In this study, we tested the hypothesis that fusion of distinct cell types would lead to alterations in the gene expression pattern for each cell and induce novel gene expression. We used Affymetrix human oligonucleotide arrays to examine the gene expression profile in triplicate samples of DC-melanoma fusion cells (DC-TC) enriched to >95% purity and compared them to DC-DC fusions and TC-TC fusions. Bioinformatics analysis methods, including a relational database, were developed to identify and functionally classify genes with a robust change in expression. Hierarchical cluster analysis of all fusion samples using the entire set of transcripts (n=22,277) separated the fusions into 3 distinct clusters, with the DC-TC cluster being closer to TC-TC than DC-DC. The DC-TC fusion samples also exhibited a higher Spearman rank correlation coefficient in pair-wise comparisons with the TC-TC samples. In addition, fewer genes were differentially expressed between the DC-TC and TC-TC samples (n=368) compared with DC-DC (n=1,927), and genes that were either upregulated or downregulated in the DC-TC vs. TC-TC or DC-DC fell into distinct functional classes. We also identified a set of 28 unique genes expressed only in DC-TC fusion cells involved in transcription, growth, signal transduction, cell adhesion, extracellular matrix and cytoskeletal organization. Interestingly, we observed novel expression of myoferlin, a protein involved in the physiologic process of Ca²⁺-mediated membrane fusion of myoblasts. These findings provide novel information about changes in and regulation of gene expression in the unique case of heterokaryon formation.</p>

ANIS, MURSALIN

1. Title:	Modulation of antigen-specific CD4+ T cell responses during pulmonary mycobacterial infection
2. Student Presenter:	Mursalin Anis
3. Co-Workers and Collaborators	Scott Fulton, Scott Reba, Clifford V. Harding, W. Henry Boom
4. Advisor	W. Henry Boom
5. Departments	Pathology and Infectious Diseases
6. Institutions	Case Western Reserve University School of Medicine
7. Support	HL07889
8. Please choose your academic program:	MD PHD
9. What Year are you in the program?	6
10. Body of Abstract (300 words or less)	<p>We hypothesized that ongoing pulmonary mycobacterial infection would modulate recruitment and activation of naïve antigen-specific CD4+ T cells. Balb/c mice were infected with aerosolized Mycobacterium bovis-BCG. Four to six weeks later, CFSE-labeled DO11.10 T cells, specific for OVA323-339:I-Ad, were adoptively transferred into naïve or infected mice. Recipient mice were challenged intra-nasally with soluble ovalbumin (OVA) over 3 days and then lungs, mediastinal lymph nodes (MLN) and spleens harvested to measure DO11.10 T cells by flow cytometry. To monitor antigen-specific T cell proliferation in vivo CFSE dye dilution and BrdU incorporation by DO11.10 cells was measured. Based on CFSE dilution profiles, responder frequencies of OVA-specific T cells in the BCG+OVA mice in MLN, lungs and spleens were 53(±2)%, 31(±3)%, 8.6(±1)% respectively. Responder frequencies in OVA mice were 46(±7)%, 13(±1)%, and 4.7(±1)%. ELISPOT showed increased frequencies of IFN-g secreting cells in the lungs of BCG+OVA vs. OVA alone mice. Pulmonary infection with BCG alone did not recruit appreciable numbers of OVA-specific T cells: recruitment required the presence of OVA. Ongoing pulmonary BCG infection increases recruitment, activation, and IFN-g secretion of pulmonary CD4+ T cells that encounter airway antigen.</p>

ANTONIANO, BRIAN

1. Title:	The Development of a Yeast Based Expression System to Investigate Potential Ligands that Activate Orphan G-Protein Coupled Receptors
2. Student Presenter:	Brian D. Antoniano
3. Co-Workers and Collaborators	Dr. Wesley Kroeze
4. Advisor	Dr. Bryan Roth
5. Departments	Biochemistry
6. Institutions	Case Western Reserve University
7. Support	Crile, and NIH Heart and Lung Research Grant
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Scientists are aware of the existence of over 700 different GPCRs. Although the sequences of these receptors are known, ligands remain unidentified. The purpose of this project was to develop a yeast based system where by drugs could be tested to deorphanize these receptors. Can we develop a yeast (<i>Saccharomyces cerevisiae</i>) based expression system to investigate the potential ligands that activate GPR40, GPR41, and GPR43? Since the putative ligands and functions have been partially elucidated, these receptors will primarily serve to establish the yeast based expression system as an effective technique in the de-orphanization of GPCRs.</p> <p>In total, two yeast strains were transformed for Gi- and Gq-coupled GPCRs. Agonists to be tested for all GPCRs included propionate, butyrate, acetate, and formate. Agonists tested specifically for GPR40 included Linoleate, Myristate, Palmitate, Oleate, and Dodecanoate. These were prepared under conditions that would allow solubilizations and dilutions in log amounts. Plates were next prepared containing 50ul of drug, and 150 ul of diluted yeast per well in doubles, incubated, and then checked for growth in a plate reader.</p> <p>In many samples the desired response was not obtained. Both 41 G-alpha-Q, and G-alpha-I yeastl grew in similar ranges regardless of drug present. Interestingly, in both 41s, samples containing formate, regardless of amount, showed the best levels of growth, while butyrate and propionate showed the least. GPCR 43i showed level amounts of growth, regardless of drug type. However 43 Q demonstrated growth responses dependent to drug amount for butyrate, propionate, and acetate. Samples 40 Q and 40 I both showed drug dependent responses at higher concentrations, myristate, laurate gave the strongest response.</p> <p>As the results show, this method of developing an agonist activated G-Protein allowing for yeast growth in a dose dependent manner was deliverable for GPCR 43Q, and GPCR 40I and GPCR 40Q. The experiment involving GPCR 43Q suggests Acetate, Butyrate, and Propionate all may activate GPCR 43Q. The experiment involving GPCRs 40Q and 40I suggest myristate, laurate may be agonists as well.</p>

ARNAUD, MAYA

1. Title:	There Is a High Correlation between the Clomiphene Challenge Test, Antral Follicle Count and Ovarian Volume to Predict the Ovarian Reserve
2. Student Presenter:	Maya E. Arnaud
3. Co-Workers and Collaborators	Arjun Khosla
4. Advisor	J. Ricardo Loret de Mola
5. Departments	Department of Reproductive Biology, Department of Obstetrics and Gynecology
6. Institutions	Case Western Reserve University, MacDonald Women's Hospital
7. Support	
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Objective: Diminished ovarian reserve is a condition occurring in women at any adult age. Among the most common tests employed to diagnose the problem are basal tests for FSH, LH, estradiol and inhibin B, or dynamic endocrine tests such as the clomiphene citrate challenge test (CCCT). The CCCT can unmask patients who might have not been detected by basal FSH screening alone, and appears to be more sensitive than day 3 FSH. In recent years, great attention has been devoted to direct ultrasound tests such as the antral follicle count and ovarian volume. Abnormal values in any of these tests are correlated with a decrease in pregnancy rates. The objective of our study is to evaluate if the CCCT correlates well with ultrasonographic studies such as the ovarian volume and the antral follicle count (AFC) to predict the ovarian reserve. Design: Retrospective cohort study in a University based tertiary Reproductive Endocrinology and Infertility Program Materials & Methods: 391 patients were enrolled in the study. The mean age of the subjects was 35.4 years +/- 4.5. Fifty subjects were smokers. On the month of their clomiphene challenge test (CCCT), antral follicle count (AFC), ovarian volume measurement by ultrasonography and basal gonadotropin concentrations were determined on day 2-3 of a spontaneous period and on day 10 after the CCCT. Serum levels of the various markers of ovarian reserve (FSH, LH, estradiol, progesterone, and antral follicle count) were measured by ELISA in a clinical laboratory. Statistical analysis was performed using simple regression analysis and analysis of variance (ANOVA). Results: There were 48 subjects who failed the CCCT. There was a strong direct correlation between age and day 3 FSH ($p < .0001$), day 10 FSH ($p < .0001$); as well as a strong reverse correlation with ovarian volume ($p < .007$), and the AFC ($p < .0001$). The mean antral follicle count among patients that passed the CCCT was statistically higher ($5.75 \pm .311$) than among patients that failed the test ($2.58 \pm .822$) ($p < .0004$). Additionally, the mean ovarian volume among patients that passed the CCCT was significantly larger ($17.36 \pm .816 \text{ mm}^3$) than among patients who failed the test ($12.944 \pm 1.36 \text{ mm}^3$) ($p < 0.04$). Discussion: There is a strong correlation between age and studies that assess the ovarian reserve. There was also a strong correlation between the CCCT, gonadotropin serum measurements and ultrasonographic measurements for the ovarian volume and the AFC. It appears that these studies can be used interchangeably to assess the ovarian reserve.</p>

AU, TINA

1. Title:	Sphingosine 1-Phosphate and its G Protein-Coupled Receptors Regulate B Cell Survival and Immunoglobulin Production
2. Student Presenter:	Tina Au
3. Co-Workers and Collaborators	Mei-Chuan Huang
4. Advisor	Edward Goetzl, M.D.
5. Departments	Division of Allergy & Immunology
6. Institutions	University of California, San Francisco
7. Support	Crile Fellowship, Case School of Medicine Summer Fellowship, American Academy of Allergy, Asthma & Immunology (AAAAI)
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>BACKGROUND: Sphingosine-1-phosphate (S1P) is a lysophospholipid produced by immune-activated mast cells, platelets, and macrophages. The CD40-CD40L interaction suppresses B cell apoptosis and promotes T cell-dependent B cells responses to antigens. Preliminary studies have shown that S1P enhances the expression of CD40 on B cells.</p> <p>OBJECTIVES:</p> <ol style="list-style-type: none"> 1) Determine if S1P signals B cells through S1P receptors to alter CD40 expression. 2) Determine if this influences CD40-mediated function, including the suppression of apoptosis and enhancement of antibody production. 3) Determine if B cells respond with increased production of IgE antibodies. <p>METHODS: Mice splenic B cells were isolated by magnetic cell sorting. Cells were treated with several concentrations of S1P. LPS and lectin were used as mitogenic activators of B cells, with anti-CD40 serving to simulate CD40L stimulation. RNA and protein were isolated for real time PCR of S1P receptors. CD40 expression of S1P-stimulated B cells was quantified by Western blot and flow cytometry. ELISA was used to detect production of IgG and IgM by B cells stimulated with LPS and anti-CD40, with and without IL-4 to target stimulation of IgG1 and IgE.</p> <p>RESULTS: Real-time PCR data show LPS stimulation leads to lower levels of mouse S1P1 and S1P4 transcript levels. Preliminary results suggest that anti-CD40 stimulation alters transcript levels of S1P receptors, with S1P1 levels decreasing over time, S1P3 levels increasing over time, and S1P4 levels staying relatively constant. No change in CD40 expression of S1P-treated B cells was detected by flow cytometry.</p> <p>CONCLUSIONS: Mitogenic activators of B cells, specifically LPS, can have an effect on the S1P receptors at the transcript level. No apparent differences were detected in the levels of CD40 expression of S1P stimulated B cells by flow cytometry. Further studies need to be done to determine CD40 expression differences and production of immunoglobulins.</p>

BALU, RAMANI

1. Title:	Two distinct classes of excitatory glutamatergic inputs onto olfactory bulb granule cells
2. Student Presenter:	Ramani Balu
3. Co-Workers and Collaborators	
4. Advisor	Ben W. Strowbridge
5. Departments	Department of Neurosciences
6. Institutions	Case Western Reserve University
7. Support	NIH predoctoral fellowship (F30-DC007274) to R.B. and by R01-DC04285 to B.W.S.
8. Please choose your academic program:	MD PHD
9. What Year are you in the program?	6
10. Body of Abstract (300 words or less)	<p>Understanding how sensory information is represented by distributed patterns of electrical activity in brain circuits represents a fundamental challenge in neuroscience. The mammalian olfactory bulb is an ideal system to study general principles of sensory coding. Sensory stimulation of olfactory receptor neurons in the nasal epithelium activates mitral cells in the olfactory bulb. Interactions between mitral cells and local inhibitory interneurons within the bulb convert this simple monotonic sensory input into a complex spatio-temporal discharge pattern of mitral cell activation that is relayed to higher order brain centers as a coded representation of odor. Granule cells—the most common local neuron in the olfactory bulb—form reciprocal dendrodendritic contacts with mitral cell secondary dendrites. These reciprocal synapses are critical for sculpting mitral cell output patterns. Despite the importance of granule cells in controlling olfactory bulb output, little is known about the fundamental properties of excitatory synaptic transmission onto granule cells. In addition, while granule cells receive mitral cell input on distal spines in the external plexiform layer (EPL), the identity and properties of excitatory inputs onto proximal spines in the granule cell layers (GCL) remain a mystery. To investigate these questions, we used whole cell patch-clamp recording from granule cells in olfactory bulb slices to study excitatory transmission at single granule cell spines. We found two distinct classes of excitatory inputs onto granule cells. Inputs onto distal spines in the EPL (presumably from mitral cell secondary dendrites) showed strong paired pulse depression that was due to an increase in transmission failures on the second stimulus. In contrast, EPSCs from proximal inputs in the granule cell layer (possibly from mitral cell axon collaterals or cortical feedback projections) showed paired-pulse facilitation accompanied by a decrease in failure rate on the second stimulus. These two types of synapses also showed markedly different responses to trains of EPSCs that mimic bursts of mitral cell action potentials during sniffing. These different classes of synapses are thus expected to have distinct effects on granule cell output and the timecourse of feedback inhibition onto mitral cells.</p>

BECK, DANIEL

1. Title:	Regional Dura Mater Differentially Regulates Suture Fate
2. Student Presenter:	Daniel Oliver Beck
3. Co-Workers and Collaborators	Derrick C. Wan MD
4. Advisor	Michael T. Longaker MBA, MD
5. Departments	Surgery
6. Institutions	Stanford University
7. Support	
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Craniosynostosis, the premature fusion of one or more cranial sutures, results in the pathologic development of the cranial vault and may appear in the context of complex syndromes with multiple system dysfunctions. The importance of a tissue interaction between the dura mater and overlying suture during early postnatal life is critical in dictating suture fate (patency versus fusion). Our study directly examined the gene expression profiles of fusing and non-fusing suture-associated regional dura mater as a means of identifying likely osteogenic agonists and antagonists, as well as their upstream or down stream signaling molecules, which may prove to be important in regulating the process of suture fusion or the maintenance of patency. Suture-associated dura was harvested from the fusing Posterior Frontal (PF), and non-fusing Coronal (COR) and Saggital (SAG) sutures of CD-1 mice (n=60) at times before (5d), during (10d) and post (20d) PF suture fusion. To elucidate potentially important differences in gene expression during this time frame an oligo-array analysis was performed on the dura tissue samples. Expression levels for genes of interest were corroborated by RT-PCR. Overall, we demonstrated up-regulation of several osteogenic agonists (e.g. FGF-2, TGF-B) associated with fusing PF dura and osteogenic antagonists (e.g. Noggin) associated with non-fusing COR and SAG dura at the 10 day time point. Gene-chip analysis is on-going and several candidate upstream regulators of our targeted osteogenic agonists and antagonists show promise for further analysis and study. Overall, we have established a strong correlation between levels of certain dural factors and overlying suture fate.</p>

BROADNAX, JEREMY

1. Title:	EMG Reliability
2. Student Presenter:	Jeremy Broadnax
3. Co-Workers and Collaborators	Yu-Tung Wong
4. Advisor	Dr. John Chae, MD
5. Departments	FES Center, Physical Medicine and Rehabilitation
6. Institutions	Case Western Reserve School of Medicine, MetroHealth Hospital
7. Support	American Federation of Aging Research, Crile
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>An EMG measures the electrical activity of a muscle in response to stimulation, to diagnose nerve disorders for example, muscle problems such as a compressed disk in the neck or back, carpal tunnel syndrome, muscular dystrophy, nerve problems associated with diabetes or anemia. If researchers believe in the validity of EMG studies what about the reliability? The goal of this study is to describe the reliability of established EMG data from the perspective of intra-reliability and inter-reliability testing analysis.</p> <p>Subjects were from a previous study on delay in start and termination of muscle contraction, motor impairment and disability in upper limb paralysis.¹ Researchers examined randomized trials from the previously recorded data and assessed the initiation and termination with respect to the EMG computer based graphical analysis for all data sets. Each examiner determined a set of rules appropriate for current techniques of EMG examination to determine if a standard technique was possible to achieve.</p> <p>The results showed; intra-rater reliability was better than inter-rater, inter-rater reliability improved over time, extensor data was more discrete than flexor data; Root Mean Square data was accurate.</p> <p>Time did not allow both researchers to complete two rounds of analysis to confirm intra-rater reliability, but would be a necessary for complete analysis. In addition, some subjects were impossible to use a standardized set of rules for measurement, so it would useful to figure out whether 10% of subjects have EMG readings that are difficult to analyze for whatever reason and eliminate them from studies that require solid EMG data analysis. Additionally, the examiner should choose a few of ubiquitous EMG samples to determine the significance of error in an analysis; if the uncertainty can be proven to be not significant, then computer-algorithms for pre-analysis of EMG data, with subsequent human-confirmation for "outliers" may be practical</p>

BUCHANAN, KELLY

1. Title:	Echo-tip vs. Standard Tip Needles in Ultrasound-guided Vascular Access
2. Student Presenter:	Kelly Buchanan
3. Co-Workers and Collaborators	Nora Colburn, John Bower M.D., Chuck Emerman M.D.
4. Advisor	Michael Phelan M.D.
5. Departments	Department of Emergency Medicine
6. Institutions	Cleveland Clinic Foundataion and MetroHealth Medical Center
7. Support	Crile Fellowship
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Background: Ultrasound is useful to help place central venous catheters. Echo-enhanced needles are available commercially, but it is unknown whether they have any advantage over standard needles. Because they are easier to visualize on the screen it has been presumed that they will improve ultrasound-guided vascular access.</p> <p>Hypothesis: It is proposed that improved visualization on ultrasound with an echo-enhanced needle tip will result in fewer needle sticks and redirections and subsequently a faster time to blood flash during central venous catheterization in a vascular access model.</p> <p>Methods: This is a prospective, randomized, observational study. Emergency medicine physicians (staff and residents) viewed a brief video on ultrasound-guided vascular access demonstration in both the long and short axis prior to participating. Subjects used both a standard and an echo-tip needle to obtain vascular access on a vascular access model in both the long and short axis view using a portable ultrasound machine. For each catheterization attempt, the number of needle sticks, redirections, and time to blood flash was measured. Following catheterization attempts, participants completed a Likert questionnaire regarding the echo-tip's performance.</p> <p>Results: There is no significant difference between needle types as measured by the number of needle sticks and redirections. There is no significant difference in needle tips in the time to blood flash as analyzed using the Mann-Whitney test. However participant perception rated the echo-tip needle's performance better than the standard tip in both axes. No Change in overall performance was reported by 39.2% of participants.</p> <p>Conclusions: Despite the enthusiasm over echo-enhancement, these needles failed to demonstrate any significant difference in objective performance measures over standard needles during ultrasound-guided vascular access, in this study. However, it is evident that participants perceived echo-tip needle performance to be superior to the standard needle.</p>

BURRAGE, LINDSAY

1. Title:	Genetic Resistance to Diet-Induced Obesity in Chromosome Substitution Strains of Mice
2. Student Presenter:	Lindsay C. Burrage
3. Co-Workers and Collaborators	Annie E. Hill (1), Jonathan B. Singer (2), Keith Shockley (3), Andrew Kirby (2), Gary Churchill (3), Karl Broman (4), Mark Daly (2), Eric S. Lander (2), Colleen(5)
4. Advisor	Joseph H. Nadeau and Colleen M. Croniger
5. Departments	(1) Department of Genetics (2) Broad Institute (4) Department of Biostatistics (5) Department of Nutrition
6. Institutions	(1) CASE School of Medicine (2) MIT and Harvard (3) The Jackson Laboratory (4) Johns Hopkins University (5) CASE School of Medicine
7. Support	This work was funded by National Institute of Health T32 GM07250-30 (L.C.B.), National Center for Research Resources RR12305, and the Charles B. Wang Foundation.
8. Please choose your academic program:	MD PHD
9. What Year are you in the program?	6
10. Body of Abstract (300 words or less)	<p>Genes that confer resistance to diseases, such as obesity, have tremendous therapeutic potential. However, most genetic studies focus on disease susceptibility. We recently discovered that the B6-Chr<A/J> panel of mouse chromosome substitution strains (CSSs), in which each A/J chromosome has been individually substituted onto the C57BL/6J (B6) inbred strain background, provides a model for genetic studies of obesity resistance. For instance, 17 CSSs are resistant to high-fat, diet-induced obesity which indicates that 17 A/J chromosomes harbor at least one quantitative trait locus (QTL) that confers resistance. Follow-up studies using F2 crosses and congenic strains derived from B6-Chr 6<A/J> revealed at least two resistance QTLs on A/J chromosome 6. Congenic and subcongenic approaches narrowed one of these QTLs from ~129 Mb (entire chromosome 6) to ~24 Mb, a segment which contains ~123 genes and less than 1% of the genome. Gene expression studies in adipose, liver, and skeletal muscle are underway in the 62B resistant congenic strain and an obese control strain after 28 and 100 days of high-fat diet exposure to identify candidate genes and pathways involved in resistance. Preliminary analysis of array data at the early time point identified several differentially expressed genes in the candidate region. Further analyses of the remaining gene expression data together with metabolic analyses will provide additional evidence indicating which of the differentially expressed genes is the strongest candidate. Overall, the CSSs provide a unique resource for studying genetic resistance to diet-induced obesity. Simultaneous studies of genetics, metabolism, and gene expression in these strains will lead to the discovery of many obesity resistance genes and perhaps, novel ways to treat this rapidly growing healthcare problem.</p>

CARTAYA, JULIA

1. Title:	Alternate Isoform Expression of the CEPB transcription factor for PEPCK In Vivo
2. Student Presenter:	Julia Cartaya
3. Co-Workers and Collaborators	Dr. Jianqi Yang, Dr. Richard Hanson, ect.
4. Advisor	Dr Richard Hanson
5. Departments	Department of Biochemistry
6. Institutions	Case Western Reserve University
7. Support	Crile Fellowship
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Background: Type II diabetes is a major public health issue affecting the United States today. The underlying problem is a lack of response to the anabolic hormone insulin, which normally functions to keep the blood sugar below a set point. When insulin insensitivity occurs, upregulation of gluconeogenic enzymes, such as PEPCK, occurs. It has been found that insulin affects the transcription of PEPCK and that this effect has, in part, been attributed to the alternate expression of PEPCK transcription factor isoforms based on the presence of insulin action. CEPB is one of those transcription factors that has been shown to regulate expression of PEPCK via alternate splicing and the production of different isoforms, CEPB β and CEPB α (LIP and LAP).</p> <p>Hypothesis: We expected to be able to show a difference in the LIP/LAP ratio in the nuclei of mice treated and untreated with insulin.</p> <p>Methods: This was achieved by using mouse liver nuclei extract and running Western blots on the samples using TBS labeled antibodies. The LIP/LAP ratio was then quantified using computer analysis.</p> <p>Results: We were able to show that CEPB isoform switching does, indeed, occur in vivo, which had previously been determined to occur in vitro in the lab.</p> <p>Conclusions: This result allows further investigation into this particular type of regulation of the PEPCK gene and potentially allows for insight into how to prevent one route of glucose production in the type II diabetic patient.</p>

CASSADA, JESSIE

1. Title:	Multifactorial Analysis of Naval Aviator Health Progression
2. Student Presenter:	Jessie L. Cassada
3. Co-Workers and Collaborators	ENS Brandi N. Olson, MC, USNR
4. Advisor	COL Roger U. Bisson, USAF, MC, CFS
5. Departments	Aeromedical Qualifications
6. Institutions	Naval Aerospace Medical Institute, Naval Aerospace Medical Research Laboratory
7. Support	United States Navy
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Naval Aviators are required to undergo a physical examination every five years in order to maintain their flight status. This yields access to longitudinal health changes that occur in a group of individuals over a given period of time. We conducted a study to observe time- and age-related changes in weight, lipids, blood pressure, and hearing loss in a cohort of 51 pilots. We also investigated significant differences between the various aircraft pilots as categorized into fighter, transport and helicopter populations. We predicted an increase in all values over the course of five years in addition to a greater hearing loss in the jet pilot population than in other aviators. The Analysis of Variance parametric test was initially utilized to compare means, followed by use of the Kruskal-Wallis nonparametric test to compare medians. Statistically significant data included an increase in LDL levels with age in all aviators—an average of 15 mg/dL over the course of 5 years, an increase in hearing impairment with time at 4 KHz in the left ear of all aviators—3.90 dB over the course of 5 years, and a significant hearing loss with time at 6 KHz in the right ear only in jet pilots—7.31 dB over the course of 5 years. A trend toward increased hearing impairment with time at 6 KHz in the right ear was observed in all aviators—3.79 dB over the course of 5 years. This indicates that all aviators experience some degree of hearing loss while jet pilots experience hearing loss at an accelerated rate as compared with non-jet aviators. Further research is required to produce more comprehensive results.</p>

CELIGOJ, FRANK

1. Title:	Future of Surgical Intervention in Heart Failure
2. Student Presenter:	Andrew Celigoj
3. Co-Workers and Collaborators	Y. Ootaki, M. Kopcak, M. Akiyama, K Kamohara, B. Duncan, L. Golding
4. Advisor	K. Fukamachi
5. Departments	Cleveland Clinic Biomedical Engineering
6. Institutions	Cleveland Clinic Foundation
7. Support	Myocor Coapsys System – Funded by Myocor, Inc. CorAide Left Ventricular Assist System – Funded by Arrow International, Inc.
8. Please choose your academic program:	PediPump Left and Right Ventricular Assist System – Funded by an NHLBI Contract, BAA NHLBI-HV-04-01 Novel Device for Left Atrial Appendage Exclusion – Funded by AtriCure, Inc.
9. What Year are you in the program?	MD 2
10. Body of Abstract (300 words or less)	<p>Heart disease afflicts more than 20 million Americans. New devices and techniques need to be developed in order to help this ever growing population of people. Current treatments are costly and do not adequately increase patients' quality of life. Therefore, I wanted to know what the future held for the treatment of heart disease. In order to pursue this question, I worked with the leading institution on heart disease, The Cleveland Clinic Foundation, to find out more. I worked with a team that investigates solutions for various causes of heart disease using artificial devices. The devices I looked at included the following:</p> <p>Myocor Coapsys System CorAide Left Ventricular Assist System PediPump Left and Right Ventricular Assist System Novel Device for Left Atrial Appendage Exclusion</p> <p>In addition to working with the team on new surgical interventions, I did background research on each of the devices.</p> <p>Each of these devices are in very early stages of development. Therefore, it is hard to determine if they will be implemented in the future. There is a lot of promise in the field of surgical treatment for heart disease. However, most of the treatments are highly invasive. Also, any foreign device placed in the body runs the risk biological incompatibility. Therefore, many of these devices require the patient to be continuously anticoagulated. As the devices are modified and improved, I believe the next step in the interventions is to develop techniques that minimize invasiveness.</p>

CHADALAVADA, SEETHARAM

1. Title:	The Prognostic Value of Peak Oxygen Consumption in Men and Women with Severe Systolic Heart Failure
2. Student Presenter:	Seetharam C Chadalavada
3. Co-Workers and Collaborators	Eileen Hsich MD, Eugene H. Blackstone MD
4. Advisor	Michael S. Lauer MD
5. Departments	Cleveland Clinic Lerner College of Medicine of Case Western Reserve University (SC), Departments of Cardiovascular Medicine (EH, MSL, and Cardiothoracic Surgery (EHB) at the Cleveland Clinic Foundation and the Department of Epidemiology and Biostatistics.
6. Institutions	The Cleveland Clinic Foundation and Case Western Reserve University School of Medicine
7. Support	National Institutes of Health grants R01 HL-66004-2, R01 HL072771-01, P50 HL-77107-1 and K12 HD049091-01. The Cleveland Clinic Foundation and Case Western Reserve University.
8. Please choose your academic program:	MD MS
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Background: Although peak oxygen consumption (VO₂) during exercise is frequently used to help predict optimal timing for heart transplantation, its prognostic value in women has not been well defined.</p> <p>Methods: We followed for 5 years 2105 adult systolic heart failure patients, including 525 (25%) women who underwent metabolic stress testing between January 1995 and December 2002. Multivariable proportional hazards modeling related VO₂ to survival with adjustments for over 30 confounders and with transplantation considered as a time-dependent covariate.</p> <p>Results: During follow-up 129 women (26%) died, as did 572 men (36%). There were 175 transplants, including 34 among women. Men and women were similar in age (55 vs. 54 years), but women less likely to have coronary disease (28% vs. 58%). VO₂ was strongly predictive of time to death in men (adjusted hazard ratio [HR] for VO₂ falling from 15 to 14 ml/kg/min 1.12, 95% CI 1.08-1.16, P<0.0001) and in women (adjusted HR 1.11, 95% CI 1.05-1.18, P<0.0001). There was no gender interaction (P=0.80), but for any given VO₂ women were at lower risk (adjusted HR for men 2.22, 95% CI 1.58-3.10, P<0.0001).</p> <p>Conclusions: Peak oxygen consumption is a useful tool to predict outcome of systolic heart failure in both men and women. However, for a given VO₂ the prognosis in men is worse than for women.</p>

CHAISSON, CLARISSA

1. Title:	Cardiovascular Disease in Women with Thyroid Cancer on Chronic Thyrotropin-Suppressive Therapy
2. Student Presenter:	Clarissa Chaisson
3. Co-Workers and Collaborators	Mira Milas, Allan Siperstein
4. Advisor	Mira Milas, M.D.
5. Departments	General Surgery
6. Institutions	The Cleveland Clinic Foundation, Case Western Reserve University School of Medicine
7. Support	Crile Fellowship, T35 Short-term Training Program HL080981 Grant
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Background: Adverse cardiac effects of both hyperthyroidism and hypothyroidism are well-recognized. Suppressing thyrotropin levels into hyperthyroid range during thyroid cancer (ThyCa) treatment minimizes cancer recurrence, but recent reports suggest even slight levothyroxine excess may provoke significant heart disease. Our interest was to analyze this trend in older women with ThyCa.</p> <p>Methods: Medical records at The Cleveland Clinic were retrospectively reviewed to identify female ThyCa patients over age 50, and compare ThyCa clinical/laboratory parameters, levothyroxine use, and cardiovascular disease (CVD) before and after starting thyrotropin-suppressive therapy (T4Rx). Data reflect mean±sd unless otherwise indicated; statistics employed Student's t-test.</p> <p>Results: Of 215 ThyCa patients, 33 women (15%) aged 64±10yrs (range 50-92yrs; 88%Caucasian) underwent thyroidectomy with median 1.3yrs follow-up (range 1mo-13yrs). After surgery, median levothyroxine dose was 112 mcg, representing body weight-based dosing of 1.6±0.6mcg/kg, and yielding TSH 0.86±1.1?U/mL. While total T4 levels were mildly elevated (13.4±2.5?g/dL), total T3 was normal (110±38ng/dL). CVD prevalence increased from 67% to 84% following T4Rx, especially for hypertension (HTN, 7%vs82%), atrial fibrillation (Afib; 12%vs24%), and congestive heart failure (3%vs6%). In 21% patients, T4Rx dosing was deliberately lowered to minimize cardiac side-effects. Compared to patients with Stage I ThyCa (n=20), patients with Stage III/IV (n=10) tended to be younger (65±8yrs vs 70±11, p=0.2), T4Rx dosing higher (1.8±0.8 vs 1.5±0.4mcg/kg, p=0.3), and TSH values more suppressed (nadirs 0.02±0.004 vs 0.6±0.5?U/mL, p<0.05). CVD disease patterns were unchanged in Stage I patients during follow-up. Afib prevalence rose from none to 29%, and HTN from 60% to 80%, in patients with Stage II/IV ThyCa while on T4Rx.</p> <p>Conclusion: Older women with ThyCa have high prevalence of CVD both before and after initiation of suppressive thyroid hormone therapy. Higher levothyroxine dosing appropriate for advanced ThyCa may influence Afib and HTN. Balancing therapy for ThyCa, now the #1 leading cancer in women by incidence rates, must recognize associated heart disease risks.</p>

CHANG, SHELLEY

1. Title:	Assessment of operationalized 3 day-recall of adherence and its association with viral rebound among HIV/AIDS patients receiving antiretroviral therapy at the Special Immunology Unit
2. Student Presenter:	Shelley Chang
3. Co-Workers and Collaborators	Barbara Gripshover, MD, Michelle Kuchia, Benigno Rodriguez, MD, Michael M. Lederman, MD.
4. Advisor	Ajay K. Sethi, PhD, MHS
5. Departments	Department of Biostatistics and Epidemiology and Center for AIDS Research (Case Western Reserve University School of Medicine); Special Immunology Unit (University Hospitals Health Systems)
6. Institutions	Case Western Reserve University
7. Support	Crile Research Fellowship, Center for AIDS Research (AI036219)
8. Please choose your academic program:	MD PHD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Although non-adherence to HAART directly correlates with treatment failure, there is no widely accepted method to assess adherence to HAART in HIV care clinics. Based on prior research, 3-day recall of medication adherence has been operationalized at the SIU, but has not been evaluated. We assessed the correlation of this current adherence measure with viral rebound and adherence to HIV care in this study. Since 2003, 833 patients on HAART have had 4,613 clinic visits in which 3-day recall was assessed at 4,103 (89%) visits for a median of 6 (IQR 3-8) visits per patient. Final cumulative adherence across all visits when adherence was assessed was 100% in 440 patients (55.63%) and <100% in 351 patients (44.37%). Using GEE, there was an association between having <100% cumulative adherence and viral rebound compared to having perfect cumulative adherence [OR=2.80, 95% CI: 1.85, 4.24]. When cumulative adherence was lagged by one clinic visit, the odds ratio remained significant [OR=1.98, 95% CI: 1.33, 2.93], indicating there exists a window of opportunity in which an intervention may improve patient adherence to HAART before the occurrence of treatment failure. When stratifying by level of imperfect adherence, there appeared to be a varying association between level of cumulative adherence and viral rebound. For cumulative adherence levels <50%, 50-70%, and 70-90%, the odds ratios were 4.91 (95% CI: 2.08, 11.62), 5.83 (95%CI: 2.60, 13.09), and 2.37 (95%CI: 1.20, 4.67), respectively, compared to having >90% cumulative adherence. When adherence is lagged, only the 50-70% cumulative adherence stratum remained significant [OR=4.32, 95%CI: 1.80, 10.36]. Significant predictors of rebound were being transgendered, missing clinic visits, lower CD4, and longer time since first ARV use. Cumulative adherence is not significantly associated with suppression. Cumulative adherence from operationalized 3-day recall measures appears to be an effective method to predict future viral rebound.</p>

COLLINS-RICHARDS, DEVON

1. Title:	Expansion of Mesenchymal Stem Cells for Bone Tissue Engineering
2. Student Presenter:	Devon Collins-Richards(1)
3. Co-Workers and Collaborators	Yusra Ahmad(2), Donald P. Lennon PhD(3), John E. George III MD (4), Davood Varghai MD (1), Arnold I. Caplan PhD(3), David Dean PhD(1)
4. Advisor	David Dean PhD
5. Departments	(1) Neurological Surgery (2) Anatomy (3) Biology (4) Surgery
6. Institutions	Case Western Reserve University
7. Support	Partial support is from a Crile Summer Fellowship to DC-R, NIH grant R01-DE13740 to DD, and the Research Foundation of the Department of Neurological Surgery, C
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Background and Rationale: Tissue engineered porous bone scaffolds may perform more reliably when seeded with mesenchymal stem cells (MSCs) than with raw bone marrow (RBM) as in our previous work (Dean D, et al. Effect of Transforming Growth Factor Beta 2 on Marrow-Infused Foam Poly(Propylene Fumarate) Tissue-Engineered Constructs for the Repair of Critical-Size Cranial Defects in Rabbits. Tissue Engineering 11:923-939, 2005). The goal of this project is to determine the most productive method of culturing canine MSCs from RBM. Hypothesis: We expect that a RBM sample with 5 million nucleated cells can be processed and cultured to result in at least 500,000 MSCs within 10 days. Methods: RBM was aspirated from the humeri of three dogs and put immediately on ice. Processing begins with the collection of a nucleated cell count via hemacytometer. The remaining marrow is centrifuged. Next, the isolated cells are resuspended and run through a percoll gradient separation. The resulting cells are plated in 100 mm petri dishes at a concentration of 5,000,000 cells per plate using two different media. These media differ only in their Fetal Bovine Serum (FBS) content. The two sera utilized were HyClone (Logan, UT) FBS and BioWhittaker (Walkersville, MD) Lot# 033F FBS. Media are changed every 3-4 days. Five plates are fixed on days 6, 10, and 14. All fixed plates are stained with crystal violet. At least one day after staining, macroscopically visible MSC colonies are counted. These colony counts are used to extrapolate MSC yield. Results: Plates representing all time points and both media are in hand and being counted. For 3 dogs this resulted in 45 plates for each of the two media, a total of 90 plates. Preliminary results suggest that with media containing either serum, the minimum desired MSC yield is obtained by day 10.</p>

CZEISLER, BARRY

1. Title:	Seizures Following Osmotic Blood-Brain Barrier Disruption in Humans
2. Student Presenter:	Barry M. Czeisler
3. Co-Workers and Collaborators	Nicola Marchi, Lilyana Angelov, Thomas Masaryk, Vincent Fazio, Tiziana Granata, Emily Oby, and Damir Janigro
4. Advisor	Damir Janigro
5. Departments	Cerebrovascular Research Center, Brain Tumor Institute, Departments of Neurological Surgery and Radiology
6. Institutions	The Cleveland Clinic Foundation, Istituto Nazionale Neurologico C. Besta
7. Support	This work was supported in part by the National Institutes of Health (NIH-NS43284, NIH-HL51614, NIH-NS46513, NIH-NS049514, and NIH-NS38195).
8. Please choose your academic program:	MD MS
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>The cerebral vasculature in epileptic patients is known to be functionally impaired in a number of ways, including defects in specific transporters as well as generalized blood-brain barrier (BBB) leakage. Whether these changes are primary factors in the pathogenesis of epilepsy or secondary effects of seizures on the BBB is not yet known. This study tested the hypothesis that acute BBB disruption (BBBD) can trigger behavioral seizures in human subjects. We monitored seizure activity in patients undergoing osmotic BBBD for the effective delivery of chemotherapy in the treatment of primary central nervous system lymphoma. Chemotherapeutic agents were administered immediately after BBB opening via hyperosmotic mannitol infusion into the cerebral arteries. Grading of BBBD was determined using CT imaging and levels of serum S100β, a peripheral marker of barrier disruption. We found that acute BBB failure may lead to behavioral seizures that occur most often contralateral to the hemisphere of the BBBD. Despite barbiturate administration prior to disruption, seizures occurred immediately after BBBD in 25% of procedures. No correlation was found between seizure occurrence and age, tumor size, or number of previous BBBD treatments. Seizures occurred prior to chemotherapy administration, and patients undergoing intra-arterial chemotherapy without BBBD did not develop seizures. Interestingly, patients with higher pre-procedure serum levels of S100β displayed resistance to seizures compared with those having normal baseline levels. These findings suggest that BBB disruption is itself pro-epileptogenic without influence from other predisposing factors such as unbalanced electrolytes or drug administration.</p>

DAUT, GREGORY

1. Title:	Prognostic Factors in Primary Pediatric Brain Tumors
2. Student Presenter:	Gregory Daut
3. Co-Workers and Collaborators	Dr. Sunil Manjila
4. Advisor	Dr. Alan Cohen
5. Departments	Pediatric Neurosurgery
6. Institutions	University Hospitals
7. Support	Crile Fellowship
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Introduction: Primary brain tumors in infants less than 12 months of age have a different distribution and prognosis than those of older children and adults. Identifying the primary prognostic factors can help modify treatment of these tumors.</p> <p>Research Question: What are the major prognostic factors for reduction in morbidity and mortality in primary brain tumors in infants?</p> <p>Study Design: A retrospective analysis was done in 14 patients diagnosed with primary brain tumors at less than 12 months of age in our hospital between 1995 and 2005. The age of onset, follow up duration, type of surgical procedure, histopathological diagnosis, adjuvant therapies and postoperative morbidities were studied from the available medical records. Therapies were assigned by tumor aggressiveness and location and age of patient.</p> <p>Results: The cases were analyzed for age at diagnosis, sex, tumor diagnosis, surgical action and adjuvant therapy against their outcome. Positive outcomes were disease-free survival for a follow-up period of at least 6 months. 3/6 diagnoses made at less than 6 months (50%) resulted in positive outcomes compared to 2/8 after 6 months of age (25%). 4/6 males (67%) had positive outcomes and 2/8 females (25%). 3/6 glial tumors (50%), including astrocytomas, gangliogliomas and desmoplastic infantile gangliogliomas, resulted in positive outcomes, 2/3 ependymomas (67%) and 2/2 choroid plexus tumors (100%); the other tumor types had only one example each. 3/5 gross total resections (60%) resulted in positive outcome, 2/5 partial resections (40%), and 1/4 biopsy (25%). Performing no adjuvant therapy resulted in 3/8 positive outcomes (38%), 2/3 patients that received chemotherapy alone (67%), 1/1 patient receiving radiation therapy alone (100%), and 0/2 patients receiving combination radiation/chemo (0%).</p> <p>Conclusions: In this small sample size, it appears that early age at diagnosis, male sex and aggressive surgical and adjuvant therapy may result in better outcomes.</p>

DENDRINOS, MELINA

1. Title:	Intraoperative Perfusion Technique and Temperament Profiles in Children with Hypoplastic Left Heart Syndrome
2. Student Presenter:	Melina Dendrinios
3. Co-Workers and Collaborators	Richard G. Ohye, Shauna Tindall, Eileen Mollen, Edward Schwartz, Cheryl Nowak, Edward Bove, Eric Devaney
4. Advisor	Caren Goldberg, MD
5. Departments	Division of Pediatric Cardiology
6. Institutions	University of Michigan, Ann Arbor, MI
7. Support	The Doris Duke Foundation, University of Michigan Research Advisory Council, Save-A-Heart Foundation, The General Clinical Research Center
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Hypoplastic left heart syndrome (HLHS) is a complex congenital heart disease requiring serial palliative operations. Impaired neurodevelopment is among the concerning morbidities. Surgical techniques, including intraoperative perfusion techniques, are among the factors which may impact neurodevelopment for children with HLHS. Purpose: The aim of this study is to describe the temperament profiles of infants with HLHS and to compare temperament between infants who underwent aortic arch reconstruction with a deep hypothermic circulatory arrest (DHCA) strategy to those who underwent aortic arch reconstruction with regional cerebral perfusion (RCP). Methods: Infants with HLHS were recruited for the clinical trial and randomized to undergo aortic arch reconstruction with RCP or with DHCA alone. Carey Temperament Scales questionnaires were completed by the parents of the patients prior to their second procedure, at approximately 5 months of age, and again at one year of age. Scores were generated for each of the nine temperament domains: activity, rhythmicity, approach-withdrawal, adaptability, intensity, mood, persistence, distractibility, and sensory threshold. Z-scores were calculated for each domain and t-tests were performed to compare DHCA to RCP groups. Results: Questionnaires were completed for 35 children at the first administration and 26 children at the second administration. The mean scores for the nine domains for both groups were within one standard deviation of the published standardized norms at both time points. Only 24 of the 549 domain scores were greater or less than 2 standard deviations from the standardized norms. At both time points, the patients in the RCP group had significantly lower distractibility scores than the patients in the DHCA group. Conclusion: Like the standard population, less than 5% of the study patients had domain scores greater or less than 2 standard deviations from the norms. The patients who underwent RCP were less distractible than the patients who underwent DHCA alone.</p>

DERAKHSHAN, JAMAL

1. Title:	Inversion-optimized, multi-slice, parallel TOSSI (T-One insensitive Steady State Imaging)
2. Student Presenter:	Jamal Derakhshan(1)
3. Co-Workers and Collaborators	M. Blaimer(2), P. Schmitt(3), J.L. Sunshine(2), J.L. Duerk(1,2), M.A. Griswold(2)
4. Advisor	Jeff Duerk, Ph.D.
5. Departments	(1)Department of Biomedical Engineering (2)Department of Radiology (3)MRI
6. Institutions	(1)Case Western Reserve University (2)University Hospitals of Cleveland and Case Western Reserve University (3)Siemens Medical Solutions, Erlangen, Germany
7. Support	NIH T32 GM07250-Case MSTP Siemens Medical Solutions-MRI
8. Please choose your academic program:	MD PHD
9. What Year are you in the program?	4
10. Body of Abstract (300 words or less)	<p>The spin-spin relaxation time (T2) of tissue is of great clinical importance for diagnosing diseased tissue from its healthy counterpart. Currently it takes 1.5 minutes to generate a T2-weighted (T2W) brain scan using a Turbo Spin-Echo (TSE) pulse sequence. Recently, a new pulse sequence called TOSSI (T-One insensitive Steady State Imaging) has been developed which is an alternative way of generating T2 contrast. This is a steady state free precession (SSFP) based MRI pulse sequence which has an inherently high signal-to-noise ratio. Pure T2 contrast is generated by non-uniformly spaced inversion pulses which align the bulk magnetization in states parallel and anti-parallel to the main magnetic field in a way that negates the T1 relaxation effect. The two previously published studies using TOSSI were limited to non-optimal inversion timing and to single-slice acquisitions. In this work we engineered several improvements into the TOSSI pulse sequence such as better image contrast, higher spatial resolution at a fixed echo time, and the ability to perform multi-slice acquisitions. We show that TOSSI can be used to obtain rapid multi-slice T2W images of the head in ~0.8 sec/slice or 16 seconds for a complete brain scan. We were able to obtain T2W brain images in a moving human subject without the need for additional motion correction; something not achievable with a TSE sequence. We also show that TOSSI is able to generate better T2W brain scans compared to other fast T2W pulse sequences such as HASTE and spin-echo EPI.</p>

DRAGE, MICHAEL

1. Title:	Interactions between mycobacterial lipoproteins and Toll-like receptors
2. Student Presenter:	Michael G. Drage
3. Co-Workers and Collaborators	Nicole D. Pecora, W. Henry Boom, Clifford V. Harding
4. Advisor	Clifford Harding
5. Departments	Pathology
6. Institutions	Case Western Reserve University
7. Support	
8. Please choose your academic program:	MD PHD
9. What Year are you in the program?	4
10. Body of Abstract (300 words or less)	<p>Mycobacterium tuberculosis (Mtb) causes chronic infection in otherwise healthy individuals. We have hypothesized that the ability of Mtb to decrease antigen processing and presentation by the host cell is one mechanism that enables Mtb to survive within the macrophage. This effect by Mtb is dependent on the presence of Toll-like receptor (TLR) 2. We have isolated several mycobacterial lipoproteins that signal through TLR2 and inhibit antigen processing and presentation.</p> <p>TLR2 is thought to signal as a heterodimer, paired with either TLR1 or TLR6. Bioassays using cells derived from TLR1 or TLR6 deficient mice suggests that TLR2/1 heterodimers bind triacylated lipoproteins and TLR2/6 heterodimers bind diacylated lipoproteins. Recent studies by our group and others suggest that there may be other ligand characteristics that influence signaling requirements by lipoproteins. The goal of this study is to examine the TLR2 heterodimer binding requirements of Mtb lipoproteins using both an in vitro bioassay using TLR deficient murine macrophages and human TLR fusion proteins.</p>

EDMISTON, LOGAN

1. Title:	Insertion of the Peptide D5-13 (KHGHGHGKHKNKGKKN) into Glutathione-S-Transferase Significantly Enhances its Antiangiogenic Activity
2. Student Presenter:	Logan Edmiston
3. Co-Workers and Collaborators	Sergei Merkulov, Anton A. Komar, Xiaoping Qi, Danyu Sun, Katya V. Gurova, Natalia D. Tararova, William C. Merrick
4. Advisor	Keith R. McCrae
5. Departments	1. Department of Medicine 2. Department of Biochemistry 3. Department of Biology 4. Department of Molecular Genetics
6. Institutions	1,2. Case Western Reserve University School of Medicine, Cleveland, OH 44106 3. Cleveland State University, 2121 Euclid Avenue, Cleveland, OH, 44115 4. Lerner Research Institute, The Cleveland Clinic Foundation, 9500 Euclid Avenue, Cleveland, OH 44195
7. Support	
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>High molecular weight kininogen (HK) is a well known cofactor in the intrinsic pathway of the blood coagulation cascade; however, its domain 5 (D5) (specifically the HGK motif-containing peptide) has been found to inhibit angiogenesis, endothelial cell proliferation, cell adhesion, invasion and metastasis. A peptide derived from domain 5, denoted H5-13, also inhibits endothelial cell proliferation and induces endothelial cell apoptosis, although these activities become apparent only at a 1000-fold greater concentration than the intact domain 5. These findings suggest that the conformational restraints placed on this peptide when presented in the context of D5 are important. Since D5 has limited solubility, we hypothesized that inserting H5-13 into another protein that may be abundantly expressed and easily purified might enhance its antiangiogenic and anti-tumor activity. Thus, we engineered a hybrid protein in which H5-13 (KHGHGHGKHKNKGKKN) had been inserted between Gly49 and Leu50 of glutathione S-transferase (GST). This protein, GSHKT, induced endothelial cell apoptosis (demonstrated using direct DNA laddering assays as well as by using a proliferation assays as a surrogate marker of apoptosis) at concentrations approximately 100-fold lower than the isolated peptide. Moreover, GSHKT blocked the metastasis and growth of B16F10 melanoma cells in a murine retroorbital vein model when used at less than 10% of the concentrations of the isolated HGK peptide (as reported in the literature). These findings suggest that incorporation of D5-13 into GST led to significant structural constraints in the peptide that enhanced its anti-endothelial cell and antiangiogenic activity. We speculate that this approach may be useful in optimizing the biological activity of a number of antiangiogenic peptides, as well as in defining the active structures of these agents.</p>

EKEODURU, RHASHEDAH

1. Title:	Using Immunohistochemical Staining to Establish the Presence of the AF1q Mitochondrial Protein in Thyroid Hurthle Cell Carcinomas and in Renal Oncocytomas
2. Student Presenter:	Rhashedah Eke-Oduru
3. Co-Workers and Collaborators	Dr. Howarad Meyerson and Dr. William Tse
4. Advisor	Dr. William Tse
5. Departments	Department of Oncology
6. Institutions	Iris and Burt Wolstein Research Center
7. Support	Crile Fellowship Program
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Thyroid oncocytic adenomas (Hurthle cell adenoma) are a class of tumors characterized by the presence of abundant mitochondria. Renal oncocytomas are benign tumors composed of large cells with granular, eosinophilic cytoplasm with abundant mitochondria. The Journal of Clinical Endocrinology and Metabolism reported an article detailing a two-step differential expression analysis that revealed a new set of genes thought to be involved in thyroid oncocytic tumors. The results were significant and confounding because AF1q was found to be overexpressed in 56% of 18 oncocytic tumors. This is significant because pediatric patients with AML who have high levels of AF1q expression have poorer prognoses than those with lower levels of AF1q. Specifically, the overall survival at 8 years for patients with a high AF1q expression is 19% versus 50% in patients with low AF1q expression. It is hypothesized that AF1q confers anti-apoptotic properties.</p> <p>Immuohistochemical staining was performed on thyroid Hurthle cell carcinomas and on renal oncocytomas using a human anti-rabbit AF1q primary antibody and a goat anti-rabbit secondary antibody. There is no established protocol for this experiment, thus optimal concentrations of primary antibody and of staining time were determined. It was demonstrated that a one hour incubation produced moderate staining, but an overnight stain proved optimal. It was questioned whether or not samples were overstained at twenty-four hours or if a three hour incubation was ideal. A 1:100 dilution of primary antibody elicited adequate staining of tissues. A rabbit anti-human polyclonal primary antibody was used, so non-specific staining was a concern. Control tissue sections stained solely with secondary, goat anti-rabbit antibody were all negative for AF1q expression. The negative controls were tonsil sections. Though all were negative, the test sections demonstrated a blushed brown appearance, with staining of superficial epithelial cells and interspersed heavily staining cells. The heavily staining cells are unknown. Flow Cytometry will be used to determine if these are B cells, T cells, or plasma cells. Future experiments involve staining of follicular, papillary and anaplastic oncocytomas, other adenocarcinomas, and small cell lung carcinomas.</p>

FADL, SAMER

1. Title:	Vertebral Artery Mobilization: Techniques and Applications in Neurosurgery
2. Student Presenter:	Samer Fadl
3. Co-Workers and Collaborators	
4. Advisor	Dr. Alan Cohen
5. Departments	Neurosurgery
6. Institutions	Rainbow Babies and Children's Hospital (UH - Case)
7. Support	Crile Fellowship T35 NIH-NHLBI
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>The vertebral artery (VA) is a crucial anatomical landmark when attempting to surgically access areas adjacent to the cervical spine or posterior fossa. The complexity of the neurovascular anatomy in these regions compounded with the limited microsurgical viewing angle have led to the employment of several operative approaches - from lesser invasive to more extensive in nature, to treat tumors and vascular diseases in this region. In order to minimize the morbidity and achieve the desired surgical benefit, a skilled neurosurgeon must be cognizant of the neurovascular anatomy and methods of adroitly maneuvering around such structures.</p> <p>In this study we compare and contrast two major operative techniques utilizing VA mobilization- extreme lateral approach and anterolateral approach- and their effectiveness in achieving the specified surgical goal. The classical far lateral techniques employing VA mobilization can be utilized for accessing the ventral foramen magnum region, with or without endoscopic assistance. The anterolateral approach through the neck will aid resection of extradural tumors of the cervical spine region, involving or encasing the V2 segment of vertebral artery. The skeletonization of the vertebral artery can also find application in the treatment of dissecting aneurysms.</p> <p>We performed human cadaveric dissections to validate the efficacy of these approaches.</p> <p>From our study it can be demonstrated that mobilization of the vertebral artery provides a wider surgical field with multiple corridors, thus making the access easy and intra-operative decisions more judicious. By carefully mapping out safe surgical corridors, amidst these vital anatomical structures, the neurosurgeon will be able to handle the intra-operative complications, even with minimal exposure.</p>

FEDERER, GREGORY

1. Title:	Incorporation of Material Properties into 3D CT-based Computer Aided Design of Large Format Cranial Implants
2. Student Presenter:	Gregory E. Federer(1)
3. Co-Workers and Collaborators	Robert L. Mullen PhD(2), David Dean PhD(1)
4. Advisor	David Dean PhD
5. Departments	(1) Neurological Surgery (2) Civil Engineering
6. Institutions	Case Western Reserve University, 10900 Euclid Avenue, Cleveland, OH 44106
7. Support	Partial support for this project was provided by a Crile Summer Fellowship to GEF and by the Research Foundation of the Department of Neurological Surgery, Case Western Reserve University, Cleveland, OH.
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Background and Rationale: Previous workers have relied on an assumption that homogenous material properties for skeletal segments are sufficient for a Finite Element Analysis (FEA) and that this would correlate well with a FEA based on the actual material properties. Radiographic intensity (i.e., radiodensity) data recorded in a patient's 3D CT-scan has been shown to be sufficiently well correlated with bone strength and stiffness to be used to create a Finite Element Model (FEM) for a boney segment with non-homogenous properties. Hypothesis: A FEM based on a skeletal segment's material properties will be less correlated with geometry than one based on the assumption of homogenous material properties. Methods: A 75 year old female cadaveric skull was 3D CT-scanned prior to processing that obtained its material properties. We then created a FEM with the actual material properties and with a homogenous material property specification based on the work of others. These two FEMs were tested at fourteen tessellation levels (i.e., 15,000 nodes to 80,000 nodes per mesh at intervals of 5,000 nodes). We then compared the distribution of strain for a given stressor over the distribution of the entire model between the radiodensity-informed and the non-radiodensity-informed FEMs. A frontal loading over 3% of the skull's total surface area was applied. Results: Across the range of mesh densities observed, the strain distribution was relatively constant. The strain distribution was roughly circular matching the shape of the loaded region. At the highest mesh density of 80,000 nodes, Von Mises stresses of approximately 5 megapascals were observed centrally in both FEMs. Conclusions: It appears that our hypothesis has been falsified and that the long-running assumption by other workers is appropriate. However, we have further tests to run before we can make this claim with confidence.</p>

FOUCHE, JOSEPH

1. Title:	The Correlation of Healthy Eating Habits and the Prevalence of Overweight Children in Urban Cleveland
2. Student Presenter:	Joseph Fouche
3. Co-Workers and Collaborators	
4. Advisor	Leslie Heinberg, PhD
5. Departments	Department of Epidemiology and Biostatistics
6. Institutions	Case School of Medicine
7. Support	Crile Summer Research Fellowship 2006 Boys and Girls Club of Greater Cleveland
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Obesity and dietary factors are associated with a substantial number of premature deaths in the United States. The accumulation of excess fat deposits in children stems from three main components: nutrition, genetic, and physical activity. Children with a body mass index above the 95th percentile are considered overweight, with those greater than the 97th percentile being severely overweight. This study was conducted to elucidate the relationship between diet, physical activity, and the development of overweight in 2 subgroups of minority children in a local Boys and Girls Club. The hypothesis of this study was that a negative correlation exists between met CDC dietary criteria and between sedentary activity and BMI percentile.</p> <p>Each participant's BMI, height, and weight were calculated. A questionnaire was administered inquiring about eating practices and daily nutritional intake. 22 adolescents and pre-teenagers were assessed. The average overall BMI was 19 (range 15-30) with no significant difference between the two groups. In the pre-teenage group, 5 of the 15 participants were overweight, and their eating habits were not different from the eating habits of healthy children. In the teenage group, the eating habits and nutritional status of the 3 overweight children did not differ from the other teenagers, but did differ significantly from the eating habits of the pre-teenage overweight and healthy weight children. Overall, the teenage group partook in less healthy eating practices in 8 of the 11 nutritional dietary criteria. 5 of the 8 overweight children reported significantly reduced hours exercising per week.</p> <p>Expectedly, a sedentary lifestyle was positively correlated with an increased BMI. Healthy eating habits did not significantly result in lower BMI percentiles, although this could be attributed to the lack of power of the study. Ideally, the results of this study helped to promote the development of healthy eating practices in the participants.</p>

FULLER, MOLLY

1. Title:	BMP4's role in astrogliosis and scar formation following spinal cord injury
2. Student Presenter:	Molly L. Fuller
3. Co-Workers and Collaborators	Rae Wang, Brian Rothstein, Anne DeChant
4. Advisor	Robert H. Miller
5. Departments	Department of Neurosciences
6. Institutions	Case Western Reserve University
7. Support	NINDS
8. Please choose your academic program:	MD PHD
9. What Year are you in the program?	6
10. Body of Abstract (300 words or less)	<p>Bone Morphogenetic Proteins (BMPs) are members of the Transforming Growth Factor-β superfamily of cytokines which have been shown to alter the proliferative, apoptotic, and differentiative states of neural stem cells. During embryonic development of the central nervous system (CNS), BMP4 promotes differentiation of neural precursors into astrocytes at the expense of oligodendrocytes. To investigate the continuing influence of BMP4 on the biology of astrocytes in the adult, we are using our established in vivo model of a demyelinating lesion of the rat spinal cord. By two days after the lesion, BMP4 levels were upregulated and glial fibrillary acidic protein (GFAP) expression was increased. Since increased GFAP expression is a sign of a "reactive astrocyte" and marks the astroglial scar that follows injury to the CNS, we looked for upregulation of other scar markers. By seven days post-lesion, chondroitin sulfate proteoglycan (CSPG), heparin sulfate proteoglycan, versican, neurocan, and phosphacan were all found to be upregulated at the lesion site. To simplify the analysis of cell types and cell signaling involved in this scar response, we prepared Type 1 astrocyte cultures from the CNS of postnatal day 2 rats. Type 1 astrocytes were shown to be responsive to BMP4 via an increase in the phosphorylation and activation of Smad1, the signaling molecule immediately downstream of the activated BMP receptor. In response to BMP4 treatment, GFAP and vimentin expression increased in treated cultures and CSPG expression was markedly upregulated. Our data show that BMP4 may play a critical role in the astroglial response of type 1 astrocytes to a CNS insult and formation of a scar. Understanding this response may allow for the development of interventions after CNS injury which would cause improved regeneration of CNS neurons and oligodendrocytes and recovery of nervous system functioning.</p>

GALLOGLY, MOLLY

1. Title:	Role of Reversible S-glutathionylation in Regulating Cellular Survival: Focus on the Aging Heart
2. Student Presenter:	Molly Gallogly
3. Co-Workers and Collaborators	Edward Lesnefsky, David Starke, Sarah Stewart, Qun Chen
4. Advisor	John Mieyal, PhD
5. Departments	Pharmacology (Case) and Medicine (VA)
6. Institutions	Case School of Medicine, Louis Stokes Cleveland Department of Veterans Affairs Medical Center
7. Support	NIH T32 GM07250 (MMG), NIH P01 AG 15885 (JJM, EJL), NIH R01 AG 024413, VA Merit Review Grant (JJM)
8. Please choose your academic program:	MD PHD
9. What Year are you in the program?	5
10. Body of Abstract (300 words or less)	<p>Post-translational modification by reversible S-glutathionylation is an emerging redox signal transduction mechanism affecting diverse cellular processes, including hypertrophy, actin polymerization, growth signaling, calcium homeostasis, glucose metabolism, and transcription factor activation. Proteomic analysis of rat heart tissue reveals that global protein-SSG (P-SSG) levels, as well as individual P-SSG levels (e.g., GAPDH, actin) are increased following ischemia-reperfusion. We have discovered that content and activity of glutaredoxin (GRx), the major intracellular de-glutathionylating enzyme, is decreased in heart tissue from Fisher 344 rats, an established model of human aging. We hypothesize that in the aging heart, decreased GRx activity leads to increased P-SSG levels following an oxidative insult such as ischemia reperfusion. We expect such changes in glutathionylation status to influence signal transduction pathways that regulate contractility and cellular survival, contributing to the increased morbidity and mortality experienced by elderly patients who suffer from myocardial infarction. We have shown in a pilot study that ischemia-reperfusion leads to increased glutathionylation of actin and a ~100 kD membrane protein (coincident with SERCA2 immunoreactivity) in adult (6 month-old) Fisher 344 rats. We intend to compare these changes in glutathionylation status with those seen in elderly (24 m.o.) rats, and use cell culture models (primary adult and elderly cardiomyocytes and embryonic cells with knocked-down GRx) to study the effects of actin glutathionylation on cytoskeletal integrity, contractility and apoptotic signaling; and the effects of SERCA2 glutathionylation on calcium homeostasis.</p>

GIMBEL, BRANDON

1. Title:	Changes in Connexin43 expression underlie Ventricular Electrical Remodeling
2. Student Presenter:	Brandon Gimbel
3. Co-Workers and Collaborators	Darwin Jeyaraj, Monica Isabella, Mark Tenforde
4. Advisor	David Rosenbaum
5. Departments	The Heart & Vascular Research Center
6. Institutions	Case Western Reserve University
7. Support	NIH-HL54807 (Dr. Rosenbaum)
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Electrical remodeling is a persistent change in the electrophysiological properties of myocardium in response to a change in rate or activation sequence. Ventricular electrical remodeling (VER) has potentially deleterious effects, but its mechanisms remain unknown. Gap junctions, which are vital for impulse propagation in the heart, turn over rapidly and are therefore candidates for involvement with VER. Previously, we found that in response to long-term pacing, the myocardial segment that undergoes the most significant VER (defined by changes in action potential duration and conduction) is always distal to the site of pacing. Since the gap junction protein Connexin43 (Cx43) is required for impulse propagation in the heart, we hypothesized that altered expression of Cx43 across the transmural wall underlies VER. Therefore, we predicted that Cx43 expression would change distal but not proximal to the site of pacing. Adult mongrel dogs were paced from the anterior wall epicardium. Samples of epicardium, midmyocardium, and endocardium were isolated from both the anterior (i.e., proximal) and posterior (i.e., distal) segments of the left ventricle. The membrane proteins were isolated, western blots were run, and the resultant radiographs of the gels were used to quantify the Cx43 expression levels in each segment. Cx43 was reduced in both proximal and distal segments, but the reduction did not achieve statistical significance in the epicardium of either: Non-paced proximal segment epicardium showed 1.61 (arbitrary units) +/- 0.16 of Cx43 expression, whereas paced proximal segment epicardium showed 1.35 +/- 0.29, demonstrating a 16.1% decrease, $p < 0.083$. Non-paced distal segment epicardium showed 1.51 +/- 0.18 of Cx43 expression, whereas paced distal segment epicardium showed 1.25 +/- 0.25, demonstrating a 17.4% decrease, $p < 0.069$. This data suggests that Cx43 reduction may play a critical role in the conduction slowing and in the action potential duration prolongation involved in VER.</p>

GOSNELL, AMY

1. Title:	Neurotransmitter Contribution to Elicitation of Nickel Allergy in Humans
2. Student Presenter:	Amy Gosnell
3. Co-Workers and Collaborators	
4. Advisor	Susan Nedorost
5. Departments	Dermatology
6. Institutions	University Hospitals/Case Western Reserve University
7. Support	Department of Dermatology at University Hospitals/Case Western Reserve University, Crile Fellowship
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Neurotransmitters are now thought to play an important role in inflammatory skin disease. Several studies have demonstrated that pharmacologic agents that interfere with these neurotransmitters can influence the development and expression of these diseases. This study was designed to investigate the role of neurotransmission in allergic contact dermatitis (ACD). We predicted that pretreatment with neurotransmitter-modulating agents would diminish the elicitation of ACD in known nickel-sensitive volunteers. We applied topical capsaicin, intradermal (id) lidocaine, Botox (id), atropine (id), and a saline control (id) to discrete locations on the back of each subject. We then placed Ni patch tests at each site for 48 hrs to determine the effects of these agents on the development of ACD. The reaction at each site was assessed by visual grading at 1-2 and 3-4 days after Ni exposure. The results of this pilot study yielded no significant difference in the treated patch sites compared to the positive patch test control sites. However, we predict that by adjusting the length of nickel exposure to better correlate with the duration of action and rate of clearance of the drugs used, effects of these interventions will be seen.</p>

GROSSMAN, JOANNA

1. Title:	Method to Reliably Identify S phase T Cells in Cryopreserved Peripheral Blood Mononuclear Cell Samples
2. Student Presenter:	Joanna K. Grossman
3. Co-Workers and Collaborators	Douglas Bazdar, Robert Asaad, MD
4. Advisor	Scott F. Sieg, PhD, Michael M. Lederman, MD
5. Departments	Division of Infectious Diseases
6. Institutions	Case Western Reserve University and University Hospitals of Cleveland, Center for AIDS Research
7. Support	Center for AIDS Research at Case Western Reserve/University Hospitals of Cleveland (grant AI-36219), National Institutes of Health (grant AI-38858)
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Very little is known about the progressive CD4+ T cell decline that characterizes HIV disease progression. While some researchers have suggested that plasma HIV viremia predicts the rate of CD4+ T cell decline, recent work at Case indicates that viremia is a poor predictor of disease progression. Dr. Scott Sieg at Case reported an increased number of circulating T cells in S phase of the cell cycle among HIV-infected persons. Because these S phase T cells are highly susceptible to cell death in vitro, we hypothesized that the frequency of S phase T cells in peripheral blood might be a good reflection of the rate of T cell decline. In order to assess whether a correlation exists between the frequency of S phase T cells and the rate of CD4+ T cell decline in HIV disease, we wished to utilize our extensive repository of cryopreserved peripheral blood mononuclear cell (PBMC) samples from HIV-infected persons who have been followed in our clinic over several years. Therefore, we needed to develop an assay that would reliably identify S phase T cells in frozen PBMCs. Although uptake of the thymidine analogue bromodeoxyuridine (BrdU) is the gold standard assay for labeling cells synthesizing DNA in S phase of the cell cycle, this method is ineffective when used on frozen cells. We suspect that this is due to the increased fragility of T cells in HIV-infected persons and of S phase T cells in particular. Thus, S phase T cells may be unable to continue DNA synthesis following the cryopreservation process. To establish an alternative method for identifying S phase T cells, we incubated PBMC preparations with BrdU, stained the cells with a fluorochrome-labeled anti-BrdU antibody, and compared the frequency of BrdU+ cells with the frequency of cells staining positive for other markers of immune activation (CD25, CD38, CD71, HLA-DR) or cell cycle progression (Ki67, cyclin A). Preliminary flow cytometric analysis indicates that concurrent Ki67 and cyclin A staining approximates the proportion of S phase T cells identified by the BrdU incorporation assay. Further testing is needed to confirm this observation and to evaluate this assay in frozen PBMC samples. If confirmed, we will apply this assay to the cryopreserved specimen repository at Case in order to ascertain the relationship between S phase frequency and CD4+ T cell decline rate in an untreated HIV-infected patient population.</p>

GUNN, PAUL

1. Title:	An Emerging Model of Primary Care for Older Adults: The House Call Practice
2. Student Presenter:	Paul W Gunn
3. Co-Workers and Collaborators	Antonnette V Graham, Shirley M Moore, Kurt C Stange, Stephen J Zyzanski
4. Advisor	Steven H Landers
5. Departments	Department of Family Medicine
6. Institutions	Case Western Reserve University/University Hospitals of Cleveland; Frances Payne Bolton School of Nursing
7. Support	American Federation of Aging Research, Crile Fellowship
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Background: House calls to the elderly have become more common, and this growth may be related to the emergence of physician-led house call practices. As the United States explores ways to meet the healthcare needs of an aging population, these practices represent an innovative and potentially beneficial model of primary care for older adults. Research in this area would be advanced by a description of existing practices.</p> <p>Objectives: To determine organizational, clinician, and patient characteristics of existing house call practices.</p> <p>Methods: We performed a cross-sectional survey of 36 clinicians representing house call practices throughout the United States. A 47-item questionnaire was administered by telephone interview, e-mail, or fax.</p> <p>Results: The response rate was 64%. The median practice age was 5 (95% CI, 5-9) years, and the median annual number of house calls per practice was 1000 (890-2946). Most practices identified themselves as the primary care providers for their patients (97%, 85-100%). The median number of physicians per practice was 1 (1-2.5), and 50% (33-67%) of practices had at least one nurse practitioner or physician assistant. The most frequent physician specialties were geriatrics (43%, 32-56%), family medicine (26%, 16-38%), and internal medicine (22%, 13-33%). The most common practice setting was urban (72%, 55-86%). Most house call patients had Medicare alone (73%, 60-80%), or Medicare and Medicaid (15%, 15-28%). The most commonly encountered diagnoses were hypertension and osteoarthritis. The most important reasons for emphasizing house calls were improved patient care, autonomy, and a past positive experience with a house call.</p> <p>Conclusions: Most house call practices are relatively new and composed of either solo physicians or small groups of physicians and nurse practitioners who primarily provide primary care to Medicare patients with chronic diseases. Clinicians are choosing this model of care in order to provide better patient care and enjoy greater autonomy.</p>

HARTWIG, KEVIN

1. Title:	Pediatric Urology Database Development and case report on Dilated Posterior Urethra in Infants Mimicking Posterior Urethral Valves
2. Student Presenter:	Kevin Hartwig
3. Co-Workers and Collaborators	Dr. Katherine Rhee, Eugene Kirkland
4. Advisor	Dr. Jeffrey S. Palmer
5. Departments	Division of Pediatric Urology
6. Institutions	Rainbow Babies and Children's Hospital
7. Support	Crile Fellowship
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Pediatric patients diagnosed with urological conditions such as nephrocalcinosis, vesico-ureteral reflux, and posterior urethral dilatation regularly undergo various radiographic imaging procedures like renal or bladder ultrasonography and voiding cystourethrography during the process of evaluation and treatment. It became apparent that establishing a database of the many pediatric urological cases that present to the hospital would be beneficial for use in evaluating surgical techniques used in treatment, in describing the presenting features and radiographic evaluation of the patients, and in assessing the accuracy of different radiographic imaging techniques in detecting certain urological conditions. It was with this objective that patient charts were reviewed and their radiographs digitized and imputed into a database. A number of the surgical procedures employed in treating the pediatric urology patients were also observed first hand.</p> <p>In the process of compiling the database, three children evaluated for prenatal hydronephrosis or proximal hypospadias were noted as having dilated posterior urethras on voiding cystourethrogram. Posterior urethral dilatation typically results from lower urinary tract obstruction due to such conditions as urethral stricture, posterior urethral valves, bladder-sphincter dyssynergia, or muscular abnormalities. These three particular cases of widened posterior urethra and prominent bladder neck had no evidence of posterior urethral valves or stricture on cystourethroscopic evaluation. A report on these cases was written and submitted for publication since it is the first report of infants with dilated posterior urethra on voiding cystourethrogram and cystourethroscopy without posterior urethral valves. It is a small and initial series so the significance cannot be fully determined at this time and requires serial follow up especially once the children are toilet trained. These findings and the relationship to voiding dysfunction need to be examined in the future.</p>

HICKEY, COLLEEN

1. Title:	Scholarly Activities of Family Medicine Faculty: Results of a National Survey
2. Student Presenter:	Colleen Hickey
3. Co-Workers and Collaborators	Kristen Brezinski, MS
4. Advisor	Jose Hinojosa, MD, Kim Marvel, PhD
5. Departments	Family Medicine Residency Program
6. Institutions	Poudre Valley Hospital, Corpus Christi Family Practice Residency
7. Support	Crile Fellowship, Health Resources and Services Administration Title VII funding
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Background and Objectives: This survey examined how family medicine residency programs define scholarly activity, the productivity of programs, and perceived barriers to scholarly work. Five types of residency programs are compared: university-based, community-based (unaffiliated, university-affiliated, university-administered), and military. Goals: The goals of the study are to 1.) Clarify activities considered to fit the criteria of scholarly; 2.) Obtain faculty productivity levels at family medicine residency programs; and, 3.) Identify perceived barriers to scholarly activity. Methods: A 13 item web-based questionnaire was sent to all 455 U. S. family medicine residency programs. The survey solicited demographic information as well as program expectations of faculty, presence of a research coordinator/director, activities considered scholarly, productivity, and perceived barriers. Results: A total of 177 surveys were completed for a response rate of 38%, similar to response rates of web-based surveys in the literature. 67.6% of programs encouraged, but did not require scholarly activity, and 44.5% indicated their program had no research coordinator/ director. University-based programs had the highest levels of productivity compared to other program types. Primary barriers to scholarly activity noted were lack of time (73/138, 53%) and lack of supportive infrastructure (37/138, 27%). Conclusions: While interpretations are limited by the response rate of the survey, results provide an increased understanding of how programs define scholarly activity as well as reference points for faculty productivity. This information can help program directors when setting criterion for scholarly work.</p>

HILL, JASON

1. Title:	The Effects of Transient Intrauterine Hypoxia-Ischemia Upon Cerebellar Development
2. Student Presenter:	Jason D. Hill
3. Co-Workers and Collaborators	Lab Assistants: Anne DeChant, MS, Qing Li, MD
4. Advisor	Shenandoah Robinson, MD
5. Departments	Neurosurgery/Neuroscience
6. Institutions	Case Western Reserve University
7. Support	Crile Fellowship
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Background: Perinatal brain injury affects a significant proportion of infants born prematurely, and frequently impairs motor and cognitive development. Though early ultrasound technology brought easily-detected white matter lesions to the forefront, modern imaging demonstrates that cerebellar damage also occurs, possibly compounding neurological deficits in premature infants. One-quarter of children with severe perinatal brain injury at our institution demonstrated cerebellar underdevelopment, impelling us to undertake this study. Using a rodent model of systemic prenatal hypoxia-ischemia, we investigated the pathogenesis of cerebellar injury in premature infants.</p> <p>Hypothesis: We predict cell populations that arise coincidental with late gestation hypoxic-ischemic injury will demonstrate a greater degree of abnormality than those cells that arise prior to or significantly after the injury.</p> <p>Methods: Fetal rat pups were subjected to 45 minutes of transient umbilical artery occlusion on embryonic day 18, and were born at term. Immunolabeling of midline sagittal posterior fossa sections was performed at P9 and P15 to compare development between post-insult and sham-control rats. Labeled cells from 4-7 animals per group were counted in lobules I, V, and X by two independent observers blinded to the insult status. Using a two-tailed t test, differences with $P < 0.05$ were considered significant.</p> <p>Results: In post-insult animals, cell populations arising late in gestation such as Golgi cells ($p < .02$), O4-immunolabeled pro-oligodendrocytes ($p < .002$), and calretinin-immunolabeled cells ($p < .002$) were decreased compared to sham-controls. Midgestation-arising Purkinje cells counts did not differ between insult and control animals. Similarly, the counts for basket and stellate cells, which arise postnatally, did not differ. A caudal-to-rostral gradient of injury was observed, co-incident with the normal cerebellar developmental gradient.</p> <p>Conclusion: Our data suggests that cell populations arising at the time of the E18 insult are most vulnerable. Selective vulnerability of the cell populations that arise late in gestation suggests targets for novel interventions for premature infants.</p>

HLAING, MAUNG

1. Title:	Educating Healthcare Providers about HIV/AIDS-related Stigma and Discrimination in Uganda
2. Student Presenter:	Maung Hlaing
3. Co-Workers and Collaborators	Meghan Gaydos (2), Winny Ngabiirwe (2), Sabrina Eagan (1, 2), and Denis Sama (2)
4. Advisor	Joyce Fitzpatrick, Ph.D., R.N., F.A.A.N. (1); Nelson Musoba, M.D. (2)
5. Departments	Frances Payne Bolton School of Nursing (1)
6. Institutions	Case Western Reserve University (1); Action Group for Health, Human Rights, and HIV/AIDS (AGHA) – Uganda (2)
7. Support	Crile Fellowship
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Human rights violations, specifically stigma and discrimination (S&D) by healthcare providers, create a formidable social barrier that prevents those most vulnerable to HIV/AIDS from diagnosis and treatment. Many health workers are unaware of discriminatory behaviors and unknowingly keep patients from seeking and receiving treatment. In Uganda significant efforts to reduce S&D have been made by state and non-governmental organizations. Nevertheless discrimination in all aspects of life prevents many individuals from receiving proper treatment. Very little literature exists on training healthcare professionals (HCP's) working with HIV/AIDS patients on the social issues of human rights and discrimination. Therefore, we attempted to identify issues most relevant to HCP's in Uganda in order to provide S&D awareness training. The project consisted of two parts. First, we performed a review of human rights literature as well as a review of regional HIV/AIDS literature to determine S&D issues specific to HIV/AIDS in Uganda. We then interviewed several individuals selected for their work with HIV-positive individuals in the healthcare field including an HIV support organization (TASO), a health and human rights organization (AGHA), a traditional healer organization (THETA), and physicians at the national referral hospital (Mulago Hospital) in Kampala, Uganda.</p> <p>The interviewees emphasized four topics: (1) the training needed to be participatory in order to elicit participants' emotions about HIV/AIDS to help recognize discriminatory behavior; (2) self-stigma amongst HCP's needed to be addressed; (3) HIV-counseling services need to be provided in healthcare settings; and (4) manuals currently used in S&D training in the community can be adapted for HCP's. With this information, we began writing guidelines for S&D training. At the end of the summer research period, preliminary guidelines and timelines were being completed. Currently, pilot training sessions with Ugandan medical students participating as trainees are being undertaken to fine-tune the training protocol.</p>

HOLMES, JESSICA

1. Title:	Evaluating Follow-up Care for Patients with Dementia
2. Student Presenter:	Jessica A. Holmes
3. Co-Workers and Collaborators	N Fisher, GNP, E. Dunlop, ANP, MA Greene, GNP, L Abood, PhD, PA Higgins, RN, PhD, TR Hornick, MD, D Kresevic, GNP, PhD, M Pallaki, MD, J Wang
4. Advisor	Dr. Thomas Hornick and Dr. Patricia Higgins
5. Departments	Department of Geriatrics
6. Institutions	Louis Stokes Cleveland Veterans Affairs Medical Center, Case Western Reserve University, NEOUCOM
7. Support	American Federation for Aging Research Medical Student Fellowship & Crile Research Fellowship
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Unlike other chronic conditions, in which there are well-established guidelines for routine assessment and follow-up care, guidelines of care for dementia patients are less well defined.</p> <p>The purpose of this study was to document type and frequency of outpatient care routinely provided as follow-up treatment for patients diagnosed with dementia.</p> <p>This clinical demonstration project was conducted by geriatric clinicians and researchers at the Cleveland Veterans Affairs Medical Center (VAMC). Approximately 34% of the patients in this interdisciplinary practice have a dementia diagnosis. Using a retrospective design, we abstracted data from the medical records of 62 dementia patients who received follow-up treatment for at least 16 months during 2002-2004. Based on a literature review and clinical experience, we assessed the frequency of documentation of 10 key indicators: Mini Mental Status Exam (MMSE), caregiver strain, patient behavior, ADLs, IADLs, competency, respite needs, referral to Alzheimer's Association services, driving status, and weapons.</p> <p>The sample reflected the general geriatric clinic population: 100% male; mean age = 79 (range = 62-87); mean MMSE = 21 (range 4-29). On the initial visit, documentation of the indicators varied from 100% (decision-making) to 3% (Alzheimer's Association). During follow-up, documentation rates dropped, with mental status most frequently recorded and caregiver needs least frequently recorded. Descriptive and graphical analyses will be used to illustrate major findings. This first phase of this project provided information about usual care practices in an academic geriatric outpatient clinic. The long-term objective is the development, implementation and evaluation of standard of care guidelines.</p>

HOWE, EVAN

1. Title:	Attitudes and Perspectives on End of Life Care among Cleveland's Homeless
2. Student Presenter:	Evan Howe
3. Co-Workers and Collaborators	Anthony D'Eramo, Julia Rose
4. Advisor	Elizabeth O'Toole
5. Departments	Department of Medicine
6. Institutions	MetroHealth Medical Center
7. Support	Crile Fellowship, AFAR Grant
8. Please choose your academic program:	MD MPH
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>The homeless population represents a unique patient group that is often not able to access health care resources to the same degree as other groups within a population. It is important to understand the unique needs and desires of this population that often has little voice in the debate over just distribution of health care resources. This qualitative study was intended to pursue the attitudes of homeless individuals towards end of life (EOL) care. Currently little research seeks to understand the interests of homeless and shelter dwelling individuals with regard to EOL care. The goal of this study was to determine the amount of knowledge and the interests of the homeless population in this area. A series of focus groups were performed at homeless shelters and drop in centers within the city of Cleveland, Ohio, USA. The questions covered three areas: life values, end of life experiences, and advanced care planning. This data was collected and the transcripts were analyzed using the NVivo software package. The focus groups and interviews highlighted the desire of homeless individuals to receive the same set of health care options as the rest of the population. However, because of the difficulty that this population has in obtaining government assistance to qualify for payment as well as the difficulty in finding a stable residence to receive the care, palliative measures are often not adequately provided. This study shows that while many of the desires of the homeless population in Cleveland, Ohio, USA towards EOL care are the same as the general population, the challenges that face the homeless in order to access EOL care are significantly greater than that encountered by the rest of the population. Special attention needs to be paid to homeless populations to assist them in gaining equal access to health care.</p>

JEFFERY, ANNITA

1. Title:	Transmural Dispersion of Repolarization as a Marker of Proarrhythmia
2. Student Presenter:	A. Nikole Jeffery
3. Co-Workers and Collaborators	Lance Wilson, MD; Tamer Said, MD
4. Advisor	David Rosenbaum, MD
5. Departments	Heart and Vascular Research Center
6. Institutions	MetroHealth Medical Center
7. Support	Pfizer
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>The potential for drugs to prolong repolarization and thus the QT interval is associated with the potentially fatal arrhythmia Torsade de pointes (TdP). Despite the lack of conclusive evidence to show that drug induced prolongation of APDs or the QT interval inevitably lead to TdP, any evidence that a new drug prolongs the QT interval raises significant concern about its safety, and is a major cause for the withdrawal of approved drugs from the market. Enhanced dispersion of repolarization has long been associated with arrhythmogenesis. Drugs that block the I_{Kr} channel enhance inhomogeneities of repolarization across the transmural wall of the ventricle, providing substrate for conduction block, reentry, and possibly TdP. To date, there has not been a standard method with which to measure dispersion. The goal of this study is to identify methods by which proarrhythmic and nonproarrhythmic QT prolonging drugs can be differentiated and to evaluate the five methods used to measure dispersion: maximal APD dispersion, epicardial to M cell APD gradient, dispersion of repolarization time, maximal local gradient of repolarization, and maximal local gradient of APD. Transmural optical mapping in a canine wedge preparation was utilized to measure APDs at a wide range of cycle lengths. Measures of dispersion were then examined at 2000 cycle lengths. Each transmural measure of dispersion allowed comparison of the drugs studied. With varying precision, each method was able to prove which drugs exhibited arrhythmogenic potential. But it was the maximal local gradient of repolarization that was most useful in identifying pockets of reentry. It was shown that measures of transmural dispersion could differentiate proarrhythmic and nonproarrhythmic drugs, but no one method was superior.</p>

KEARY, JONATHAN

1. Title:	Responses to Gram-negative Bacteria are Distinct From Responses to Soluble Lipopolysaccharide
2. Student Presenter:	Jonathan Keary
3. Co-Workers and Collaborators	Beidelschies, M.A.; Islam, A.S.
4. Advisor	Ed Greenfield
5. Departments	Orthopaedics
6. Institutions	Case Western Reserve University, Cleveland, OH University Hospitals of Cleveland, Cleveland, OH
7. Support	NIH RO1 AR043769
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Lipopolysaccharide (LPS), the primary immunostimulatory molecule produced by Gram-negative bacteria, is virtually inactive in the absence of LPS binding protein (LBP). Since LBP is a serum protein, it is unclear how Gram-negative bacteria stimulate host responses in the relatively avascular microenvironments often encountered during infection.</p> <p>Intact bacteria present LPS in a manner that does not require LBP to activate host responses. Polymyxin B (PMB), which prevents LPS binding to LBP, was incubated with RAW264.7 macrophages during stimulation with soluble LPS, intact heat killed <i>E. coli</i>, or titanium particles with adherent LPS in the presence or absence of bacterial debris. TNFα secretion was measured to assess host responses.</p> <p>As expected, PMB completely blocked TNFα secretion induced by soluble LPS in a dose dependent fashion, yet had no effect on responses to intact bacteria. To determine if this is due to LPS interaction with other bacterial molecules or LPS on particulates, we compared metal particles with adherent LPS in the presence or absence of bacterial debris. PMB blocked responses to highly purified LPS adherent to metal particles in a dose dependent fashion but had no effect on responses to metal particles with adherent bacterial debris.</p> <p>These results show that intact bacteria present LPS in a manner that does not require LBP to activate host responses. This may explain how Gram-negative bacteria stimulate host responses in the relatively avascular microenvironments often encountered during infection. These results may also explain how metal particles with adherent bacterial debris stimulate inflammatory bone loss in the relatively avascular tissue surrounding loosened orthopaedic implants. These results, together with our lab's recent finding that TLR-4, the primary LPS receptor, associates with lipid rafts in response to soluble LPS but not in response to intact bacteria, show that mammalian responses to Gram-negative bacteria are distinct from responses to soluble LPS.</p>

KENNER, STACI

1. Title:	The Effects of Gender, Ethnicity and Socio-economic status on Body Mass Index, Self-esteem, Body Image and Self-efficacy in Overweight Children and Adolescents
2. Student Presenter:	Staci Kenner
3. Co-Workers and Collaborators	Eve Kutchman, M.Ed.; Sarah Lawhun, M.Ed.,RD,LD; Naveen Uli,MD
4. Advisor	Leslie Heinberg, PhD
5. Departments	Departments of Epidemiology and Biostatistics and Pediatrics
6. Institutions	Case Western Reserve University School of Medicine and Rainbow Babies and Children's Hospital
7. Support	Funding for this project was provided by the Crile Summer Research Endowment with supplemental support provided by the P35 Short Term Training Program HL080981
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>This study investigated the ethnic, gender and socio-economic factors that may differentiate the experience of pediatric obesity, self image and self-efficacy in children referred for obesity treatment. It was hypothesized that: 1) African Americans, boys, and low socio-economic status (SES) individuals will be more overweight (higher BMI z score) and 2) African Americans, boys, and high SES individuals, would have higher ratings of: a) self esteem; b) body image; and c) self-efficacy to change one's diet and activity level. Participants included 64 families (46% African-American; 58% female; Mean children's age=11.31; SD=2.97) referred for evaluation to enter the Healthy Kids Healthy Weight intervention. This 12-week, behavioral intervention focuses on increasing physical activity, improving dietary intake and increasing behavior-change skills. The following questionnaires were completed during the initial 2 visits: 1) Rosenberg Self-Esteem Inventory 2) The Self Image Questionnaire for Young Adolescents-Body Image Subscale, 3) Self-Efficacy Questionnaire: Physical activity subscale, and 4) Weight Efficacy Life-Style Questionnaire. As hypothesized, African Americans had significantly higher BMI z scores (mean=2.54, SD=0.24) than Caucasians (mean=2.35, SD=0.36; t=2.67, p=.01). Similarly, boys had significantly higher BMI z scores (mean=2.58, SD=.38) than girls (mean=2.38, SD=.28; t=2.55 p<.02). The hypothesis that children from a lower SES would be more overweight was not supported. Further, contrary to hypothesis, no racial differences were found on the measures of interest. Boys had much higher self-efficacy about managing their weight (mean=72.07, SD=8.04) than girls (mean=56.60, SD=14.79; t=3.56, p=.001). However, there were no gender differences on body image, self esteem or physical activity self-efficacy. Finally, there no SES differences on any of the measures of interest. In conclusion, even though boys had significantly higher BMI z scores than girls, they also had significantly higher self-efficacy to change their lifestyle. Future research should investigate whether this greater self-efficacy predicts greater success with the weight management program.</p>

KHOSLA, ARJUN

1. Title:	In Women with the Polycystic Ovarian Syndrome (PCOS) the Body Mass Index (BMI) is an independent risk factor for elevated High Sensitivity C-Reactive Protein (HS-CRP)
2. Student Presenter:	Arjun Khosla
3. Co-Workers and Collaborators	Maya Arnaud
4. Advisor	J. Ricardo Loret de Mola
5. Departments	Department of Reproductive Biology, Department of Obstetrics and Gynecology
6. Institutions	Case Western Reserve University, MacDonald Women's Hospital, Cleveland, Ohio
7. Support	
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Introduction: Polycystic ovarian syndrome (PCOS) is the most common metabolic reproductive abnormality in women of reproductive age. Symptoms include chronic anovulation, hyperandrogenism, and insulin resistance, leading to compensatory hyperinsulinemia and dyslipidemia. These patients are, therefore, at increased risk for developing cardiovascular conditions. Evidence has shown that arterial thrombosis, in addition to being caused by lipid accumulation, represents a chronic inflammatory process. C-reactive protein (CRP) is a marker of inflammation that has been shown to predict cardiovascular events. In fact, CRP is a stronger predictor than LDL, it is a simple and inexpensive method, and can be used to improve global risk prediction and compliance with preventive approaches. Therefore, given the high incidence of cardiovascular disease in PCOS and the high correlation of CRP in predicting cardiovascular events, we studied this particular marker in women with PCOS.</p> <p>Methods: This was a sixty-seven patient retrospective cohort study performed in a university-based tertiary reproductive endocrinology and infertility program. Menstrual and medical histories were obtained and physical examinations were performed. No medications were taken for at least one month prior to providing a fasting serum sample, which was analyzed for high-sensitivity/c-reactive protein (HS-CRP), fasting glucose, fasting insulin, testosterone, DHEAS, and 17-hydroxyprogesterone levels.</p> <p>Results: BMI appears to be a risk factor for cardiovascular disease, since there was a highly statistically significant independent correlation between BMI and HS-CRP ($P < .0001$). There was also a highly statistically significant correlation between BMI and fasting insulin and fasting glucose/insulin ratio ($P < .0001$).</p> <p>Conclusion: There is currently no definitive evidence that lowering CRP levels will reduce cardiovascular events, however studies are underway. There is also no data on the use of CRP in clinical management of PCOS, however these initial observations may help identify a population that is at risk for developing cardiovascular disease and whether treatment regimes should focus on weight loss and/or Metformin to reduce HS-CRP levels and, therefore, cardiovascular risk.</p>

KIM, MICHELLE

1. Title:	Clinical Benefit of Palliative Radiation Therapy in Advanced Gastric Cancer
2. Student Presenter:	Michelle M. Kim
3. Co-Workers and Collaborators	Sunil Krishnan, M.D., Nora A Janjan, M.D., Alexandria T. Phan, M. D., Prajnan Das, M.D., Marc E. Delclos, M.D., Linus Ho, M. D., Peter W. Pisters, M.D., Paul F. Mansfield, M. D., Jaffer A. Ajani, M.D., Christopher H. Crane, M.D.
4. Advisor	Sunil Krishnan, M.D.
5. Departments	Departments of Radiation Oncology, Medical Oncology and Surgical Oncology
6. Institutions	The University of Texas M.D. Anderson Cancer Center, Houston, TX
7. Support	The University of Texas M. D. Anderson Cancer Center, Summer Research Program
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Local progression of gastric cancer causes considerable morbidity. We retrospectively evaluated clinical outcomes after palliative radiotherapy (RT) among patients with gastric cancer. From 1996 to 2004, 37 gastric cancer patients were treated with palliative RT to the primary site. There were 32 men and 5 women. Median age was 66.9 years (range, 32.5–89.4). At baseline, 73% of patients had nodal involvement, 78% had metastatic disease. Symptoms before treatment included gastric bleeding in 54% of patients, dysphagia in 43% of patients, and pain in 19% of patients. The median radiation dose was 35 Gy (range, 20-36 Gy) in 14 fractions (range, 5-15). Concurrent chemoradiation therapy (CRT) was administered in 65% of patients and 41% received additional cycles of chemotherapy. Median follow-up was 3.1 months (range, 0.1-93.2 months). Rates of control were 70% (14/20) for bleeding, 81% (13/16) for dysphagia and 86% (6/7) for pain. Control of bleeding and dysphagia was sustained for a median duration of 6.2 and 11.4 months respectively. Five (26%) of 19 assessed patients progressed at the primary tumor, 17 (89%) in regional lymph nodes, and 7 (32%) of 22 distantly. Median actuarial times to local, nodal and distant progression were 11.9, 11.9 and 4.6 months. Median actuarial overall survival (OS) was 5.2 months (95% CI: 2.7-6.8 months). There was no treatment-related mortality. Grade 3 toxicities were noted in 2 (15%) of 13 RT patients (both nausea) and 5 (21%) of 24 CRT patients (2 neutropenia, 2 nausea and 1 dehydration). Patients receiving CRT had a modest improvement in median OS over those receiving RT alone (6.7 vs. 2.4 months, p=0.08). Dysphagia and gastric bleeding are controlled with palliative RT in the majority of patients and this relief is durable. CRT to the primary tumor is well tolerated and merits consideration even in metastatic gastric cancer patients treated palliatively.</p>

KIRKLAND, EUGENE

1. Title:	Methoxyamine Potentiates the Therapeutic Efficacy of Fludarabine in Human Lymphoid Malignancies
2. Student Presenter:	Eugene B. Kirkland
3. Co-Workers and Collaborators	Alina D. Bulgar
4. Advisor	Lili Liu, Stanton Gerson
5. Departments	Department of Hematology/Oncology
6. Institutions	Case Western Reserve University, Case Comprehensive Cancer Center
7. Support	American Cancer Society Joseph S. Silber Fellowship; Crile Fellowship
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Fludarabine is a nucleotide analogue used in the treatment of leukemia and lymphoma. It incorporates at the 3' end of a growing DNA strand where it inhibits replication. We hypothesize that methoxyamine (MX) is able to enhance the cytotoxic effects of fludarabine because: (i) randomly incorporated fludarabine is processed by base excision repair (BER) as an abnormal base, resulting in the production of AP sites; and (ii) MX binds to the AP sites, leading to interruption of BER repair. These effects were analyzed using a leukemia cell line (HL60) and blood samples from a lymphoma patient and a normal donor. Comet Assay, which quantifies DNA damage, revealed that fludarabine alone generated a moderate amount of damage, whereas fludarabine plus MX increased DNA strand breaks 2-5 fold. We then correlated this with the induction of AP sites formed after treatment. Our data showed that the levels of AP sites in both nuclear and mitochondrial DNA (detected using ARP reagent) increased proportionally with the fludarabine concentration and a significant portion of these sites were bound by MX. Since bound sites persist and are resistant to BER, these sites are lethal lesions. Western blots assessing the induction of BER proteins demonstrated elevated protein levels with fludarabine treatment and further augmentation with the addition of MX. Changes in the levels of proteins involved in mitochondrial induced apoptosis were also evident with combined treatment. JC-1 assay was then used to assess direct mitochondrial damage, showing the greatest effects for the combined treatment. To confirm these results, apoptotic death was measured using Annexin V staining. A 2-3 fold increase in Annexin V positive cells was observed in cells treated with fludarabine plus MX. Because such potentiation was observed, these studies indicate that the combination of MX with fludarabine is a novel and promising therapeutic strategy for malignant lymphoid disorders.</p>

KUMAR, ARYAVARTA

1. Title:	The Design and Engineering of Novel Nucleobase Biomaterials
2. Student Presenter:	Aryavarta Kumar
3. Co-Workers and Collaborators	Sona Sivakova, Jenny E. Green, Justin Fox, Stuart J. Rowan, Roger E. Marchant
4. Advisor	Roger E. Marchant
5. Departments	Biomedical Engineering Macromolecular Science and Engineering
6. Institutions	Case Western Reserve University
7. Support	NIH (NIBIB-EB-001466-01) and Case MSTP (T32 GM07250)
8. Please choose your academic program:	MD PHD
9. What Year are you in the program?	3
10. Body of Abstract (300 words or less)	<p>The goal of this project is to develop a new class of novel biomimetic nucleobase materials that can coat hydrophobic materials and reduce thrombotic and infectious complications from an implanted device in vivo.</p> <p>Peptide Nucleic Acids (PNAs) are novel polynucleobase molecules that can mimic DNA double helices. A major difference between the two is that PNAs have an uncharged peptide backbone compared to a charged phosphoribose backbone in DNA. The only similarities between the two materials are the nucleobases which can follow Chargaff's pairing rules. The DNA nucleobases, Adenine (A), Cytosine (C), Guanine (G), and Thymine (T), can form hydrogen bonds that do not follow Chargaff's rules as well; however, the complementary base pairings G-C and A-T are the more energetically favorable.</p> <p>We have designed PNA materials that can spontaneously self-assemble on a hydrophobic surface to form a supramolecular polymer. The molecules have three domains - a surface adsorbing hydrocarbon, a single PNA-nucleobase component that mediates certain intermolecular interactions, and a biological component to mediate a specific biological effect. We plan to characterize these model molecules by varying lengths and interaction strengths of each section. Molecular models of the surface assemblies are constructed to explain the molecular and nano-scale phenomena. The final design of the system will use complementary nucleobases to ensure a well-defined surface organization with well-defined positioning of biological components.</p> <p>If this research is successful, we will be able to 'program' the molecular system to surface self-assemble the PNA biomaterials in a specific manner, enabling more complex surface epitope reconstruction. This could ultimately be used to improve cell adhesion between a hydrophobic biomaterial and endothelial cells, and would reduce thrombotic, infectious, and biocompatibility complications that currently plague patients.</p>

KUNG, THEODORE

1. Title:	Rapid Attenuation of Circadian Clock Gene Oscillations in the Rat Heart Following Myocardial Ischemia
2. Student Presenter:	Theodore A. Kung
3. Co-Workers and Collaborators	Jiajia Cui, Oluwaseum Egbejimi, David J. Durgan, Chad A. Shaw
4. Advisor	William C. Stanley, Ph.D. & Martin E. Young
5. Departments	Department of Physiology and Biophysics, Department of Pediatrics, Department of Molecular and Human Genetics
6. Institutions	Case Western Reserve University School of Medicine, Baylor College of Medicine
7. Support	1. American Heart Association Student Scholarship in Cardiovascular Disease and Stroke 2. Crile Fellowship
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Circadian clocks are intracellular molecular mechanisms that confer the selective advantage of anticipation. In doing so, circadian clocks allow cells/organs/organisms to adapt appropriately to environmental stimuli. These intrinsic clocks have been identified in a wide array of mammalian cell types, including various components of the cardiovascular system (e.g. cardiomyocytes, vascular smooth muscle cells). The purpose of the present study was to test the hypothesis that ischemia/reperfusion (I/R) impairs the circadian clock within the ischemic, versus non-ischemic, region of the heart. Male Wistar rats were housed in a 12hr/12hr light/dark cycle (lights on at zeitgeber time 0; ZT0), and divided into two groups: naïve (n=40) and I/R (n=54) rats. Anesthetized I/R rats were subjected to ligation of the left main coronary artery at ZT15; the ligation was removed at ZT15.5. Naïve rats did not undergo surgery. Hearts were isolated from both naïve and I/R rats at 3hr intervals after ZT15, for up to 24hrs. Left ventricular ischemic (anterior) and non-ischemic (posterior) regions were separated for subsequent quantification of mRNAs encoding for various circadian clock components (bmal1, npas2, clock, rev-erba?, per1, per2, cry2, dec1, dbp). The surgical intervention caused a rapid phase shift (3hr delay) in all circadian clock genes investigated, for both ischemic and non-ischemic regions. I/R rat hearts exhibited a rapid induction (2.2-fold within 6hrs) of dec1 in the ischemic, versus non-ischemic, region. Consistent with induction of dec1 (a negative component of the mammalian circadian clock), circadian clock gene oscillations (i.e. peak-to-trough fold differences) were rapidly attenuated in the ischemic, versus non-ischemic, region. These data show that in a rodent model of myocardial infarction (MI), the circadian clock within the ischemic region becomes rapidly impaired. We speculate that asynchrony between circadian clocks within different regions of the heart may contribute towards the pathogenesis of heart failure following MI.</p>

LARSEN, COBY

1. Title:	RGD fluorosurfactant polymer modification of ePTFE facilitates endothelial cell adhesion and growth
2. Student Presenter:	Coby Larsen
3. Co-Workers and Collaborators	Faina Kligman, Kandice Kottke-Marchant, Roger E. Marchant
4. Advisor	Roger E. Marchant
5. Departments	Department of Biomedical Engineering
6. Institutions	Case Western Reserve University
7. Support	presenters gratefully acknowledge the financial support provided by NIH grant 5R01EB002067 and the facilities provided by the Center for Cardiovascular Biomaterials.
8. Please choose your academic program:	MD PHD
9. What Year are you in the program?	5
10. Body of Abstract (300 words or less)	<p>We have synthesized and characterized a novel peptide fluorosurfactant polymer (PFSP) modification that facilitates the adhesion and growth of endothelial cells on ePTFE vascular graft material. This PFSP consists of a poly(vinyl amine) (PVAm) backbone with integrin binding RGD peptides and perfluorocarbon pendant branches for adsorption and stable adhesion to underlying ePTFE. Aqueous PFSP solution was used to modify the surface of fluorocarbon substrates. Following subconfluent seeding, endothelial cell (EC) adhesion and growth on PFSP was assessed by determining cell population at different time points. Spectroscopic results indicated successful synthesis of PFSP. PFSP modification of ePTFE reduced the receding water contact angle measurement from 120° to 6°, indicating successful surface modification. Quantification of cell population demonstrated reduced EC attachment efficiency but increased growth rate on RGD PFSP compared with fibronectin (FN). Five day cell population on the RGD PFSP surface approached confluence and was significantly greater than on FN surfaces. There was no appreciable cell population on unmodified fluorocarbon and RGE PFSP surfaces for all time points. Our results indicate successful synthesis and surface modification with PFSP; this is an attractive and effective approach to modifying ePTFE to encourage endothelial cell attachment and growth.</p>

LARSON, BENJAMIN

1. Title:	Blood Pressure Surges during Office-based Transurethral Microwave Thermotherapy Treatments of the Prostate																																
2. Student Presenter:	Benjamin Larson																																
3. Co-Workers and Collaborators	B. Larson (a), L. Mynderse (b), M. Jaff (c), V. Sommers (d) , W. Evans (e), T. Larson (f)																																
4. Advisor	T. Larson																																
5. Departments	a Cleveland Clinic Lerner College of Medicine of Case Western Reserve University, Cleveland, OH b Department of Urology, Mayo Clinic Rochester, Rochester, MN c Department of Cardiology, Massachusetts General Hospital, Boston, MA d Department of Cardiology, Mayo Clinic Rochester, Rochester, MN e Southwest Florida Urologic Association, Fort Meyers, FL																																
6. Institutions	f Institute of Medical Research, Scottsdale, AZ																																
7. Support	Grant from Institute of Medical Research, Scottsdale, AZ																																
8. Please choose your academic program:	MD																																
9. What Year are you in the program?	2																																
10. Body of Abstract (300 words or less)	<p>Objective: Approximately 70,000 transurethral microwave thermotherapy (TUMT) procedures for the treatment for lower urinary tract symptoms (LUTS) related to benign prostatic hyperplasia (BPH) were done last year in the U.S., with an average patient age between 65 -70. There is a high prevalence of underlying cardiovascular disease in this patient population. To assess the potential risk TUMT poses to patients, a retrospective quality control study analyzing changes in blood pressure during TUMT treatment for BPH was conducted.</p> <p>Methods: Vital signs of 185 patients receiving TUMT treatment from 6 different devices at four institutions were analyzed. Maximum change and percent change in systolic (SBP), diastolic (DBP) and mean arterial pressure (MAP) were analyzed. Results were stratified by device used.</p> <p>Results:</p> <table border="1"> <thead> <tr> <th colspan="4">Changes in Blood Pressure During TUMT Treatment (n=185)</th> </tr> <tr> <th>Change</th> <th>Systolic Blood Pressure</th> <th>Diastolic Blood Pressure</th> <th>Mean Arterial Press</th> </tr> </thead> <tbody> <tr> <td>>30 mmHg</td> <td>77 (42%)</td> <td>29 (16%)</td> <td>44 (24%)</td> </tr> <tr> <td>>50 mmHg</td> <td>30 (16%)</td> <td>2 (1%)</td> <td>8 (4%)</td> </tr> <tr> <td>>70 mmHg</td> <td>10 (5%)</td> <td>2 (1%)</td> <td>1 (0.5%)</td> </tr> <tr> <td>> 20%</td> <td>95 (51%)</td> <td>103 (56%)</td> <td>91 (49%)</td> </tr> <tr> <td>> 30%</td> <td>55 (30%)</td> <td>61 (33%)</td> <td>51 (28%)</td> </tr> <tr> <td>> 40%</td> <td>31 (17%)</td> <td>33 (18%)</td> <td>27 (15%)</td> </tr> </tbody> </table> <p>Conclusions: TUMT elicits striking increases in blood pressure, although there were differences depending on the treatment modality. Given the older age and high prevalence of stabilized cardiovascular disease in patients undergoing TUMT, these increases may be potentially harmful. These responses to TUMT have been hitherto unrecognized, and the mechanisms responsible remain to be determined. The results of this study suggest blood pressures should be monitored during TUMT procedures and the procedure or anesthesia should be adjusted according to health risks factors.</p>	Changes in Blood Pressure During TUMT Treatment (n=185)				Change	Systolic Blood Pressure	Diastolic Blood Pressure	Mean Arterial Press	>30 mmHg	77 (42%)	29 (16%)	44 (24%)	>50 mmHg	30 (16%)	2 (1%)	8 (4%)	>70 mmHg	10 (5%)	2 (1%)	1 (0.5%)	> 20%	95 (51%)	103 (56%)	91 (49%)	> 30%	55 (30%)	61 (33%)	51 (28%)	> 40%	31 (17%)	33 (18%)	27 (15%)
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LIU, EUGENE

1. Title:	Vertical Distribution of West Nile Virus Mosquito Vectors in Suburban Trees in Cuyahoga County
2. Student Presenter:	Eugene Liu
3. Co-Workers and Collaborators	Joe Keiper, Joe Lynch
4. Advisor	Charles King
5. Departments	Entomology Section of Invertebrate Zoology Department, Division of Epidemiology and Surveillance, Center for Global Health and Diseases
6. Institutions	Cleveland Museum of Natural History, Cuyahoga County Board of Health, Case Western Reserve University School of Medicine
7. Support	Crile Fellowship
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Epidemiologic data suggests vegetation is an important factor in transmission of West Nile Virus (WNV). This may be due to the behavior of the primary WNV vector, Culex genus mosquitoes. During the summer breeding season, ornithophilic Culex mosquitoes are found primarily in tree canopies. However, at the end of the annual reproductive cycle in late summer, female Culex are hypothesized to become less selective in feeding, migrating down from the canopy to feed on humans in addition to birds. This experiment sought to test this theory. CDC light traps were suspended 0.5m and 5.0m above the ground from a tree located in a suburban medium risk zone (determined the Local Moran's Test of neighborhoods based on human data from the 2002 Cuyahoga County WNV epidemic). Traps were hung dusk to dawn approximately twice a week, starting July 19 and ending October 21. Trapped mosquitoes were identified and separated according to genus and sex. Females of each genus were tested for WNV by PCR. Using MANOVA, a significant difference in female Culex abundance was found by height ($p < 0.001$), with a season total of 27.22 times more females at 5.0m than 0.5m. Abundance by minimum daily temperature was also significant ($p < 0.02$). Two samples, both from traps at 5.0m were determined positive for WNV by PCR. The results suggest Culex preference for tree canopies and a decrease in abundance with decreasing temperatures. The anticipated late summer increase in ground level Culex was not observed, suggesting the increase in human cases of WNV seen near the end of the summer is not due to an increase in abundance of infected mosquitoes near the ground. Instead, it may be due to a total (ground + canopy) increase in the proportion of infected mosquitoes.</p>

LOVE, ZACHARY

1. Title:	Multimodal Imaging of Mesenchymal Stem Cell Transplants
2. Student Presenter:	Zac Love
3. Co-Workers and Collaborators	J Dennis, F Wang, A Awadallah, J Molter, Y Lin, J Auletta, A. Weisenberger, S. Majewski, S. Gerson, Z. Lee
4. Advisor	Zhenghong Lee
5. Departments	UH Radiology UH Orthopaedics UH Medicine
6. Institutions	University Hospitals of Cleveland Case Western Reserve University
7. Support	NIH Grant
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Human mesenchymal stem cells (hMSC) isolated from donor bone marrow hold promise as a novel source of tissue for treatment of diseases affecting a broad spectrum of tissues including: bone, heart, nervous tissue, skin, liver and connective tissue. This study aimed to show that radiographic visualization can be used as a non-invasive and longitudinal means of assessing growth and trafficking of human mesenchymal stem cell allografts in vivo. We produced virus using a 2nd generation lentiviral vector containing the gene LRT (fLuc-erfp-HSVtk, from S. Gambhir), encoding a firefly luciferase-eRFP-HSV thymidine kinase fusion protein. Six ceramic cubes loaded with either LRT-transduced hMSCs, untransduced (wt), and mixed hMSCs were subdermally implanted in each of 6 NOD-SCID mice. Additionally, LRT-transduced and wt hMSCs were transplanted into 2 NOD-SCID mice by subdermal injection, and 8 mice by intravenous infusion. Parallel samples of LRT-transduced and wt hMSCs were assessed for pluripotentiality by osteogenic, chondrogenic and adipogenic assays. Subsequently, all transplants were serially imaged using bioluminescent imaging (BLI) to assess luciferase expression. Selected transplants were imaged by computed tomography (CT) and x-ray to correlate BLI signal with cube location. Cubes containing LRT-transduced cells were visible by BLI starting 30 minutes after implantation, peaked in signal intensity at 2 weeks post-transplant, and continued to be visible with diminished signal beyond 10 weeks post-transplant. Subdermally injected LRT-transduced hMSCs were visible at the injection site starting 24 hours post-injection, but were less durable, lasting only 4 weeks post-transplant. Intravenously injected LRT-transduced hMSCs were visible in the thorax starting 30 minutes post-injection and remained visible there 1 week post-transplant. We conclude that transduction with LRT affords a means of longitudinally tracking hMSCs in allograft models. Subsequent experiments will quantitatively assess engraftment of LRT-transduced hMSC using positron emission tomography (PET) and will focus on hMSC homing in ischemic and trauma models.</p>

LU, ELAINE

1. Title:	Defining the “Community” in Community Consultation for Emergency Research: Findings from the Community VOICES Study
2. Student Presenter:	Elaine Lu
3. Co-Workers and Collaborators	Deborah Ragin, Ilene Wilets, Jennifer Holohan, Rosamond Rhodes, Margaret Smirnoff, Gary Winkel, Maggi Rodriguez, Edmund Ricci, Lynne D. Richardson
4. Advisor	Lynne D. Richardson
5. Departments	Department of Emergency Medicine, Division of Bioethics, Nursing, Behavioral & Community Health Sciences
6. Institutions	Mount Sinai School of Medicine
7. Support	NIH
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Objective: Federal rules allowing emergency research without informed consent require “community consultation” but do not provide specific guidance for operationalizing “community” for this purpose. The Community VOICES Study explored public attitudes towards exception from consent for emergency research.</p> <p>Methods: Participants were recruited from residential buildings that took part in the Public Access Defibrillation Trial, answering questions on the definition of community and appropriate methods of community consultation in a 30-minute interview conducted in English or Spanish. Respondents were asked, “How do you define “community?”.</p> <p>Results: 355 interviews were obtained from a socioeconomically diverse sample that was 66% female; 42.3% White, 29.3% African American, 22.0% Hispanic, and 6.5% other ethnic groups. Community was defined variably as: location, people/demographics, family/friends, interests/activities, professions, similar experiences or religious beliefs. Respondents’ views differed according to race/ethnicity and place of birth. White respondents were significantly more likely to describe their community based on location ($p < .01$) or interests/activities ($p < .01$) whereas African Americans were significantly more likely to describe their community as family/friends ($p < .001$). Other ethnic groups were significantly more likely to define community according to interests/activities ($p < .01$). Differences in definition of community were found also for foreign vs. U.S. born participants. U.S. born respondents were significantly more likely to describe their communities by interests/activities ($p < .01$), professions ($p < .05$) and similar experiences ($p < .05$) than were foreign born respondents.</p> <p>Conclusion: Conducting community consultation for emergency research among immigrant and minority groups requires an understanding of their definitions of community. These findings will assist investigators in developing appropriate consultation processes for emergency research.</p>

LUO, ALBERT

1. Title:	Association of a single nucleotide polymorphism in the LGALS2 gene with myocardial infarction in an American population
2. Student Presenter:	Albert K. Luo
3. Co-Workers and Collaborators	Vivek Rajagopal, Gong-Qing Shen, Qing Wang
4. Advisor	Eric J. Topol
5. Departments	Department of Molecular Cardiology, Department of Genetics
6. Institutions	The Cleveland Clinic Foundation, Case Western Reserve University School of Medicine
7. Support	National Heart, Lung, and Blood Institute, National Institutes of Health
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Myocardial infarction (MI) is a leading causes of death in the Western world. Its pathogenesis includes the chronic formation of plaque inside the coronary artery vessel wall and subsequent acute rupture of the plaque complex, implicating a number of inflammation-mediating molecules, including the cytokine lymphotoxin-a (LTA). It has recently been shown in a Japanese population that functional variation in the LGALS2 gene, whose product is galectin-2, a ligand that binds to LTA, is associated with susceptibility to MI. Reproducibility of case-control genetic polymorphism study results is especially crucial given the relative ease of introducing bias into such studies and the heterogeneity of different study populations. Our aim therefore was to attempt to validate this result in a predominantly Caucasian American population. 1230 individuals who have suffered MI and 951 normal control individuals were genotyped for one single nucleotide polymorphism (SNP) in the noncoding region of LGALS2 which was found to be significantly associated with MI. This C?T substitution affects the transcriptional level of galectin-2 in vitro, potentially leading to altered secretion of LTA, which would then affect the degree of inflammation. The pending data will then be analyzed to determine significant association with MI, if any.</p>

MAHMOOD, SYED

1. Title:	Computerization of Ugandan HIV/AIDS patient charts and clinical data for efficient patient care and research.
2. Student Presenter:	S. Saad Mahmood
3. Co-Workers and Collaborators	
4. Advisor	Benigno Rodriguez, M.D. and Michael M. Lederman, M.D.
5. Departments	Kampala International AIDS Clinical Trials Unit & Center for AIDS Research
6. Institutions	Joint Clinical Research Center (Kampala, Uganda) & Case Western Reserve University (Cleveland, Ohio)
7. Support	Crile Summer Research Fellowship
8. Please choose your academic program:	MD MPH
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>The first case of HIV infection in Uganda was reported in 1982. Prevalence soon rose to 30% in urban areas. Since then, prevalence has fallen but an estimated 1.4 million infected persons live in Uganda. There is an urgent need in Uganda to provide a standard of medical care that permits safe administration of complex antiretroviral therapies (ART).</p> <p>The Joint Clinical Research Center (JCRC) in Kampala, Uganda is an HIV/AIDS research facility developed in 1991 by Makerere University and Ugandan Ministries of Health and Defense. Providing ARTs to approximately 7,000 HIV-infected individuals, JCRC has extensive patient care medical record collections. We propose that a computerized patient record will enhance patient care and enrich JCRC research infrastructure. We also propose that a patient care and research database system used at an academic HIV clinic in Cleveland, Ohio, could be adapted for use at JCRC.</p> <p>The Patient Care and Research Database is a custom-built SQL application designed at CASE. The relational database is maintained through a Microsoft SQL Software back end and an SP.NET/web browser front end for editing and browsing. Separate tables are maintained for basic patient information, the patient intake questionnaire, allergies, visits, medications, co-morbidities, inter-current illnesses, vaccinations, screens, test results, repository samples, HIV resistance genotype results and phenotype testing. The investigators traveled to JCRC, deployed a customized version of the application and conducted changes in application structure in response to local providers' and scientists' input. An interface was created to import existing electronic records, and record-by-record validation was conducted for data quality. Customized version acceptability was excellent, as assessed by interviews with local providers and directives. Over 17,000 records were included, representing a range of clinical stages and demographics. The database was used to support a successful grant application, led by Dr. Rodriguez, from the President's Emergency Plan for AIDS Relief.</p>

MARINA, OVIDIU

1. Title:	A High-Throughput Tool for the Analysis of the Humoral Immune Response to Chronic Myelogenous Leukemia
2. Student Presenter:	Ovidiu Marina (1,2,3)
3. Co-Workers and Collaborators	Niroshan Ramachandran (4), Melinda Biernacki (3,5), Wandi Zhang (3), Eugenie Hainsworth (4), Catherine J. Wu (3,6)
4. Advisor	Catherine J. Wu, MD
5. Departments	1 Case Western Reserve University School of Medicine 2 Division of Aging, Brigham and Women's Hospital 3 Division of Hematologic Malignancies, Dana Farber Cancer Institute 4 Harvard Institute of Proteomics, Department of Biological Chemistry and
6. Institutions	Molecular Pharmacology, Harvard Medical School 5 University of Connecticut School of Medicine 6 Departments of Medicine and Pathology, Brigham and Women's Hospital Case School of Medicine Crile Summer Research Fellowship Case School of Medicine Office of Geriatric Medicine, American Federation for Aging Research (AFAR) program
7. Support	Brigham and Women's Hospital, Division of Aging, NIH NRSA Grant 1 T35 AG02681-01 National Cancer Institute grant NCI-1 R21 CA 115043-01 (Dr. Catherine J. Wu,
8. Please choose your academic program:	MD MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Background: Treatment with donor lymphocyte infusion (DLI) for patients with chronic myelogenous leukemia (CML) provides an example of a clinically effective tumor response, which is associated with the development of potent humoral immunity. In previous studies, we identified over 50 B-cell defined CML-associated antigens from 7 CML DLI responders. At the same time, a novel method for expressing protein onto a glass slide, enabling the testing for multiple antigens in parallel, has been developed.</p> <p>Hypothesis: A high-throughput screening tool can be developed for CML-associated antigens and reliably used for the measurement of antibody levels in patient sera.</p> <p>Methods: We cloned target sequences from the previously-characterized CML-associated antigens into a Gateway GST-fusion protein expression vector. To simultaneously express these antigens for serologic screening, plasmid DNA encoding the antigens of interest was spotted as an array onto a glass slide. GST-fusion proteins were then expressed in situ by in vitro transcription and translation, and locally bound to the slide with anti-GST antibodies. Reactivity against serum antibodies was detected by immunofluorescence. Test sera were derived from patient samples whose pattern of reactivity had been previously characterized using standard ELISA.</p> <p>Results: 25 DNA sequences, representing 19 previously-identified antigens, were successfully cloned, sequence-verified, and tested for GST expression in array format. Ongoing studies are under way to refine the detection of antibody binding to these antigens while minimizing background noise.</p> <p>Conclusions: This promising technology is currently undergoing validation. The development of a large-scale array of CML-associated antigens would enable rapid evaluation of the immunogenicity of different CML-directed treatments, including allogeneic transplant, DLI and novel vaccine approaches. Analyses using this tool may provide insight into the breadth and extent of the humoral immune response that develops following effective clinical immunity, and may potentially identify reliable surrogate markers against which immunity consistently develops following immune intervention.</p>

MARTIN, MATTHEW

1. Title:	The Role of NMDA in stimulation of Colon Motility In Rats with Irritable Bowel Syndrome
2. Student Presenter:	
3. Co-Workers and Collaborators	
4. Advisor	Robert Caudle, PhD
5. Departments	Department of Neuroscience
6. Institutions	University of Florida (Gainesville, FL)
7. Support	
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>The expression of receptor subtype for the neurotransmitter NMDA changes following development of irritable bowel syndrome (IBS) in the rat model. Specifically, there is a shift from NMDA receptors composed of NR1-2a/NR2B subunits to receptors composed of NR1-1a/NR2A and NR1-1b/NR2A subunits. The hypothesis in my study was that the altered NMDA receptor expression secondary to gut inflammation leads to enhanced motility in the rat colon when exposed to NMDA. From both control rats and rats given IBS (via rectal mustard oil injection 14 days in advance), I harvested small segments of the distal colon. I placed a force transducer within these colon segments, and placed the segments in a heated buffer bath. The colon segments were subsequently exposed to buffer solution, a 200 μM NMDA solution, a 200 μM acetylcholine solution, and a solution of 200 μM NMDA and 200 μM acetylcholine. Colon segments from rats with IBS showed the most motility when in the acetylcholine solution. Colon segments from control rats did not demonstrate increased motility in any of the various solutions when compared to buffer solution. Because NMDA administration failed to stimulate motility in colon segments from rats with IBS, the results do not support my hypothesis that binding of NMDA to an altered NMDA receptor is the causative factor in enhanced colon motility. I therefore conclude that an alternative mechanism is likely responsible for the symptoms of IBS in the rat model.</p>

MCINTYRE, WILLIAM

1. Title:	Abnormal Liver Transaminases in Alaska Natives with Type 2 DiabetesMellitus
2. Student Presenter:	William D. McIntyre II
3. Co-Workers and Collaborators	Stephen E. Livingston M.D., Julien L. Naylor M.D., Henry H Cagle, Chriss E. Homan, James L. Williams, Brian J. McMahon M.D.
4. Advisor	Stephen E. Livingston M.D.
5. Departments	Liver Disease and Hepatitis Program, Alaska Area Diabetes Program
6. Institutions	1. Liver Disease and Hepatitis Program, Alaska Native Tribal Health Consortium, Anchorage, AK 2. Alaska Area Diabetes Program, Alaska Native Tribal Health Consortium, Anchorage, AK 3. Arctic Investigations Program, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Anchorage, AK
7. Support	1. Liver Disease and Hepatitis Program, Alaska Native Tribal Health Consortium, Anchorage, AK, 2. Alaska Area Diabetes Program, Alaska Native Tribal Health Consortium, Anchorage, AK
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Few past studies have looked at the prevalence of abnormal liver function tests (LFTs) in patients with type 2 diabetes mellitus (DM). We conducted a population-based retrospective study to determine the prevalence of abnormal LFTs, if a medical evaluation had occurred and if an etiology were found in a cohort of Alaskan Natives (AN) with type 2 DM. A computerized hospital system and a diabetes registry were used to review patient records between 1/1/2000 and 12/31/2001. Study group patients included those who had = 2 ALT or AST values > 40 U/L drawn at least 90 days apart. Test results for causes of chronic liver disease, body mass index (BMI), medication use and ethanol use history were noted. Of 644 AN who had at least 1 ALT or AST drawn, 114 (18%) met the study group criteria. Screening for hepatitis B, hepatitis C virus (HCV) and fatty liver (by imaging) was performed in over 50% of patients, but screening for less common diseases was performed in < 50%. Probable diagnoses were assigned to 48% of patients. These included ethanol abuse (55%), nonalcoholic fatty liver disease (NAFLD, 14%), HCV or HCV and ethanol (7%), and metastatic cancer (5%). Mean BMI for study patients with NAFLD (39.7) was significantly higher compared to those with other probable diagnoses (34.6, p = 0.0179). This retrospective study showed a significant prevalence (18%) of elevated ALT or AST in a cohort of Alaska Natives with type 2 DM. Only half of the patients with abnormal ALT or AST had enough of a medical evaluation to allow us to assign a probable diagnosis. A more inclusive prospective study would more accurately assess the prevalence and etiology of liver disease in this underserved population with a large disparity in liver disease death compared with other ethnic groups in the US.</p>

MCWHORTER, PETER

1. Title:	Differentiation of Human Adult Stem Cells to Hepatocytes
2. Student Presenter:	Peter McWhorter
3. Co-Workers and Collaborators	
4. Advisor	Paul Lucas, PhD
5. Departments	Department of Orthopaedic Surgery
6. Institutions	New York Medical College
7. Support	NYMC grant
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Adult stem cells (ASCs) are found in a variety of human tissues and they have the potential to differentiate into the different cell types of that tissue. Recent research has shown that, additionally, ASCs are capable of differentiating into tissues from other germ layers. Specifically, Jiang et al. showed that a particular type of ASC from human bone marrow called Mesenchymal stem cells can differentiate into cells with visceral mesoderm, neuroectoderm and endoderm characteristics in vitro. My group's experiment tried to determine two things:</p> <ol style="list-style-type: none">1) Can ASCs other than mesenchymal stem cells differentiate into hepatocytes? The ASCs which we used were isolated from human bone marrow, human skin, and human skeletal muscle.2) Are there culture conditions other than those used by Jiang that can generate the same kind of pluripotency that his cells achieved? <p>To address these issues, ASCs from human bone marrow, human skin and human skeletal muscle were grown in one of two different culture media for four weeks and then assayed for evidence of differentiation to hepatocytes. The first medium contained horse serum and differing concentrations of dexamethasone (between 10^{-10} M and 10^{-6} M) while the second contained the liver-specific cytokines FGF-4 and hepatocyte growth factor (HGF). The assay involved determining how many cells stained positively for a variety of hepatocyte-specific membrane proteins. Initial results failed to show evidence of differentiation to hepatocytes. However the experiment could not be carried to conclusion due to the time constraints of a ten week work period. Future stem cell research will continue trying to determine the differentiation potentials of ASCs as well as the culture conditions that are necessary for driving differentiation to the desired cell type.</p>

METHENY, LELAND

1. Title:	BRCA 1/2 testing as a tool to reduce mortality in carriers
2. Student Presenter:	Leland Metheny
3. Co-Workers and Collaborators	
4. Advisor	Dr. Georgia Wiesner
5. Departments	Genetics
6. Institutions	University Hospitals
7. Support	
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>BACKGROUND: Cancer is the second leading cause of death among Americans. Because of this, medical science has focused its efforts to identify high risk populations. Many techniques are available to identify those who are at risk for cancer; one such technique is genetic testing, such as for the BRCA1 and BRCA2 gene. The somatic presence of these altered genes increases the risk of developing breast cancer by 3 to 7 times over the general population. However, to date there is little evidence that BRCA testing results in a decrease in mortality. Although there are prophylactic treatments (1, 2) available for this high risk population, it is unclear whether genetic testing influences the patient's decision to undergo treatment. This study was undertaken to evaluate whether women who test positive for BRCA1/2 mutations undergo risk-reducing oophorectomy or mastectomy at a higher rate than those women that test negative for BRCA 1/2 mutations. METHODS: Female patient, who were seen at the Center for Human Genetics during 1996 to 2006 were abstracted for information on test results, age and prophylactic treatment taken. Three prophylactic treatments were considered: mastectomy, oophorectomy, and tamoxifen. Patients were restricted to 30-70 years of age and will categorized 10 year periods for analysis purposes. Our analysis confidence interval is 95% and the power is 80%. RESULTS: 600 patient records have been abstracted to date. Results are yet to be obtained. We have abstracted the patient charts through 2004 and have moved on to analyzing the individual prophylactic treatment history of the patient. Once this has been accomplished, the information will be organized into a spreadsheet and analyzed. It is our hypothesis that BRCA+ younger women will tend to undergo tamoxifen treatment, BRCA+ menopausal women will tend to undergo mastectomy, BRCA+ women over 60 will tend to not undergo prophylactic treatment and BRCA- women of all ages will tend not to undergo prophylactic treatment. We expect to see that women who are carriers for BRCA1/2 will undergo prophylactic treatment more commonly than those that are not carriers. We also expect to see that younger women will elect to undergo less surgical treatment while those that are older will undergo more surgical treatments.</p>

MEYER, JACOB

1. Title:	Propofol Directly Activates Recombinant PKC-E
2. Student Presenter:	Jacob Meyer
3. Co-Workers and Collaborators	Peter J. Wickley
4. Advisor	Derek Damron, Ph.D
5. Departments	Center for Anesthesiology Research
6. Institutions	The Cleveland Clinic Foundation
7. Support	Crile Fellowship Anesthesia and Cardiomyocyte Signal Transduction NIH-HL65701
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Background: Myocardial protection by anesthetics (anesthetic preconditioning) is known to involve activation of protein kinase C (PKC). Recent evidence has implicated the PKC-E isoform as playing the most significant role in anesthetic preconditioning. Our objective was to identify whether or not the intravenous anesthetic agent, propofol, directly activates recombinant PKC-E. Hypothesis: The activity of recombinant PKC-E will be enhanced following incubation with a solution containing propofol</p> <p>Methods: The activity of purified recombinant PKC-E was assessed before and after exposure to propofol using a enzyme-linked immuno-absorbant assay kit. The activity was measured as phosphorylation of cAMP response element binding protein (CREB), which serves as a readily phosphorylated PKC substrate.</p> <p>Results: Propofol (1, 10, 30, 100 micro-M) directly increased activity of recombinant PKC-E (50 ng) -dependent phosphorylation of CREB in vitro in a dose-dependent manner causing phosphorylation of CREB. Moreover, the PKC activators, phorbol myristate acetate (PMA, 100 nM) and dioctanoylglycerol (DOG, 50 micro-M), increased recombinant PKC-E-dependent phosphorylation of CREB to a similar extent. Pretreatment of the recombinant PKC-E with propofol (10 micro-M) potentiated DOG (50 micro-M) and PMA (0.1 micro-M) stimulated, PKC-E-dependent phosphorylation of CREB.</p> <p>Conclusions: These data indicate that propofol directly increases PKC-E activity via a direct intermolecular interaction with the enzyme. Moreover, propofol potentiates PKC-E activity following pre-treatment with the classical activators, DOG and PMA.</p>

MILLER, KYAUNA

1. Title:	Alcohol Consumption in Mid-Life and Alzheimer's Disease
2. Student Presenter:	Kyauna S. Miller
3. Co-Workers and Collaborators	Petot, G.J.*, Fritsch, T.
4. Advisor	Friedland, Robert
5. Departments	Departments of Nutrition Department of Neurology
6. Institutions	Case Western Reserve University School of Medicine, University Memory and Aging Center, University Hospitals
7. Support	NIH (R01AG017173-04A2), The Joseph and Florence Mandel Research Fund, The Nickman Family, The Institute for the Study of Aging and Phillip Morris, USA.
8. Please choose your academic program:	I received research support for the summer project from the Crile Fellowship, Case Western U. School of Medicine and also American Federation for Aging Research Summer Fellowship for Medical Students.
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Alcohol consumption has been shown to have physiological effects on the central nervous system, cognition, and behavior. Moderate alcohol consumption has been associated with decreased cognitive decline in older persons, whereas greater consumption has shown increased cognitive decline. Few studies have investigated associations between alcohol consumption and Alzheimer's disease (AD). In a case-control study of genetic and lifestyle risk factors of Alzheimer's disease (AD), we studied associations between patterns of alcohol consumption in mid-life (40-59 years) in Alzheimer's cases (n=179) and healthy controls (n=284). Cases were recruited from clinical settings and from the community, and controls were friends or neighbors of the cases or members of the same organizations to which cases belonged. Persons with histories of alcoholism were not enrolled in the study. A food frequency questionnaire was used to gather data on servings per day of beer, wine and spirits. Controls responded for themselves and surrogates responded for cases. We have previously shown that this method does not introduce systematic reporting biases in our sample. Of 463 subjects in the study, 146 people reported no alcohol consumption during this age period. Servings of beer ranged from 0 to 5 per day, servings of wine ranged from 0 to 1 per day and servings of spirits ranged from 0 to 4.3 per day. Logistic regression analysis indicated that, adjusting for year of birth, gender and education, consumption of alcoholic beverages in this population during midlife did not increase odds of AD (Odds Ratio 1.076, 95% Confidence Interval 0.812-1.43). Results were similar when controlling for APOE and the interaction of APOE and mid-life alcohol consumption. Although past research has shown a protective effect of moderate alcohol consumption on cognition, we did not find evidence that alcoholic beverage reduces the odds of AD in this group.</p>

MIOCINOVIC, SVJETLANA

1. Title:	Model-designed parameters for selective deep brain stimulation of the subthalamic nucleus
2. Student Presenter:	Svjetlana Miocinovic
3. Co-Workers and Collaborators	Martin Parent, André Parent, Christopher R. Butson, Gary S. Russo, Jerrold L. Vitek
4. Advisor	Cameron C. McIntyre
5. Departments	Dept of Biomedical Engineering, Dept of Biomedical Engineering, Centre de Recherche, Center for Neurological Restoration
6. Institutions	Case Western Reserve University, Cleveland, Ohio Cleveland Clinic Foundation, Cleveland, Ohio Université Laval Robert-Giffard, Beauport, Québec, Canada Cleveland Clinic Foundation, Cleveland, Ohio
7. Support	NIH (T32 GM07250; R01 NS-47388; R01 NS-37019) and IRSC (MOP-5781)
8. Please choose your academic program:	MD PHD
9. What Year are you in the program?	5
10. Body of Abstract (300 words or less)	<p>Despite the clinical effectiveness of subthalamic nucleus (STN) deep brain stimulation (DBS) in the treatment of Parkinson's disease, the underlying neuronal response linked to therapeutic benefit remains unclear. Therapeutic DBS electrode contacts are typically positioned in the dorsal STN/fields of Forel (H2)/zona incerta region, making both STN projection neurons and pallidothalamic (GPi) fibers viable candidates as the therapeutic target of the stimulation. We built a comprehensive computational model of DBS to design selective stimulation parameters for activation of either STN projection neurons or GPi fibers of passage. The goal of this model is to provide guidance in experimental studies addressing the therapeutic neural element(s) in STN DBS of parkinsonian macaques.</p> <p>Our model of STN DBS consists of three fundamental components: 1) a 3D anatomical model of monkey basal ganglia, 2) a finite element model of the DBS electrode and resulting electric field, and 3) multi-compartment biophysical models of STN projection neurons and GPi fibers of passage. The STN models include a 3D geometry derived from biotin dextran amine labeled STN neurons of a cynomolgus monkey. Fifty STN neurons and 50 GPi fibers were positioned within the 3D anatomical model. The DBS voltage field in the tissue medium was calculated for Itrel II stimulus waveforms with the Fourier finite element method and applied to the neuron models to evaluate their firing response to the stimulation.</p> <p>Monopolar, cathodic, 1V, 90us, 136Hz stimulus trains generated varying degrees of selectivity. Electrode contacts deep within the STN activated 72% of STN neurons and only 19% of GPi fibers. Stimulation applied in H2 activated 60% of GPi fibers and only 2% of STN neurons. These results suggest that appropriate selection of the stimulating contact can substantially bias activation of either STN neurons or GPi fibers. Given the common location of therapeutic contacts for clinical STN DBS in H2, our results suggest that GPi fibers may represent an important target of the stimulation.</p>

MONTANEZ, MARJORIE

1. Title:	LMO4 is necessary for maintenance of Cyclin D1 expression in breast cancer cells
2. Student Presenter:	Marjorie E. Montanez-
3. Co-Workers and Collaborators	Melissa D. Landis, Darcie D. Seachrist
4. Advisor	Ruth A. Keri
5. Departments	Pharmacology
6. Institutions	Case Western Reserve University
7. Support	Continuing Umbrella of Research Experiences (CURE) supplemental grant to NIH RO1-CA90398
8. Please choose your academic program:	MD PHD
9. What Year are you in the program?	5
10. Body of Abstract (300 words or less)	<p>ErbB2/Neu is an orphan receptor of the EGFR tyrosine kinase family. It is overexpressed in 20-30% of human breast cancers and its overexpression correlates with poor patient prognosis and resistance to chemotherapy. To investigate molecular mechanisms of ErbB2-induced tumorigenesis in the breast, transgenic mice that overexpress c-Neu under direction of a mammary gland-specific promoter (MMTV) were used for gene expression profiling. Among the genes differentially regulated in tumors, LMO4, a member of the LIM-only family of transcriptional regulators, is upregulated 5 fold when compared to wild-type glands. This data has been confirmed by RT-PCR, in situ hybridization and western blotting and suggests that LMO4 is a potential ErbB2 transcriptional target in the mammary gland. Supporting this notion, previous studies have revealed that 65% of ErbB2-overexpressing human tumors also overexpress LMO4. In vitro, LMO4 upregulation is associated with lack of expression of differentiation markers in mammary epithelial cells, while its silencing is associated with decreased proliferation, migration and invasion. In transgenic mice, LMO4 overexpression in the mammary gland induces epithelial hyperplasia and tumors. However, the mechanisms by which LMO4 regulates cell proliferation remain unknown. We postulated that LMO4 is required for ErbB2-mediated induction of proliferation. To identify the mechanisms by which LMO4 regulates proliferation of breast cancer cells, we have reduced LMO4 by 85% in ErbB2-dependent breast cancer cells using siRNA. Loss of LMO4 induces a concomitant decrease in Cyclin D1 protein levels by 70%. This reduction in Cyclin D1 expression may involve transcriptional regulation because Cyclin D1 mRNA is also affected by the reduction in LMO4. Current studies are focused on determining if Cyclin D1 mRNA synthesis is regulated by LMO4. In summary, these data show that maintenance of LMO4 expression is necessary for continued expression of Cyclin D1, a key regulator of mammary epithelial cell proliferation and ErbB2-induced tumorigenesis.</p>

MORRISSEY, KELLY

1. Title:	Pc 4-Photodynamic Therapy Induced Selective Killing of Malignant Lymphocytes in Sézary Syndrome
2. Student Presenter:	Kelly Morrissey
3. Co-Workers and Collaborators	Andrew Hsia, Heather Scull
4. Advisor	Elma Baron, MD
5. Departments	Department of Dermatology
6. Institutions	University Hospitals of Cleveland
7. Support	The Skin Study Center/Translational Research Core, Skin Disease Research Center, Department of Dermatology
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Background: Photodynamic therapy (PDT) is currently being utilized in the treatment of several cutaneous diseases. The silicon phthalocyanine Pc 4 [HOSiPcOSi(CH₃)₂(CH₂)₃N-(CH₃)₂] is a second generation photosensitizer that has demonstrated preferential killing of tumor cells in vitro. Previous experiments by our group and others have shown that transformed lymphocytes (Jurkat cells) were more sensitive to Pc 4-PDT-induced killing than epidermoid carcinoma A431 cells.</p> <p>Purpose: This study aims to determine if Pc 4-PDT selectively kills the malignant lymphocytes that characterize Sezary syndrome while sparing normal cells.</p> <p>Methods: Peripheral blood mononuclear cells (PBMCs) were obtained from three patients with Sézary Syndrome. PBMCs were treated with Pc 4-PDT in vitro and then analyzed using fluorescence flow cytometry to detect apoptosis in T lymphocytes and monocytes.</p> <p>Results: We observed a dose-dependant preferential induction of apoptosis (Apo 2.7+) in the malignant T cells (CD4+CD7-) compared to other cells.</p> <p>Conclusion: The selective killing of malignant lymphocytes over other cells from Sézary patients indicates that Pc 4-PDT holds promise to be an effective non-invasive targeted therapy for patients with this variant of cutaneous T-cell lymphoma.</p>

MUKERJI, SHIBANI

1. Title:	Activin in Cerebral Ischemic Injury and Hypoxia
2. Student Presenter:	Shibani Mukerji(1)
3. Co-Workers and Collaborators	Ekaterina Katsman(1) and Alison Hall(1,2)
4. Advisor	Alison Hall
5. Departments	Neuroscience(1) Pharmacology(2)
6. Institutions	Case Western Reserve University
7. Support	MSTP training grant and NIH (NS-39316)
8. Please choose your academic program:	MD PHD
9. What Year are you in the program?	4
10. Body of Abstract (300 words or less)	<p>Stroke is a major health challenge in the United States, accounting for a third of all deaths and resulting in many individuals living with significantly compromised neural functions. Growth factors such as the Transforming Growth Factor beta family member, activin, are attractive potential therapeutics following acute CNS insult. The filament model of middle cerebral artery occlusion (MCAO) was used to study activin involvement after transient focal ischemia in mice. One hour occlusion followed by 24hours of reperfusion gave rise to reproducible infarct volumes. To begin to understand the temporal characteristics of activin expression, brain samples from adult mice that had a 1 hour occlusion followed by 1 or 24 hours reperfusion were taken for quantitative real-time PCR. Activin mRNA expression increases were detected at 1 hour of reperfusion but not at 24hours. Western blot analysis reveals that 24hours after MCAO in mice there is ipsilateral activation of smad 2/3 protein detected. Further, following brief exposure to hypoxia that has recently been identified to confer protection from subsequent focal cerebral injury, rapid activin mRNA increases were observed. Adult mice placed in sealed normobaric chambers were exposed to 11% O₂ for 2 hours. Activin mRNA showed increases at 1 hour but not at 4 or 24 hours following hypoxic exposure. In addition, a cell culture model that simulates some aspects of free radical stress following ischemia demonstrated that exogenous activin prevented neuronal death. Cortical cells at 24hours were pretreated with activin or medium, challenged with hydrogen peroxide (H₂O₂), and counted at 48 and 72 hours. Activin treatment given prior to H₂O₂ prevented free radical-induced cell death. These data suggest that endogenous activin is involved in both acute ischemic injury responses and changes with hypoxia, and point to a possible role for activin in providing neuronal protection after injury.</p>

OKADA, HARUKO

1. Title:	Radiofrequency Microtenotomy Coblation and Arthroscopic Synovectomy of the Radio-Capitellar Joint for the Treatment of Recalcitrant Lateral Epicondylitis
2. Student Presenter:	Haruko Okada
3. Co-Workers and Collaborators	William H. Seitz, Jr., M.D.
4. Advisor	William H. Seitz, Jr., M.D.
5. Departments	Orthopaedics
6. Institutions	Cleveland Orthopaedic and Spine Hospital at Lutheran (Cleveland Clinic Health Care System), The Cleveland Clinic Beachwood Family Health and Surgery Center
7. Support	Crile Fellowship, Case Western Reserve University School of Medicine
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Lateral epicondylitis is a tendinosis of the confluent origin of the forearm extensors caused by their overuse and repetitive supination. Surgery is indicated for the 5% of patients with persistent symptoms who fail conservative treatment. Techniques such as lateral epicondylectomy or fasciotomy have risks of posteriolateral instability of the elbow from excessive debridement and are painful after surgery, thus requiring a long recovery time of six (6) to twelve (12) months.</p> <p>Recently, evidence of success using the radiofrequency microtenotomy coblation technique has been shown to be clinically effective in laboratory studies . Radiofrequency waves emitted from a small probe produce plasma from saline vapor which breaks tissue bonds and stimulates angiogenesis . Additionally, the recalcitrant cases have shown radiocapitellar synovitis directly beneath the area of lateral epicondylitis . The recognition of this suggests that a minimally invasive procedure can be performed at the same time of lateral epicondylitis surgery to assess the presence of a synovial plica which can be resected. We sought to look at the outcomes of radiofrequency microtenotomy coblation using the Arthrocare Topaz Wand paired with arthroscopic synovectomy of the radiocapitellar joint by a single surgeon (WHS). The goal of this study is to evaluate the rate of patients' early recovery and decrease in pain.</p> <p>We followed forty-five (45) patients who underwent surgery at the Cleveland Orthopaedic and Spine Hospital at Lutheran Hospital, Cleveland Clinic Health System, and Cleveland Clinic Beachwood Family Health and Surgery Center since January 2003. Patients were asked to fill out a questionnaire regarding their pre and post-operative pain at one (1) day, one (1) week, six (6) weeks, three (3) months, and six (6) months, and they were asked to rate their function and satisfaction with treatment.</p> <p>Preliminary results indicate a rapid decrease in pain post operatively with an average drop of six (6) points (on a VAS scale of 1-10), at 6 months after the operation. This represents a significant improvement over other existing surgical techniques. A future randomized control study should be performed to further validate these findings.</p>

PADOVANI-CLAUDIO, DOLLY

1. Title:	Modulation of Oligodendrocyte Lineage, Myelination, and Repair after CXCR2 Chemokine Receptor Inhibition
2. Student Presenter:	Dolly Ann Padovani-Claudio
3. Co-Workers and Collaborators	*Liping Liu, *Richard Ransohoff
4. Advisor	Robert H. Miller
5. Departments	Department of Neurosciences, *Department of Neurosciences
6. Institutions	Case School of Medicine; *Lerner Research Institute-Cleveland Clinic Foundation
7. Support	NIH NS36674-08 grant to Robert H. Miller. NRSA F31 NS047928-01-02 grant to Dolly Ann Padovani-Claudio. Myelin Repair Foundation support.
8. Please choose your academic program:	MD PHD
9. What Year are you in the program?	6
10. Body of Abstract (300 words or less)	<p>The regulation of oligodendrocyte precursor cell (OPC) proliferation, migration, and differentiation is critical for normal central nervous system (CNS) myelination. Previous studies suggest that in the developing spinal cord, localized expression of the chemokine CXCL1 inhibits migration and enhances OPC proliferation by binding the CXCR2 chemokine receptor. We have characterized the structural and functional CNS alterations resulting from a lack of CXCR2 signaling in mice. In CXCR2-KO adult mice there are regional alterations in oligodendrocyte lineage cell densities in the CNS as well as an increase in the spinal cord white matter density and arborization of NG2 positive cells, an endogenous population that may be involved in oligodendrocyte replacement. CXCR2-KO mice, however, exhibit a significant decrease in spinal cord white matter area, reduced thickness of myelin sheaths, and a slowing in the rate of conduction of somatosensory-evoked-potentials (SSEPs) despite no significant changes in axonal size or number. Biochemical analyses show decreased expression of myelin basic protein, increased expression of sodium channels, and decreased expression of glial fibrillary acidic protein (GFAP). In vitro studies revealed a reduction in the number of differentiated oligodendrocytes, which may account for the observed hypomyelination. These findings suggest that the chemokine receptor CXCR2 is important for the development and maintenance of the oligodendrocyte lineage in the vertebrate CNS. Modulation of chemokine signaling may alter CNS cellular responses in adulthood and its manipulation may serve to enhance CNS repair. We hypothesize that after a demyelinating injury to the CNS, CXCR2 inhibition may decrease immune cell infiltration, increase NG2+ OPC availability, enhance OPC migration into demyelinating lesions, and reduce gliosis; all of which could result in enhanced repair. Our preliminary data consistently shows decreased GFAP upregulation and decreased lesion sizes in CXCR2-KO after chemical demyelination suggesting that inhibition of CXCR2 is either protective or enhances CNS remyelination repair.</p>

PATEL, NIRAJ

1. Title:	GPCRs - TSH and TRH Receptor
2. Student Presenter:	Niraj Patel
3. Co-Workers and Collaborators	Susanne Newmann, Bruce Raaka, Elizabeth Geras-Raaka
4. Advisor	Marvin Gershengorn
5. Departments	NIDDK Bethesda MD
6. Institutions	NIH
7. Support	
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Background The hypothalamic-pituitary-thyroid (HPT) axis controls the production of T4 and T3 for the body; these biogenic amines regulate the set point for basal metabolic rate. Excess of these amines can lead to diseases such as Graves (stimulation to excess production of T4/T3 due to LATS) or Hashimoto's Thyroiditis (autoimmune destruction of thyroid gland). While many diseases of the HPT axis exist, very little is known about the structure of the TRH and TSH G protein coupled receptors (GPCR). As part of a collaboration of chemists to create compounds and computer structure scientists for structure integration we sought to further explore the structure of the receptors.</p> <p>Methods Analysis of the structure of these receptors using normal methods of X-ray crystallography is not possible due to their membrane bound properties. We used an intelligent design – using two libraries of organic compounds we screened for agonistic and antagonist activity. Relative affinities of ligand binding to receptor were examined using relative measurements of second messenger's of the GPCRs; intracellular Ca²⁺ and cAMP using special dyes serving as reporters. Modifications including substitutions, deletions, and additions were made to any hits. The information was then given to the computer structure scientists and modifications were made to the structure of the bound receptor. This allowed us to describe the binding pocket of the receptor.</p> <p>Results & Conclusions Using the preliminary work that we have done using two libraries of compounds, we have a platform to build new structures. These structures will allow for better visualization of the binding pocket of the receptors and allow for the interdisciplinary team to elucidate more about the GPCRs.</p>

PEACOCK, ELIZABETH

1. Title:	Postoperative Analgesia Using the ON-Q® Pain Buster in Aesthetic Plastic Surgery
2. Student Presenter:	Elizabeth K. Peacock
3. Co-Workers and Collaborators	
4. Advisor	Dr. James Zins, M.D.
5. Departments	Department of Plastic Surgery
6. Institutions	Cleveland Clinic Foundation
7. Support	I-Flow Corp., Lake Forest, CA, USA
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Improving and minimizing pain after surgery had been shown to be a benefit to a patient's recovery. Currently, most of post-operative pain is managed by parenteral opioids and oral narcotics, which are associated with a high rate of side effects including nausea, excessive sedation, and respiratory distress.</p> <p>The ON-Q® pain management system, which uses a temporary porous catheter placed by the surgeon in the incision site, delivers a continuous dose of long acting local anesthetic that has been shown to be effective in controlling post-operative pain without nausea, breathing problems, drowsiness, constipation, or sleepiness. While well documented in other surgery types, there are no reports of its efficacy in the plastic surgery literature.</p> <p>This prospective randomized study was designed to evaluate the efficacy of the ON-Q® Pump in post-operative pain management in five types of plastic surgery: browlift, facelift, abdominoplasty, breast augmentation, and breast reduction. Pain and nausea levels, both ranked on a scale from zero (no pain/nausea) to ten (the worst pain/nausea), were collected at six separate times – PACU arrival, one hour after PACU arrival, discharge, day one, day three, and day seven. The amount of analgesic use was also recorded for each of these times.</p> <p>Statistical analysis was done on 116 patients, with 57 of these being controls. Only one surgery type was found to have a statistically significant difference between those who used the pain pump and those that did not. There is some evidence that patients using the pain pump were more likely to use perioperative analgesics ($p=0.11$) and antiemetics ($p=0.10$), but these differences were not statistically significant. Patients undergoing breast reduction and using the pain pump tended to have less pain leaving the PACU than those not using the pain pump. No other statistically significant differences in pain entering or leaving the PACU were observed.</p>

PIFER, MATTHEW

1. Title:	Secondary Supratip "Pollybeak" Deformity: A closer look at etiology.
2. Student Presenter:	Matthew A. Pifer M.S.
3. Co-Workers and Collaborators	David Moose M.D. D.M.S., Steven T. Constantine, D.O.
4. Advisor	Brent D. Kennedy M.D.
5. Departments	Facial, Reconstructive and Cosmetic Surgery
6. Institutions	Institute of Facial and Cosmetic Surgery 5929 South Fashion Rd. Murray, UT 84107 (801) 261-3637
7. Support	Case School of Medicine Crile Fellowship. Summer 2005
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Background: The secondary supratip deformity, or "Pollybeak", is defined as fullness or convexity of the dorsum immediately cephalic to the nasal tip. It is a hallmark of a poorly executed rhinoplasty or unpredictable postoperative wound healing. Although numerous etiological factors for the supratip deformity have been forwarded in the literature, it remains one of the most frequent complications of rhinoplasty necessitating secondary revision. We report a retrospective chart review of patients requiring revision rhinoplasty for correction of supratip deformity.</p> <p>Methods: Retrospective chart analysis was conducted on 28 patients requiring revision rhinoplasty for correction of supratip deformity from January 1998 to July 2005. Data collection points included patient demographics, preoperative clinical findings, surgical findings, and techniques employed for surgical correction.</p> <p>Results: 28 patients (100%) showed extensive supratip fibrosis at the time of surgery. 23 patients (82%) demonstrated inadequate tip support at the time of surgery. In 21 cases (75%) surgical correction involved excision of fibrotic scar tissue accompanied by reconstruction of tip support mechanisms. Tip defining techniques such as cephalic trim, tip grafting, or domal sutures were utilized as part of revision surgery in 20 cases (71%). 17 cases (63%) required resection of dorsal cartilage in addition to fibrous scar tissue for adequate surgical correction while only two cases (7%) required dorsal grafting of a previously overresected dorsum as a means of surgical correction.</p> <p>Conclusions: Fibrotic scar tissue was observed to be the most predictable etiological cause for the secondary supratip deformity being present in 100% of our cases. The next most predictable etiological cause was observed to be lack of tip support. By in large, we found that resection of fibrotic supratip scarring accompanied by reconstruction of tip support mechanisms to be the mainstay of surgical correction. Techniques to improve the overall gestalt such as tip defining measures also play an important role in optimal surgical correction of the supratip deformity.</p>

QUADRI, MAHEEN

1. Title:	Visual Dissection of Ebola Virus Assembly
2. Student Presenter:	Maheen Quadri
3. Co-Workers and Collaborators	Keith Olszens, Hyun Yu, Morgan Reuter
4. Advisor	Dr. David McDonald
5. Departments	Molecular Biology and Microbiology
6. Institutions	CASE School of Medicine
7. Support	CFAR (Center for AIDS Research) Crile Fellowship
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Although the HIV and Ebola virus are members of distinct viral families, they both reproduce by enveloping themselves within a membrane derived from the infected cell. Both viruses accomplish this by hijacking the cellular ESCRT (endosomal sorting complex required for transport) machinery. ESCRT proteins catalyze the inward budding of endosomes into intracellular vesicles known as multivesicular bodies (MVBs). The major structural proteins HIV Gag and Ebola VP40 direct viral assembly by recruiting cytoplasmic ESCRT complexes to the plasma or MVB membrane, resulting in virus particles being extruded out of the cell or into MVBs. Strikingly, while HIV budding generally results in spherical structures, Ebola virions bud off the cell in long filamentous strands. Recently, the endosomal trafficking regulator Adaptin-3 (AP-3) has been shown to direct HIV Gag to sites of assembly before engagement of the ESCRT machinery. To determine whether AP-3 is involved in Ebola VP40 trafficking, we developed a visual assay based on the expression of green fluorescent protein (GFP) fusions with the viral structural proteins. As expected, expression of these fusions resulted in assembly and budding of viral-like particles (VLPs) from the cells. HIV Gag-GFP produced bright punctae both at the cell surface and within MVBs whereas Ebola VP40-GFP expression resulted in dramatic filamentous particles emanating from the cell surface. Expression of dominant-negative ESCRT proteins blocked the formation of both HIV and Ebola VLPs, confirming the validity of the assay. When a dominant-negative AP-3[?] subunit was expressed, HIV VLP budding was dramatically reduced, whereas Ebola VLP formation was not affected. These results suggest that Ebola VP40 does not require AP-3 complexes to accumulate at sites of viral assembly. Further, they confirm the validity of this visual approach for characterizing viral assembly. When used along with quantitative viral production assays, these tools provide a powerful approach to envisioning viral assembly.</p>

RADOVIC, ANA

1. Title:	Trans Fat Education Campaign
2. Student Presenter:	Ana Radovic
3. Co-Workers and Collaborators	Sanjum Sethi, Maria Abraham
4. Advisor	Gail Goldstein, Sonia Angell
5. Departments	Cardiovascular Disease Prevention & Control Bureau of Chronic Disease Prevention
6. Institutions	New York City Department of Health & Mental Hygiene
7. Support	New York City Department of Health & Mental Hygiene, Crile Fellowship
8. Please choose your academic program:	MD MPH
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>In New York City, 25% of adults have elevated cholesterol, which has been linked to the risk for cardiovascular disease. Trans fat contributes to this risk as has been shown by numerous epidemiological studies and national scientific advisory bodies that trans fat increases harmful cholesterol while decreasing beneficial cholesterol. Restaurant food contributes significantly to the typical NYC diet, and so the aim of our research and intervention was to determine the prevalence of use and awareness of health risks of trans fats in restaurants and food distributors. Our intervention was directed towards educating restaurants, distributors, and consumers about the health risks of trans fats and offering strategies to eliminate them from the diet. We conducted a phone survey to determine the baseline knowledge about trans fats of food suppliers who distribute to restaurants. We also employed the use of NYCDOHMH restaurant inspectors to conduct a 5 week survey during their routine inspection of 529 city restaurants. Of the 109 suppliers contacted, 47 sold cooking oil and 30 sold margarine, shortening or prepared foods. Most of the suppliers who sold cooking oil did not know if these oils contained trans fat (almost 75%). We determined that 1/3 of restaurants surveyed used at least one product which contained trans fat. We advanced our intervention by sending out specifically targeted educational mailings to consumers, food distributors, and restaurants. We followed up with educational phone calls to 105 local suppliers who sold bulk oil and/or prepackaged foods to restaurants, and sent a more detailed mailing. A trans fat module has been added to regular food safety courses which restaurants are required to participate in. Our research determined that the NYC trans fat intake is contributed to greatly by restaurants. Follow up of our intervention methods will further determine whether they were effective at decreasing prevalence of trans fat use by restaurants and sale by food distributors.</p>

RANDA, JESSICA

1. Title:	Pediatric Mental Health and the Primary Care Pediatrician: Development of a Web-Based Resource for the Pediatric Practice
2. Student Presenter:	Jessica Randa
3. Co-Workers and Collaborators	Andrew Garner, MD/PhD; Sarah Horwitz, PhD
4. Advisor	Amy Heneghan, MD
5. Departments	Department of Pediatrics; Rainbow Research Network
6. Institutions	University Hospitals of Cleveland
7. Support	Crile Fellowship Grant, Woodruff Foundation Grant, American Academy of Pediatrics CATCH Grant
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Background: The majority of children in Cuyahoga County requiring mental health services are unable to access care in the current system. To address this concern, experts in pediatrics and mental health convened to form the Cleveland Coalition for Pediatric Mental Health (CCPMH). As part of their county-wide action plan, CCPMH recognizes a need to link primary care pediatricians (PCP) and their patients to private and public mental health resources. Objective: 1) Identify community resources for children's mental health, 2) Create a web-based database of pediatric mental health resources and 3) Inform local pediatricians about mental health resources for children. Methods: Resources were identified from pre-existing resource guides and key-informant interviews. "Snowball technique" was used to ensure completeness of the final list. Representatives from each community agency were interviewed using standardized questions. Information gathered included: services offered, referral process, patients' inclusion/exclusion considerations, and cost of services. Individual providers received a mailed survey. The resources identified represented all those providing mental health services, enrichment and support to children and their families. Results: 25 community organizations with 72 programs/services, five healthcare systems and 34 providers consented for inclusion in the database. Four organizations declined to participate. Information from consenting resources was entered into the Child Health and Development Interaction System (CHADIS), an existing platform housing national mental health resources. Keywords were assigned to all organizations, programs and providers, allowing PCPs to search by program type, age, diagnosis, geographic location, or insurance. This online compendium will be available to all Cuyahoga County PCPs in April 2006. Conclusions: Creation of an online database addresses an identified need to link PCPs and their patients with appropriate public and private resources as outlined in CCPMH's action plan. Further data will be collected following launch of this online resource, to evaluate its usefulness to PCPs and their patients.</p>

RAUCH, JULIA

1. Title:	Physiological Changes in the Practicing Reiki Practitioner
2. Student Presenter:	Julia Rauch
3. Co-Workers and Collaborators	Didier Alexandre, Emily Fox, Jim Bena, and Joan Fox
4. Advisor	Joan Fox, PhD
5. Departments	Integrative Medicine Research, The Department of Molecular Cardiology
6. Institutions	The Cleveland Clinic Foundation
7. Support	This research was supported by in part by funding from the National Institutes of Health, National Center for Complementary and Alternative Medicine Grant AT-001884 and in part by the National Institutes of Health, National Center for Research Resources, General Clinical Research Center Grant M01 RR-018390
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Background: With the increasing popularity of energy healing therapies, such as Reiki, research on their effects is increasing. Reiki is based on the yet unproven premise/belief that a trained practitioner can channel “life-force” into a client’s body with the purpose of providing therapeutic benefit. A major deficiency in the research on Reiki is that abilities of the practitioner are determined only by time spent practicing and by subjective references from teachers and clients. With the goal of finding specific markers to better characterize practitioners’ abilities, this pilot study looked at physiological and psychological changes of Reiki practitioners and Reiki-naïve controls being guided through the centering and heart-focused intentions of Reiki practice. Questions/hypothesis: 1) Reiki practitioners will show decreased sympathetic and increased parasympathetic responses and decreased salivary cortisol. 2) They will show improved well-being, as measured by psychometric instruments and elevated melatonin, DHEA and atrial natriuretic peptide. 3) The changes in practitioners will be greater than those in Reiki-naïve controls.</p> <p>Methods: The intervention was performed in 2 sessions with ~ 15 Reiki practitioners and 15 controls in each. Blood, saliva, and psychometric questionnaires were obtained before and after the intervention.</p> <p>Psychometric Instruments: A 25-item state-anxiety version of the Profile of Moods Survey (POMS) was used as well as the SRSI, which addresses positive emotions.</p> <p>Heart Rate: Electrodes were attached and electrocardiograms recorded throughout the session.</p> <p>Salivary Cortisol and Melatonin: Saliva was collected by passive drool and stored at -80°C. Assays were performed en masse by enzyme-linked immunoassay (ELISA) using commercial kits.</p> <p>Plasma Atrial Natriuretic Peptide (ANP): Plasma was isolated and stored at -80°C prior to assay of ANP using a commercial radioimmunoassay kit.</p> <p>Serum DHEA: Serum was prepared and DHEA assayed using a commercial ELISA kit.</p> <p>Results: The data will be presented after final analysis by biostatisticians at The Cleveland Clinic Foundation.</p>

REDDY, SUJAN

1. Title:	Human Rights Education in Ugandan Health Professional Schools
2. Student Presenter:	Sujan Reddy
3. Co-Workers and Collaborators	Nelson Musoba, MD, MPH; Sabrina Eagan RN, MPH
4. Advisor	Joyce Fitzpatrick PhD, RN, FAAN
5. Departments	School of Nursing
6. Institutions	Case Western Reserve University; Action Group for Health, Human Rights, and HIV/AIDS (AGHA) - Uganda
7. Support	Crile Research Fellowship
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>BACKGROUND: As highlighted by the HIV/AIDS epidemic, human rights abuses contribute to poor health outcomes, while discrimination based on health status has infringed upon patients universally recognized rights. In order to effectively manage their patients' well-being, health professionals need to be educated about this relationship between the health of their patients and the fulfillment of their human rights.</p> <p>QUESTION: Do Ugandan health professional schools address human rights topics in their curricula? This study will qualitatively describe the coverage of human rights topics in the curricula and the factors influencing the inclusion of such material.</p> <p>METHODS: Methods utilized were literature review, key-informant interviews, and focus groups. Interviews were conducted with faculty and students from health professional schools (medicine, nursing and public health). Focus groups consisted of human rights advocates and health professional students.</p> <p>RESULTS: When human rights topics are covered, ethics courses are the most likely setting. However, not all schools have ethics courses and the material may not be a stated learning objective in the syllabi. Factors limiting the incorporation of human rights topics include higher priorities, time restraints, and limited resources, such as funding and faculty expertise. Resources for incorporating this material include student interest, student groups, and partnerships with other schools, institutions or non-governmental organizations. Based upon these findings, a quantitative survey was developed in order to assess the extent to which specific human rights topics are covered.</p> <p>CONCLUSIONS: By ascertaining the inadequacies in human rights training and the factors influencing the inclusion of such material, this baseline information will be useful for future educational interventions.</p>

REED, JANICE

1. Title:	African American Attitudes toward Clinical Research: Implications for recruitment
2. Student Presenter:	Janice Lindsay Reed
3. Co-Workers and Collaborators	Pamela Jackson, RN, BSN, MA and Katherine Mathews, MD
4. Advisor	Dorothy F. Edwards, PhD
5. Departments	Alzheimer's Disease Research Center- Department of Neurology
6. Institutions	Washington University School of Medicine – St. Louis, Missouri
7. Support	Grant # 2 P50 AG05681-17 from the National Institute on Aging, U.S. Public Health Service; Crile Fellowship
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>This study investigates the attitudes of African Americans who reside in the St. Louis metropolitan region. One of the goals of the African American Outreach Satellite (AAOS) at Washington University School of Medicine is to increase enrollment of African American participants in the research activities of the Alzheimer's Disease Research Center (ADRC). Therefore, this study has the potential to improve recruitment by enabling researchers to approach the African American community in a way that resolves the identified barriers and addresses the concerns of the community. Due to the historical accounts of unethical practices experienced by African Americans in the United States, it was hypothesized that African American participants in this study would cite the Tuskegee study of untreated syphilis in the negro male (1932-1972) as a source of apprehension toward research. In this qualitative study, seven survey questions were administered as a semi-structured interview among 36 key informants to elicit the general views of African Americans about research. Preliminary results demonstrate that African Americans in the St. Louis metropolitan region regard research participation as beneficial; however, lack of trust in the institution conducting research was noted as a prominent barrier. While a few participants referred to the Tuskegee Syphilis Study based in Alabama, most interviewees shared their personal experiences in navigating local hospitals. The connection between research attitudes, personal experiences, and difficulties regarding the health care system raise interesting questions that will be explored further through focus groups with community residents and interviews with minority physicians.</p>

RICCI, KRISTIN

1. Title:	Systemic Antioxidants in Tibetan Highlanders
2. Student Presenter:	Kristin Ricci
3. Co-Workers and Collaborators	Cynthia Beall, Suzy Comhair, Allison Janocha
4. Advisor	Serpil Erzurum
5. Departments	Department of Pathobiology
6. Institutions	Lerner Research Institute, Cleveland Clinic Foundation, Cleveland, Ohio
7. Support	Crile Fellowship
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Background: High altitude hypoxia is a major stimulus of systemic oxidative stress, which imparts free radical induced damage at all levels of tissue complexity. Antioxidants provide cells with the ability to neutralize these destructive compounds through redox reactions.</p> <p>Hypothesis: We hypothesized that populations exposed chronically to high altitude hypoxia may have different levels of systemic antioxidant molecules than those living at sea level, enabling them to better combat oxidant stress.</p> <p>Methods: To test this hypothesis, plasma superoxide dismutase (SOD) activity and proteins and the glutathione peroxidase (GPx)/glutathione antioxidant system were measured in 20 Tibetan healthy, nonsmoking, native residents at 4,200 m (13,900 ft) and in 25 sea level controls using spectrophotometric and enzyme-linked immunosorbent assays.</p> <p>Results: SOD activity, but not Mn-SOD or Cu,Zn SOD protein was higher in Tibetan subjects than in sea level controls. While Cu,Zn SOD protein was higher in controls, the specific activity of the enzyme was significantly higher in Tibetans. GPx activity was significantly lower in Tibetan subjects than controls, while extracellular GPx concentration was not significantly different. Total glutathione levels were also similar between groups.</p> <p>Conclusions: These results are consistent with our initial hypothesis that those living at high altitude may possess enhanced responses to oxidative stress. Tibetans have SOD specific activities that are much higher than those of sea level controls. Increased enzymatic activity could provide systemic protection against the abundant free radicals of high altitude living. While lower activity levels of GPx, a selenoprotein, were measured, these paradoxical decreases could be accounted for from established low levels of selenium in the indigenous Tibetan diet. These enzymatic variations could indicate potential molecular changes facilitating high altitude adaptation.</p>

ROBERTS, BRANDON

1. Title:	Auditory and Vestibular Function Evaluation in Patients with Solid Tumors Treated with Oxaliplatin-Containing Chemotherapy
2. Student Presenter:	Brandon A. Roberts
3. Co-Workers and Collaborators	Joanna Brell, Matthew Cooney, Afshin Dowlati, Pingfu Fu, Cheryl Henkin, Smitha Krisnamurthi, Gail Murray, Scot Remick, Stephen Sagar, Paula Silverman, Judith Wh
4. Advisor	Panayiotis Savvides
5. Departments	Department of Medicine ; Department of Neurology; Department of Surgery Audiology Services; Head and Neck Institute
6. Institutions	University Hospitals of Cleveland; Cleveland Clinic
7. Support	Case Comprehensive Cancer Center
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>The development of chemotherapy-induced peripheral neuropathy (CIPN) is a significant dose limiting toxicity in patients treated with oxaliplatin. The evaluation of peripheral neuropathy is almost exclusively based on the grading system described in the NCI's Common Terminology Criteria for Adverse Events (CTCAE). This grading system has significant drawbacks since grading cannot be objectively verified and multiple biases can be introduced by both the patient and the clinician.</p> <p>In the other platinum compounds approved for clinical use, ototoxicity has been observed in addition to peripheral neuropathy with varying degrees of subclinical and clinical manifestations. We hypothesize that neuropathy is a class effect for these platinum compounds and that audiometric detected hearing loss is common in patients treated with oxaliplatin. The goal of this study is to determine if there is an association between clinician-rated CIPN and audiometric detected hearing loss.</p> <p>Patients answer a series of questionnaires regarding their hearing, dizziness, and peripheral neuropathy complaints and an overall grade is assigned based on the CTCAE. Audiograms are then performed to determine if their hearing is abnormally deficient.</p> <p>Currently, 27 patients are enrolled in our study. Each has completed the questionnaires and been assigned an overall grade. Many have had an audiogram, but not all of their results have been returned. We anticipate reaching our goal of 60 patient evaluations, audiograms, and audiogram results by the end of July 2006. At that time, the analysis will be performed on the data to determine if there is indeed an association between clinician-rated CIPN and audiometric detected hearing loss.</p> <p>If an association between ototoxicity and CIPN is established and the toxicity is found to precede the CIPN, our study has the potential to help change clinical practice by reliably predicting patients who are at an increased risk of developing CIPN based on audiological evaluation prior to and during treatment. This would be valuable since it would allow for clinical intervention before the CIPN becomes severe and possibly irreversible.</p>

ROTTKAMP, CATHERINE

1. Title:	Role of the Hox cofactors in the development of spinal motor circuits
2. Student Presenter:	Catherine Rottkamp
3. Co-Workers and Collaborators	Cynthia L. Wladyka, Katherine J. Lobur, Amy K. Lucky
4. Advisor	Stephen O'Gorman
5. Departments	Department of Neurosciences
6. Institutions	Case Western Reserve University
7. Support	NIH RO1 GM056525
8. Please choose your academic program:	MD PHD
9. What Year are you in the program?	6
10. Body of Abstract (300 words or less)	<p>It has been demonstrated that differential expression of Hox genes plays an important role in motor pool identity, both rostrocaudally between segments and mediolaterally within segments of the spinal cord. However, the expression pattern of Hox genes by itself is not diverse enough to account for the large number of motor pools. We propose that differential expression of two families of cofactors, the Meis and Pbx proteins, that affect binding affinity and specificity by forming heteromultimers with members of the Hox family, may provide the necessary diversity. We have demonstrated that in general Pbx and Meis factors are widely expressed in ventral spinal neurons. A striking exception exists in the brachial and lumbar expansions where groups of motor neurons fail to express Pbx or Meis. Retrograde transport studies demonstrated that groups lacking expression represent motor pools projecting to specific muscles, while adjacent motor pools express varying combinations of Pbx and Meis proteins. The functional consequences of misexpression of Pbx1 and Meis1 in a normally negative pool were assessed in ovo electroporation into pectoral motor neurons. While misexpressing neurons settled in the pectoral pool, they were less likely to project to the appropriate target. Electromyographic studies showed that motor neurons of overexpressing chicks displayed abnormal spontaneous firing.</p> <p>We have also decided to look at the consequences of lack of Pbx3 function in the adult mouse. This question cannot be addressed in Pbx3 null mice because they die perinatally due to respiratory failure caused by defects in the hindbrain respiratory circuit. We have therefore developed mice with a conditionally null Pbx3 allele. By crossing this mouse with a Hoxb1-Cre line we have eliminated Pbx3 expression in >90% of spinal cord neurons from early stages. These mice are viable into adulthood, but demonstrate gross motor abnormalities including hypokinesia, hind limb splaying and posturing of the forelimbs and tail. We are in the process of characterizing these mice with the goal of isolating the cause of the motor dysfunction.</p>

ROULETTE, GREGORY

1. Title:	Determining the Environmental Context for P2X7 Receptor Sensitization in Rat Macrophages
2. Student Presenter:	Dante Roulette
3. Co-Workers and Collaborators	Sylvia Kertesy
4. Advisor	George Dubyak
5. Departments	Department of Physiology and Biophysics
6. Institutions	Case Western Reserve University
7. Support	NIH-GM36387
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>The purpose of this preliminary study was to determine ability of exogenous ATP to stimulate cell surface ATP receptors that are coupled to degranulation via mobilization of intracellular calcium stores. RBL-2H3 cells, a cell found in the in-vivo environment of macrophages containing the P2X7 receptor, were used in these experiments. Stimulation of RBL-2H3 cells by ATP causes degranulation via a process mediated by phospholipids. Several potential agonists were chosen based on this pathway, and tested at different concentrations and conditions to see how well they stimulated calcium mobilization in the RBL cell. Changes in cytosolic calcium concentration due to either efflux from the ER or influx across the plasma membrane, as measured by FURA-2 calcium indicator, determined the experimental outcome.</p> <p>Initially, response was not seen with stimulation by ATP, at any concentration. It was theorized the cells were constitutively desensitized to ATP. Apyrase, an enzyme that catalyses the hydrolysis of ATP, reversed this process. After adding apyrase, stimulating the cells with ATP yielded the expected positive result. Exogenous lysophosphatidic acid (LPA) also yielded a positive result, though at a diminished level when compared to ATP. Sphingosine-1-phosphate (S1P) was shown to induce calcium mobilization as well. Both LPA and S1P are phospholipids linked to calcium mobilization thru other cell receptors. There are plans to complete similar experiments using different enzymes and IgE to see how well they stimulate the degranulation process.</p> <p>Conceptually, the next steps in the process are to complete similar experiments on two other cells found in the local environment, murine splenic T-lymphocytes and bone marrow derived mast cells. Following completion of the assays, it is anticipated each cell type will be co-cultured with cells containing the macrophage P2X7 receptor to achieve the long-range goal of defining the context for the positive modulation of P2X7 affinity for ATP.</p>

RUSZCZYCKY, MARK

1. Title:	How do enzymes make alcohols more nucleophilic? Secondary deuterium V/K isotope effects in the case of serine acetyltransferase
2. Student Presenter:	Mark W. Ruszczycky
3. Co-Workers and Collaborators	
4. Advisor	Vernon E. Anderson
5. Departments	Department of Biochemistry
6. Institutions	Case Western Reserve University
7. Support	Case MSTP NIH NSF
8. Please choose your academic program:	MD PHD
9. What Year are you in the program?	6
10. Body of Abstract (300 words or less)	<p>The enzymatic activation of alcohols as nucleophiles is an area of enzymology that has received relatively little attention. This is primarily due to the relative inaccessibility of the transition states in the corresponding reactions to direct experimental analysis. The most direct and reliable way of investigating transition state structure is through the measurement of kinetic isotope effects; however, in the case of nucleophilic alcohols, the hydroxyl proton is rapidly exchanged with solvent precluding one's ability to isotopically label it for these types of experiments. We circumvent this difficulty by replacing C-H bonds adjacent to the nucleophilic hydroxyl group with C-D bonds and measuring the beta-secondary deuterium V/K isotope effects using whole molecule isotope ratio mass spectrometry. By synthesizing (2S,3R)-[3-2H]serine and (2S)-[3,3-2H2]serine, we have measured the V/K isotope effects stereospecifically for both beta hydrogens of L-serine in the reaction catalyzed by serine acetyltransferase using internal competition and analysis of both residual starting material and product formed. These were found to be 0.993 ± 0.04 and 0.978 ± 0.03 respectively, suggesting that the serine is not fully ionized in the most sensitive transition state and that the pro-S beta C-H bond in the transition state is slightly tightened while the bond order of the pro-R beta C-H bond is relatively unaffected compared to serine free in solution.</p>

SAMANT, UMA

1. Title:	Risk of Poor Outcome Due to Hypotension Burden Following Severe Pediatric Traumatic Brain Injury
2. Student Presenter:	Uma Samant
3. Co-Workers and Collaborators	Christopher Mack, Saipin Muangman, Pilar Suz
4. Advisor	Monica S. Vavilala
5. Departments	Departments of Anesthesiology, Pediatrics and Neurological Surgery, University of Washington, and Harborview Injury Prevention and Research Center, Seattle, WA
6. Institutions	University of Washington, and Harborview Injury Prevention and Research Center, Seattle, WA
7. Support	Support was Provided by Foundation of Anesthesia Education and Research (UBS, CM), and NIH/NICHHD K23 (MSV)
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Background and Rationale: Children presenting to the ED with hypotension following traumatic brain injury (TBI) have a higher mortality compared to patients with blood pressure appropriate for age. The objective of this study was to examine the influence of hypotension burden (hypotension intensity and duration) on outcome using a constructed hypotension burden index (HBI). Methods: This retrospective cohort study took place at Harborview Medical Center (level I pediatric trauma center) Seattle, WA (1998-2005). Participants (n=133) were children < 18 years of age with TBI, head abbreviated injury score (AIS) > 3, and PICU admission Glasgow Coma Scale (GCS) score < 9. HBI was calculated as average rate ratio for poor outcome. Each available systolic blood pressure (SBP) value from field through the first 72 hours of PICU admission, was recorded for every patient. The primary outcome measure was hospital discharge (D/C) Glasgow Outcome score (GOS) where D/C GOS < 4 reflects poor outcome. We also examined deaths. Results: Any SBP < 5th percentile (RR 1.9; 95% CI 1.4-2.6) and any SBP < 50th percentile (RR 1.7; 95% CI 1.2-2.6) were associated with increased risk of poor D/C GOS. However, HBI predicted poor GOS (100% specificity for HBI > 1.6) better than any single episode of hypotension, defined either as any SBP < 5th percentile (94% specificity) or any SBP < 50th percentile (68% specificity). HBI also predicted death (HBI 100% specificity for HBI > 1.9) better than any single episode of SBP < 5th percentile (90% specificity) or any SBP < 50th percentile (59% specificity). Conclusions: The HBI was a better early predictor of poor GOS and death than the currently recommended definition of hypotension in severe pediatric TBI. Clinical use of the HBI, early following severe TBI, might be important to the triage, care and prognosis of these children.</p>

SCHUB, DAVID

1. Title:	SUTURE PULLOUT STRENGTHS FROM HUMAN FASCIA LATA USING MULTIPLE TECHNIQUES
2. Student Presenter:	David Schub
3. Co-Workers and Collaborators	Dr. Joseph Iannotti, Dr. Kathleen Derwin
4. Advisor	Dr. Kathleen Derwin
5. Departments	Lerner Research Institute and Orthopaedic Research Center
6. Institutions	Cleveland Clinic Foundation, Cleveland, OH
7. Support	We thank The Musculoskeletal Transplant Foundation (Edison, NJ) for funding and donation of the fascia samples, as well as The Crile Fellowship for its support.
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>INTRODUCTION Tissue banks and autogenous sources currently provide the human fascia lata utilized in clinical practice, though thorough investigation of a commercially available product is underway. The aim of this study is to determine the pullout strengths of three different suturing methods currently used in various soft tissue repair surgeries when placed in this developed material.</p> <p>METHODS Twenty-four 2 cm x 3 cm strips of human fascia lata were obtained from the iliotibial tract of a human donor, treated with antibiotics and lyophilized, then randomly divided into three groups of eight, and assigned a different suture technique. Groups were named according to the method used, the simple suture, the modified Mason Allen technique, and the Massive Cuff technique. The samples were tested using an Instron 5543 machine until complete suture failure was observed and maximum load was achieved.</p> <p>RESULTS Simple suture had a mean failure load of 12.9 ± 4.0 N with individual failure loads ranging from 5.9 – 18.1 N. Modified Mason Allen technique showed a mean failure load of 39.5 ± 10.4 N with individual failure loads ranging from 22.8 – 55.7 N. Massive Cuff technique showed a mean failure load of 34.5 ± 14.5 N with individual failure loads ranging from 18.2 – 67.0 N. The pullout strength of the simple suture was significantly lower than both the modified Mason Allen and the Massive Cuff techniques. Differences between the median pullout strengths of the Massive Cuff and modified Mason Allen groups were not statistically significant.</p> <p>CONCLUSIONS While potentially more complicated to implement internally than a simple suture, both the modified Mason Allen and Massive Cuff stitches provide significant improvements in the maximum loads achieved before total failure is recognized, and when planning further research of processed human fascia lata for in vivo usage, this information should be taken into account.</p>

SCOTT, JACOB

1. Title:	Modelling of Proximal Tibiofibular Joint Motion Due to Tibiofemoral Loading
2. Student Presenter:	Jacob Scott
3. Co-Workers and Collaborators	Antonie (Ton) van den Bogert, Wael K Barsoum
4. Advisor	Antonie (Ton) van den Bogert
5. Departments	Biomedical Engineering and Orthopaedic Surgery
6. Institutions	Cleveland Clinic
7. Support	Crile Fellowship, NIH #1T32AR050959-01 , Stryker Biomedical
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Introduction: The posterolateral part of the knee joint has been largely ignored in past biomechanical studies. Specifically, little is known about the proximal tibiofibular joint (PTFJ) and its relationship to overall knee joint mechanics. The proximal fibula serves as the insertion for several key muscles and ligaments integral to knee stability. Our recent work has shown that significant PTFJ motion exists during physiologic loading conditions, the greatest displacements occurring during combined varus and external tibial rotation moments. Changes in the motion of this joint may be a surrogate marker for pathologic changes in overall knee mechanics.</p> <p>Methods: Fresh frozen cadaveric knee specimens were tested with the knee joint fully intact. The tibia was mounted vertically on a six degree of freedom force/torque sensor (SI-2500-400, ATI, Industrial Automation, Apex, NC) mounted to the floor. The distal fibular connections to the tibia were undisturbed during dissection and subsequent testing. Reflective markers were driven into the tibia and proximal fibula, respectively. Relative motion between the two was captured by a high speed video camera (DALSA model #CL-C3 running Epix Framegrabber software) and motion analysis was carried out using custom MATLAB software. Camera and force data were both recorded at 10Hz and subsequently synchronized. The knee joint was then subjected to manual loading conditions and the data were subjected to quadratic regression analysis allowing for comparison of standardized loading conditions consistent with gait and stair climbing.</p> <p>Results: Significant PTFJ motion exists at torques consistent with gait and stair climbing that is consistent across specimens. Deeper flexion angles cause more error in our model, possibly due to knee joint geometry changes due to femoral head rolling and raising on the tibial plateau. Use of this model allows for more standardized comparison of future knee joint testing and for broader application of data.</p>

SHEU, MIKE

1. Title:	Langerhans' Cell Histiocytosis: Characterization of a Patient Population at a Metropolitan Children's Hospital
2. Student Presenter:	Mike Sheu, MS, MPH
3. Co-Workers and Collaborators	Rima Jubran, MD, MPH
4. Advisor	Rima Jubran
5. Departments	Hematology/Oncology
6. Institutions	Childrens' Hospital of Los Angeles
7. Support	Case Western Reserve University, Children's Hospital of Los Angeles/University of Southern California
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Langerhans' Cell Histiocytosis (LCH) is predominately pediatric condition characterized by the abnormal tissue infiltration and clonal proliferation of bone marrow derived histocytes known as Langerhans cells. The organ systems affected by LCH are wide-ranging and can include skin, bone, lymph nodes, spleen, brain, and liver. There have been very few epidemiological studies of LCH and consequently the identification of a definitive causal factor or agent for LCH remains elusive. Currently available literature associates LCH with infections, solvent exposure, and pesticide exposure. In addition, studies have linked poor prognosis to multiple organ involvement and lesions in certain organs such as the liver and spleen. To better understand the LCH patient population at CHLA we undertook a review of records of known cases treated at the hospital in the last ten years. Data gathered included age at diagnosis, gender, location of lesion(s), diseases reactivation, and treatment modality. Data analysis revealed a mean age at diagnosis of 4.48 years and the male to female ratio was relatively even. In our population we found that patients with multiple organ involvement of LCH were more likely to have reactive disease when compared to patients with single organ involvement. We also found that patients with skull lesions were more likely to have disease reactivation when compared to patients without skull lesions. A small subgroup of patients with reactive LCH was treated with 2-cholor-2'-deoxyadenosine (2CdA) instead of the usual treatment with prednisone and vinblastine. Our analysis revealed that 2CdA treatment in reactive LCH appeared to be a viable and possibly superior treatment to prenidstone/vinblastine. Our characterization of the LCH patient population at LCH builds upon earlier findings and points to area of research and clinical interest that may be pursued in the future.</p>

SHULTZ, DAVID

1. Title:	The role of IKKbeta in IFN-gamma signaling
2. Student Presenter:	David Shultz
3. Co-Workers and Collaborators	Nywana Sizemore
4. Advisor	George Stark
5. Departments	Pathology
6. Institutions	Case School of Medicine, Cleveland Clinic Foundation
7. Support	NIH
8. Please choose your academic program:	MD PHD
9. What Year are you in the program?	6
10. Body of Abstract (300 words or less)	<p>Sizemore et al (PNAS, 101(21), 2004) recently identified a subset of ISGs that are not induced in response to interferons (IFNs) in mouse embryonic fibroblast cells (MEFs) doubly null for the expression of IβB kinase α and β (IKKα and IKKβ). Induction of one such gene, ip-10, was undiminished in MEFs that stably expressed the super repressor of IβBα, as was induction in p65$^{-/-}$ MEFs, indicating that IKK dependence for induction of that gene was unrelated to NFβB activation. Further microarray work has revealed that the IFN-induced transcription of other IKK-dependent ISGs is specifically dependent on IKKβ expression. In an experiment conducted using CodeLink technology, of 584 ISGs induced in a pool of IKK$\beta$$^{-/-}$ cells stably restored for IKKβ expression, 370 (63%) were not induced in IKK$\beta$$^{-/-}$ cells. Several of these genes have been confirmed by Northern analysis. We hypothesize that IFNγ activates IKKβ to produce a distinct signal, unrelated to NFβB activation, that leads to the activation of as of yet unknown transcription factors, thus helping to stimulate the transcription of a subset of ISGs. We are currently working to identify upstream signals that activate IKKβ by IFNs, the factors downstream of that event, and the cis-regulatory elements required for the IKKβ-dependent response of certain ISGs .</p>

SOPKO, NIKOLAI

1. Title:	Increased Accuracy of Pulmonary Imaging using Sub-Regional Analysis via Three Dimensional Volume Warping
2. Student Presenter:	Nikolai Sopko
3. Co-Workers and Collaborators	
4. Advisor	Zhenghong Lee
5. Departments	Biomedical Engineering
6. Institutions	Case Western Reserve University
7. Support	
8. Please choose your academic program:	MD PHD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Computerized Tomography (CT) provides excellent three-dimensional anatomical information by making use of the inherent variance of densities between tissues found in the human body. Its acuity for imaging dissection is strongest for denser structures, namely bone and organ parenchyma. Human lungs can occupy a quarter of total body volume and facilitate oxygen equilibration between outside air and our blood by providing a large surface area for gas exchange. Therefore the corresponding form to this function is one of air filled sacs surrounded by thin layers of tissue with very low density. Hence, healthy lungs are "transparent" to x-rays. In order to visualize the fissures that separate lung lobes and obtain a more accurate position within the lung, a high intensity CT scan must be used, which greatly exceeds normal x-ray exposure and could significantly increase health risks due to radiation especially in individuals that need multiple scans within a short period of time. Lung models, which provide precise anatomical landmarks, have been developed by averaging high intensity CT scans of healthy volunteers. We used such a lung model by warping its volume to several juvenile CT scans using a control point algorithm, which gave us lobular definition in our patient's normal resolution CT. One of the many advantages of this technique is its use in conjunction with Single Photon Emission Tomography (SPECT). We used these combined modalities to monitor acute inflammations in cystic fibrosis (CF) patients by tagging polymorphic nuclear cells (PMN) with a radioactive anti-body that SPECT could detect and simultaneously locating their aggregations within lobular regions of the lung using our CT warping technique. Patients underwent two imaging regimens that were pre and post IV antibiotic treatment. We compared pulmonary function tests with PMN activity determined by SPECT/CT regional analysis and we obtained mixed results.</p>

STEVENSON, RYAN

1. Title:	Preoperative Evaluation of Hip Fracture Patients. Is a Medical Consult Really Necessary?
2. Student Presenter:	Ryan Stevenson
3. Co-Workers and Collaborators	Sam Akhavan, MD, James Rowbottom, MD
4. Advisor	Patrick Getty MD
5. Departments	Orthopaedics, Anesthesia
6. Institutions	University Hospitals of Cleveland
7. Support	Crile Fellowship
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>In patients undergoing surgical fixation of hip fractures, medical consultation has traditionally been obtained to optimize the patient in order to reduce perioperative complications. This evaluation, however, often leads to delays in operative fixation. This study was designed to determine whether obtaining a preoperative medical evaluation in patients with an American Society of Anesthesia (ASA) score of II or III decreased the rate of complications. Sixty-eight patients with hip fractures undergoing operative fixation were evaluated for time from admission to operative fixation, overall length of hospital stay and perioperative complications. Thirty-eight patients underwent medical evaluation prior to surgery (Group 1) and thirty patients did not (Group 2). Criteria for selection: ASA scores II and III and age over 65. Patients were similar in distribution between the two groups in terms of ASA scores, sex, age and medical problems. Patients in Group 1 had a significantly longer time from admission to the operative fixation, 23.6 hours (range 3-152 hours) vs. 11.13 hours (range 2-25.5 hours), $p < 0.001$; total length of hospital stay 6.1 days (range 3-21 days) vs. 4.6 days (range 3-8 days), $p = 0.02$. There was no significant difference in complication rates. (Group 1, 31.7% vs. Group 2, 10%, $p = 0.25$). There was one death in group 2. Medical evaluation is a crucial part hip fracture management, especially in patients with multiple medical problems. Results of this study, however, indicate that medical evaluation in patients with an ASA score of II and III does not reduce the risk of complication and leads to greater preoperative delays. It is our current plan to retrospectively evaluate all hip fracture patients between 1999-2004. The plan is to then proceed with a randomized prospective trial.</p>

STULBERG, JONAH

1. Title:	Knowledge Is Power: Educating Uninsured Patients Living with Diabetes in Greater Cleveland
2. Student Presenter:	Jonah Stulberg, M.P.H.
3. Co-Workers and Collaborators	Ione Freedman, N.P., Matt Sebastian, R.D., L.D., Leanne Chrisman-Khawam, M.D., M.Ed.
4. Advisor	Susan Flocke, Ph.D.
5. Departments	Epidemiology and Biostatistics, Family Medicine
6. Institutions	Free Medical Clinic of Greater Cleveland, Case Western Reserve University
7. Support	Crile Summer Fellowship, 2005
8. Please choose your academic program:	MD PHD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Background: Rapidly increasing numbers of uninsured individuals are turning to safety net organizations for ongoing care of Type II Diabetes. Formal patient education and patient empowerment curriculum are currently lacking but critically needed. This study evaluates the efficacy and effectiveness of a new diabetes education program implemented in the Free Medical Clinic of Greater Cleveland (Free Clinic).</p> <p>Methods: The Knowledge is Power diabetes education program was designed specifically to meet the needs of the patients of the Free Clinic and to fit the natural patient flow of the clinic. 37 participants enrolled and received 9 hours of education. Evaluation outcomes included: attendance rates, satisfaction with the course, readiness to change, change in participant knowledge and staff impressions of program effectiveness. A planned review of the medical records of participants and a sample of non-participants will assess fasting blood glucose, hemoglobin A1C, blood pressure and consistency of medication refills at four time points: baseline, completion of the program, and three- and six-months after the intervention.</p> <p>Results: Initial analysis suggests the Knowledge Is Power program was feasible in this setting and successful in motivating participants to make productive changes in their health care habits. The program achieved over a 50% retention rate, a 10 fold increase over previous programs in this setting. Participant satisfaction was high. Anecdotally, the Free Clinic staff report higher medication adherence rates and a higher level of engagement in self-care by program participants. The medical record review is scheduled for the last week in March so that all program groups will have 6 month results.</p> <p>Conclusions: Though complete results are currently pending, the findings reported thus far were positive enough to encourage the Free Medical Clinic of Greater Cleveland to pursue future Knowledge Is Power classes and stimulated development of ongoing diabetes support groups. If this program has an effect on important biomedical markers, it could be implemented to meet the needs of patients with diabetes seeking care in other safety net clinics.</p>

TARABISHY, BISHER

1. Title:	An Anatomic Study of Healed Clavicle Fractures
2. Student Presenter:	Bisher Tarabishy
3. Co-Workers and Collaborators	Mike Chen, MD; John Wilbur, MD; Daniel Cooperman, MD
4. Advisor	Daniel Cooperman, MD
5. Departments	Orthopedic Surgery
6. Institutions	Case Western, University Hospitals, Cleveland Museum of Natural History
7. Support	
8. Please choose your academic program:	MD
9. What Year are you in the program?	3
10. Body of Abstract (300 words or less)	<p>PURPOSE: Fractures of the clavicle are common injuries. Most are treated with closed methods. Many heal with some degree of deformity. This study evaluates the osseous results of healed clavicle fractures that were most certainly treated non-operatively.</p> <p>METHODS: Clavicles from the Hamann-Todd Osteological Collection at the Cleveland Museum of Natural History were examined for fractures. All patients died between 1893 and 1938. None of the clavicles revealed any signs consistent with surgical treatment. We identified 77 unilateral clavicle fractures for analysis from 3100 specimens. Measurements of length for the fractured and unfractured clavicle were performed on a digital osteometric board. As a control, the clavicles of 80 normal specimens were also measured to compare side-to-side variation in length. Digital images were made of all fractured specimens. Fracture displacement (any visually detectable cortical offset) and angulation (>5 degrees difference when compared with the normal clavicle) were measured using an image processing program.</p> <p>RESULTS: Fractures occurred in 66 men and 11 women. Forty-three fractures occurred in the left clavicle and 34 in the right clavicle. In normal specimens, the mean difference in length between clavicles was 3.75mm (range 0.11mm to 10.12mm, $p=0.00089$, correlation coefficient = 0.925). Forty (52%) of 77 fractures healed with displacement. The mean displacement was 93.15% (range 26.28% to 176.98%) of the apparent clavicle diameter. Fifty-seven (74%) fractures healed with angulation. The mean angulation was 19.88 degrees (range 5 to 68 degrees).</p> <p>CONCLUSION & SIGNIFICANCE: Presumed non-operative treatment of clavicle fractures resulted in shortening, displacement and angulation that averaged 12.02mm, 93.15%, and 19.88 degrees respectively, and resulted in extremes of 36.55mm, 176.98%, and 68 degrees respectively. Functional studies should elucidate the significance of the average and extremes. In addition, outcomes of operative and non-operative treatment should be compared with this study where almost certainly minimal treatment was given.</p>

THOMSON, JODI

1. Title:	Multiple Substitutions at Ambler Position 244 in SHV β -lactamase Provide Insight into Importance of Arg244 in Inhibitor and Substrate Binding
2. Student Presenter:	Jodi M. Thomson
3. Co-Workers and Collaborators	Anne M. Distler, Fabio Prati
4. Advisor	Robert A. Bonomo
5. Departments	Department of Pharmacology, Division of Research Service, and the Department of Chemistry,
6. Institutions	Case Western Reserve University School of Medicine, Louis Stokes Cleveland Department of Veterans Affairs Medical Center, and the University of Modena, Modena,
7. Support	Jodi Thomson was supported in part by NIH T32 GM07250 and the Case Medical Scientist Training Program. Special thanks to the National Institutes of health for
8. Please choose your academic program:	MD PHD
9. What Year are you in the program?	5
10. Body of Abstract (300 words or less)	<p>Background: Inhibitor resistant class A β-lactamases are an emerging threat to β-lactam/ β-lactamase inhibitor treatment of gram negative infections. Based on clinical isolates of inhibitor (clavulanate) resistant TEM enzymes with mutations at Ambler position Arg244, we used site-saturation mutagenesis to explore the importance of this residue in substrate and inhibitor binding and recognition in SHV, an enzyme found most notably in the hospital pathogen <i>Klebsiella pneumoniae</i>.</p> <p>Materials and methods: We constructed 19 mutants at position 244 by site-saturation mutagenesis of the blaSHV-1 gene. Agar dilution MICs were performed on all isolates. Enzymes were expressed in <i>Escherichia coli</i> DH10B and purified using preparative isoelectric focusing. Steady state kinetics were performed and K_i and k_{inact} values determined through competition with the substrate nitrocefin. Mass spectrometry was performed on SHV-1 and SHV R244S with and without clavulanate inactivation, and tryptic digests of the inhibitor/ β-lactamase complexes were performed and analyzed.</p> <p>Results: 16 variants at Arg244 had increased MIC values against ampicillin/clavulanate. In contrast, all 19 mutants had decreased MIC values to ampicillin, cephaloridine, and piperacillin. Kinetic studies on clavulanate resistant variants Arg244Ser, -Gln, and -Glu showed a decrease in affinity for both inhibitor and substrates (60-1000 fold lower than SHV-1). Unexpectedly, the k_{inact} values of the mutants were all elevated, arguing against a mechanistic basis for resistance, as has been shown in TEM. Employing mass spectrometry, we showed a large portion of the Arg244Ser enzyme is inactivated and multiple products are formed after 15 minutes incubation (1000:1 inhibitor:enzyme ratio).</p> <p>Conclusion: Arg244 is essential for both antibiotic and inhibitor binding to the active site of SHV. These data allow us to predict the future development of inhibitor resistant enzymes in this emerging family and provides novel insight into the design of more potent β-lactamase inhibitors.</p>

TUNG, CHRISTIE

1. Title:	Angiopoietins promote neurite outgrowth in neuronal cells in a Tie2-independent manner
2. Student Presenter:	Christie E. Tung
3. Co-Workers and Collaborators	
4. Advisor	Nicole L. Ward
5. Departments	Dermatology and Neurosciences
6. Institutions	Case School of Medicine This work was supported by a Crile fellowship, an American Academy of Neurology award, and an American Foundation of Aging Research scholarship to CET and grants to NLW from the National American Heart Association (0435103N) and the National Institutes of Health (NIAMS P&F project; P30-AR39750).
7. Support	
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>The role of the vasculature is important to consider in neurological diseases. Many similarities exist between the nervous and vascular systems, including anatomical patterning and concurrent participation in disease. However, little is known about the mechanisms governing the relationship between the two systems. Recent work using vascular endothelial growth factor (VEGF) and angiopoietins suggests that nerves and blood vessels exert reciprocal control of their own growth in a paracrine fashion, thereby playing a pivotal role during development and following injury. Angiopoietin (Ang)-1 is a growth factor that binds to its endothelial cell specific receptor Tie2, recruiting pericytes to developing vessels, and stabilizing the vasculature. Conversely, Ang2 acts as a context specific antagonist, leading to competitive inhibition of Ang1 signaling. Previous in vivo work done by our lab suggests that Ang1 overexpression in the brain leads to altered dendritic patterning in addition to increased vascularization. We hypothesize that Ang1 acts directly on neurons to induce neurite outgrowth. Using a traditional neurite outgrowth bioassay, we tested the abilities of Ang1 and Ang2 to induce neurite outgrowth of PC12 cells from rat pheochromocytoma. Nerve growth factor (NGF) stimulation lead to a 3-fold increase in neurite length compared to unstimulated cells. Ang1 stimulation induced a 2.8-fold increase and Ang2, a 2.3-fold increase, in neurite length. Western blotting and RT-PCR confirmed the absence of Tie2 expression and the presence of expression of β1-integrin in cultures of Ang1-treated PC12s. Furthermore, Ang1-mediated outgrowth was attenuated by functional inhibition of β1-integrin signaling and not by inhibition of Tie2. Our results suggest that angiopoietins induce neurite outgrowth in PC12 cells independent of known Ang/Tie2 signaling pathways, possibly through β1-integrin signaling. Thus, angiopoietins may provide a novel therapeutic target capable of protecting or repairing neurons and vessels during neuro-vascular insults such as ischemic injury, stroke, or traumatic brain injury.</p>

TUTEN, CARRIE

1. Title:	Development of a Cancer Communication and Decision-Making Assessment Scale
2. Student Presenter:	Carrie Tuten
3. Co-Workers and Collaborators	Marie Caputo, Gregory Graham
4. Advisor	Laura Siminoff
5. Departments	Department of Bioethics
6. Institutions	Case Western Reserve University
7. Support	National Cancer Institute grant #R01-CA78517
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Families play an important role in the healthcare decision-making process and the degree of conflict between patients and their family members in terms of treatment and care decisions is an important factor in the health of the patients. Disputes over treatment and care decisions can jeopardize the psychological well-being and quality of life of patients, strain the family, and hinder subsequent treatment planning. If health care providers were able to accurately assess the dynamics of family decision-making they would be better equipped to help patients and their families fully understand the treatment and care options and ensure that they make decisions truly reflective of patients' wishes and treatment goals.</p> <p>To address this issue, and focusing specifically on the lung cancer patient population, Dr. Siminoff is conducting research into the development of an assessment scale that will allow clinicians to quickly and reliably evaluate patient and family treatment decision-making dynamics and measure the level of discord during cancer treatment and care planning. My interest focused on determining the kinds of conflicts present and examining how the number of overall conflicts, the average intensity of those conflicts, and the quality of the patient-physician relationship each affect the overall conflict level.</p> <p>A coding sheet was developed to analyze transcribed interviews of lung cancer patients and their families and data describing the treatment and care conflicts was collected. In the next phase of this project, this data will be used to confirm the accuracy and reliability of the assessment scale.</p> <p>We found that overall conflict surrounding care decisions occurs more often than overall conflict surrounding treatment decisions. More families overall (48.6%) had issues around care decisions than treatment decisions (43.2%). The single most common source of conflict, however, was treatment decisions concerning chemotherapy (18%) followed by care decisions concerning smoking (10.9%). Data analysis is on-going. Conclusions will be made once these analyses are completed.</p>

VO, MICHELLE

1. Title:	Patient Perceptions of the Marketing of Cosmetic Procedures and the Doctor Patient Relationship
2. Student Presenter:	Michelle Vo
3. Co-Workers and Collaborators	
4. Advisor	Jennifer Fishman, PhD.
5. Departments	Bioethics
6. Institutions	Case Western Reserve University
7. Support	Crile Fellowship
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Trends of commercialization are shaping the practice of medicine for many contemporary physicians. Concurrently, cosmetic procedures in medicine are becoming increasingly mainstream in television and print media. Factors contributing to this phenomenon include direct-to-patient marketing strategies for cosmetic procedures, media portrayals of skincare procedures and remedies as “anti-aging” and beauty products, and the promotion of skincare lines launched by physician-entrepreneurs. The intent of this study is to examine the trends of commercialization in medicine and the undefined boundary between the consumerism of the beauty industry and the traditional professionalism of medical practice. The practice of cosmetic medicine and its alignment with beauty industry marketing may encourage patients and their physicians to adopt a more consumerist approach to the doctor-patient relationship, opposing the traditional shared decision-making models of the doctor-patient relationship. The literature regarding historical and contemporary attitudes toward the doctor-patient relationship, the debate surrounding direct-to-consumer marketing of pharmaceuticals, and discussions concerning the place of cosmetic procedures in medical practice were all examined. It was determined that a study examining patient perception of the doctor-patient relationship in the context of contemporary cosmetic practice may help define a portion of the debate surrounding direct-to-consumer marketing and cosmetic procedures. Consequently, a survey was developed to assess patient exposure to media and marketing influences relating to cosmetic medicine. Patients seeking cosmetic procedures are asked to assess on a 6-point scale their exposure to print and television media relating to cosmetic medicine and exposure to direct-to-consumer advertising of cosmetic procedures, and to assess their perceptions and expectations of their individual doctor-patient relationship within this context. This ongoing study is being prepared for implementation.</p>

VORA, PARAG

1. Title:	Effectiveness of Homebound Primary Care In Preventing Avoidable Hospitalizations in Chronic Disease Management
2. Student Presenter:	Parag Vora
3. Co-Workers and Collaborators	
4. Advisor	Dr. Steven Landers
5. Departments	Department of Family Medicine
6. Institutions	Case Western Reserve University, University Hospitals Health Systems
7. Support	
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>BACKGROUND Chronic diseases like diabetes and hypertension cause high levels of morbidity and mortality. Homebound patients with chronic diseases may face barriers to reaching clinical goals of care because of difficulty accessing primary care. The perceptions of homebound patients and their caregivers about the barriers they face in managing their chronic diseases are unknown.</p> <p>OBJECTIVES Objective 1: To determine the effects of homebound primary care on both the utilization and type of hospitalizations by homebound patients with chronic disease. Objective 2:</p> <p>METHODS/PROCEDURES A cross sectional-survey of homebound patients and their caregivers with hypertension, diabetes, or both, of a large academic primary care practice. The exact patient selection process and questionnaire are not yet developed. The study will compare hospitalization data of homebound patients both in the HCP and on the waitlist in order to determine if homebound patients with homebound primary care are less likely to have avoidable hospitalizations, thus making the house call program effective.</p> <p>SIGNIFICANCE An improved understanding of the utilization of care and hospitalizations by homebound patients in achieving chronic disease care goals, may provide insight into how to better address the primary care needs of this population. This information may help policymakers and public health officials decide on best models of care for chronic diseases in the homebound.</p>

WALKER, HOLLIS

1. Title:	The treatment of Multiple Sclerosis with Lisinopril peptide derivatives
2. Student Presenter:	Hollis Walker
3. Co-Workers and Collaborators	Peggy Ho, PhD
4. Advisor	Dr. Lawrence Steinman
5. Departments	Neurology
6. Institutions	Stanford University School of Medicine
7. Support	
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Background: It had previously been shown that some naturally occurring peptides, with concentrations that increased in the presence of an ACE inhibitor, can actually reverse inflammation in rats with experimentally induced colitis and those with heart failure after myocardial infarction.</p> <p>Hypothesis: Can small peptide derivatives of Lisinopril, an angiotensin-converting enzyme inhibitor, but used to treat an inflammatory neurological disease like Multiple Sclerosis.</p> <p>Methods: 50 female SJL-strain mice were induced with PLP 139-1514, a peptide used that would produce EAE (an animal model of multiple sclerosis), and then subsequently treated with one of the 5 possible treatment options. The options included PBS (control group), Lisinopril, Ac-SDKP, MIF, Tuftsin.</p> <p>Results: The in vivo data collected showed some indication that mice treated with MIF and Ac-SDKP helped to prevent the onset and severity of disease.</p> <p>Conclusions: This preliminary data looks very promising in showing that certain peptide derivatives can reduce the inflammatory processes seen in an animal model of Multiple Sclerosis.</p>

WANG-PETERMAN, JENNY

1. Title:	Diffusion Tensor Imaging and Tractography - Generation and Analysis
2. Student Presenter:	Jenny Wang-Peterman
3. Co-Workers and Collaborators	Jean Tkach, PhD
4. Advisor	Jeffrey Ross, MD
5. Departments	Department of Radiology Center for Imaging Research
6. Institutions	The Cleveland Clinic Foundation University Hospitals of Cleveland
7. Support	Crile Fellowship
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Diffusion tensor imaging (DTI) is a relatively new magnetic resonance technique that allows white matter bundles in the brain to be identifiable in vivo. Combined with fiber tractography technique, DTI has been proposed as a preoperative planning protocol for brain tumor resections as well as a diagnostic tool for brain abnormalities. However, current limited understanding of DTI has minimized its translation into clinical practice. The aim of this study is to develop a normal anatomy atlas of the major white matter bundles and to demonstrate the variability of the white matter tractography to changes in the fractional anisotropy (FA) setting and angle of deflection (AOD) setting. Diffusion images with 12-direction encoding of both control subjects and brain tumor patients were processed and generated. White matter tractography was performed using a tensor deflection algorithm, in which the FA and AOD thresholds were varied, while step length and number of samples per voxel length were held constant. Individual regions of interest (ROIs) were regenerated in three dimensions and in three planes from a single seed point for multiple iterations of FA and AOD values. Tractographies of corticospinal tract, internal capsule, cingulum, and corpus callosum were obtained and illustrated. Threshold values of FA and AOD showed to have a significant impact on the number of fiber tracts and the boundaries of the fibers. Although the number of fiber tracts was increased by a decrease in FA threshold or an increase in AOD threshold, it reached maximum and stayed constant when FA threshold was less than 0.20, or when AOD threshold was greater than 20 degrees. Additionally, the contour of a tumor was better defined at a lower FA threshold, where the amount of aberrant fibers was also increased. Future studies should be focused on the appropriateness of fiber tracts and their clinical correlations. Further streamlined DTI and tractography software and a high-capacity workstation are highly recommended.</p>

WEI, DANIEL

1. Title:	Physician Perspectives on Primary Care Physician Involvement in the Care of Advanced Cancer Patients
2. Student Presenter:	Daniel Wei
3. Co-Workers and Collaborators	Melissa Cappaert
4. Advisor	Elizabeth O'Toole, MD, Julia Rose, PhD, MA
5. Departments	Department of Medicine, Metrohealth Medical Center
6. Institutions	Case Western Reserve University School of Medicine, Cleveland, OH
7. Support	2005 Crile Fellowship 2005 Medical Student Summer Research Training in Aging Research (AFAR) NCI-R01-CA102828: Aging and Supportive Care in Advanced Cancer (Julia Rose, PI, Elizabeth O'Toole, Co-PI)
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>As the American population ages, cancer is becoming a major source of morbidity and mortality and poses an increasing challenge in health care delivery. The comprehensive care and treatment of cancer patients may require involvement of primary care physicians (PCPs) as well as oncologists. The involvement of PCPs may be especially important in the care of elderly patients for whom frailty and comorbidities are important considerations in care goals and treatment decision making. In this preliminary study, the role of the PCP in the care of advanced cancer patients was examined. Key questions were about level of involvement of PCPs in the care of advanced cancer patients, whether this involvement should differ for older patients, and if and how communication occurs between oncologists and PCPs. Eighteen generalists (PCPs) and 25 oncologists were interviewed face-to-face to assess their perspectives in these areas. Overall, the two physician groups were similar in their demographic and external pressures in clinical care. Compared to oncologists, generalists felt that PCPs should be more involved in discussing care goals with their advanced cancer patients (83% of generalists felt they should be fairly or very involved as compared to 52% of oncologists). In contrast, 50% of generalists and only 28% of oncologists felt that the PCP should have this level of involvement in cancer treatment decision making. Only a small percentage of generalists or oncologists saw any unique need for involvement of PCPs in the care of older patients. Generalists were less likely to communicate with oncologists on a frequent basis than vice versa. These findings highlight the need to train both types of physicians about the unique challenges in caring for older patients. Study results also inform a conceptual framework that proposes unique and shared roles for PCPs and oncologists in the care of older cancer patients.</p>

WEINBERG, BRENT

1. Title:	Liver tumor treatment with combined radiofrequency ablation and doxorubicin-containing polymer implants
2. Student Presenter:	Brent D. Weinberg
3. Co-Workers and Collaborators	Elvin Blanco, Scott Lempka, James Anderson, Jinming Gao
4. Advisor	Agata Exner
5. Departments	Biomedical Engineering (Weinberg, Lempka) Institute of Pathology (Anderson) Simmons Comprehensive Cancer Center (Blanco, Gao) Department of Radiology (Exner)
6. Institutions	Case Western Reserve University (Weinberg, Lempka, Anderson) University of Texas-Southwestern Medical Center (Blanco, Gao) University Hospitals of Cleveland (Exner)
7. Support	Department of Defense Predoctoral Fellowship BC043453
8. Please choose your academic program:	MD PHD
9. What Year are you in the program?	5
10. Body of Abstract (300 words or less)	<p>Radiofrequency (RF) ablation has been developed as a minimally-invasive treatment for refractory liver cancer. However, treatment efficacy is limited by frequent tumor recurrence around the ablation boundary. To improve the therapeutic outcome of the treatment, we have developed biodegradable polymer implants (millirods) that can be placed directly into tumors to release chemotherapeutic agents. Cylindrical implants releasing their drug contents over 24 hours were fabricated using 60% poly(D,L-lactide-co-glycolide) (PLGA), 26.5% NaCl, and 13.5% doxorubicin. To test local drug distribution and treatment efficacy of these implants, we treated VX2 liver tumors (11 mm diameter) in rabbits with RF ablation insufficient to treat the entire tumor (8 mm treatment diameter). Following the ablation, drug-free or doxorubicin-containing implants were placed in the tumor center. Tumors were removed 4 or 8 days after millirod implantation, and treatment efficacy was assessed using tumor size, histology, and fluorescence measurement of drug distribution. Tumors in both test groups recurred around the boundary of the RF ablated region. High doxorubicin concentrations were found within the ablation region at both 4 and 8 days, but the concentrations declined rapidly at the boundary between normal and ablated tissue. This region was characterized by a thick inflammatory layer with extensive collagen deposition, which appeared to restrict drug transport out of the ablated zone and limit drug spread to viable tumor tissue. Although the outcome of the combined treatment did not offer significant improvement over ablation alone, the extensive drug distribution in the ablated tissue shows promise for future investigation into the approach.</p>

WEISS, ANNA

1. Title:	Aberrant cholesterol transport in CF cells as a possible source for increased inflammatory signaling
2. Student Presenter:	Anna Weiss
3. Co-Workers and Collaborators	Nicole White, Deborah Corey, Latresa Lang, Kristie Ross
4. Advisor	Thomas J. Kelley
5. Departments	Pediatric Pulmonology of UH
6. Institutions	Case Western Reserve University, University Hospitals
7. Support	Research Grant from the Cystic Fibrosis Foundation
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Previously it has been demonstrated that there are many cell-signaling alterations in Cystic Fibrosis. The goal of this study was to investigate the hypothesis that aberrant cholesterol transport in CF cells is a source for inflammatory signaling. We tested this hypothesis by using pCEP (wt) and pCEP-R (CF-phenotype) 9/HTEo- cells either treated or untreated with the cholesterol transport inhibitor U18666a (U18). Cells were challenged with Pseudomonas Aeruginosa (PA) and assayed for IL-6 and IL-8 production. U18 had no effect on the CF cell type, which is already deficient in cholesterol transport, but did increase the inflammatory response in the wt cells in response to PA challenge. Wild-type pCEP cells showed an 11.9 ± 1.25 fold increase when challenged with PA, as compared to pCEP cells treated with U18 and challenged with PA showing an 18.4 ± 2.28 fold increase in IL-6 cytokine production. pCEP-R cells did not show a statistically significant increase in IL-6 production when treated with U18 prior to bacterial challenge. The effect of correcting cholesterol transport on cytokine production was also assessed. Recent data in the lab shows that the cathepsin substrate glycine-phenylalanine-B-naphthylamide (GPN) corrects the cholesterol accumulation phenotype observed in CF cells. GPN lyses lysosomes specifically, releasing calcium and potentially releasing the accumulated cholesterol. A preliminary experiment, using an IL-8-luciferase construct and treating pCEP and pCEP-R cells with IL-1?, TNF-?, and IFN-? (cytomix), demonstrated that GPN drastically reduced the IL-8 expression in both cell types. CF cells treated with cytomix produced 62% more IL-8 promoter activation than control cells. IL-8 promoter activation was significantly reduced in the presence of GPN. This suggests that GPN may reverse the cholesterol accumulation and reduce the inflammation response in CF cells. Further studies determining whether GPN will effect the signaling alterations in CF models are needed.</p>

WIANT, AMANDA

1. Title:	Development of an Educational Program for Medical Students to Increase Awareness of and Comfort with Personal Biases
2. Student Presenter:	Amanda Wiant
3. Co-Workers and Collaborators	
4. Advisor	Ash Sehgal, MD
5. Departments	Center for Reducing Health Disparities
6. Institutions	MetroHealth Medical Center
7. Support	Crile Research Fellowship
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>BACKGROUND: Cross-cultural educational interventions addressing health disparities are delicate matters for all involved. When the validity of deeply ingrained social identities such as race, class, and gender are challenged, negative feelings can arise in protest of this questioning. Strong emotions and lack of insight make fruitful dialogue and introspection on discrimination difficult. An honest, open, respectful, and safe environment where feelings are explicitly acknowledged and biases are pointedly explored may be helpful in facilitating medical students' acceptance of their biases and willingness to change them. Therefore, the goals of this program are (1) to provoke self-reflection on racial, class, and gender identity and (2) to facilitate comfort with the feelings that arise from introspection.</p> <p>PROGRAM OUTLINE: Groups of 10 students, each with a facilitator, will meet for a total of 1.5 hours. Pre-session assignment: take the Implicit Association Tests (IAT) for gender, race, and sexual orientation. Students will complete a form in which they write down their "scores" and thoughts on the tests. First activity: in large group setting, a 10-minute introduction will be given on the purpose and goals of the session; followed by a 15-minute presentation on the neurobiology and psychology of bias; followed by a 15-minute interval for small-group discussion. Topics of discussion will be provided to facilitators. Second activity: in small groups, a clinical scenario using free association will be used as a tool to explore personal biases and assumptions (20 minutes). Final activity: in small groups, students will be encouraged to reflect upon their thoughts and feelings regarding their own reactions to information presented and discussed (30 minutes). Groups are to discuss strategies for reducing individual biases.</p> <p>ASSESSMENT: Feedback on the program will be elicited from students and facilitators by a survey administered after the session. IAT forms will be collected.</p>

WIGHTMAN, AARON

1. Title:	Parental Protection of Extremely Low Birth Weight Children at age 8 years
2. Student Presenter:	Aaron Wightman
3. Co-Workers and Collaborators	Mark Schluchter PhD, Dennis Drotar PhD, Laura Andreias MD,H. Gerry Taylor PhD, Nancy Klein PhD, Deanne Wilson-Costello MD, Maureen Hack, MB.ChB
4. Advisor	Dr. Maureen Hack
5. Departments	Department of Pediatrics
6. Institutions	Case Western Reserve University
7. Support	Crile Fellowship Supported by grants RO1 HD39756 and M01 RR00080, General Clinical Research Center of the National Institutes of Health
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Abstract</p> <p>Title: Parent Protection of Extremely Low Birth Weight Children at Age 8 Years.</p> <p>Objective: Parents of extremely low birth weight (ELBW, <1kg) infants may overprotect their children, but this has not been systematically studied. We sought to examine parent protection and its correlates among 8 year old ELBW children as compared to that of normal birth weight (NBW) controls.</p> <p>Design/Methods: The population included 217 8 year old ELBW born 1992-1995 (92% of the surviving birth cohort, mean birth weight: 811g; mean gestational age 26.4 weeks) and 176 NBW controls. The Parent Protection Scale (PPS) questionnaire, the primary outcome measure includes a total score and 4 domains including Supervision, Separation, Dependence and Control. Multivariate analyses were performed to examine the predictors of parent protection.</p> <p>Results: After adjusting for sociodemographic factors (SES), race and sex of the child, parents of ELBW children reported significantly higher mean scores than parents of NBW children on the total Parent Protection Scales (31.1 vs 29.7, $p=0.03$) and on the Parent Control subscale (8.0 vs 7.5, $p=0.04$). These differences were not significant when the 36 children with neurosensory impairments were excluded. Parents of ELBW children also reported higher rates of over protection ($>1SD$, 12% vs 3%, $p=0.001$), findings which remained significant even after excluding children with neurosensory impairments (8% vs 3%, $p<0.014$). Multivariate analyses revealed that lower SES predicted parent protection in both the ELBW ($p<0.001$) and NBW ($p<0.05$) groups. Additional predictors included the number of functional limitations in the ELBW group ($p<0.001$), and black race ($p<0.05$) and maternal depression in the NBW group ($p<0.01$).</p> <p>Conclusions: The increased parent protection of ELBW children indicates a need for anticipatory guidance to help prevent the development of child-parent relationship disorders and other psychopathology later in life.</p>

WILLIAMS, EMMA

1. Title:	A Novel Approach to Growth Competition Assay as a Measure of HIV type 1 Viral Fitness
2. Student Presenter:	Emma R. Williams
3. Co-Workers and Collaborators	Jan Weber, Ph.D.
4. Advisor	Miguel Quinones-Mateu, Ph.D.
5. Departments	Department of Molecular Genetics - Section of Virology
6. Institutions	The Cleveland Clinic Foundation
7. Support	Funding for this project was provided by the T35 Short-term Training Program HL080981 for NHLBI Research Opportunities for Minority Students with supplemental support provided by the Crile Student Summer Research Endowment
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Fitness is a parameter defining the replicative capacity of an organism. In the case of human immunodeficiency virus type 1 (HIV-1), in vitro characterization of replicative fitness could lead to a better understanding of how specific mutations emerge during therapy, and whether or not less fit viruses are beneficial for HIV-infected individuals. Currently, one of the techniques used to measure HIV fitness in vitro is growth competition experiments involving head on competitions in cell culture between two viral isolates. The novel approach to competition assay as a measure of viral fitness taken in this project involved the introduction of fluorescent proteins into viral genome. Experimental protocol involved amplification of the pol or envelope region from DNA template through Expand High Fidelity PCR and purification of the PCR product. The 2.5Kb fragment purified pol or env region of the virus isolated from an HIV patient was subsequently inserted via transfection-electroporation into a 10,000Kb vector containing either green fluorescent protein or dsRed but lacking the pol/env region. The forward primers used in the expand PCR were 1811U24 and Env B while the reverse primers were 4335L24 and HIV 8726. Three out of four amplification attempts using 1811U24 and 4335L24 were unsuccessful while those with Env B and HIV 8726 were successful up to the pretransfection phase of the project. These results suggest that the most sensitive stage was during the high fidelity PCR and the type of forward and reverse primers used had an impact on the success of the gene amplification process. Transfection experiments are still ongoing, therefore, competition assays using fluorescent virus to ascertain fitness remains in the development phase.</p>

WING, AIMEE

1. Title:	Site Specific Variations in Bone Loss of the Distal Radius With Age
2. Student Presenter:	Aimee Wing
3. Co-Workers and Collaborators	Gary Deutsch, Danielle Casagrande
4. Advisor	Karl Jepsen
5. Departments	Leni & Peter W. May Department of Orthopaedics, Department of Geriatrics
6. Institutions	Mount Sinai School of Medicine, Case Western Reserve University
7. Support	American Federation for Aging Research Grant, Crile Fellowship
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Bone fractures are common in the elderly and can cause significant morbidity and mortality. Fractures of the upper extremities in an older population require prolonged hospitalization and account for one-third of the total incidence of fractures due to osteoporosis in that population. The aim of this study was to characterize site specific bone loss of the distal radius with age in order to identify patterns that might put certain populations at a greater risk for fracture. Thirty four radii were harvested from male and female cadavers ranging in age from 51-102 years. Cross sections of the distal radial shaft were made and embedded in a polyester resin. The sections were stained and imaged with microscopy. Sections were divided into anterior, posterior, ulnar, and radial quadrants then analyzed for presence of original endosteum, intracortical resorption, and thickness of intact cortex. The ulnar quadrant showed a significant increase in resorption space, but did not decrease in thickness. There was a decrease in cortical thickness in the anterior and radial quadrants with increasing age. There was a significant difference between the cortical thickness of the anterior vs. ulnar, posterior vs. ulnar, and radial vs. ulnar quadrants. Further analysis of trends specific to females included a significant decrease in the presence of original endosteum in the anterior and posterior quadrants with increasing age. Female cadavers had increased anterior intracortical resorption and a significant decrease in posterior cortical thickness with age. These data indicate a pattern of site-specific resorption and remodeling of the radius with age that might impact how a fracture of the forearm is more likely to occur. The changes specific to females give insight into the increased forearm fracture risk and greater likelihood of certain types of fracture in the aging female population.</p>

WONG, YU-TUNG

1. Title:	Quantification of Human Sciatic Nerve Anatomy: Implications for Neural Prostheses Utilizing Nerve Cuff Electrodes
2. Student Presenter:	Yu-Tung Wong (1a)
3. Co-Workers and Collaborators	Kenneth J. Gustafson (1b,2); Ronald J. Triolo (1b,1c,2); Yanina Grinberg (1b); Matthew Stone (1b)
4. Advisor	Kenneth J. Gustafson (1b,2); Ronald J. Triolo (1b,1c,2)
5. Departments	(a) Case School of Medicine; (b) Department of Biomedical Engineering; (c) Department of Orthopedics
6. Institutions	(1) Case Western Reserve University, Cleveland, OH; (2) Louis Stokes Cleveland Department of Veterans Affairs Medical Center, Cleveland, OH
7. Support	Supported by Crile Research Fellowship (YTW), NIH HD40298 (KJG), and EB001889 (RJT). Special thanks to Jennifer Neville and Brendan Masini for their assistance.
8. Please choose your academic program:	MD MS
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>The next generation of neural prostheses utilizing nerve cuff electrodes to restore standing in individuals with spinal cord injury (SCI) and to prevent footdrop or provide active propulsion after hemiplegia require detailed knowledge of lower sciatic nerve neuroanatomy. The objectives of this study were to quantify the fascicular anatomy and morphology of the human lower sciatic nerve, and evaluate the potential of selective activation of ankle musculature with a multicontact nerve cuff electrode.</p> <p>Four complete sciatic nerves and all distal branches were dissected from the piriformis to each muscle entry point to characterize their branching patterns and diameters. Fascicle maps were created for three samples from serial sections from each distal terminus below the knee through the junction of the tibial and common fibular nerves above the knee. Branching pattern and nerve size data were also obtained from four additional lower sciatic nerves.</p> <p>Consistent branching patterns were observed between specimens. Distal nerves were represented as individual fascicles or distinct fascicular areas in proximal nerve sections; however fascicular plexusing in one sample limited the ability to trace individual fascicles proximally past the branching point of the tibial and common fibular nerves. Isolated functional grouping of fascicles from plantar flexors and dorsiflexors were more readily identified in the tibial and common fibular nerves than the sciatic nerve. Branch-free lengths of the distal sciatic, tibial and common fibular nerves from the bifurcation to the first branch were 5.1 ± 1.5 cm (range 3.7-6.7), 7.4 ± 1.0 cm (6.5-8.5), and 5.0 ± 2.2 cm (2.7-7.0), respectively.</p> <p>The lower sciatic nerve fascicular anatomy and morphology are conducive to selective activation of dorsiflexion and plantar flexion with cuff electrode(s) on the lower sciatic nerve, which may improve current systems for walking after hemiplegia as well as the next generation of standing and walking systems for SCI.</p>

WOOLRIDGE, STEFANIE

1. Title:	Evaluation of laboratory quality improvement program for sputum smear microscopy in Kampala, Uganda.
2. Student Presenter:	Stefanie Woolridge
3. Co-Workers and Collaborators	Deus Lukoye, Nicholas Ezati
4. Advisor	Achilles Katamba, Christopher Whalen
5. Departments	Department of Epidemiology and Biostatistics
6. Institutions	CWRU
7. Support	1. Supported in part by an Alpha Omega Alpha Student Research Fellowship. 2005 CAROLYN L. KUCKEIN AOA STUDENT RESEARCH FELLOWSHIPS 2. Crile Summer Research Fellowship through the medical school.
8. Please choose your academic program:	MD MPH
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>BACKGROUND: Well functioning laboratories are required for the successful management of tuberculosis. Without accurate detection of cases through sputum smear microscopy, the efficacy of all standardized treatment and prevention programs are compromised. OBJECTIVE: To assess the outcomes of a laboratory quality improvement program. METHOD: A standardized on-site quality assessment survey was conducted at fifteen tuberculosis diagnostic laboratories in Kampala in 2002 and in again in 2005 after implementation of targeted interventions based on the 2002 survey. The targeted interventions included skills and knowledge training, implementation of regular support supervision, and provision of supplies through a revamped centralized system. Results of the surveys were compared between 2002 and 2005. RESULTS: A marked improvement in almost all categories of laboratory performance was observed; particularly in supply provision, record keeping, external quality control measures, and worker knowledge and motivation. CONCLUSION: Targeted interventions implemented in response to periodic standardized quality assessment surveys are an important step forward in improving the performance of diagnostic microscopy laboratories in Kampala, Uganda.</p>

YE, PEGGY

1. Title:	Disclosure of Prognosis in Childhood Leukemia
2. Student Presenter:	Peggy Ye
3. Co-Workers and Collaborators	Michelle Eder, Ph.D.
4. Advisor	Dennis Drotar, Ph.D.
5. Departments	Department of Pediatrics
6. Institutions	Rainbow Babies and Children's Hospital
7. Support	Crile Fellowship
8. Please choose your academic program:	MD
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Disclosure of prognostic information protects patient autonomy by facilitating informed decision making. Physicians, however, may find it difficult to be honest regarding a patient's prognosis, fearing that honesty about poor news may cause loss of hope.</p> <p>Childhood AML is associated with a five-year event-free survival rate of 50%. Childhood ALL, on the other hand, has a much higher event-free survival rate, depending on the risk categorization: standard-risk ALL has a cure rate of around 85% while high-risk ALL has a cure rate around 70%.</p> <p>These differences in disease survival may impact the way a clinician approaches the informed consent conference (ICC). Because of the modest cure rates for AML and high-risk ALL, physicians may communicate prognosis using more hopeful language; for example, by framing prognosis in terms of survival rather than mortality.</p> <p>Data was gathered from the multi-site, NCI-funded study entitled Informed Consent in the Children's Cancer Group (R01 CA083267, PI: Eric Kodish, MD). Transcripts of 140 observed and audiotaped ICCs were reviewed for instances when the physician gave the disease prognosis to the patient's family. Analysis of the language physicians used supplemented quantitative data gathered from an observer checklist instrument. Cases were analyzed in two groups based on cure rates: high-risk ALL and AML (higher-risk group, n = 80), and standard-risk ALL (standard-risk group, n = 60).</p> <p>Preliminary results indicate that physicians tended to discuss the likelihood of a cure in general terms, rather than applying the concept specifically to the patient. This was particularly true for the higher-risk group. Physicians were also more likely to broach the possibility of death from leukemia in the higher-risk group. Further analysis will examine the specific language used in describing the child's prognosis in terms of survival and/or mortality.</p>

YERUKHIMOVICH, MICHAEL

1. Title:	Identification and Characterization of Mouse Cochlear Stem Cells
2. Student Presenter:	Michael Yerukhimovich
3. Co-Workers and Collaborators	Daniel Chen, Lianhua Bi, Robert Miller, Kumar Alagramam
4. Advisor	Kumar Alagramam
5. Departments	Otolaryngology – Head and Neck Surgery, Neuroscience
6. Institutions	Case Western Reserve University
7. Support	Crile Fellowship Center for Stem Cell and Regenerative Medicine
8. Please choose your academic program:	MD MA
9. What Year are you in the program?	2
10. Body of Abstract (300 words or less)	<p>Background: Genetic, noise and drug induced loss of hair cells in the mouse and human cochlea leads to permanent hearing loss because these hair cells are not replaced. Vestibular epithelia from adult mouse show limited regenerative ability following injury, which is thought to be due to the presence of vestibular epithelial stem cells. Lack of regeneration of cochlear hair cells may be due to reduced number and/or loss of regenerative ability of stem cells in the adult cochlea. We hypothesize that: 1. Mouse neonate cochlea harbor stem cells that are capable of differentiating into hair cells and 2. Number of cochlear stem cells decreases with age. Aim: To test whether cochleae obtained from mice after birth harbor cells that are capable of self-renewal and express markers associated with developing hair cells. Methods: This study focused on neonates. Cochlea from 1-3 day old mice (FVB/N strain) were dissected and cultured under conditions selective for sphere formation, a standard assay for identification of stem cells. Spheres obtained after passage were analyzed for expression of markers of various stages in hair cell differentiation. Cells from the spheres were allowed to differentiate under conditions that would permit differentiation of neuronal cell types. Results: Spheres were obtained from cells isolated from neonate cochlea. These cells could be passaged to give rise to new spheres. RNA isolated from cochlear sphere cells was positive for several markers, including Sox2, Otx2 and Myo7a, but failed to show markers that are expressed exclusively in mature cochlear tissue. Cochlear sphere cells were capable of differentiating into astrocytes and oligodendrocytes, but not neurons. Conclusions: Cochlea from neonate mice harbor cells capable of forming spheres, which give rise to cells expressing some of the markers associated with developing inner ear neuroepithelia and hair cells. These cells could potentially be used for replacement therapy in deaf mice.</p>

