

ORAL PRESENTATION

Abstract Title: **Azithromycin Attenuates the Inflammatory Response After Myocardial Infarction**

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Abstract: Background: Myocardial infarction (MI) is a leading cause for congestive heart failure (CHF). Pro-inflammatory macrophages (M1), chemoattracted by MI, initiate inflammation and ECM damage, thus leading to CHF. On the other hand, anti-inflammatory macrophages (M2) enhance healing. Shifting the balance between M1 and M2 remains an elusive therapeutic target. Azithromycin (AZM) polarizes macrophages towards M2 phenotype after inflammation in animal and human studies. Methods: We hypothesize that using AZM can shift macrophages towards M2 phenotype and decrease adverse cardiac remodeling. To test this hypothesis, male mice (C57BL/6, 6–8 weeks old) were treated with AZM orally (160 mg/kg/day) or vehicle for 4 days prior to myocardial infarction or sham surgeries, continuing daily up to 7 days post surgeries. Fluorescent-activated cell sorting and quantitative real-time PCR were performed for cell phenotypic analysis at days 1, 3, and 7. To assess the infarct mass and apoptosis, histological examinations were done at days 3 and 30. Results: AZM-treated mice showed a significant increase in anti-inflammatory and significant decrease in pro-inflammatory macrophages. Anti-inflammatory cytokines were increased significantly, while pro-inflammatory cytokines were decreased significantly in AZM-treated mice. Moreover, apoptosis and scar size were significantly reduced in Azithromycin-treated mice. Conclusion: This study indicates Azithromycin may play an important role as cardioprotective agent following cardiac ischemic injury. Long term and human translational studies are planned to examine the therapeutic applications of azithromycin in MI patients.

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ORAL PRESENTATION

Abstract Title: **Novel Applications of MRI Techniques in the Detection of Neuronal Dysfunction before Tangle Pathology in Tau Transgenic Mice.**

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Abstract: Background: Tauopathic patients have significant cognitive decline accompanied by severe, irreversible brain atrophy. Neuronal dysfunction is thought to occur years before diagnosis. A major obstacle in the treatment of tauopathies is that current diagnostic tools are ineffective at detecting pre-pathological changes. We previously developed a MEMRI (manganese-enhanced magnetic resonance imaging) protocol coupled with R1-mapping to measure the extent of neuronal dysfunction that occurs before appearance of cognitive deficits and tau pathology associated with the rTg4510 tau model. In this study, we performed MEMRI with mangafodipir, an FDA-approved contrast. Methods: We used MEMRI to measure neuronal dysfunction in rTg4510 mice tau transgenic mice at 2 months (no pathology/cognitive deficits), and 3 months (presymptomatic pre-tangle pathology detectable). We measured MEMRI R1 changes before (baseline) and after (time-course) injecting mangafodipir (50mg/kg) intraperitoneally. We focused on the superior cortex and hippocampal sub-regions. Results: We found mangafodipir to be an effective contrast for MEMRI of mouse brains. Optimal enhancement of the cortex and hippocampus occurs 12-24 hours post-injection. Conclusions: This study builds upon our previous work showing that MEMRI (with MnCl₂) reveals important functional differences between tau transgenic and non-transgenic mice. Here we found that mangafodipir is as effective as MnCl₂ in performing MEMRI. Mangafodipir exhibits less toxicity than MnCl₂ due to structural similarity to EDTA (used to treat manganese toxicity), making mangafodipir a target for translation of MEMRI for tauopathy into human subjects.

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ORAL PRESENTATION

Abstract Title: **Neuroprotective effects of inhibition of $\alpha 5\beta 1$ integrin following experimental stroke: A dual center pre-clinical study.**

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Abstract: Blood-brain barrier (BBB) dysfunction after ischemic stroke exacerbates brain damage by contributing to edema and inflammation. The $\beta 1$ integrin receptor family on brain endothelial cells may contribute to this dysfunction via alteration of BBB-forming tight junction proteins. We hypothesize that inhibition of the $\beta 1$ integrin receptor subtype $\alpha 5\beta 1$, which is acutely expressed in infarct and peri-infarct vasculature after experimental stroke, reduces BBB permeability, improves functional recovery and reduces infarct volume. Objective: Our aim was to determine the therapeutic potential of inhibiting integrin $\alpha 5\beta 1$ with the small peptide, ATN-161, following experimental stroke. Methods: In vivo, transient middle cerebral artery occlusion (MCAO) was performed in mice and rats, and permanent MCAO in rats. ATN-161 (1mg/kg) was administered IV immediately upon reperfusion and on post-stroke day (PSD) 1 and 2. Infarct volume was determined by cresyl violet staining and T2 weighted MRI at PSD3. BBB breakdown was determined by immunohistochemical analysis of IgG and claudin-5 and MRI at PSD3. Behavior was determined by multipoint neuroscore. In vitro, barrier permeability was determined by FITC-dextran after oxygen-glucose deprivation. Results: ATN-161 significantly reduced infarcts, decreased BBB permeability in vivo and in vitro, and improved functional outcomes. Therefore, inhibition of $\alpha 5\beta 1$ by ATN-161 could represent a novel stroke therapeutic target worthy of further investigation.

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ORAL PRESENTATION

Abstract Title: **Steroid Therapy Limits Stem Cell Activation Required to Enact Mucosal Healing in Inflammatory Bowel Disease**

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Abstract: Background/Objectives: Intestinal stem cells (ISC) primarily act in the repair of ulcerated epithelium, and their proliferative capacity relies on Wnt/ β -catenin signaling. However, the role of GCs on basal epithelial cell signaling has not been fully characterized. The objective of this study was to interrogate a mechanism by which steroids may limit ISC activation. We hypothesized that GCs limit Wnt/ β -catenin signaling required for ISC activation and epithelial restitution by inhibiting NF κ B activation in epithelial cells. Methods: To examine the effects of GCs on intestinal epithelial cells, we NCM460 cells with dexamethasone and observed the effects on NF κ B and Wnt/ β -catenin signaling events. We isolated mouse epithelial cells from the distal colon for stem cell culture as 3D "organoids." We obtained pure epithelial cell preparations from mucosal biopsies isolated from patients treated at GI clinics at the University of Kentucky and VA Medical Center. Results: In steroid-treated NCM460 cells, we saw a significant decrease in transcripts for Wnt target genes, including Axin2 and cmcyc; NF κ B target genes, including IFNG and IL6; and the shared NF κ B and Wnt pathway co-activator CREBBP, despite unchanged transcript levels for β -catenin (CTNNB1). This data was corroborated in 3D stem cell cultures from cells isolated from mouse colon tissue, which had significant decreases in transcripts for stem cell markers Lgr5 and Ascl2, proliferative markers KI67 and PCNA, and Wnt target Axin2. NCM460s transfected with a lentivirus carrying a TCF/LEF luciferase construct showed a 2.5-fold decrease in TNF-stimulated luciferase activity with dexamethasone treatment. Interestingly, this effect can be rescued by glucocorticoid receptor (GR) blockade with RU-486. Intestinal epithelial cells from patient biopsies showed significant decreases in colitis-induced Axin2, p-LRP6 (a positive marker of Wnt Signaling) and nuclear β -catenin. Conclusion: Together, these data suggest that steroid therapy inhibits Wnt/ β -catenin signaling at multiple levels, and effects stem cell proliferation in pure stem cell cultures. Decreases in TCF/LEF transcriptional activation (nuclear β -catenin's DNA binding target) can be reversed with steroid receptor blockade with RU-486, suggesting that a receptor level interaction may be occurring. While steroids play a significant role in regulating the amount of inflammatory damage that occurs during IBD treatment, our data suggest that they may be limiting pathways required for effective healing as well.

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ORAL PRESENTATION

Abstract Title: **Early Clinical Signatures of Stroke and Bleeding in Patients on Left Ventricular Assist Device Support**

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Abstract: Hypothesis: Platelet function and thromboinflammatory biomarkers will help predict clinical complications due to Left Ventricular Assist Devices (LVAD). Methods: June 2014-August 2016, 66 patients received Heartmate II(n= 48), Heartware(n=18). Median age 55. 86% Male. Blood collections: baseline (BL); 1, 24, 72, 168-hours and follow-up 30-180-days post-operation. Platelet function analyzed via impedance aggregometry and agonists (thrombin, ADP, collagen, ristocetin). Plasma biomarkers (TNF-a, CD40L, IL-6, CRP, IL-10, IL-1b, PF4, Angiopoietin-1,-2, ST2) analyzed via immunoassays. Clinical data correlated via functional data analysis, multiple linear regression. Results: Median values reported. Platelets decreased 42.0% (SD 208.0±77;120.9±50)(p<0.001) while WBC increased 67.1% (SD 8.2 ±2.9;13.7±3.6)(p<0.0001) BL to 72-hours. Platelet ristocetin aggregation decreased 52% (SE 515.0±79.7;247.1±45.7)(p=0.0006) BL to 24-hours without BL recovery by day 7. To demonstrate a few biomarkers: IL-6 increased 796.9% (SE 25.4±72.4;227.8 ±94.6)(p=0.004) BL to 72-hours without BL recovery by follow-up. Angiopoietin-1 decreased 35% (SE 1279±136.4;837.2±84.7)(p=0.01) while Angiopoietin-2 increased 235.7% (SE 3143.9±813.5;10555.4±7556.1)(p=0.03) BL to 72-hours. Angiopoietin-2/angiopoietin-1 was increased 273% from healthy levels at BL (SE 0.46±0.07;1.72±0.65)(p=0.05) without return by follow-up. One-year outcomes: stroke 18.2%, gastrointestinal bleeding (GIB) 19.7%, thrombosis 9.1%, drive-line infection (DLI) (10.6%) mortality 15.2%. Analysis revealed significant associations of platelet function with GIB, DLI; also, between biomarkers and stroke, GIB, mortality. Further data will be presented. Conclusions: LVADs are crucial for patients with limited cardiac function, however significant complications exist. Study results suggest that early platelet function and biomarker analysis may help predict complications such as stroke and bleeding, and thus serve as risk-stratification or targeted therapy tools for patients on LVAD support.

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ORAL PRESENTATION

Abstract Title: **The Significance of Na/K-ATPase Signaling in Obesity-induced Hypertension**

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Abstract: Systemic oxidative stress is strongly associated with obesity-induced hypertension. We have demonstrated that oxidative stress and Na/K-ATPase signaling forms a positive feedback loop. However, it is not clear if, or how, this oxidant stress-Na/K-ATPase axis affects obesity-induced hypertension. Our hypothesis is that obesity induces oxidative stress via the activation of Na/K-ATPase signaling, leading to salt-sensitive hypertension. In this pilot study, obese mice showed a right-shifted renal function curve in response to a high salt (HS) diet, exhibiting more sensitivity to salt than the control lean mice in terms of blood pressure elevation. In high fat diet-induced obese (DIO) C57BL/6J (B6) mice, a HS diet (4% NaCl, 1 week) led to a significant increase in blood pressure. Protein carbonylation is a widely used marker for oxidative stress. In the kidney cortex of B6 mice, we observed that a high fat diet (HF, 58% fat diet, 8 weeks) stimulated α 1 carbonylation ($n=4/\text{group}$, $p<0.05$) and phosphorylation of c-Src ($n=4/\text{group}$, $p<0.01$), which is a Na/K-ATPase signaling molecule. Importantly, the Na/K-ATPase signaling antagonist, pNaKtide (25mg/kg body weight, every 8 days), is capable of attenuating α 1 carbonylation and c-Src phosphorylation induced by a HF diet ($n=4/\text{group}$, $p<0.01$). TALLYHO/JngJ (TH) mice are believed to mimic human obesity with a polygenic background of type 2 diabetes. In comparison to wild type B6 mice, TH mice had a higher basal level of α 1 carbonylation ($n=4/\text{group}$, $p<0.05$) and activation of c-Src ($n=4/\text{group}$, $p<0.01$). Additionally, obese TH mice, prior to onset of diabetes, were also hypertensive in response to a HS diet, characterized by a reduced slope in the renal function curve (HS, 2% NaCl 3 days, $p<0.01$, TH normal chow vs TH HS). We conclude that Na/K-ATPase signaling contributes to oxidative stress-induced hypertension in obesity.

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ORAL PRESENTATION

Abstract Title: **Cannabinoid Modulation of the Analgesic Effects of Opioids in Humans**

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Abstract: Aims: There is a rich literature of preclinical studies demonstrating cannabinoid agonist-enhancement of the analgesic effects of μ -opioid agonists. The aim of this study is to examine the analgesic effects of dronabinol alone and in combination with oxycodone in humans, using an array of laboratory pain models predictive of the clinical pain response. Methods: Healthy participants (n=7) without current drug use or pain conditions completed this ongoing within-subject, double blind, placebo-controlled, randomized outpatient study. Nine 8-hr sessions were completed during which oral dronabinol (0, 2.5, 5 mg) was administered 1hr prior to oral oxycodone (0, 5, 10 mg) for a total of 9 test conditions. Sensory threshold and tolerance outcomes from a battery of experimental pain measures (cold pressor, pressure algometer, menthol-induced cold hyperalgesia, heat testing) were collected. Participant-rated, performance and physiological outcomes were also assessed. Results: Oxycodone (5, 10 mg) produced miosis and analgesic responses. Dronabinol alone did not produce consistent analgesic or pupillary effects. Depending on the dose combination, dronabinol either attenuated or did not alter oxycodone analgesia. For example, dronabinol blocked the analgesic effects of 10 mg of oxycodone on heat threshold, pressure tolerance, and cold pressor tolerance. Oxycodone-induced miosis and nausea/vomiting (n=4) were not altered by dronabinol. Conclusions: In contrast to previous animal research, this human study demonstrates that dronabinol attenuated the analgesic effects of oxycodone at select dose combinations. These data suggest that dronabinol may not be an effective opioid adjuvant and could potentially even increase opioid dose requirements necessary for pain relief. Future studies should examine chronic pain models and cannabinoid modulation of opioid analgesic tolerance.

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Abstract Title: **Coronary Artery Calcification on Non-gated CT Scan Predicts Mortality and Acute Myocardial Infarction After Sepsis.**

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Abstract: Background: Cardiac complications are common after hospital admission for sepsis, especially in those with elevated troponin. Coronary artery calcification (CAC) is an easily identifiable imaging finding, even on non-gated CT scans, but has not been studied in this population. Methods: This is a single center, retrospective cohort study of 899 patients admitted for sepsis with a detectable TnI level from January 2013-December 2013. CT scans of the chest or abdomen done for other clinical indications within 6 months of admission were reviewed for the presence of CAC. Medical records were individually reviewed for mortality and type I acute myocardial infarctions (AMI) at 1 year. Results: 144 patients (mean age 57 +/- 14.8 years, 48% female) were included in the analysis. CAC was seen in 59% of these scans. Compared to those without detectable CAC, the CAC group had similar APACHE score (18 vs 16.6, p=0.259), peak TnI (3.64 vs 2.11 mg/dL, p=0.363), aspirin (63% vs 51%, p=0.144) and beta blocker use (90% vs 85%, p=0.357) with higher statin use (48% vs 27%, p=0.013). CAC was associated with increased all-cause mortality (59.5% vs 38.9%, p=0.016) and type I AMI (10.6% vs 1.7%, p=0.039) compared to those without CAC. Conclusion: Coronary artery calcification is often seen when patients present with a non-cardiac acute illness, such as sepsis, often making a new diagnosis for these patients. Mortality and acute MI after sepsis can be predicted by coronary calcification, and identify patients who should be targeted for therapy and close follow-up.

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ORAL PRESENTATION

Abstract Title: **Patient Outcomes and Treatment Efficacy for Outpatient Parenteral Antimicrobial Therapy (OPAT) at UK HealthCare**

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Abstract: BACKGROUND Outpatient Parenteral Antimicrobial Therapy (OPAT) is a convenient method of delivering intravenous (IV) antimicrobials as an alternative to inpatient care. The success of OPAT is dependent on important key elements that include patient identification and selection, OPAT/Infectious Diseases (ID) team consultation, outpatient monitoring and OPAT program assessment. Important outcomes measures include clinical cure, bacteriologic clearance, compliance, OPAT program success, adverse events and readmission rates. Currently, at UK HealthCare, there is no formal OPAT-service or consultation and to our knowledge, a formal evaluation of prescribing practices, patient outcomes and financial implications for OPAT at UK HealthCare has not been performed. **OBJECTIVE** The primary objective of this research project is to compare patient outcomes and treatment efficacy with ID-consult service involvement in patients being discharged on OPAT with existing literature. **METHODS** This is an IRB-approved, retrospective review of electronic medical records (EMR) from July 1, 2013 to July 1, 2016 in patients ≥ 18 years of age admitted to UK HealthCare Enterprise who were prescribed outpatient parenteral antimicrobials. Patients with inpatient antimicrobials that were not continued as an outpatient were excluded. Demographics, microbiology data, vital signs, indication for antibiotics, duration of inpatient and outpatient antibiotics, consultation by an ID service, insurance provider, cost, adverse events including drug-related and infection-related, patient follow-up service and readmission rates were collected from the electronic medical records including Allscripts Electronic Health Records (AEHR), and Sunrise Clinical Manager (SCM). All analyses were performed using Redcap and R statistical software (3.12). **RESULTS** Preliminarily, 100 patients have been included in the study. Male and female genders were equally divided amongst our population. Majority of the population was Caucasian (74%) with Medicare and/or Medicaid as the primary insurance providers (38% and 40%, respectively). Medicine services accounted for majority of discharges with IV antimicrobials (55%). An ID service was consulted on 69% of all patients on OPAT. S.aureus was the most frequently isolated organism (29%). Organisms were most commonly isolated from the bloodstream (34%), wound (29%) and bone (20%). Vancomycin was the most frequently prescribed antimicrobial for inpatient and outpatient therapy (27% and 19%, respectively). 81% of patients had follow-up at discharge; of these, 64% were with an ID-service. 26% percent of patients were readmitted within 30 days and majority were due to worsening infection (40%). **CONCLUSIONS** Majority of the patients discharged on IV antimicrobial therapy had an ID-service consult and follow-up. Rates of readmissions due to adverse events, specifically worsening infection are concerning and warrant further investigation.

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ORAL PRESENTATION

Abstract Title: **The Impact of Prescription Drug Monitoring Program Characteristics on Rates of Opioid-Related Poisonings**

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Abstract: Background: Prescription drug monitoring programs (PDMPs) are state-level interventions that track the dispensing of controlled substances and may assist in identifying drug diversion, abuse, or aberrant prescribing practices. Prior studies assessing the impact of PDMPs on opioid-related poisonings (ORPs) have failed to consider the wide heterogeneity of program features. The objective of this study is to examine the impact of specific PDMP characteristics on the rate of ORPs. Methods: This retrospective study utilized nationally representative private and Medicare claims data over the years 2004-2014. The main outcome of interest was the incidence rate of ORPs in each state in each month over the 11 year study period. Covariates of interest included age, sex, use of Schedule II opioids, diagnoses associated with opioid use, and PDMP characteristics related to program administration, data access, and reporting. Data on PDMP characteristics were gathered from the Prescription Drug Abuse Policy System. Covariates assessed at the individual level were aggregated into state-level rates and measures. Generalized estimating equation Poisson regression models were used to assess the impact of PDMP characteristics on rates of ORPs while controlling for other covariates of interest. Results: Rates of ORPs per 100,000 beneficiaries ranged from 0 to 24.8 (median 0.94) over the 6,732 state-month pairs. State-months with operational PDMPs had significantly higher mean rates of ORP. Several PDMP characteristics, including monitoring more drug Schedules, requiring more frequent data reporting, and generating unsolicited reports were significantly associated with lower relative risks of ORPs relative to states without operational PDMPs. Conclusion: PDMPs offer a valuable tool to reduce opioid-related morbidity and mortality. Results of this study may be used to improve the efficacy of existing PDMPs and to guide best practices for future programs.

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ORAL PRESENTATION

Abstract Title: **Positive associations between serum levels of dioxin-like pollutants and the circulating cardiometabolic disease risk biomarker Trimethylamine-N-oxide**

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Abstract: Cardiovascular disorders are largely caused by genetic and environmental factors. Understanding how these factors intersect to determine individual disease risk is a critical challenge. Well-studied 'lifestyle dependent' determinants of increased cardiovascular disease risk include smoking, physical inactivity, and poor nutrition, but emerging data now implicate exposures to persistent environmental pollutants as an important contributor to inter-individual variability in cardiovascular disease risk. It is also critical to identify novel biomarkers that link nutrition, toxicant exposure, and cardiometabolic disease risk. Interestingly, emerging diet-derived biomarkers such as trimethylamine-N-oxide (TMAO), carnitine, certain fatty acids, and choline have strong positive relationships with heart disease risk, whereas plasma levels of other nutrients, for example plant-derived carotenoids, sterols and polyphenols are correlated with reduced risk. Quantitating levels of these nutrient biomarkers in individuals with well-defined environmental exposures and well documented metabolic disease histories may shed light on why certain people are more or less prone to environmentally induced diseases. For example, recently, we published that in preclinical models, exposure to dioxin-like pollutants can increase circulating levels of TMAO. In our preclinical studies, dioxin-like PCBs strongly increase the enzyme responsible for TMAO production, FMO3, resulting in amplified increases in TMAO levels. We have now begun to investigate if these associations between pollutant exposure and TMAO are evident in the highly exposed Anniston, Alabama population. We have used mass spectrometry methods to quantitate TMAO in archived plasma samples, and have determined that higher body burden of dioxin-like pollutants is significantly associated with increased circulating TMAO levels in humans.

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Abstract Title: **Infective Endocarditis as a Complication of Injection Drug Use in a Rural Population**

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Abstract: Background: The epidemic of Injection Drug Use (IDU) is increasing across the United States. Severe medical complications of IDU require significant utilization of hospital resources. We characterized the demographics, clinical course and inpatient hospital utilization of Persons Who Inject Drugs (PWIDs) with Infective Endocarditis (IE) admitted to a major referral center in the Southeastern United States. Methods: We reviewed the electronic medical records of PWIDs' most recent admissions with IE to the University of Kentucky Medical Center in Lexington, Kentucky between 2013 and 2015. We extracted data on baseline characteristics, microbiology results, length of hospital stay, intensive care unit (ICU) stay, need for heart valve replacement surgery, hospital mortality, and total cost to the hospital in this population. We used the mean (\pm standard deviation) and percentages as measures of central tendency. Results: We analyzed 168 confirmed cases of PWID with IE. The mean age was 36.4 ± 11.2 years, 49.4% were females and 97.6% were white. The most common organisms isolated in PWID with IE were *Staphylococcus aureus* (60.7%), *Streptococcus* spp. (22.6%), Gram-negative bacilli (16.1%), *Enterococcus* spp. (14.9%), *Candida* spp. (6.5%). On average, the length of hospital stay was 32.2 ± 28.7 days, total bed days in the ICU were 5.1 ± 9.4 days. A total of 25% of PWIDs with IE had heart valve replacement and 13.7% died in the hospital. The average total cost for hospitalization of one PWID with IE was $\$76702.18 \pm 65553.64$. Conclusions: Hospitalized PWID with IE are critically ill and require many hospital resources for their treatment. Interventions to control the IDU epidemic in the US are much needed.

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POSTER PRESENTATION #21

Abstract Title: **Vivitrol® Initiation Among KY Offenders in Corrections-based Substance Abuse Treatment**

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Abstract: In March 2015, the Kentucky Department of Corrections received funding to offer Vivitrol®, a medication assisted treatment (MAT), to inmates prior to release into the community. Inmate eligibility was determined based upon reported alcohol or opioid dependence prior to incarceration, and completion of corrections-based substance use program. This study describes the differences between eligible offenders who initiated Vivitrol® and those who refused. This analysis includes secondary data collected as part of the Criminal Justice Kentucky Treatment Outcome Study (CJKTOS). Data was collected during the intake assessment for individuals entering KY corrections-based substance abuse treatment programs (N=247) who were determined to be “eligible” for Vivitrol® initiation. Bivariate analysis focused on differences in demographic characteristics, drug use patterns, and criminal history between individuals who initiated Vivitrol® (n=54) and those who refused (n=193). Vivitrol® initiators were predominately white (81.5%), and unmarried (53.7%). Majority of initiators reported stable housing (87.0%) and living in rural areas (53.7%). Furthermore, Vivitrol® initiators were more likely to be female 33.3% vs. 3.6% p<.001, and during 12 months prior to incarceration, reported higher rates of prescription opiate use (68.5% vs. 48.2% p<.001), and spent more nights incarcerated (71.1 vs. 36, p<.001). Research has shown significant benefits of MAT for offenders leaving prisons and transitioning to the community. These study findings suggest that there are important differences between Vivitrol® initiators and refusers. Further research should focus on exploration and comparison of Vivitrol® initiators to refusers in regards to initiation motivators, relapse rates, and overall health status between the two groups.

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POSTER PRESENTATION #22

Abstract Title: **Altered Frontal Brainwave Patterns during Working Memory in Veterans with Brain Injury**

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Abstract: Veterans who sustain mild Traumatic brain injury (mTBI), primarily from blasts, have increased probability of developing neurological pathologies and early onset of dementia. Specific damage of neural mechanisms associated with working memory and attention (core cognitive functions) have not been well understood. The current study utilizes previously identified ERP signatures associated with currently relevant working memory target, and currently irrelevant memory distractors to investigate differential brain responses among mTBI compared to combat controls. A battery of neuropsychological tests (assessing attention, processing speed, and executive function) and 32-channel scalp EEG were collected in 10 veterans with mTBI and 10 combat healthy controls (mean age=30.6 vs 37.5, $p=.11$). We found that in the mTBIs, left frontal ERPs show reduced mean P3 amplitude compared to those of combat control during retrieval of memory targets (4.37 vs 0.59 mV, $p<.05$), and the distractors (4.28 vs -.03 mV, $p=.05$). Right frontal ERP differences trended towards significance in response to memory target ($p=.09$) but were not statistically significant in response to distractors. There is a significant correlation between left frontal P3 for retrieving target ($r=-.457$, $p=.025$), and distractor ($r=-.489$, $p=.015$), and the Trail Making Test (frontal executive functions). Interestingly, Connors performance test correlates with the parietal P3 (attention related measures; $p<.05$), but not with the frontal ERPs in mTBIs. Our current findings revealed altered frontal brainwaves of veterans with mTBI from those of combat control, during working memory. The mTBI brainwaves of working memory are also distinct from reported patterns in older adults with mild cognitive impairments.

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POSTER PRESENTATION #23

Abstract Title: **Detecting Malingered Neurocognitive Deficit with Delayed Brain Responses**

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Abstract: Traumatic brain injury affects about 1.7 million people in the United States each year. It has been reported that over one-third of individuals undergoing evaluations following TBI may be malingering deficits. Thus, new ways of detecting brain injury beyond currently successful behavioral testing are needed. The current study aims to apply latency of brain responses during an old-new memory recognition task to detect fake brain injury. Event-Related Potentials (ERPs) time-locked to memory recall of a visual item, were used. We hypothesize that the reaction times and latency of brain responses of malingerers are delayed due to extra processing time. Age- and education- matched subjects were grouped into three cohorts: healthy controls with no history of head injury (n=16), otherwise healthy subjects malingering cognitive deficits (n=16), and those with documented mTBI (n=15). Subjects were fitted with a 32-channel electrode EEG cap and asked to perform a computerized old-new memory recognition task. Data were recorded using Neuroscan 4.5 and analyzed using EP Toolkit 2.0. We found that latency of the onset of the ERP P300 component (associated with cognitive function) was 236.25 ms in honest group, versus 359.50 ms in malingered group, both to studied (old) images at the frontal sites (Fz). These latency differences indicate additional cortical processes time associated with malingering. Future direction of the project is to compare the delayed ERP responses with behavioral reaction times to memory recognition task. The results have potential for clinical application for detection of malingered neurocognitive deficit.

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POSTER PRESENTATION #24

Abstract Title: **Low Arousal Positive Emotional Stimuli Ameliorate Working Memory Processing Dysfunction in Persons with Mild Cognitive Impairment**

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Abstract: Emotional enhancement effects have been proposed to be robust to the pathophysiology of Alzheimer's disease. Others have suggested that such effects are dysfunctional in this context, especially when other memory faculties are simultaneously engaged. Participants with and without mild cognitive impairment presumed to be due to Alzheimer's disease performed an emotionally-valenced delayed-match-to-sample repetition task while encephalography was performed to assess alterations in synaptic activity linked to discrete memory faculties in these groups. Results indicated that for persons with mild cognitive impairment, high arousal negative stimuli led to working memory processing patterns previously associated with mild cognitive impairment presumed due to Alzheimer's disease and dementia of the Alzheimer's type, but that low arousal positive stimuli evoked a processing pattern similar to MCI participants' unaffected spouses. We suggest that low arousal positive stimuli attenuate working memory processing manifestations of MCI due to Alzheimer's disease.

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POSTER PRESENTATION #25

Abstract Title: **Assessment of NICU Inter-Provider Communication and Patient Safety**

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Abstract: Background: Medical errors are frequently a direct result of errors in communication.1-3 Disparate attitudes about teamwork and communication exist between medical providers and may contribute to sub-optimal communication and overall patient outcomes.4 Personality may also be a key determinant of individual communication.5 Verbal and nonverbal communication choices are often distinct for each person 6,7 and may reflect an individual's communication style.8 Specifically, in neonatal critical care, the importance of effective communication cannot be overemphasized; premature infants are arguably most vulnerable and leave little room for errors in care. 9 Lack of effective communication and collaboration has been linked to increased medical errors and compromised patient care.10 A recent study by Riskin, et al. demonstrated that rudeness significantly compromised diagnostic and procedural performance in NICU team members.11 Alternatively, high-reliability organizations promote a culture of safety by being evidence-based, focused on system improvements and ensuring positive working environments for medical staff.12 Objectives: Primary: To determine the association between inter-provider personality-based communication and safety culture. Secondary: 1. To assess provider perspectives on communication and safety in the NICU. 2. To increase inter-provider awareness of shared and differing perspectives. Study design: The study is a survey-based, prospective observational study. All personnel in the University of Kentucky NICU will be eligible to take the online Safety Attitudes Questionnaire through University of Kentucky RedCap, a standardized assessment to reflect the existing safety culture. A target population of medical personnel will also be eligible to take the online DISC assessment, a standardized questionnaire used to assess preferred individual personality and communication styles. In the target population, both assessments will be linked (using de-identifiers) to assess the association between communication and safety by personality style.

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POSTER PRESENTATION #26

Abstract Title: **Assessment of Disruptive Behavioral Problems in Children with Hearing Loss**

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Abstract: HYPOTHESIS: The hypothesis of this study was that preschool-aged children with hearing loss (HL) have a higher prevalence of disruptive behavior problems than those with normal hearing (NH). PARTICIPANTS: Caregivers of children (2-5 years old) with NH (n=39), HL using hearing aid(s) (n=29), or cochlear implant(s) (n=21) were recruited at a tertiary academic center, while obtaining demographic information and a childhood mental health history. Childhood behavior and child language development were assessed utilizing The Child Behavior Checklist, the Young Child-Diagnostic Interview Schedule, and the MacArthur-Bates Communication Development Inventory (MBCDI). RESULTS: Similar distributions of race, socioeconomic status, insurance status, and parental home situation (single v. two parent family) were observed across all three groups. Parents of children with HL were significantly more likely to report disruptive behavior problems (HA=41%, CI=38%) than parents of NH children (10%) (p=0.002). Children with HL were significantly more likely to meet criteria for oppositional defiance disorder (HA=48%, CI=48%) than NH children (23%) (p=0.02). Very few NH children (8%) and no hearing impaired children had accessed mental health services (p=0.08). NH children were found to have more advanced language development on MBCDI than hearing impaired children (p=0.01), but controlling for MBCDI percentiles, the observed behavioral differences remained. CONCLUSIONS: Controlling for language development, children with HL have higher prevalence of disruptive behaviors than their NH peers. These children are less likely to receive appropriate behavioral interventions. Further research is warranted to investigate the impact of disruptive behavioral problems on speech and hearing rehabilitation and to explore methods to improve access to effective behavioral intervention.

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POSTER PRESENTATION #27

Abstract Title: **The Mediating and Moderating Effect of Volunteering between Pain and Depression, Life Purpose, Well-being and Physical Activity**

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Abstract: Background: To improve function and quality of life in patients with chronic pain, a prevalent and costly condition, an understanding of the relationships between well-being, physical activity, depression and life purpose with pain is needed. Due to the role loss experienced by people with chronic pain, activities such as volunteering could have an important role in improving health and well-being. In one study, chronic pain patients who participated in volunteer activities reported both decreased pain and “a sense of purpose”. Methods (Aims, Design, Setting, and Sample): This observational study tested the relationship between pain and well-being, physical activity, depression, and life purpose and then aimed to determine if volunteering activities mediated or moderated these relationships in a sample of 200 women over the age of 50. Results: We found that people with higher pain were more depressed and had lower life purpose and well-being. People who volunteered less had more pain, lower perceived life purpose, more depressive symptoms, and decreased physical activity. Volunteer activities did have a significant mediating effect on the relationship between pain and depression; approximately 9% of the relationship between pain and depression can be accounted for by volunteering. Moderation by volunteering was found between pain and life purpose. Conclusion: We identified important relationships between pain, volunteering and health outcomes and found that volunteering has a role in improving depressive symptoms and life purpose in women with pain.

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POSTER PRESENTATION #28

Abstract Title: **Parental Psychosocial Experiences in Pediatric Hearing Healthcare: A Qualitative Analysis**

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Abstract: Purpose: For parents of children with hearing loss, fragmentation of services is challenging to navigate. Within the hearing healthcare system, parents must coordinate multiple encounters with clinicians, therapists, and other team members. Parents may lack access to medical information and social support, leading to anxiety and social isolation. The objective of this research was to investigate the psychosocial experiences of parents of children with hearing loss during the diagnostic and treatment process using a qualitative approach. Methods: One-hour semi-structured key informant interviews (N=20) with parents of children with cochlear implants or hearing aids were transcribed. Research team members developed a codebook to identify recurring psychosocial themes (i.e. anxiety, isolation). Two research team members completed sample coding, with reliability exceeding 80%. Each transcript was then coded by a primary coder and reviewed for agreement by a second coder. Representative quotations for codes were compiled and assessed to identify connections between psychosocial and clinical experiences. Results: The majority (85%) of parents were non-Hispanic White. Age of children was equally distributed (2-5) and just over half (60%) were male. Parent experiences differed between two distinct groups: (a) proactive, well-resourced parents, and (b) overwhelmed, under-resourced parents. The proactive parents were strong advocates and described family support and resources. In contrast, the overwhelmed parents described feelings of isolation, either in reference to social support or lack of information. In both groups, parents attributed success in gathering information to financial resources or to their own health literacy. Conclusion: Some parents of children with hearing loss report negative psychosocial experiences in navigating the hearing healthcare system. Integrated psychosocial interventions to expand information and support, such as clinically facilitated support groups, could reduce isolation and frustration in this patient population.

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POSTER PRESENTATION #29

Abstract Title: **Effect of Glaucoma on Identification of Ophthalmic Medications**

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Abstract: Purpose: To elucidate the effect of varying degrees of glaucoma on color vision and patients' ability to distinguish bottle cap color of ophthalmic medications. Methods: Prospective, nonrandomized, observational trial. Patients were recruited from a university glaucoma service. Each eye was tested independently for the ability to correctly identify the bottle cap color of ten commonly used ophthalmic medications. These results were correlated with most recent logMAR visual acuity, visual field mean deviation, and Enhanced Glaucoma Staging System-2 score (GSS2). Data/Results: 103 eyes from 60 patients were evaluated. A lower visual acuity (higher logMAR) showed a significant relationship with lower cap color score ($p < 0.0001$) and lower score for 7 of 10 cap colors individually. A lower mean deviation was correlated with lower cap color score and lower score for orange and green caps. Multiple linear regression showed the effect of mean deviation ($p = 0.212$) did not correlate with cap color score when effect of visual acuity was considered. GSS2 did not show relationship with cap color score ($p = 0.567$). Conclusions: This study attempted to measure the effect of glaucoma on discrimination of colored caps used to distinguish glaucoma eyedrop medication classes. Results showed that patients were less likely to correctly identify the color of caps as visual acuity and mean deviation worsened; however, this could not be attributed to mean deviation independently of visual acuity. The clinical significance of these findings is that patients with adequate visual acuity should be able to differentiate cap colors regardless of glaucoma severity.

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POSTER PRESENTATION #30

Abstract Title: **Understanding Associations Between Depression and Eating Disorder Risk Among College Women: The Indirect Effect of Self-Disgust**

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Abstract: Research has demonstrated a link between depression and eating disorder risk, particularly among women. However, limited research has investigated mechanisms that underlie this relationship. In particular, self-disgust has been separately linked to both depression and eating disorder symptomatology, but has not been examined as a potential link between these two symptom dimensions. The current study examined whether there was an indirect effect of depression on eating disorder risk through the pathway of self-disgust in a sample of 150 undergraduate women ($M_{age} = 19.37$, $SD = 2.57$). Measures included the Patient Health Questionnaire – 9 as a measure of depression, the Eating Attitudes Test-26 as a measure of eating disorder risk, and the Self-Disgust Scale, measuring self-disgust facets of disgusting self (disgust with self-concept) and disgusting ways (disgust with one's behavior). Results demonstrated that depression was significantly positively associated with disgusting self and disgusting ways (path a1 and a2), and greater eating disorder risk (path c). When accounting for depression, disgusting self (path b1) was significantly associated with eating disorder risk, whereas disgusting ways (path b2) was not significant. As hypothesized, there was a significant indirect effect of depression on eating disorder risk through disgusting self (path ab1 = .04, SE = .02, BC 95% CI [.01, .08]). No significant indirect effect was found for depression on eating disorder risk through disgusting ways (path ab2). These findings suggest disgust with self-concept may serve as one pathway through which depressive symptoms relate to eating disorder risk. Further research is needed to understand additional pathways in this relationship.

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POSTER PRESENTATION #31

Abstract Title: **Hormones and Hearing: Central Auditory Processing in Women**

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Abstract: INTRODUCTION: Estrogen has been found to play a role in many organ systems. Recently, estrogen has been found to be produced in the human brain and plays an important role in the auditory processing system. After menopause, a low estrogen state, many women report hearing loss but demonstrate no deficits in hearing sensitivity, which supports the notion that estrogen plays an effect on auditory processing. While animal research on estrogen and hearing loss is extensive, there is little in the literature on the human model. Our aim was to evaluate relationships between hormonal changes and hearing as it relates to higher auditory function in pre and post-menopausal females. METHODS: A prospective, group comparison study was conducted on 26 women between the ages of 18 and 70 at the University of Kentucky. Participants were separated into premenopausal and peri/postmenopausal groups. Patients had normal peripheral hearing sensitivity and underwent a behavioral auditory processing battery and electrophysiologic evaluation. RESULTS: Results from the study demonstrated statistically significant difference between groups in spatial hearing abilities as reflected on the LiSN-S test. In addition, electrophysiological measures reflected statistically significant differences between groups, as well as a decreased amplitude in the Pa waveform in the middle latency response in post-menopausal females. CONCLUSIONS: Results from the current study demonstrate significant differences between groups, particularly listening in noise. Females who present with auditory complaints in spite of normal hearing thresholds should have a more extensive audiological evaluation to further examine for possible central deficits.

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POSTER PRESENTATION #32

Abstract Title: **Influence of a Walking Campaign on College Students' Perceptions of and their Actual Walking Behaviors**

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Abstract: Background/Purpose: Research concerning college students' (CS) walking behaviors is scarce; however, walking is recommended to obtain health benefits and meet physical activity requirements. Research suggests youth are more apt to walk when the environment is complimentary and a destination is walkable from their home, yet no similar studies exist with CS. Thus, the purpose of this study was to evaluate the influence of a campus-based campaign on CS' perceptions of walkability and walking behaviors. Method: College participants (n= 503; 69% female) completed an online survey regarding their walking behaviors before (n=366) and after (n=137) the WalkUK campaign, a point-of-decision prompt initiative to promote awareness and opportunities to walk for transportation. Descriptive statistics and t-tests were conducted. Analysis/Results: Students reported fairly high levels of walking for transportation during past 7 days: M=5.3(SD=2.6) vs. M=4.1(SD=2.6); $p<.0001$. Students perceived some behavioral control over walking for transportation: M=3.39(SD=1.5) vs. M=3.1(SD=1.5). Perceptions of ease ($p<.001$) and self-efficacy ($p=.01$) to walk for transportation decreased slightly, while perceptions of crime rate and structural barriers slightly increased ($p<.05$). Post-campaign, 25% reported seeing the prompts. Conclusions: CS report high levels of walking for transportation. CS' perceptions of walkability were slightly lower post-campaign; awareness of the surrounding environment and potential barriers to walking for transportation for those who observed the signs may have been increased. Only 25% observed campaign signs, reinforcing the need for future research to determine efficacious messaging and strategies to promote walking for transportation among CS. Furthermore, campaigns must be conducted in environments which support walking.

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POSTER PRESENTATION #33

Abstract Title: **Salivary Markers of Stress in Grandparents Raising Grandchildren in Rural Appalachia: Associations with Mental Health**

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Abstract: Appalachian communities are known to be at higher risk for poor health outcomes and lower quality of life. Within this region there is a growing subpopulation known as “grandfamilies,” family units where the grandparents now serve as the primary caregivers for their grandchildren because the middle generation is absent. This absence is often due to substance abuse, incarceration, or neglect. Grandfamilies tend to have elevated risk of poverty, stress, and mental and physical health problems. This study focuses on the higher rates of stress and corresponding mental health problems reported by the grandparents of this unique population. The allostatic load theory proposes that chronic activation of the body’s response systems to stress leads to physical and mental disorders—such systems include the hypothalamic-pituitary-adrenal axis, the immune system, and the sympathetic nervous system. Biometric indicators of these activated systems, obtained from saliva samples, are used in this pilot study to quantify allostatic load and to identify any existing correlations with grandparents’ mental health. Mental health status, markers of psychosocial stress and possible protective factors were assessed through standardized questionnaires and instruments. Data analysis indicated that increased levels of c-reactive protein were associated with depression. Higher levels of interleukin-6 were associated with greater impairments due to mental health problems. Marital conflict and food insecurity also correlated with higher impairments. Elevated interleukin-6 was associated with marital conflict, consistent with these findings. Depression and impairment were negatively associated with physical activity, suggesting that exercise may serve as a protective factor. Overall, results complement the literature relating allostatic load to mental health outcomes using biomarkers.

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POSTER PRESENTATION #34

Abstract Title: **Adapting an Evidence-Based Recovery Intervention for Rural Women With Depression**

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Abstract: Introduction: Rural women experience depression at higher rates than the general U.S. population, but also face extensive social and structural barriers that restrict their ability to receive adequate treatment. Interventions centered on recovery, self-determination, de-stigmatization, and positive outcomes show promise for engaging rural women outside traditional treatment. Wellness Recovery Action Plan is one such intervention with a robust evidence base. Using the Replicating Effective Programs Framework, we adapted WRAP for rural Appalachian women and evaluated its feasibility and acceptability in a proof-of-concept trial. Methods: 15 Appalachian women who screened positively for depression participated in a 6-session program in fall 2016. Participants were split between 2 groups facilitated by two Community Health Workers certified as WRAP facilitators. Participants completed pre- and post-intervention surveys measuring mental health symptoms and program satisfaction, and were interviewed post-intervention about their experiences in the program. Results: Surveys indicated improvement on measures of depression severity (Patient Health Questionnaire-9, $p=0.04$), rumination on depression (Ruminative Responses Scale, $p=0.02$), ability to deal with daily problems (Experience of Care and Health Outcomes [ECHO], $p=0.04$), and ability to accomplish goals (ECHO, $p=0.02$) by paired t-tests. In interviews participants responded positively to WRAP's content and peer delivery, describing how they gained pragmatic skills to manage the demands of stressful relationships, acknowledge individual needs, and prioritize self-care. Participants reported that the group format offered critical peer support and de-stigmatized their depression. Participants commented that adaptations for feasibility—session timing, reminder calls, location, gas cards—reduced barriers to participation. Conclusions: Participant satisfaction and symptom improvement support the feasibility and acceptability of WRAP among rural women with depression, demonstrating the need for larger-scale testing.

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POSTER PRESENTATION #35

Abstract Title: **Development of an Ultra-Brief Screening Tool for Preschoolers' Behaviors: Expanded Provider Survey**

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Abstract: Background: Behavioral problems in children are drastically under-identified, and only a small fraction of children receive treatment. Although pediatric primary care is an ideal venue to identify disruptive behavior problems (DBPs), existing instruments require too much time to deliver. To aid in early identification in a primary care setting, an ultra-brief screening tool was developed. This project assessed primary care providers' acceptance of the Young Child Brief Behavioral Screen (YCBBS) and identified characteristics of providers associated with willingness to incorporate the tool into their practices. Methods: An online survey assessed acceptability ratings and provider characteristics, attitudes, and behaviors in addressing DBPs in primary care practice. Active physicians and nurse practitioners (N=212) in the specialties of family medicine and pediatrics were randomly selected from state licensure records. Proportionate random sampling was used to select participants from Appalachian rural, non-Appalachian rural, and metropolitan regions of Kentucky. Dillman's Tailored Design Method was used to improve response rates for medical providers. Results: 72 eligible providers completed the survey (34% response rate), the majority of which identified as white (93%) and female (51%). Most respondents were family practitioners (49%) or pediatricians (42%), and time in practice ranged from 2-43 years. Although 96% of providers reported assessing behavioral disorders in their practices, only 56% reported using a standardized questionnaire. Regarding acceptability of the YCBBS, 97% thought the screening tool was brief enough to use in primary care, and 96% thought pediatric primary care was an appropriate venue. Ultimately, 78% of providers responded that they would use this screening tool in their practices, with non-metropolitan providers more frequently endorsing use compared to metropolitan providers (89% vs. 72%, $p=0.1$). Conclusions: This information regarding providers' attitudes and beliefs will help inform future implementation strategies for integrating this measure into clinical practice.

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POSTER PRESENTATION #36

Abstract Title: **Public Understanding and Opinions of Genetic Research for Alzheimer's Disease**

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Abstract: Alzheimer's disease (AD) is a progressive brain disorder with several genetic risk factors identified. Volunteers are needed for AD genetic research to help identify new approaches to prevent and treat the disease. However, relatively little is known about the public's understanding of research or willingness to engage. The purpose of this study was to explore understanding and acceptance of genetic research for Alzheimer's disease among the public. Surveys were mailed to 1,278 individuals either actively engaged in the Alzheimer's Disease Center longitudinal program or from an aged-matched voter registration list of older adults in the community. Surveys included a mock Alzheimer's disease genetic consent with modified Quality of Informed Consent scale, opinion questions on many aspect of genetic research including privacy concerns and use of data, as well as basic demographics. 523 surveys were returned (41% response rate). An overwhelming majority believed it was important to participate in genetic research (92.3%) and wanted to know the details of any genetic information that could affect their risk for disease (82.4%). Older individuals, those of a minority status, and those with less than a college education scored significantly worse on the informed consent knowledge questions, $p < .001$. The public recognizes the importance of genetic research and would like to learn about their own risk for developing disease. Clinical trial design should consider individuals' desire to know about their own risk factors when making decisions about disclosures.

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POSTER PRESENTATION #37

Abstract Title: **The Bayesian Method for Confounding as Applied to Personality and Substance Use Data to Estimate Average Causal Effect**

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Abstract: Purpose: To investigate possible correlations between substance use and personality trait measurements in students attending the University of Kentucky using the Bayesian Adjustment for Confounding. Methods: The analysis was done in the statistical analysis software R using the Bayesian Adjustment for Confounding as developed by Dr. Chi Wang et al. The resulting model related the personality trait measures with substance use while accounting for a multitude of confounders. Data/Results: There were 449 individuals in the data. The dataset contained 10 different personality measurements from two different models. These variables were the exposure variables. The four outcome variables used were frequency of alcohol use, frequency of marijuana use, frequency of tobacco use, and audit total score, a measure of how harmful the subject's alcohol use is. 37 confounders were also included in the model, including sex, race, age, and quite a few variables involving the subject's friends' usage and opinions of alcohol, marijuana, and stimulants. This resulted in evaluating 40 associations/relationships, each relating one exposure variable to one outcome variable. The results showed which confounders were selected often in each model. The average causal effect (ACE) was also calculated from the models, providing a measurement of the actual level of causation between the two variables. Conclusions: Overall, the Bayesian Adjustment for Confounding is a method useful for eliminating confounders in observational studies and establishing causation with more certainty. The relationship that showed the highest positive effect was between positive urgency and audit total score. The relationship showing the most negative effect was between conscientiousness and audit total score. An example of a relationship with no effect was between marijuana use frequency and extraversion. Through the BAC method, the direct effects of personality traits on substance use can be accurately estimated.

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POSTER PRESENTATION #38

Abstract Title: **Optimal Transcranial Direct Current Stimulation Polarity for Enhancing Motor Recovery from Severe Post-Stroke Hemiparesis**

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Abstract: Transcranial direct current stimulation (tDCS) has been shown to enhance outcomes of motor training for subjects with mild to moderate post-stroke motor deficit. To determine which tDCS configuration optimizes motor training in cases of severe post-stroke hemiparesis (≤ 19 out of 60, Fugl-Meyer Assessment (FMA) upper extremity motor score), this study randomized 26 subjects to 1 of 4 conditions: 1) “anodal” (anodal tDCS to the ipsilesional motor cortex); 2) “cathodal” (cathodal tDCS to the contralesional motor cortex); 3) “dual” (anodal tDCS to the ipsilesional motor cortex and cathodal tDCS to the contralesional motor cortex); or 4) “sham” tDCS. In 10 sessions total, each on a consecutive weekday, tDCS preceded 3 hours of intensive, task-oriented motor training. Outcome measures included FMA and Action Research Arm Test (ARAT). Evaluations took place at baseline, post-intervention, and 1-month follow-up. Pre-post FMA improvement was significant for “anodal,” “cathodal,” and “sham”; and 1-month follow-up was significant for “sham.” There were no significant differences between groups on FMA at post or at 1-month follow-up. Pre-post ARAT improvement was significant for “cathodal”; and 1-month follow-up was significant for “cathodal” and “sham.” There were no significant differences between groups on ARAT at post; however, at 1-month follow-up, “cathodal” was significantly better than all other groups. In sum, cathodal tDCS may optimize motor training for people with severe post-stroke hemiparesis. Larger studies are recommended to substantiate these preliminary results.

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POSTER PRESENTATION #39

Abstract Title: **Neuromodulation paired with locomotor training improves muscle strength after motor complete spinal cord injury: A case report.**

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Abstract: The adult central nervous system can reorganize to a degree formerly thought possible only during the early post-natal period. This capacity for plastic change can play a crucial role in recovery of function after neurological injury. Plastic change in cortical motor areas can occur after incomplete spinal cord injury (SCI) because unlesioned fibers in the spinal cord remain connected with the intact brain and responsive to sensorimotor stimuli. Several lines of evidence indicate that plastic change supporting motor recovery after stroke can be driven by a non-invasive neuromodulatory intervention called transcranial direct current stimulation (tDCS). However, there is no available data about tDCS to enhance recovery of lower extremity motor function for people with SCI. The present study investigated the effects of tDCS paired with robot-assisted locomotor training on a treadmill (Lokomat). A slower-than-standard treadmill speed was used in order to provide sufficient time for the corticomotor system to process information and adjust motor behavior in response to internal and external feedback (e.g., proprioception; therapist input). The primary outcome measure was manual muscle test (MMT) of bilateral lower extremities at baseline, post, and 1-month follow-up. The present case study reports on findings for a woman who was 34 years of age at enrollment and who had sustained motor complete SCI (C6; American Spinal Injury Association (AIS)-B) in a motor vehicle accident 2 years prior to enrollment. After the entire intervention period (i.e., 36 daily sessions), she demonstrated active bilateral muscle activation for the first time since injury (scores at baseline, post-intervention, and follow-up: left MMT summative grades 0, 7, 11; right MMT summative grades 0, 7, 12). This data has positive implications for the translational potential of the intervention and warrants further systematic evaluation to determine the beneficial impact of tDCS on outcomes of locomotor training in cases of motor complete SCI.

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POSTER PRESENTATION #40

Abstract Title: **The choline acetyltransferase inhibitor BW813U suppresses the growth of lung adenocarcinoma from smokers**

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Abstract: The clinicopathological profile of lung adenocarcinoma (LAC) in smokers is completely different from those in non-smokers. One of the unique features of LAC in smokers is that it is relatively resistant to therapies. For example, targeted therapeutic agents like EGFR-inhibitors (erlotinib and gefitinib) are highly effective in LACs which develop in non-smokers. However, these EGFR-inhibitors display much lower anti-tumor activity in LACs in patients who are active smokers. Similarly, lung cancer patients (who are active smokers) show lower response to chemotherapy than those who are non-smokers. However, majority of LAC patients are smokers. This underlines the need to identify novel molecular targets relevant for LAC therapy in patients who are exposed to cigarette smoke via active smoking or exposure to secondhand smoke. Several convergent studies show that nicotine (the addictive component of cigarette smoke) accelerates the growth of lung cancers, as well as confers resistance to chemotherapy. One of the mechanisms underlying these biological activity of nicotine is that it promotes the secretion of the neurotransmitter acetylcholine (ACh) from LAC cells. ACh is known to be an autocrine growth factor for LAC cells and is synthesized by the enzyme choline acetyltransferase (ChAT). The present study investigates the feasibility of ChAT as a molecular target for LAC in smokers. We find that ChAT levels are upregulated in human LAC cell lines and tissues in a manner dependent on the smoking history. Finally, the ChAT inhibitor BW813U causes robust apoptosis in human LAC cells. The magnitude of BW813U-induced apoptosis is similar across LAC cell lines (irrespective of smoking history); however, the concentration of BW813U which causes apoptosis is lower in LAC cell lines belonging to heavy smokers. Our studies validate choline acetyltransferase (CHAT) as a viable drug target for the majority of population of lung cancer patients who are smokers.

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POSTER PRESENTATION #41

Abstract Title: **Increased Accuracy in Computational Drug Discover: Towards the Prediction of Adverse Drug Reactions**

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Abstract: In this work we have developed a multi-tiered computational platform to study protein-drug interactions. At the beginning of the workflow more efficient and less accurate methods are used to enable large libraries of proteins in many conformations and massive chemical libraries to be screened. At each subsequent step in the workflow a subset of input data is investigated with increased accuracy and more computationally expensive methods. In this work we demonstrate the developed workflow with the investigation of the lymphocyte-specific kinase LCK, which is implicated as a drug target in many cancers and also known to have toxic effects when unintentionally targeted.

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POSTER PRESENTATION #42

Abstract Title: **Activation of FASN/SPHK/S1P axis promotes metastatic potential of primary colorectal cancer cells**

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Abstract: Introduction: Development of metastasis is the most common cause of death in colorectal cancer (CRC) patients. Fatty acid synthase (FASN) and Sphingosine Kinases (SPHKs) are upregulated in many cancers including CRC. However, the contribution of FASN-mediated upregulation of sphingolipid metabolism to CRC metastasis is not known. The purpose of this study is to determine (i) correlation of FASN, SPHK1 and SPHK2 expression in human CRC tissues, (ii) the effect of FASN on sphingolipid metabolism and (iii) functional significance of the FASN/SPHK axis in CRC. Methods. Expression of FASN, SPHK1 and SPHK2 was evaluated in CRC TMA. Primary CRC cells were treated with TVB-3664, a novel FASN inhibitor, or with FTY-720, an S1P mimetic that inhibits SPHK1 and the S1P receptor, and proliferation and migration capabilities of cells were assessed. Formation of focal adhesions was evaluated by TIRF microscopy. Results. We showed that FASN, SPHK1 and SPHK2 are highly expressed in primary tumors and liver metastasis as compared to normal colon tissues. TVB-3664 and FTY-720 treatments significantly inhibited cellular proliferation and reduced migration capabilities of primary CRC cells. Consistently TVB-3664 and FTY-720 significantly reduced formation of focal adhesions and reduced activation of p-MET, p-FAK, and p-PAX. Conclusions. Our data demonstrate that upregulation of the FASN/SPHK axis promotes CRC progression by enhancing cellular proliferation, adhesion and migration. Therefore, these findings provide a strong rationale for further investigation of interconnection of de novo lipid synthesis and sphingolipid metabolism that would potentially lead to identification of new therapeutic targets and strategies for CRC treatment.

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POSTER PRESENTATION #43

Abstract Title: **EMT and resistance to androgen-directed agents in CRPC - a mechanistic study on TGF inhibition and AR signaling in a mouse model of prostate tumorigenesis**

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Abstract: Castration-resistant prostate cancer (CRPC) is the most advanced, lethal manifestation of prostate cancer with a median overall survival of 18-24 months. Enzalutamide, a potent androgen receptor (AR) antagonist (antiandrogen), is one of six FDA-approved drugs for the treatment of CRPC. Despite improvements in survival offered by therapies such as enzalutamide, tumors inevitably develop strategies to circumvent inhibitions posed by these medications, ultimately resulting in disease progression and eventually death. Epithelial-mesenchymal-transition (EMT) is a TGF β signaling-driven process underlying tumor interactions with the host microenvironment, and has been implicated in antiandrogen resistance and tumor progression. We investigated the therapeutic value of targeting TGF β -mediated EMT by LY2157299, a TGF β inhibitor, by examining its potential to reverse EMT (a process known as MET, mesenchymal-epithelial-transition) and overcome resistance to enzalutamide in a preclinical model. TGF β receptor wild type (TGFwt) and TGF β receptor II mutant (TGFRII mut) TRAMP (model for prostate tumorigenesis) mice 16-20 weeks of age were dosed with LY2157299 or vehicle twice daily for 14 days and sacrificed (day 15). Their prostates were excised, sectioned, and stained for characterization with H&E, TUNEL (apoptosis), Ki-67 (proliferation index). In addition, immunohistochemistry was also performed for EMT markers E-cadherin, N-cadherin, and Smad-4, as well as for the AR. Statistical analysis shows general trend of increased apoptosis and decreased proliferation in prostates treated with LY2157299.

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POSTER PRESENTATION #44

Abstract Title: **Capsaicin suppresses the metastasis of human NSCLC in vivo**

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Abstract: Non small lung cancer (NSCLC) is characterized by aggressive clinical course, rapid doubling time and a propensity for extrapulmonary metastasis. A substantial proportion of NSCLC present with metastatic disease at the time of their diagnosis. Metastasis is a complex multistep process. One of the earliest events of the metastatic process is the invasion of malignant cells through the surrounding stroma into the blood and lymph. The long-term goal of our laboratory is to identify nutritional compounds (as single agents or in combination with standard chemotherapy) which will suppress metastasis of NSCLCs. Capsaicin is the pungent ingredient of chili peppers. Several convergent studies have shown that capsaicin inhibits the invasion and metastasis of several types of human cancers including melanoma, prostate cancer and cholangiosarcoma. The present study examines the anti-invasive properties of capsaicin and two capsaicin-like compounds, capsiate and capsiconiate, found in select variety of chili peppers on NSCLC. We measured the anti-invasive activity of these compounds by the Boyden chamber assay and spherical invasion assays. We found that capsaicin and capsiate displayed equivalent anti-invasive activity in NSCLC cells. In contrast, capsiconiate did not suppress the invasion of NSCLC cells. Furthermore, we tested the anti-metastatic activity of capsaicin in a syngenic mouse model of metastasis. We observed that the dietary administration of capsaicin potently decreased the area of lung metastatic foci relative to control untreated mice. Our data may form the basis of novel nutrition-based therapeutic regimens in NSCLC metastasis.

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POSTER PRESENTATION #45

Abstract Title: **Comparison of Bottom-Up and Top-Down Approaches to the Synthesis of Carbon Quantum Dots and Photodynamic Effect on Cancer Cells**

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Abstract: Carbon quantum dots (CQDs) have recently drawn significant interest in pharmacological and energy conversion applications due to their unique optical and catalytic properties. For our study, these zero-dimensional nanomaterials are synthesized by two approaches. The top-down approach utilizes the harsh oxidation of bulk carbons to produce graphene quantum dots (GQDs) whereas the bottom-up approach uses the condensation of small organic molecules like glucose or citric acid to produce carbon nanodots (CNDs). With a unique balance of low natural cytotoxicity and strong photodynamic (PDT) effect, CQDs can be employed as antibacterial and anti-cancer agents. However, their potential cannot be fully realized without the knowledge of the mechanism for prominent photodynamic effects. This work uses spectroscopic and chemical methods to characterize the similarities and differences of the CQDs produced by a top-down approach and a bottom-up approach. By coupling biological methods such as cell viability, singlet oxygen measurements, and gel electrophoresis with the results from chemical analyses, we investigated the structure-function relationship and anti-cancer activities of CQDs. In cell viability studies, it was observed that GQDs were generally better PDT agents than CNDs due to a larger sp²-carbon nano-domains and vastly different functional group distributions. Interestingly, the incorporation of nitrogen atoms into the carbon network enhanced PDT efficiency in CNDs but GQDs were negatively impacted. Singlet oxygen (¹O₂), which is one of the primary chemicals responsible for inducing cancer cell death, was quantitatively measured and show a similar trend to the cell viability studies. The results presented herein imply that fundamental understanding of structure-function relations of CQDs is required to develop potential low-cost and non-toxic anti-cancer and anti-bacterial agents.

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POSTER PRESENTATION #46

Abstract Title: **Memantine, the dual $\alpha 7$ -nAChR/NMDAR antagonist displays potent anti-angiogenic activity in lung cancer**

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Abstract: Non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC) bear a strong etiological association with smoking habits. Nicotine, the addictive component of cigarettes, promotes angiogenesis in lung cancer via the $\alpha 7$ -nicotinic acetylcholine receptor ($\alpha 7$ -nAChR) subunit on human lung endothelial cells. Therefore, we conjectured that $\alpha 7$ -nAChR-antagonists should display potent anti-angiogenic and anti-tumor activity in lung cancers. Memantine is a dual $\alpha 7$ -nAChR/NMDAR antagonist, which is used in the clinic for the treatment of patients suffering from mild-to-moderate Alzheimer's disease. Receptor binding assays have shown that the affinity of Memantine for $\alpha 7$ -nAChR is greater than NMDAR. Here we show that memantine attenuates nicotine-induced angiogenesis in human microvascular endothelial cells of the lung (HMEC-Ls). Most interestingly, the levels of $\alpha 7$ -nAChR in tumor-associated endothelial cells was greater than normal lung endothelial cells. The anti-angiogenic activity of memantine was mediated by the $\alpha 7$ -nAChR (and not by NMDARs) on lung endothelial cells. Furthermore, the $\alpha 7$ -nAChR antagonist memantine displayed potent anti-angiogenic activity in chicken chorioallantoic membrane (CAM) model. Our studies show that $\alpha 7$ -nAChR antagonists may be useful anti-tumor agents relevant for the treatment of human lung cancer.

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POSTER PRESENTATION #47

Abstract Title: **Targeting leucine-stimulated Mechanistic Target Of Rapamycin (mTOR) to suppress breast cancer in obesity**

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Abstract: Background: Approximately one out of every three cancer deaths are linked to excess body weight and Appalachia and West Virginia have some of the highest rates of obesity in the country. Obese women (especially postmenopausal women) have higher rates of breast cancer incidence, are less responsive to cancer therapy and have worse clinical outcomes than non-obese women. Leucine is an essential amino acid that is elevated in obesity and is required for the activation of Mechanistic Target Of Rapamycin (mTOR), a kinase that is critical for tumor growth. Breast cancer cells absorb extracellular leucine through L-Type Amino Acid Transporter 1 (LAT1). Our hypothesis is to inhibit LAT1/leucine-stimulated induction of mTOR to suppress breast cancer development in obese women. Methods/results: Using western blot analysis, we have uncovered that the adipocyte secretome upregulates the expression of LAT1 (by ~40%) and mTOR1 (by ~6-fold) activity in cultured human breast cancer cells. Using qPCR, western blot analysis and chromatin immunoprecipitation assays, we provide evidence that the aryl hydrocarbon receptor (AHR) and estrogen receptor (ER) promote LAT1 transcription. The LAT1 inhibitor BCH reduced MCF7 colony formation by 70% and omitting leucine from cell culture medium reduced MCF7 colony formation by 97%. This supports our hypothesis that leucine transporters are critical for breast cancer cell survival and proliferation. Ongoing work: These findings provide the basis for our current/ongoing work that will establish the regulation and function of leucine-stimulated mTOR1 activation in breast cancer in obesity using clinically relevant cancer cell models and clinical samples.

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POSTER PRESENTATION #48

Abstract Title: **Non-pungent long chain capsaicin-analogs arvanil and olvanil display better anti-invasive activity than capsaicin in human small cell lung cancers**

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Abstract: The nutritional compound capsaicin inhibits the invasion of many types of human cancers. The clinical development of capsaicin as an anti-cancer drug is limited due to its unfavorable side effects like burning sensation, stomach cramps, gut pain and nausea. This study compared the anti-invasive activity of capsaicin to non-pungent long chain capsaicin analogs, namely arvanil and olvanil, in human small cell lung cancer cells. Boyden chamber invasion assays revealed that arvanil and olvanil displayed improved anti-invasive activity relative to capsaicin in human SCLC cells. The results of the Boyden chamber assay were confirmed by the spherical invasion assay, and similar results were obtained. The anti-invasive activity of arvanil, olvanil and capsaicin were independent of TRPV and CB1 receptors. Furthermore, the anti-invasive activity of arvanil, olvanil and capsaicin was mediated by the AMPK pathway. Depletion of AMPK levels by siRNA methodology abrogated the anti-invasive activity of arvanil, olvanil and capsaicin. The non-pungent capsaicin analogs arvanil and olvanil display improved anti-invasive activity relative to capsaicin in human SCLC cells. These agents may represent the second generation of capsaicin-like compounds which are more potent than the parent molecule and have a better side effect profile.

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POSTER PRESENTATION #49

Abstract Title: **McCrearamycins A-D, novel cyclopentenone ansamycin polyketides from an underground coal mine reclamation site**

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Abstract: McCrearamycins A-D (1-4), four new cyclopentenone-containing ansamycin polyketides, and six new geldanamycin analogs (5-10), were characterized as metabolites of the Rock Creek (McCreary County) underground coal mine acid mine drainage isolate *Streptomyces* sp. AD-23-14. Biomimetic chemical conversion studies using both simple synthetic models and complex ansamycin polyketides confirmed the core cyclopentenone to derive from benzilic acid rearrangement of the conventional ansamycin ortho-quinone and thereby provides compelling support for the involvement of a potential novel biocatalyst in ansamycin ring contraction. Four known compounds were also isolated from *Streptomyces* sp. AD-23-14, including geldanamycin as the predominate product (92.5 mg/L). All the isolated compounds were evaluated in a standard cancer cell line (human non-small cell lung A549) cytotoxicity assays, Hsp90 α binding assay and a recently developed axolotl embryo tail regeneration assay. Compound isolation, structure elucidation, biomimetic ring contraction studies and bioactivity assays will be presented.

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POSTER PRESENTATION #50

Abstract Title: **Divergence of cAMP Signaling Pathways Mediating Augmented Nucleotide Excision Repair and Pigment Induction in Melanocytes**

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Abstract: Loss-of-function melanocortin 1 receptor (MC1R) polymorphisms are common in UV-sensitive fair-skinned individuals and are associated with blunted cAMP second messenger signaling and higher lifetime risk of melanoma because of diminished ability of melanocytes to cope with UV damage. cAMP signaling positions melanocytes to resist UV injury by up-regulating synthesis of UV-blocking eumelanin pigment and by enhancing the repair of UV-induced DNA damage. cAMP enhances melanocyte nucleotide excision repair (NER), the genome maintenance pathway responsible for the removal of mutagenic UV photolesions, through cAMP-activated protein kinase (protein kinase A)-mediated phosphorylation of the ataxia telangiectasia mutated and Rad3 related (ATR) protein on the S435 residue. We investigated the interdependence of cAMP-mediated melanin upregulation and cAMP-enhanced DNA repair in primary human melanocytes and a melanoma cell line. We observed that the ATR-dependent molecular pathway linking cAMP signaling to the NER pathway is independent of MITF activation. Similarly, cAMP-mediated up-regulation of pigment synthesis is independent of ATR, suggesting that the key molecular events driving MC1R-mediated enhancement of genome maintenance (e.g. PKA-mediated phosphorylation of ATR) and MC1R-induced pigment induction (e.g. MITF activation) are distinct.

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POSTER PRESENTATION #51

Abstract Title: **Immune checkpoint inhibition and the prevalence of autoimmune disorders among lung and renal cancer patients**

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Abstract: Purpose: Immune checkpoint inhibition reactivates the immune response against cancer cells in multiple tissue types and has been shown to induce durable responses. However, for patients with autoimmune disorders, their conditions can worsen with this reactivation. We sought to identify, among lung and renal cancer patients, how many harbor a comorbid autoimmune condition and may be at risk of worsening their condition while on immune checkpoint inhibitors such as nivolumab and pembrolizumab. Methods: An administrative healthcare claims database, Truven MarketScan, was used to identify patients diagnosed with lung and renal cancer from 2010 - 2013. We assessed patients for diagnosis of autoimmune diseases one year prior to or after diagnosis of cancer using ICD-9 codes for 41 autoimmune diseases. Baseline characteristics and other comorbid conditions were recorded. Results: More than 25% of both lung and renal cancer patients had a comorbid autoimmune condition between 2010 and 2013 and were more likely to be female, older and have more baseline comorbidities. Conclusions: This population presents a dilemma to physicians when deciding to treat with immune checkpoint inhibitors and risk immune-related adverse events. Future evaluation of real-world use of immune checkpoint inhibitors in cancer patients with autoimmune diseases will be needed.

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POSTER PRESENTATION #52

Abstract Title: **Cancer Pathway Analyses Based on Alterations in Squamous Cell Lung Cancer in Appalachian Kentucky**

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Abstract: The Kentucky Lung Cancer Genomics (KLCG) study is the first to characterize the genomic alterations in squamous cell carcinoma (SQCC) of lung from Central Appalachian Kentucky (AppKY) where 26.4% of all lung cancers are SQCC compared to 22.6% of all lung cancers nationally [1]. The KLCG study includes whole exome sequencing of 51 lung SQCC samples from AppKY, which we compared to the The Cancer Genome Atlas (TCGA) study of lung SQCC [2]. In the KLCG study, genes with recurrent mutations in order of statistical significance include: TP53, PCMTD1, IDH1, PIK3CA, RNF43, MLLT10, STK11, NFE2L2, DEK, POT1, ATP2B3, HRAS, HOXA11 and HOXA13. In contrast to the TCGA study, we find that PCMTD1 (18%) and IDH1 (12%) are more frequently altered in the AppKY cohort, suggesting that pathways including these genes are likely important for cancer development in this population. Therefore, we looked for mutational patterns in related genes based on known protein-protein interactions and gene-products with related function. We found mutually exclusive mutational patterns between PCMTD1 and related histone methylases and between IDH1 and related histone demethylases, suggesting that mutations in these pathways directing histone methylation and demethylation are important in SQCC cancer development and may be related to AppKY-specific environmental factors. These findings have been reported for the first time in lung SQCC, indicating population differences in the genetics of lung SQCC between AppKY and the US and highlighting the importance of the relevant population when developing personalized treatment approaches in this disease.

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POSTER PRESENTATION #53

Abstract Title: **Patient Satisfaction: 'Accentuating the Positive' in Patient Care**

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Abstract: Background: Hospitals identify areas of strengths and weaknesses through patient surveys. Normally, weaknesses receive more attention than strengths. While sometimes successful, this can lead an organization to overlook strengths, which may lead to a negative organizational culture. Appreciative Inquiry (AI) is a positive alternative to this method. The aim of this project is to identify positive aspects of patient care in the cancer center in an academic medical center. Methods: Interviews were conducted in the chemotherapy infusion and bone marrow transplant units in a large, university-based cancer center. No identifying information was collected. Patients were asked about a time they were a part of excellent patient care and asked to identify people who contributed during this time. Additionally, patients were asked three wishes that could enhance their experience. Responses were analyzed qualitatively using a standard method. Two iterations were performed. Results: 102 interviews were conducted, with 78 (77%) in chemotherapy infusion and 24 (23%) in bone marrow transplant. The common themes regarding positive experiences were caring (68%), personalized care (50%), communication (41%), and professionalism (38%). The themes regarding improvements were wait time (28% of patients), facilities (15%), scheduling (10%), availability of staff (10%), and staff performance (8%). 49% of patients did not identify an improvement. Conclusion: Patients most appreciated the way they were treated by their healthcare providers rather than the level of healthcare they received. Additionally, improvements were more related to operational improvements such as wait time and facility improvements rather than to the performance of their healthcare providers.

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POSTER PRESENTATION #54

Abstract Title: **The Geographic Management of Cancer Health Disparities Program (GMaP): Advancing the Next Generation of Cancer Researchers through Promotion of the National Cancer Institute (NCI) Continuing Umbrella of Research Experiences (CURE) Program**

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Abstract: Introduction: A major goal of the GMaP Region 1 North (R1N) Hub, based at the University of Kentucky Markey Cancer Center, is to facilitate the career development of the next generation of underrepresented cancer researchers by promoting and increasing applications to the NCI CURE Program. The CURE Program provides funded training opportunities to students and investigators at all career levels to ensure a continuum of career development opportunities in cancer health disparities research. Procedures: GMaP investigators are implementing multi-faceted programming to increase awareness of the CURE Program throughout the GMaP R1N coverage area. GMaP R1N has developed a listserv to increase promotion of the CURE Program; has implemented surveys to assess awareness of the CURE Program and associated funding mechanisms such as Diversity Supplements, K-series awards, and F-series awards; and has developed a tracking and referral system to track applicant interest and readiness to apply for CURE Program funding opportunities. Potential applicants are referred directly to a Training Navigator at NCI, who provides individualized advice on the most suitable funding mechanism. Results to date: 1) A Listserv including 800 plus members has been developed to promote CURE funding opportunities. 2) 172 senior investigators and 40 students/trainees have completed initial surveys assessing awareness of the CURE Program, interest in serving as mentors, or interest and readiness to apply for CURE funding opportunities. 3) 27 students/trainees have been referred to the NCI Training Navigator for further encouragement and additional discussion of the CURE Program and application requirements.

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POSTER PRESENTATION #55

Abstract Title: **Incidence and epigenetic factors associated with endometrial cancer in Appalachian Kentucky.**

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Abstract: Background: Data from the US Cancer Statistics Working Group shows that age adjusted incidence of endometrial cancer was 25.6/100,000, 2009 to 2013 for the US and 24.9/100,000 for Kentucky. However, for the Kentucky River Area Development District (KR) in the Appalachian region, the rate was higher at 34.2/100,000. This investigation was designed to explore epigenetic factors related to the elevated incidence of endometrial cancer in KR region. Methods: With IRB approval, retrospective data on women with endometrial cancer abstracted from tumor registry for the period 2005 to 2015. Data including age at diagnosis, family history of cancer, smoking, diabetes and demographic characteristics were analyzed using SPSS. Results: Data on 41 cases of endometrial cancer from 2005 to 2015 were included in the analyses. The age range was 37-87 with mean age 62. Of the 41 cases, 19.5% (8/41) were under age 50 at diagnosis. 2 out of 8 (25%) had family history of Lynch syndrome associated malignancies. 9 (22.0%) had family history of cancer. No significant associations between smoking, age at diagnosis and diabetes were noted. Conclusions: There is an increased incidence of endometrial carcinoma in Appalachian Kentucky in general, and elevated rates in women under age 50 compared to statewide and US rates. We have shown from our previous research that there is a higher incidence of Lynch syndrome among young patients with colon cancer in Appalachian Kentucky. Similar findings were observed with endometrial cancer analysis. Further evaluation and genetic testing for any association with Lynch syndrome is needed.

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POSTER PRESENTATION #56

Abstract Title: **The Effects of Polychlorinated Biphenyl 126 on a Compromised Liver**

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Abstract: Exposure to environmental pollutants, including Polychlorinated Biphenyls (PCBs), is correlated with the occurrence of liver disease, hypertension and metabolic disorders. The liver is crucial for xenobiotic metabolism and energy homeostasis. Previously, our group demonstrated that PCB126 (4.9mg/kg) disrupted energy homeostasis and worsened steatohepatitis in a compromised liver mouse model. The purpose of this study was to examine the effects of a lower dose of PCB126 on energy homeostasis and metabolic parameters, over a longer time-course. Male C57Bl/6 mice (n=10) were fed either an amino acid control diet (CD) or a methionine-choline deficient diet (MCD) in this 14-week study. Mice were exposed to PCB126 (0.5mg/kg) via oral gavage. The chronic and low dose of exposure was designed to mimic human PCB exposure patterns. Body weight, fat composition, glucose uptake, and blood pressure (BP) were assessed. Future studies will look at histology and tissue analysis for metabolic endpoints. The MCD diet decreased body weight (~8% loss) while co-exposure to PCB126 exacerbated this body weight loss (~12%). The % fat composition was measured using Echo-MRI and the MCD group showed a ~1.5 fold decrease in % body fat composition while the MCD+PCB126 group had a ~2.1 fold decrease. The MCD+PCB126 group also exhibited decrease basal blood glucose levels (fasted and non-fasted) while there was no effect in the CD+PCB126 group. Interestingly, the MCD+PCB126 group also displayed a trend towards higher systolic blood pressure versus its CD counterpart when measured on Week 8. In terms of glucose metabolism, the CD+PCB126 group showed a higher Area Under the Curve (Glucose tolerance test) versus the MCD groups, indicating resistance to glucose metabolism. This was counterintuitive to our previous study utilizing a higher dose and a shorter time-point. PCB126 at the dose used exacerbated effects of wasting as demonstrated by body weight and fat composition. PCB126 also appeared to disrupt glucose metabolism irrespective of the liver state and these effects were time- and dose- dependent. These current findings will enable us to further elucidate the metabolic and toxic effects of PCBs, particularly coplanar congeners, in humans. (The current study is supported by the NIEHS/NIH grant P42ES007380 and NIGMS/NIH grant 8 P20 GM103527-06).

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POSTER PRESENTATION #57

Abstract Title: **Lineage Tracking of Fibroblasts in the Aorta During Angiotensin II Infusion**

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Abstract: Objective: The purpose of this study was to determine whether cells tracked with a S100A4 driven Cre retain markers for fibroblasts or expressed characteristics of smooth muscle cells. The S100A4 promoter is used to drive Cre recombination in fibroblast specific gene expression. However, the S100A4 promoter is potentially active in cell types in addition to fibroblasts. Our previous studies have demonstrated angiotensin II (AngII) infusion increases aortic medial cells expressing S100A4 promoter driven Cre in mice ubiquitously expressing a conditional LacZ gene. Approach and Results: Mice expressing Cre under the control of the S100A4 promoter were bred into transgenic mice with a repressed lacZ gene at the Rosa26 locus. At 8-10 weeks of age, mice were infused subcutaneously with either saline or AngII (1,000 ng/kg/min) for 28 days. Following infusion, aortas were dissected free and sections were obtained from the ascending, descending, and abdominal aortic regions. As noted previously, AngII infusion increased β -galactosidase tissue staining in the ascending and abdominal aortic regions, but not the descending region. β -galactosidase immunostaining was more closely colocalized with α -smooth muscle cell actin immunostaining than with ERTR7 immunostaining in all aortic regions. Conclusions: AngII infusion drives an increased expression of S100A4 in medial cells tracked with a S100A4 promoter driven Cre. Despite S100A4 being defined as a fibroblast specific gene, lineage tracked cells primarily had expression of a smooth muscle cell marker.

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POSTER PRESENTATION #58

Abstract Title: **Sex difference in the patho-physiological consequences of adipocyte PRR deficiency**

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Abstract: Obesity increased the expression of the (pro)renin receptor (PRR), a component of the renin-angiotensin system, in adipose tissue. In male mice, the deletion of adipocyte PRR prevented the development of obesity and the accumulation of fat mass but led to a fatty liver and an elevated systolic blood pressure (SBP). The objective of our study was to determine whether this remarkable phenotype was sustained in female. Male PRRAdi/Y mice expressing adiponectin-driven Cre recombinase were bred with female mice PRRfl/fl to generate female control (PRRfl/fl) and adipocyte-PRR deficient mice (PRRAdi). Female mice were fed a standard diet (SD) or a high fat diet (HF) for 23 weeks (n=6-13/groups). The deletion of adipocyte PRR in females did not change body weight in SD-fed mice, but prevented the development of high fat diet-induced obesity. Interestingly, the resistance to obesity in female mice was less pronounced than in male. Similar to males, the deletion of adipocyte PRR in female mice decreased by over 85% adipose tissue mass and resulted in hepatomegaly associated with an increase of liver lipid contents. At 22 weeks, radiotelemetry devices were implanted in female mice. In contrast to males, the increase in systolic blood pressure was not significant in SD-fed PRRAdi female mice (PRRfl/fl, 129 ± 3 mmHg; PRRAdi, 141 ± 9 mmHg) suggesting a sex difference in PRR mediated-regulation of blood pressure. Blood pressure measurement in HF-fed mice are under investigation. Future studies will define whether sex difference in blood pressure regulation mediated by PRR depends on the renin angiotensin system and on hormonal regulation. Mechanism by which PRR regulates lipid metabolism will also be explored.

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POSTER PRESENTATION #59

Abstract Title: **Regulation of claudins in renal TJ by Na,K-ATPase alpha 1 subunit**

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Abstract: Tight junctions (TJs) are located at the uppermost portion of the lateral membrane of epithelial cells that seal the intracellular interspace between adjacent cells, transforming the epithelial cells into an effective permeable barrier. Tight junctions regulate the movement of substances through the paracellular pathway, and claudins (Clns) are major determinants of TJ permeability. Renal expression of different Cln isoforms is in a tubule-specific manner. The distribution of Cln on nephron is involved in physiological and kidney related diseases. Little is known about what controls the composition of TJ along the nephron. Previous reports have shown that ouabain, a cardiac glycoside that acts by inhibiting the Na⁺,K⁺-ATPase (NKA) pump activity, increases TJ sealing degree (10-100 nM), suggesting the participation of NKA in TJ regulation. Results: Using TER measurement, western blot and confocal microscopy we found that A420P and A425P mutation decreases the ion permeability and changes the molecular composition of TJ proteins when compared to wild type NKA alpha1. The expression levels and cellular localization of Cln 2 and Cln 4 were altered. Src inhibitor PP2 and pNaKtide were able to decrease the TER values in A425P cell line comparable to wild type. In A425P, Cln 2 is downregulated in transcriptional manner, while Cln 4 is upregulated. Thus, this work shows that the N domain of NKA alpha-1 has an important role in tight junction function and this regulation implicates NKA-Src-Caveolin-Claudin pathway. Taken together, these observations have a significant relevance to the altered function of kidneys in physiological and pathological conditions, in which the transport of ion and nutrients are significantly altered.

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POSTER PRESENTATION #60

Abstract Title: **Early life stress (ELS) promotes lack of protective factors against obesity-induced hypertension in female mice**

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Abstract: Early life stress (ELS) exposure has been recognized as an independent risk factor for obesity and cardiovascular disease. Maternal separation and early weaning (MSEW) is used as a mouse model of ELS. This study tests the hypothesis that male and female mice subjected to MSEW will display exacerbated high fat (HF) diet-induced obesity, being female mice protected against the development of hypertension (HT). MSEW was performed in C57Bl/6 mice from postnatal days 2-16. Undisturbed litters served as control (C) group. Mice were placed on a low-fat (LF) or HF diet for 16 weeks upon weaning. In response to HF diet, obesity and HT were exacerbated in both male and female MSEW mice vs. C. However, these increases were greater in females. Vascular reactivity assessed by wire myography showed increased serotonin-induced vasoconstriction in female MSEW mice vs. C (73 ± 15 vs. 36 ± 3 %maximal constriction, $p < 0.05$) but not in male MSEW mice (59 ± 8 vs. 51 ± 3 %maximal constriction, $p < 0.05$). Metabolic function measurements revealed that female MSEW mice, but not male MSEW mice, displayed hyperinsulinemia, reduced insulin sensitivity, plasma inflammatory markers (PAI-1, resistin) and greater central adiposity and adipocyte hypertrophy vs. C ($p < 0.05$, respectively). Although the renin-angiotensin system was activated in both male and female MSEW mice, the mineralocorticoid metabolism (aldosterone, mineralocorticoid receptors) was upregulated only in females. These data indicate that female mice exposed to MSEW and fed a HF diet are particularly susceptible to undergo accelerated metabolic disease and HT by lacking protective factors such as reduced central fat deposition and attenuated vascular reactivity.

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POSTER PRESENTATION #61

Abstract Title: **The Significance of Na/K-ATPase Signaling and ROS in Obesity Development**

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Abstract: It has been demonstrated that chronic oxidative stress contributes to the development of obesity and related complications. We have demonstrated that oxidative stress and Na/K-ATPase signaling forms a positive feedback amplification loop. It is not clear how amplification loop affects obesity and associated complications. We hypothesize that activation of the loop exacerbates obesity development, which can be ameliorated by attenuation of this amplification loop. In 3T3-L1 preadipogenic cells, oxidant stress caused by activation of Na/K-ATPase signaling increases adipogenesis, seen through the increase in adipogenic markers and increase of adipocyte presence by oil red O staining. pNaKtide, a designed peptide to block Na/K-ATPase signaling function, decreased adipogenesis, in both the presence and absence of ouabain (a specific Na/K-ATPase ligand). Our results suggest a potentially complex interaction between the Na/K-ATPase and oxidative stress in the development of obesity that has not been previously explored. Age matched C57BL6 mice were placed on a normal diet, or a high fructose western diet (HF/WD) for 12 weeks to induce obesity; pNaKtide was targeted to adipocytes by an adiponectin driven lentivirus. Compared to mice fed with normal chow, mice fed HF/WD showed significant weight gain, along with increases in liver weight, heart weight, and subcutaneous and visceral fat weights. Treatment with pNaKtide delivered via lentivirus showed a significant decrease in weight gain compared to HF/WD mice, along with a decrease in the above mentioned side effects. Previous data has shown that a HF/WD activates Na/K-ATPase signaling and increases protein carbonylation, and administration of pNaKtide by i.p. decreases the effect.

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POSTER PRESENTATION #62

Abstract Title: **A Novel Autotaxin Inhibitor Reduces Inflammation in Myocardial Infarction Pre-Clinical Model: Potential Therapeutic Targets in Ischemic Heart Disease**

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Abstract: Introduction: Acute myocardial infarction (AMI) is the leading cause of death. AMI is associated with increased circulating inflammatory cells such as monocytes (monocytosis) in peripheral blood (PB). This pathological inflammation exacerbates tissue damage and is correlated with the development of heart failure through poorly understood pathways. Lysophosphatidic acid (LPA), produced by autotaxin (ATX), regulates monocytosis and promotes inflammation. However, the role of ATX/LPA signaling nexus in cardiac inflammation has not been previously explored. Methods and Results: Following AMI, mice were randomized to receive PF-8380 (a potent ATX inhibitor) 10 mg/kg twice daily or placebo. AMI was associated with increased ATX activity and plasma LPA levels, as assessed by enzymatic assay and mass spectrometry. ATX inhibition reduced plasma LPA level which was associated with reduced numbers of circulating and cardiac inflammatory monocytes (CD115+/CD11b+) and neutrophils (Ly-6G+/C+) during peak post-AMI inflammation, as assessed by flow cytometry. PF-8380 significantly reduced pro-inflammatory gene expression (IL-1 β , IL-6, MCP-1, TNF- α) and Interferons (IFN- α , IFN- β , IFN-R), assessed using RT-PCR at the peak of inflammatory response in BM, PB and cardiac tissues. Mechanistically, reduced inflammatory cells and inflammation was related to significant reduction in BM progenitor count and proliferation with ATX inhibition. Finally, PF8380 treatment lead to significant improvement in cardiac functional recovery and reduction in infarct size. Conclusion: AMI leads to upregulation of ATX/LPA signaling and associated inflammatory response. ATX inhibition reduces the deleterious effects of inflammation on the injured myocardium. These results support the use of small molecule pharmacological inhibitors as potential therapeutic target in AMI.

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POSTER PRESENTATION #63

Abstract Title: **The Role of Adipose-Derived Autotaxin on Inflammation Associated with Cardiovascular Disease**

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Abstract: Obesity is an established risk factor for cardiovascular disease (CVD) and stroke, and the cardiovascular complications of obesity are a leading cause of potentially preventable death. Recent evidence suggests that increased cardiovascular mortality in patients with obesity may not be fully explained by associated risk factors such as dyslipidemia, hyperglycemia, insulin resistance and hypertension. In addition to contributing to traditional CVD risk factors, obesity is also characterized by a chronic sub-acute inflammatory state termed "metainflammation" involving increased circulating inflammatory cytokines. Autotaxin (ATX), encoded by the ecto-nucleotide pyrophosphatase/phosphodiesterase 2 (ENPP2) gene, is a potent cell motility-stimulating factor that is secreted by adipose tissue. ATX hydrolyzes lysophosphatidylcholine (LPC), a lipid that is abundant in the circulation, to lysophosphatidic acid (LPA). The main objectives were to investigate if ATX may be involved in metainflammation and whether adipose ATX further contributes to physiological attributes of adipose cells and cardiovascular disease. We established two animal models with reduced ATX expression: MX1 Cre-mediated deletion of the gene encoding ATX to generate a global loss (MX1-r) and AdipoQ-Cre mediated loss of ATX expression in adipocytes (AdipoQ-r). Mice were fed a high fat diet for up to 20 weeks. RNA and proteins were extracted, qPCR and western blots were performed for ATX and inflammatory cytokines, and plasma ATX activity was determined. Results showed MX1- Δ and AdipoQ- Δ mice had a reduced level of inflammatory cytokines and decreased adipose cell size. The data generated from these experiments will provide important insight into potential mechanisms of how ATX and adipose tissue influence obesity induced inflammation and results from this and future projects may identify potential therapeutic targets to prevent and treat obesity induced inflammation.

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POSTER PRESENTATION #64

Abstract Title: **Pitfalls of big data: ICD-9 codes miss large percentage of in-hospital cardiac arrests**

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Abstract: Introduction: Electronic health records are increasingly being used for research and quality improvement purposes, largely through diagnostic and billing codes. However, the accuracy of this data is not known. This study intended to assess the comprehensiveness of ICD-9 codes for identifying in-hospital cardiac arrests (IHCA). Methods/Materials: In-hospital cardiac arrests from 2012-2015 (over 45 months) were identified from review of cardiac arrest sheets. All rapid response team (RRT) notes, coded and billing data were compiled and reviewed for these patients. Demographics and survival to hospital discharge were compared to coded data to identify factors that influenced likelihood to code this data accurately. Results: 782 patients with IHCA were included. ICD9 code for cardiac arrest was identified in 446 patients (57%). RRT note was identified in 86% of IHCA. ICD-9 codes were more likely to be documented in younger patients (58+/-15.6 years vs 61 +/- 14.7 years, p=0.0016) and if the patient survived to hospital discharge compared to those who expired in house (66% vs 53%, p=0.0008). Gender, ethnicity, or initial rhythm was not associated with decreased coding. 41% of those who had multiple cardiac arrests during a hospitalization did not get an ICD-9 code for cardiac arrest. Discussion: While ICD-9 codes are commonly used for patient identification and outcomes, this analysis suggests that over 40% of true IHCA are missed using this criteria alone with likely higher rates amongst older patients and those who do not survive to hospital discharge.

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POSTER PRESENTATION #65

Abstract Title: **HERD2020: Evaluating cardiometabolic risk factors in rural, college-aged students at Marshall University**

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Abstract: Throughout the US, obesity and diabetes rates continue to rise, especially in West Virginia. In fact, West Virginia's obesity and diabetes rates exceed 40 percent of its population. Previous literature has demonstrated that childhood and early adult lifestyles, including poor dietary choices and reduced physical activity, predict future metabolic and cardiac issues. Therefore, we sought to determine the levels of risk factors for diabetes and cardiometabolic disease in college students in southern WV via a 4-year longitudinal study termed HERD2020 (Higher Education Reducing Diabetes). Freshmen were recruited Fall 2016 at Marshall University and were stratified by BMI status to assess differences in physiological, molecular, and psychological status (BMI<25 kg/m² vs BMI>25 kg/m²). To date, 76 freshmen have enrolled into the study [age= 18.5±2.36 years; female=60.5% (n=46); BMI= 26.5±5.85 kg/m²]. Fifty three percent (n=40) of the students were deemed overweight or obese (BMI>25 kg/m²). No significant differences were found between BMI category and fasting glucose (p=.31); cholesterol (p=.473); triglycerides (p=.38); or HDL (p=.56). Strikingly, students with a BMI>25 kg/m² recorded fasting insulin levels twice as high as students with a BMI<25 kg/m², (.42 vs. .96ng/ml, p=.003). This data suggests students that overweight/obese are in a state of insulin-resistance, placing them at greater risks for future cardiometabolic diseases. Continual recruitment and analysis of this study will provide more insight into the strength of these associations following lifestyle intervention. Also, plasma bile acid levels, FGF21 concentrations, and cytokine levels in the blood will be evaluated to determine their contribution to disease status.

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POSTER PRESENTATION #66

Abstract Title: **QRS Duration Alterations After Left Ventricular Assist Device Implantation In Patients With Advanced Heart Disease**

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Abstract: Introduction: A left ventricular assist device (LVAD) is a mechanical pump that takes blood from the left lower chamber of the heart and pumps it via the aorta to the body and vital organs, supporting heart function and general blood flow. LVADs are indicated for individuals with significant heart disease who are recovering after heart surgery, waiting for a heart transplant, or whom are ineligible for a heart transplant. On EKG, patients with ventricular heart disease show broad QRS durations. We examined changes to the QRS duration in patients who underwent LVAD implantation. Methods and Results: We conducted a retrospective chart review of 144 patients with ventricular heart disease who underwent LVAD implantation. ECG results were reviewed prior to LVAD implantation when available, and after LVAD implantation at 1 week, 1 month, 3 months, 6 months, 1 year, and 2 years, when available. 140 ECGs were reviewed pre-implant, and 29 patients were excluded due to variable conduction throughout patient chart history (paced vs. intrinsic heart rhythm). A total of 113 patients were analyzed (paired t-test was completed for patients with initial and follow up ECGs). After LVAD implantation patients with native rhythm had a significant reduction in QRS width to 85.9 ± 14.9 ms $P < 0.001$ at 1 week, 92.6 ± 19.7 (P=0.006) at 1 month, and 77.3 ± 23.4 (P=0.032) at 2 years. For patients with a paced rhythm a significant reduction in QRS duration was seen to be 142.2 ± 21.8 (P<0.001) at 1 week, 138.4 ± 24.1 (P<0.005) at 6 months, and 132.5 ± 25.1 (P=0.022) at 1 year. The fluctuation in the significance of the reduction was due to a low count (<20 cases per group). Conclusion: Alteration in QRS duration after LVAD implantation demonstrates the effect of load put on the human heart and consequent signaling registered on an electrocardiogram. Significant reduction seen in QRS width after device implantation at various time points reflects decreased overall loading on the heart and improved contractile performance. Reduction seen in individuals of both native and extrinsically paced heart rhythms demonstrates LVAD value in variable heart disease patient settings.

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POSTER PRESENTATION #67

Abstract Title: **Nuanced Antibody Responses to Apolipoprotein A-I in Patients with Cardiovascular Disease**

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Abstract: Antibodies targeting apolipoprotein A-I (ApoA-I) have been identified in patients with cardiovascular disease (CVD). Anti-ApoA-I antibodies are thought to be markers of disease, but their exact role is unclear. We hypothesize that antibodies targeting ApoA-I are both protective and pathologic and unraveling the nuanced response to ApoA-I will provide insight into improved risk stratification of patients suffering from CVD. To test our hypothesis we screened serum samples by ELISA collected from patients with CVD to identify anti-ApoA-I antibody responses toward the full length protein along with immunogenic epitopes including the lecithin cholesterol acyl transferase (LCAT) domain and the C-terminal peptide of ApoA-I. These epitopes are of particular interest due to their propensity to undergo oxidative post-translational modification. Antibodies were affinity-purified toward ApoA-I, and their role in reverse cholesterol transport elucidated. Our data indicate that serum collected from patients with CVD enrolled in multiple clinical trials possess a highly nuanced immune response. We find that these antibody responses change over time in some patients who present with an AMI and antibodies correlate with outcomes. The mechanisms of these observed effects are currently under investigation. A full report on correlations between patient characteristic and antibody level will be presented. This work highlights the complexities of anti-ApoA-I antibodies in patients, which will guide development of a CVD risk stratification tool.

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POSTER PRESENTATION #68

Abstract Title: **Assessing Dietary Effect on Myocardial Function**

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Abstract: Obesity has been an ever-growing health concern in the United States with major complications such as cardiovascular and metabolic diseases. The current clinical evaluation of cardiovascular health relies upon ultrasound assessment of cardiac output by measuring systolic ejection fraction. However, this assessment fails to appreciate the compensatory remodeling process that precedes the loss of global cardiac function. This experiment aims to assess dietary effect on cardiac function using various physiologic markers. Thirty male C57B6 mice were randomized to either a high-fat diet or a low-fat diet for a period of 3 months. Interventricular septal thickness, septal-ventricular radius ratio, and fractional shortening, which directly correlates with ejection fraction, were measured via MRI monthly to track growth progress. We observed a significant body mass difference between the two diet groups. Both diet groups had significant increase in septal thickness over the 3 month period. However, this difference can be attributed to the fact that the mice were still growing during this experiment. On the other hand, the temporal trajectories for the diet groups are approximately parallel with respect to fractional shortening, indicating that there is no measurable difference in ejection fraction. Overall, we saw a mismatch between body mass and cardiac function, suggesting that ejection fraction maybe maintained in obese patients during the early cardiac remodeling phase.

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POSTER PRESENTATION #69

Abstract Title: **Pulmonary Embolism Response Team: An Initial 12-Month Review**

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Abstract: Background: Acute pulmonary embolism (PE) is a common cause of death in hospitalized patients, with an estimated occurrence of 1-2/1000 adults per year, and associated with a mortality rate of 10-30% within 1 month. Treatment of PE has remained stagnant, thus new paradigms must be instated to better detect and treat acute PE. In late 2015, UK HealthCare launched an OptimalCare® approach to management of PE that included a pulmonary embolism response team (PERT) interdisciplinary team model to treat acute submassive or massive PE utilizing the most appropriate treatment modalities based on patient-specific features. Hypothesis/Primary Objective: This study seeks to compare outcomes in the PERT era with those in previous years before PERT implementation. The primary variables examined are inpatient mortality, morbidity, intensive care utilization, and length of stay. We hope to demonstrate that the implementation of the PERT improves patient outcomes across these variables. Methods: This study is a retrospective analysis of patient data from PERT activations during the 2016 calendar year. We have compared outcomes in the PERT era with those in previous years before PERT implementation in regards to the primary variables examined. Results: In the first year following the OptimalCare® implementation, there were 56 unique PERT activations. Data from these activations was collected retrospectively through chart review and compared to historic retrospective review data on patients at UKHC. Conclusions: Preliminary data analysis indicates no significant change in morbidity or mortality but did reveal LOS decreased in PERT patients. Data analysis is ongoing to determine clinical significance.

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POSTER PRESENTATION #70

Abstract Title: **Early Clinical Signatures of Stroke and Bleeding in Patients on Left Ventricular Assist Device Support**

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Abstract: Hypothesis: Platelet function and thromboinflammatory biomarkers will help predict clinical complications due to Left Ventricular Assist Devices (LVAD). Methods: June 2014-August 2016, 66 patients received Heartmate II(n= 48), Heartware(n=18). Median age 55. 86% Male. Blood collections: baseline (BL); 1, 24, 72, 168-hours and follow-up 30-180-days post-operation. Platelet function analyzed via impedance aggregometry and agonists (thrombin, ADP, collagen, ristocetin). Plasma biomarkers (TNF-a, CD40L, IL-6, CRP, IL-10, IL-1b, PF4, Angiopoietin-1,-2, ST2) analyzed via immunoassays. Clinical data correlated via functional data analysis, multiple linear regression. Results: Median values reported. Platelets decreased 42.0% (SD 208.0±77;120.9±50)(p<0.001) while WBC increased 67.1% (SD 8.2 ±2.9;13.7±3.6)(p<0.0001) BL to 72-hours. Platelet ristocetin aggregation decreased 52% (SE 515.0±79.7;247.1±45.7)(p=0.0006) BL to 24-hours without BL recovery by day 7. To demonstrate a few biomarkers: IL-6 increased 796.9% (SE 25.4±72.4;227.8 ±94.6)(p=0.004) BL to 72-hours without BL recovery by follow-up. Angiopoietin-1 decreased 35% (SE 1279±136.4;837.2±84.7)(p=0.01) while Angiopoietin-2 increased 235.7% (SE 3143.9±813.5;10555.4±7556.1)(p=0.03) BL to 72-hours. Angiopoietin-2/angiopoietin-1 was increased 273% from healthy levels at BL (SE 0.46±0.07;1.72±0.65)(p=0.05) without return by follow-up. One-year outcomes: stroke 18.2%, gastrointestinal bleeding (GIB) 19.7%, thrombosis 9.1%, drive-line infection (DLI) (10.6%) mortality 15.2%. Analysis revealed significant associations of platelet function with GIB, DLI; also, between biomarkers and stroke, GIB, mortality. Further data will be presented. Conclusions: LVADs are crucial for patients with limited cardiac function, however significant complications exist. Study results suggest that early platelet function and biomarker analysis may help predict complications such as stroke and bleeding, and thus serve as risk-stratification or targeted therapy tools for patients on LVAD support.

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POSTER PRESENTATION #72

Abstract Title:	Utilization of Appalachian Clinical and Translational Science Institute Data Warehouse to More Accurately Predict Disease Processes Important for Central Appalachia.
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Abstract: Background: Metabolic syndrome (MetS) is a significant risk factor for multiple morbidities such as heart attack, stroke, diabetes and some cancers (e.g. liver cancer in men and endometrial in women). MetS also increases risk of all causes of cardiovascular disease and mortality. Obesity is central to MetS and West Virginians have the second highest rate of obesity in the U.S. Thus, it is important to accurately diagnose MetS in our central Appalachian population. Hypothesis: ACTSI Data Warehouse (ACTSI-DW) can be utilized to more accurately determine the number of patients with MetS. Methods: We utilized the ACTSI-DW to more accurately determine the number of patients with possible MetS at Marshall Health/Cabell Huntington Hospital patient population. ACTSI-DW was queried for MetS ICDcodes (277.1 or E88.81), for criteria necessary (e.g. BMI, hypertension, dyslipidemia, hyperglycemia) for the diagnosis of MetS recommended by different agencies (World Health Organization (WHO), National Cholesterol Education Program (NCEP), European Group for the Study of Insulin Resistance (EGIR), American Council on Exercise (ACE)) over the last 6.5 years. Results: By ICD code alone, only 232 patients were diagnosed with Met S in the last 6.5 years. However, based on criteria by each of the following agencies, we identified MetS as follows NCEP = 13,833; WHO = 5,131; EGIR = 20,182; and ACE = 23,110 unique patients during the same 6.5 years. Conclusions: The ACTSI-DW may be used to specifically identify characteristics of a disease entity more accurately than ICD codes alone. This has potential implication for better diagnosis, and thus, provision of proactive preventative and concurrent care for these patients.

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POSTER PRESENTATION #73

Abstract Title: **Metabolic Benefits of Timed Exercise**

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Abstract: The circadian system synchronizes physiology and behavior with the environment. However, modern lifestyles cause people to live against their circadian system. As a result, more than 70% of the population has social jetlag, which occurs when the alarm clock wakes us early for work, even though our internal clock intends for us to sleep later. Importantly, social jetlag is associated with obesity and metabolic dysfunction. Thus, alleviating social jetlag is a novel way to treat these deleterious health conditions. One way to eliminate social jetlag is to change the timing of the internal circadian clock so an individual naturally wakes up earlier. It is known that mid-day exercise changes the timing of the circadian clock. The goals of this study are to determine if mid-day exercise alleviates social jetlag and improves metabolism. Sedentary men and women (BMI>18.5; ages 18-35 years) will be randomized to either morning or mid-day exercise (relative to internal clock time) at 70% VO₂max, 5 days per week for 4 consecutive weeks. We will measure circadian and metabolic parameters before and after the exercise intervention. We predict mid-day exercise will advance the timing of the circadian clock, resulting in earlier bed and wake times and reduction in social jetlag when compared to morning exercise. We predict participants exercising at mid-day will also have improved glucose tolerance and decreased blood pressure and fasting FFAs. This study will identify the best time of day to exercise and could thereby improve the efficacy of exercise regimens.

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POSTER PRESENTATION #74

Abstract Title: **Effects of Adrenergic Stimulation and Acute Hyperglycemia on Murine Cardiac Electrophysiology.**

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Abstract: Elevated level of glucose in the blood is known to be associated with a variety of cardiovascular morbidities including higher incidence of electrical disturbances. Although effects of chronic hyperglycemia have been widely investigated, relatively less is known in terms of electrophysiological effects of acute hyperglycemia. Further, whether acute increase in glucose affects adrenergic response is also not clearly known. We used excised ventricular tissues from mice to record trans-membrane potentials during a variety of pacing protocols to investigate cellular/tissue level electrophysiological effects of acute hyperglycemia and adrenergic stimulation (1 μ M Isoproterenol, a β -adrenergic agonist). A custom program was used to compute action potential durations (APD), maximal rates of depolarization, and action potential amplitudes (APA) from the recorded trans-membrane potentials. From these computed measures, electrical restitution and alternans threshold were quantified. Restitution was quantified using the Standard Protocol (BCL= 200ms), Dynamic Protocol (200-40ms or till block) and a novel DI control protocol with Sinusoidal Changes in DI. Results from 3 mice show that acute hyperglycemia causes prolongation of the APD. Effects of adrenergic stimulation during acute hyperglycemia were partially blunted compared with non-hyperglycemic state. Similar, but less consistent effects were seen in other electrophysiological parameters. Our results show that acute hyperglycemia may itself alter cellular level electrophysiology of myocytes and importantly, modify adrenergic response. These results support further investigation into the electrophysiological effects of acute changes in glucose levels

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POSTER PRESENTATION #75

Abstract Title: **Prediction of All-cause Mortality from Clinical MRI-derived Left Ventricular Ejection Fraction: 15 Years of Data from a Large Regional Health System**

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Abstract: Background: Despite the widespread use of magnetic resonance imaging (MRI) to assess cardiac function, few studies have evaluated the ability of left ventricular ejection fraction (LVEF) derived from MRI to predict all-cause mortality. We used 15 years of MRI data from a large regional health system to assess the relationship between clinical MRI-derived LVEF and subsequent mortality. Methods: Records from the Geisinger Health System were reviewed to identify all instances where LVEF was measured clinically using MRI. Either date of death or last living encounter were obtained as well as patient characteristics and active diagnoses. The relationship between LVEF and mortality was assessed with Cox Proportional Hazards Regression. Results: We identified 3405 MRI studies from 3052 unique patients with clinically reported LVEF. Median follow-up time was 4.0 years. Death occurred in 707 patients representing 765 MRI studies. Including adjustments for confounders, LVEF was a significant predictor of all-cause mortality. The highest hazard ratio was observed in the lowest (<25%) LVEF interval (hazard ratio = 2.74, 95% confidence interval: 2.04 – 3.70). The hazard ratio steadily declined with increasing LVEF up to the reference 55–65% interval. There was no significant difference in the hazard ratio between the 55-65 and ≥65% intervals. Conclusions: Based on outcomes from over 3000 patients in a large regional health system, clinical MRI-derived LVEF is a significant predictor of all-cause mortality. MRI-derived LVEF can stratify patients according to their risk of all-cause mortality, with improved survival for higher LVEFs, up to an LVEF between 55-65%.

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POSTER PRESENTATION #76

Abstract Title: **Clinical Variables and Interventions That Predict Survival in Cardiac Arrest**

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Abstract: Introduction: Prognostic factors in out of hospital cardiac arrest have been investigated, however, significantly less is known about prognostic factors with in-hospital cardiac arrest (IHCA). This project investigated survival-to-discharge factors for patients experiencing in-hospital cardiac arrests (CA) including C-Graph score, initial rhythm, occurrence of re-arrest, witnessed versus unwitnessed events, and arrest time. Methods: Code sheets were manually reviewed of all IHCA at the University of Kentucky from January 2012 to September 2015. Demographics, clinical risk factors, laboratory findings, and details of the code itself were documented for each patient. C-graph score was calculated for each patient. The primary outcome was survival to hospital discharge. Dichotomous and continuous independent variables were compared with chi-square analysis and t-test respectively. Results: 839 IHCA occurred over 45 months (Age 59 +/-15.6 years, 40% female). 81% survived the initial code, and survival to hospital discharge was 30%. Non-survivors had higher C-Graph score than survivors (2.62 vs 2.51, p=0.032). PEA/asystolic arrests were less likely to survive to discharge compared to VT/VF (29% vs 38%, p=0.01) and time to ROSC of > 20 minutes were less likely to survive than shorter codes (18% vs 37%, p=0.006). Interestingly, of those who survived the initial arrest, a recurrent arrest was highly predictive of those unlikely to survive to discharge (13% vs 53%, p<0.001). Discussion: Higher C-graph score, initial non-shockable rhythm, time to ROSC of >20 min, and recurrent cardiac arrest are predictive of survival to hospital discharge and should be clearly documented to aide in clinical management.

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POSTER PRESENTATION #77

Abstract Title: **Evaluation of Mechanical Thrombectomy Trends at University of Kentucky**

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Abstract: INTRODUCTION: Ischemic stroke is a devastating condition resulting in significant morbidity and mortality. The strong positive results of randomized trials have established mechanical thrombectomy as a mainstay for large vessel occlusive stroke. Our aim was to examine our thrombectomy procedures, and to evaluate relationships in practice change and development that could inform the adoption and selection of techniques. METHODS: Retrospective review was conducted on mechanical thrombectomy cases from 07-2011 to 12-2015. Patients must have been 18 years old, diagnosed with ischemic stroke, and were treated with thrombectomy. Primary outcomes were final TIC1 score, procedural complications, NIHSS improvement, mortality, and incidence of single pass thrombectomy. RESULTS: 130 procedures were performed. 79.1% had a TIC1 score of at least 2b. 30% of thrombectomies were single pass. When evaluated by technique, single pass recanalization was achieved with reperfusion catheter alone in 52%, with stent-triever alone in 27%, and with combination techniques in 26% (Chi-squared 6.04, $p = 0.048$). Median NIH stroke scale improvement with the procedure improved each year with a significant linear correlation (Pearson $r = .915$, $p = 0.029$). Procedural mortality was 0.77% (one patient). CONCLUSIONS: Preliminary data suggest that thrombectomy is a safe procedure that results in extremely low mortality and significant decreases NIH score over time, which may point to better functional outcome. Overall, there was an improvement in NIHSS reduction with time. There was a significant difference in the ability of different techniques to achieve first-pass recanalization, though this may reflect clinical judgments about when to use each technique.

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POSTER PRESENTATION #78

Abstract Title: **Elucidating Subtypes and Risk Factors of Brain Arteriolosclerosis**

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Abstract: Cerebrovascular pathologies are often seen in aged brains. Here, we focus on brain arteriolosclerosis (B-ASC), i.e., degenerative thickening of cerebral arterioles. We recently reported that severe B-ASC pathology is associated with global cognitive status (PMID 26738751). To study risk factors of B-ASC, we analyzed 2,390 cases with clinical and neuropathological autopsy data from the National Alzheimer's Coordinating Center. Cases were analyzed according to age at death (< 80 years and ≥ 80 years) using logistic regression modeling. Gender was associated with B-ASC pathology in both age at death groups after controlling for covariates including age at death, and conventional vascular risk factors: hypertension, diabetes, smoking, and hypercholesterolemia. In a subset of cases with genetic information (n = 925), the ABCC9 gene variant (rs704180), previously associated with hippocampal sclerosis, was also associated with B-ASC pathology in the ≥ 80 year-old group. To address in finer detail the heterogeneous arteriolar morphologies that could be classified as B-ASC, we analyzed 74 cases from the University of Kentucky Alzheimer's Disease Center (UKADC) and UK Pathology Department. Within this convenience sample, the median age at death was 56.5 years with a range of 20 – 96 years. One of the subtypes of B-ASC pathology in this cohort consisted of arteriolar profiles with multiple internal lumens, which we refer to as multi-lumen vessels (MLVs, which generally have ≥ 3 lumens in a single vascular profile). In this sample, 62.1% (n = 46) of cases had ≥ 5 MLVs per brain section, as operationalized using CD34 immunohistochemistry in the frontal neocortex (Brodmann area 9). Interestingly, MLV densities increased with advanced age of death (r = 0.51; p < 0.0001). We conclude that B-ASC is a complex pathologic phenotype in advanced age with both genetic and clinical risk factors, as well as morphologic subtypes, that require further study.

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POSTER PRESENTATION #79

Abstract Title: **Aneurysmal Subarachnoid Hemorrhage Patients and an Increased Risk for Potentially Harmful Ionizing Radiation**

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Abstract: Purpose: The purpose of this study is to define the prevalence of potentially harmful ionizing radiation exposure (PHIRE) from diagnostic tests and therapeutic procedures in patients admitted with aneurysmal subarachnoid hemorrhage (aSAH) and to evaluate baseline demographics, common co-morbid or pre-existing medical conditions, and disease-specific features as risk factors for PHIRE in this patient population. Methods: This was a retrospective, observational study of patients with documented SAH who survived to hospital discharge at UK Chandler Medical Center (CMC) from 01/01/2012 to 12/31/2015. For each patient, the total effective dose of ionizing radiation (IR) was calculated based on the number of tests ordered and the radiation exposure of each type of test or procedure that was ordered. Patients were considered to have received PHIRE if their calculated total effective dose of ionizing radiation was greater than 50 mSv (the recommendation for permissible occupational radiation by the NCRCP). Risk factors were considered from baseline demographics, common co-morbid or pre-existing medical conditions, and disease-specific features. Results: 272 patients with SAH at UKCMC were evaluated and 109 patients (40.0%) met inclusion and exclusion criteria for this study. Patients received, on average, 47.5 mSv of IR during their hospitalization. The maximum calculated IR exposure for any patient was 132 mSv. 42 patients (38.5%) developed PHIRE during their initial hospitalization. No baseline demographic features or co-morbid or pre-existing medical conditions were associated with an increased risk of PHIRE. In univariate analysis, several disease-specific risk factors including, a high Hunt-Hess Score (OR=3.9; CI=1.6-9.6), a high Fischer score (OR=10.8; CI=1.4-85.8), a ventriculostomy drain (EVD) (OR=20.6; CI=4.6-92.2), a ventriculoperitoneal shunt (VPS) (OR=3.9; CI=1.4-10.5), and intracranial vasospasm (HR=9.5; CI=3.5-29.6) was also associated with PHIRE. In multivariate analysis, only EVD (OR=7.4; CI=1.3-43.8) and vasospasm (OR=6.4; CI=2.1-19.0) were associated with PHIRE. Conclusions: This is the first report of PHIRE in hospitalized patients with aSAH. In this study, we were able to demonstrate that approximately 39% of patients with aSAH have a significant exposure to IR from diagnostic tests and therapeutic interventions. Overall, it was observed that baseline demographics and the presence of common co-morbid and pre-existing medical conditions do not increase the risk of PHIRE. A number of disease-specific risk features, including severe HH score, severe Fischer score, EVD, VPS and intracranial vasospasm, are all associated with an increased risk of PHIRE. In general, each of these disease-specific features increase the complexity of clinical care and decrease the likelihood of a good clinical recovery. This data is limited by the single-center, retrospective nature of this data collection. Future studies might be expanded to multiple centers to evaluate PHIRE in a more generalized subset of patients. In addition, while we used NCRCP guidelines to define PHIRE in this population, it is not clear that this threshold is accurate to evaluate whether patients have negative clinical outcomes related to their IR exposure. Future studies should therefore consider various thresholds of IR exposure to determine IR exposure levels that are definitely associated with negative clinical outcomes in this population.

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POSTER PRESENTATION #80

Abstract Title: **Biosynthetic Potential and Biocatalyst Discovery from Terrestrial Microbes for Drug Development**

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Abstract: Terrestrial bacteria represent a rich reservoir for bioactive natural products (NPs), biosynthetic genes and tailoring biocatalysts. Identifying the genes involved in the biosynthesis of NP helps to explain the mechanisms these compounds are made. Furthermore, NP tailoring enzymes with relaxed substrate specificities encoded in these genomes can be used for drug development. As part of our ongoing effort at the Center for Pharmaceutical Research & Innovation (CPRI) at the University of Kentucky, we explore the biosynthetic potential of terrestrial microbes to identify unique tailoring biocatalysts and novel mechanisms. We have identified the gene clusters for the enediyne antitumor esperamicin, the polyketide antifungal scopafungin, the neuroprotective terphenyl terfestatins and a prenylated indole glycoside. We have characterized the functions of two promiscuous enzymes from these clusters; TerL, a phenylalanine methyltransferase and PriB a 6-C-tryptophan prenyltransferase. TerL was able to methylate both l- and d-phenylalanine, tryptophan and tryptophan analogs while PriB was shown to utilize natural and unnatural prenyl donors and accommodate substrates including anthranilic acid, naphthalene anthracene, and phenazine moieties. PriB was used to derivatize two indole-containing drugs; a beta blocker pindolol (Visken®) and the potent antibiotic daptomycin (Cubicin®). The crystal structure of PriB was solved at 1.5 Å resolution and was shown to adopt a conserved β/α fold. This work highlights the significance of genome mining and novel tailoring enzymes in drug development and diversification.

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POSTER PRESENTATION #81

Abstract Title: **Modified HIV drugs to treat blindness: Novel anti-inflammatory therapeutics**

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Abstract: Purpose: Nucleoside reverse transcriptase inhibitors (NRTIs) are mainstay therapeutics for HIV that block retrovirus replication. Surprisingly, we found that NRTIs as a class inhibit P2X7/NLRP3-mediated inflammation independent of reverse transcriptase inhibition (Fowler et al. Science 2014). Multiple FDA-approved NRTIs, including stavudine (d4T) and zidovudine (AZT), were efficacious in a mouse model of geographic atrophy (GA), a type of age-related macular degeneration (AMD) and leading cause of blindness in the elderly. However, d4T and AZT use in humans is associated with toxicity attributed to off-target host cell polymerase inhibition, which limits their therapeutic potential. Therefore, we rationally redesigned NRTIs in order to harness their anti-inflammatory properties and abrogate "off target" polymerase inhibition. We synthesized novel methoxy-substituted NRTI variants and tested whether this modification eliminates their ability to block polymerases, and tested the efficacy of modified-NRTIs in cell culture and mouse models of AMD. Methods: Methoxy-NRTI synthesis: Methoxy-substituted 3TC, d4T, AZT were synthesized from parental NRTI and methoxy-structures confirmed by H1 NMR/LC-MS. iGluc assay and western blotting were performed to assess inflammasome activation. Enhanced green fluorescent protein cell culture L1 retrotransposition assay and lentivirus GFP assay were analyzed by flow cytometry and on Biotek plate reader. mtDNA depletion measured by real-time qPCR of total DNA from cells in culture. Mouse model of dry AMD: RPE degeneration induced by subretinal injection of a plasmid expressing Alu RNA and assessed by fundus photography/ZO-1 staining of RPE flat mounts. Results: Modified NRTIs were protective in the Alu-induced mouse model of geographic atrophy. Novel NRTI variants retained inflammasome inhibition, however, unlike their parental NRTI counterparts, did not inhibit polymerases. Conclusion: NRTIs possess two distinct functions as reverse transcriptase inhibitors and anti-inflammatory compounds. The specificity of methoxy-NRTI derivatives as anti-inflammatories bolsters their therapeutic potential as a safer alternative to NRTIs. Also, modified NRTIs are useful tools for dissecting the effect of nucleosides on inflammasome vs. polymerase inhibition and could be advantageous in targeting other P2X7/NLRP3-driven diseases.

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POSTER PRESENTATION #82

Abstract Title: **Inhibition of Human Metapneumovirus Binding to Heparan Sulfate Blocks Infection in Human Lung Cells and Airway Tissues**

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Abstract: Human metapneumovirus (HMPV), a recently discovered paramyxovirus, infects nearly 100% of the world population and causes severe respiratory disease in infants, the elderly, and immunocompromised patients. We previously showed that HMPV binds heparan sulfate proteoglycans (HSPGs) and that HMPV binding requires only the viral fusion (F) protein. To characterize the features of this interaction critical for HMPV binding and the role of this interaction in infection in relevant models, we utilized sulfated polysaccharides, HS mimetics and occluding compounds. Iota-carrageenan had potent anti-HMPV activity by inhibiting binding to lung cells mediated by the F protein. Furthermore, analysis of a minilibrary of variably sulfated derivatives of Escherichia coli K5 polysaccharide mimicking HS structure revealed that the highly O-sulfated K5 polysaccharides inhibited HMPV infection, identifying a potential feature of HS critical for HMPV binding. The peptide dendrimer SB105-A10, which binds HS, reduced binding and infection in an F-dependent manner, suggesting occlusion of HS at the target cell surface is sufficient to prevent infection. HMPV infection was also inhibited by these compounds during apical infection of polarized airway tissues, suggesting these interactions take place during HMPV infection in a physiologically relevant model. These results reveal key features of the interaction between HMPV and HS, supporting the hypothesis that apical HS in the airway serves as a binding factor during infection, and HS modulating compounds may serve as a platform for potential antiviral development.

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POSTER PRESENTATION #83

Abstract Title: **Mapping Unique Interaction Domains in the Sterol Biosynthetic Pathway for Antifungal Development**

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Abstract: Invasive mycoses are becoming a significant cause of patient morbidity and mortality, indicating a need for the development of novel antifungal therapeutics. Squalene synthase catalyzes the first committed step in sterol biosynthesis. While the overall architecture of this enzyme is similar throughout eukaryotes, it has been shown that the plant and human enzymes can only complement a knockout mutation in yeast if the non-catalytic carboxy-terminal domain is swapped for one of fungal origin. This implies that there is a region within this domain that is unique to the fungal Kingdom. In order to characterize this potential therapeutic target, we used the model organism *Saccharomyces cerevisiae* with a squalene synthase knockout mutation and expressed chimeric squalene synthase genes originating from fungi, plants, animals, and algae under the control of a galactose inducible promoter. We have shown that all enzymes tested can complement the knockout mutation when expression levels are low. When the promoter is induced, it appears that overexpression of non-native squalene synthases in yeast may lead to the toxic accumulation of a sterol intermediate or by-product. We have also shown that this phenotype is specific to a 26 amino acid hinge region adjacent to the catalytic domain, and that the region can be mimicked to inhibit the growth of wild-type yeast. Our results suggest that the hinge region is a promising lead for the production of a broad spectrum antifungal therapeutic that would not disrupt cholesterol synthesis in humans.

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POSTER PRESENTATION #84

Abstract Title: **The Axolotl as a New Model for the Discovery and Validation of Chemical Genetics Tools for Regenerative Biology**

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Abstract: Amphibian vertebrates are important models in regenerative biology because they present exceptional regenerative capabilities throughout life. However, it takes considerable effort to rear amphibians to adulthood for regeneration studies and the relatively large sizes that frogs and salamanders achieve during development make them difficult to use in chemical screens. Here we introduce a new tail regeneration model using early hatchling stage Mexican axolotl larvae. We show that axolotl hatchlings completely regenerate amputated tails in 5-7 days before they exhaust their yolk supply and gain competency to feed. Further, we show that axolotl hatchlings can be efficiently reared in microtiter plates to achieve moderate throughput screening of chemicals to investigate toxicity and identify molecules that alter regenerative outcome. Importantly, the use of pre-feeding salamanders circumvents the need for an Institutional Animal Care and Use protocol and the screen has also been adapted as an undergraduate student teaching laboratory exercise. As proof of principle, we report preliminary results from screening four compound collections: the Tocriscreen Stem Cell Toolbox (80 compounds), Selleckchem Epigenetics library (151 compounds), the representative sets from the MicroSource Discovery Systems Spectrum Collection (2650 compounds) and the Center for Pharmaceutical Research and Innovation (CPRI, 210 natural products). Several tail regeneration and developmental modulators were identified where subsequent dose response, expression-profiling and/or juvenile limb regeneration studies for select agents have been pursued. Our study establishes the axolotl hatchling as a chemical screening model to investigate signaling pathways associated with tissue regeneration and also implicates utility for toxicology screening.

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POSTER PRESENTATION #85

Abstract Title: **Microbial Natural Products Discovery from Unique Terrestrial Environments**

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Abstract: Natural products remain a major inspiration and source for drug leads and bioactive probes by virtue of their rich molecular and functional diversity. While the trends in microbial natural products discovery over the last decade have moved away from terrestrial microbes, we seek to explore the microbial diversity (and corresponding biosynthetic potential) of untapped terrestrial microbes from environments. As part of our ongoing natural product discovery program at the Center for Pharmaceutical Research and Innovation (CPRI) at the University of Kentucky, we examined soil samples collected from different sites in Kentucky (including thermal vents from underground coal mine fires, coal and lead mine reclamation sites, active underground and surface coal mines, and deep subterranean drilling sites as unique access to the rich biodiversity of Appalachian Kentucky and throughout the Commonwealth) with a focus upon culturable actinomycetes capable of producing novel secondary metabolites. Cumulatively, this program has led to the deposition of >800 non-redundant bacterial strains and >270 pure bacterial metabolites (nearly half of which are new natural products exclusive to the CPRI collection). This CPRI natural product repository represents broad chemical diversity and includes several chemical classes (terpenes, macrolides, macrolactams, aminocoumarins, indolocarbazoles, peptides, piericidins, aromatic polyketides, glycosides). CPRI has enabled University of Kentucky investigators with novel biochemical, cell-based and/or animal-model based assays access to the repository and this broad collaborative effort has led to discoveries of relevance to chemical probe and/or early stage lead development in the areas of cancer, infectious disease, neurodegenerative disease, spine/limb regeneration and drug addiction.

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POSTER PRESENTATION #86

Abstract Title: **Identification of a Small-molecule Inhibitor of Latexin as Regulator of Hematopoietic Stem Cells**

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Abstract: Objectives: Latexin (LXN) is the only known inhibitor of carboxypeptidase A3 (CPA3) in mammalian. In our previous study, LXN was identified as a negative regulator of hematopoietic stem cells (HSCs) population and can influence lifespan through its action on stem cell aging. We also found that LXN-knockout causes irradiation (IR) resistance of mouse and increases CPA3 protein level in HSCs. However, mechanism of how LXN regulating HSCs function is still unclear. In this study, by using high throughput screening (HTS) method and LXN knockout mice, we are aiming to 1) find potential pharmacological compound which can enhance HSCs IR resistance through LXN regulated pathway; 2) investigate what the role of LXN and CPA3 interaction in HSCs function. Methods: LXN inhibitor 911742 was selected using HTS method and its interactions with LXN and CPA3 were determined by molecular docking. Mouse leukemogenic cell line FDC-P1 harboring TAP tag LXN and empty vector will receive 6.5Gy IR, and after 24h 911742 treatment apoptosis changes will be determined by flow cytometry. HSCs (Lin⁻Sca1⁺c-kit⁺, LSK cells) from WT and LXN knockout mice will be treated with 911742 for 24h and harvested for colony forming assay and western blot. Results: Molecular docking revealed that interaction between 911742 and LXN can block LXN and CPA3 binding. 911742 increases FDC-P1 cell IR resistance and HSCs colony forming ability in a LXN dependent manner and causes CPA3 and Bcl-2 accumulation in cells. Conclusion: LXN inhibitor 911742 enhances HSCs proliferative potential and IR resistance by regulating LXN-CPA3 interaction. This will provide new potential pharmacological targets for patients received radiation therapy and reveal the new mechanism underlying LXN-CPA3 pathway in HSCs function.

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POSTER PRESENTATION #87

Abstract Title: **Evaluation of the combinational therapy cyclosporine A and phenelzine on protection of mitochondrial respiration following severe controlled cortical impact injury in rats**

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Abstract: Traumatic brain injury (TBI) represents a significant health crisis in the United States and there are currently over five million people living with a TBI related disability. However, acute treatment of TBI remains supportive and there are no FDA-approved pharmacotherapies available to prevent the devastating neurologic consequences of TBI. Following TBI, mitochondria buffer increases in intracellular calcium in an attempt to maintain homeostasis, however, increases in intra-mitochondrial calcium lead to generation of reactive oxygen and nitrogen species (ROS/RNS), induction of lipid peroxidation (LP), and formation of the LP-derived aldehydes, 4-HNE and acrolein. 4-HNE and acrolein covalently bind mitochondrial proteins, exacerbating production of ROS/RNS, mitochondrial dysfunction, and energy impairment. Eventually, mitochondrial dysfunction leads to opening of the mitochondrial transition pore (mPTP), extrusion of calcium back into the cytosol, activation of calpain, cytoskeletal degeneration, neuronal death, and neurologic impairment. Therefore, mitochondria are promising therapeutic targets for prevention of cellular death and dysfunction following TBI. Individual administration of cyclosporine A (CsA), an immunosuppressant with the ability to inhibit mPTP, or phenelzine (PZ), an antidepressant with aldehyde scavenging properties, has been shown to partially attenuate mitochondrial respiratory function following experimental TBI. Here, the ability of the combination of CsA (15min 20mg/kg i.p. loading dose + 10mg/kg/day s.c. osmotic pump) and PZ (15min 10mg/kg s.c. loading dose + 10mg/kg/day s.c. osmotic pump) to improve mitochondrial respiration 72h following severe controlled cortical impact injury in three month old male Sprague-Dawley rats is assessed in comparison to either agent alone.

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POSTER PRESENTATION #88

Abstract Title: **Comparison of Etest® and Broth Microdilution for Polymyxin Susceptibility against Carbapenem-resistant Enterobacteriaceae**

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Abstract: Background: Polymyxins are being revitalized to combat carbapenem-resistant Enterobacteriaceae (CRE). However, evaluating the activity of these agents by traditional broth dilution methods is not practical for busy clinical laboratories. We compared two quantitative susceptibility testing methods, Etest® and broth microdilution (BMD), against CRE isolates from patients at UK HealthCare. Methods: Polymyxin activity against CRE isolates was determined with Etest® by the UK HealthCare clinical microbiology laboratory as part of routine patient care. In addition, these isolates had polymyxin activity determined by BMD in our central research laboratory according to CLSI guidelines. The CLSI breakpoint of non-fermenting gram-negative bacteria (<2 mg/L) was used for polymyxin B and colistin. Very major errors were defined as a false susceptible result in Etest® compared to gold-standard BMD, and major errors were defined as a false non-susceptible result in Etest® compared to BMD. Essential agreement was defined as an MIC measured within 1 log₂ dilution. Categorical agreement was defined as the percentage of isolates classified in the same susceptibility category (susceptible or resistant) by BMD and Etest®. Results: Isolates collected from 2010-2014 (n=20) were primarily tested by colistin whereas isolates from 2014-2016 (n=11) were tested by polymyxin B. Susceptibility to polymyxin B and colistin was 60% in both BMD groups, but 100% and 90%, respectively, by Etest®. There were no major errors between testing methods, but the very major error rate of Etest® was surprisingly high – 100% and 75%, respectively. Essential agreement for polymyxin B and colistin Etest® compared to BMD was 30% whereas categorical agreement was 70% and 60%, respectively. Conclusions: Gradient diffusion methods, like Etest®, exhibit lower sensitivity for the detection of resistance against polymyxins when compared to dilution methods, like BMD. Better optimization of gradient diffusion methodology may be warranted to more effectively evaluate polymyxin B and colistin activity.

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POSTER PRESENTATION #89

Abstract Title: **Association of Liver Cirrhosis with In-hospital Outcomes and Costs in ICU Patients Requiring Renal Replacement Therapy**

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Abstract: Introduction: Critically ill patients with liver cirrhosis have higher morbidity and mortality than non-cirrhosis patients and frequently develop acute kidney injury requiring renal replacement therapy (AKI-RRT). We aim to compare in-hospital outcomes of critically ill cirrhosis and non-cirrhosis patients with AKI-RRT in the ICU setting. Methods: We conducted a retrospective cohort study of ICU patients admitted to the UK Chandler Hospital between September 2014 and December 2016. Data were electronically extracted from the UK Healthcare Enterprise Data Warehouse. We defined liver cirrhosis and AKI-RRT based on ICD-9/10 codes. We analyzed in-hospital mortality, length of ICU and hospital stay and cost associated with inpatient visits. We compared in-hospital outcomes in cirrhosis versus non-cirrhosis patients with AKI-RRT. Results: A total of 5229 patients were admitted to the ICU during the study period. Of these, 345 (6.6%) patients received renal replacement therapy and 74 (21.5%) patients had a diagnosis code of liver cirrhosis and AKI-RRT (hemodialysis or continuous renal replacement therapy). Compared to non-cirrhosis patients, cirrhosis patients with AKI-RRT had significantly higher in-hospital mortality (70.3% versus 45%, $p < 0.001$). However there was no significant difference in the ICU length of stay (17.15 ± 15.79 days versus 17.68 ± 21.12 days) or total hospital length of stay (30.19 ± 32.71 versus 29.63 ± 33.65). While average direct cost associated with hospitalization was slightly higher among patients with cirrhosis (\$77,426 versus \$73,104), this difference was not statistically significant. The results were similar when comparing cirrhosis vs non-cirrhosis AKI-RRT survivors. Conclusions: Liver cirrhosis patients with AKI that required RRT have significantly higher mortality than non-cirrhosis patients in the ICU. Further evaluation of patient-specific and treatment-specific modifiable risk factors is needed.

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POSTER PRESENTATION #90

Abstract Title: **Incidence of Acute Kidney Injury among Critically Ill Patients Receiving Vancomycin combined with Piperacillin-Tazobactam or Cefepime**

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Abstract: Background: Combination therapy with piperacillin-tazobactam (TZP) and vancomycin (VAN) has been associated with increased AKI incidence when compared to cefepime (CFP) and VAN. However, this was not seen in critically ill patients, we hypothesized that critically ill patients receiving TZP+VAN would have a higher AKI incidence compared to those receiving CFP+VAN. Methods: Clinical and demographic data were collected from the University of Kentucky Center for Clinical and Translational Science Enterprise Data Trust. Adult patients were included if they received TZP+VAN or CFP+VAN for ≥ 48 hours in the ICU. Patients were excluded for initial CrCl < 30 mL/min, receipt of other beta-lactam agents, past medical history of CKD. AKI cases were identified via the RIFLE criteria. Variables were analyzed via appropriate statistical tests. Patients were propensity score matched on a 1:1 basis on variables that were significantly different at baseline or associated with AKI. Results: Overall, 1,282 patients were included in the matched cohort with 641 patients in each group. The cohorts were similar in baseline AKI risk factors, except age (TZP+VAN 53.2 years vs. 51.3 years, $p=0.04$), hypertension (TZP+VAN 59.4% vs. 53.4%, $p=0.03$), and loop diuretic exposure (53.4% vs 46.7%, $p=0.02$). AKI was significantly more common in TZP+VAN patients (34.2% vs 17.8%, $p<0.00001$) and after controlling for remaining confounders, TZP+VAN had 2.51 times the odds of experiencing AKI than those in the CFP+VAN (95% CI 1.9-3.34). Conclusion: TZP+VAN therapy is associated with significant increases in AKI in critically ill patients compared to those who received CFP+VAN.

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POSTER PRESENTATION #91

Abstract Title: **Fluid Overload is Associated with Impaired Acute Kidney Injury Recovery in Critically Ill Sepsis Survivors**

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Abstract: Introduction: Fluid overload (FO) has been associated with increased mortality in ICU patients. FO can be a consequence of acute kidney injury (AKI) or may predispose to AKI by causing abdominal compartment syndrome or tissue edema. We aim to examine the association of FO with AKI recovery in critically ill sepsis survivors. Methods: We conducted a retrospective cohort study of ICU patients with severe sepsis or septic shock admitted to a tertiary hospital from May 2007 to April 2012. AKI was defined within 72 h of ICU admission utilizing serum creatinine (SCr)-KDIGO criteria. AKI recovery was evaluated using the ratio of follow-up SCr (from discharge to 90 days post-discharge) / baseline SCr (before indexed admission). A ratio ≥ 0.5 indicated impaired AKI recovery. FO percentage increase (%FO) was determined using the following formula: $\%FO = [(W + CFB/W) - 1] \times 100\%$, where W is the ICU admission weight and CFB is the cumulative fluid balance at 72 h of ICU admission. The independent variable was %FO in quartiles and the dependent variable was AKI recovery. Results: 6139 critically ill septic patients were evaluated. Of these, 3561 (58%) suffered from AKI. Hospital mortality increased with higher %FO quartile as follows (from 1st to 4th quartile): 12.5%, 18%, 27.3%, and 42.2% (P-trend < 0.001). A similar trend was observed for impaired AKI recovery (from 1st to 4th quartile): 22.2%, 22.1%, 25.1% and 30.6% (P-trend < 0.001). After adjustment for important confounders, sepsis survivors that suffered from AKI and had the highest quartile of %FO had 45% increased odds of impaired AKI recovery within 90 days post-discharge (adjusted OR 1.45, 95% CI 1.16 – 1.82, $p = 0.001$). Conclusion: Higher fluid overload is associated with impaired AKI recovery in critically ill sepsis survivors. Timely recognition and intervention to prevent worsening fluid overload is needed in ICU patients.

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POSTER PRESENTATION #92

Abstract Title: **Characterization of Idiopathic Tracheal Stenosis (ITS) and the Success of Its Therapy**

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Abstract: Objective: To assess presentation, delays in diagnosis and treatment outcomes of idiopathic tracheal stenosis. Study Design: Cross-sectional survey. Methods: 238 participants were recruited from the ITS Facebook group between September 2016 and February 2017 to complete a questionnaire regarding their experiences with diagnosis and treatment of their disease. Results: 235 of 238 participants completed the survey. 98% were female with a median age of 48 years old. The median BMI was 29.0. ~58% of the participants had onset of symptoms in their 30s and 40s. The most common presenting symptoms were wheezing (97%), coughing (94%) and shortness of breath (94%). On average, participants experienced symptoms for 6-12 months prior to seeing a medical provider with >50% reporting another 12 months before being diagnosed with ITS. Participants saw ~4 different medical providers prior to diagnosis, which was most commonly made by an Otolaryngologist (63%). After diagnosis, 94% underwent surgical management within 1 month. Most common initial procedure was endoscopic dilation (61%). Participants had undergone a median of 4 total procedures. ~80% of participants were satisfied or very satisfied with their treatment. Conclusions: ITS is predominantly diagnosed in Caucasian females in their 30s to 40s. Time from symptom onset to correct diagnosis and treatment is often greater than two years. Patients with ITS undergo multiple procedures but most are satisfied with their treatment. Efforts are needed to decrease delay in diagnosis and increase awareness of ITS among medical practitioners.

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POSTER PRESENTATION #93

Abstract Title: **Liquid-Phase Laser Ablation for the Controlled Synthesis of Upconverting Nanomaterials**

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Abstract: Upconverting luminescent nanoparticles are useful for many biomedical applications including targeted drug delivery, bio-imaging and sensing, and photodynamic therapy, among others. This type of material utilizes the energy transfer upconversion mechanism where a Yb³⁺ sensitizer absorbs near-infrared (NIR) photons and transfers its energy to an activator ion (Er³⁺, Nd³⁺, Dy³⁺, Ho³⁺, and Tm³⁺) which emits photons in the visible range. By utilizing a NIR excitation source these nanoparticles are able to be excited in the optical window where light has maximum depth of penetration for biological tissue, avoiding the limitations present in materials excited with shorter wavelength photons that exhibit low depths of penetration. Thermal decomposition, coprecipitation, and solvothermal synthesis have widely been used for producing upconverting nanoparticles, but these methods have limitations of toxic byproducts, high reaction temperatures, long reaction times, and/or poor control of morphology. We report liquid-phase laser ablation synthesis of NaYF₄:Yb³⁺/Er³⁺ nanoparticles with various Yb³⁺/Er³⁺ ratios. In this synthesis, a target material is produced through coprecipitation, followed by annealing at 600 °C and then 532 nm pulsed nanosecond laser ablation in water. The laser causes the formation of plasma plumes that quickly expand, cool and condense into nanoparticles. The resultant nanoparticles show stronger emission at 652 and 669 nm and weaker bands at 407, 488, 523, 544, 556 nm which can easily be assigned to various atomic transitions of the Er³⁺ ion. Our experiments show that the Yb³⁺/Er³⁺ ratios and laser ablation parameters (laser power and wavelength as well as laser ablation duration) allow control of the upconversion efficiency, chemical structures, and sizes of the nanoparticles.

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POSTER PRESENTATION #94

Abstract Title: **Using Calibrated Proton Density Imaging to Measure Blood-Brain Partition Coefficient in Aging and Alzheimer's Disease Mice**

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Abstract: Purpose: In the present study, we determine the blood-brain partition coefficient (BBPC) in aging C57Bl6/N mice and the transgenic 129S6/Tg2576 mouse model of Alzheimer's disease using a calibrated proton density imaging approach. This parameter is an important coefficient in the quantification of cerebral blood flow (CBF) derived from arterial spin labeling (ASL) acquisitions. Previous studies have shown both regional and age-related differences in BBPC in humans, yet the current consensus in the field does not correct for these differences but instead assumes a single constant value for all regions and all patients. Arterial spin labeling has become particularly relevant in the study of brain aging where it has been used to image the vascular dysfunction that occurs with advanced age. In Alzheimer's disease it has also shown sensitivity to the vascular dysfunction which precedes amyloid and tau pathologies. This has been recapitulated in small animal models such as the 129S6/Tg2576 mice which have the human Swedish amyloid precursor protein (hAPP) mutation. However, the limitations of small animal scanners and the inherent low signal of ASL techniques require quantification models to be as precise as possible. Furthermore, any uncorrected variation in BBPC could potentially bias CBF measurements. For this reason, we test the hypothesis that BBPC will be reduced in aged C57Bl6/N mice and transgenic 129S6/Tg2576 mice. Methods: Imaging Protocol- Male C57Bl6/N wild type mice aged 3 months (n=8) and 12 months (n=8) as well as male 12-month-old 129S6/Tg2576 (n=6) with their 129S6 wild type controls (n=3) were imaged using a 7T Bruker ClinScan (Bruker Biospin, Ettlingen, Germany) with a 39mm diameter birdcage transmit/receive coil. Inside the coil was placed a series of phantoms with 0, 10, 20, 30, and 40% deuterium oxide in water that were also doped with gadobutrol (Gadavist, Bayer Healthcare Pharmaceuticals, Whippany NJ, USA, 0.07 mM) such that the T1 was approximately 2.0s. Blood was drawn from the facial vein of each subject and placed in a capillary tube alongside the deuterated phantoms. A series of image stacks were acquired with a phase-spoiled, FLASH-GRE sequence (FOV = 2.8cm x 2.8cm, matrix = 256 x 256, slice thickness = 1mm, number of slices = 10, flip angle = 90°) with a very short TE (3.2ms) and 6 different TR values (125, 187, 250, 500, 1000, 2000ms). Image Analysis- For each transverse slice, the TR-series was fit to the mono-exponential recovery curve $S = M0 * [1 - e^{-(TR/T1)}]$ in a voxel-wise manner yielding maps of both apparent T1 and relative proton density, M0. The relative M0 maps were calibrated to a regression line of the average M0 values in regions of interest (ROIs) drawn in the deuterated phantoms. Therefore, the calibrated M0 values represent the percent water content of each voxel. The BBPC value is then calculated by dividing by the average M0 value in the blood sample and the average density of brain tissue, i.e. $BBPC = M0_{brain} / (M0_{blood} * 1.04g/mL)$. An ROI was then drawn manually for each transverse slice excluding any susceptibility artifacts. BBPC values were averaged over all ROIs for each mouse. Results: The calibrated proton density imaging protocol was able to produce high resolution, low noise maps of BBPC despite reducing scan time from 2 hours, as in Leithner et al., to 25 minutes. The 12 month old mice demonstrated a 5.5% reduction in BBPC ($\mu = 0.94 \pm 0.04$ mL/g) compared to the 3 month old mice ($\mu = 0.99 \pm 0.04$ mL/g, $p = 0.02$). Preliminarily, the Tg2576+ mice demonstrate an elevated BBPC ($\mu = 0.103 \pm 0.04$ mL/g) compared to WT ($\mu = 1.00 \pm 0.05$ mL/g), though more subjects are needed. Discussion/Conclusion: The variability of BBPC values from these data demonstrates the potential error in assuming a constant value for all patients when calculating CBF. When measuring CBF in aging mice, failing to correct for the reduced BBPC will overestimate CBF resulting in reduced sensitivity. However, it appears that in the 129S6/Tg2576 model the elevated BBPC may be a confounding factor. Scan time can be reduced further by reducing the resolution to match ASL acquisitions making this technique a potentially viable method of correcting CBF measures for differences in BBPC.

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POSTER PRESENTATION #95

Abstract Title: **White Matter Abnormalities Associated with Subclinical Metabolic Syndrome in Healthy Older Adults**

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Abstract: Metabolic syndrome has been estimated to effect about 34% of adults in the US and is associated with increased rates of cerebrovascular disease and cognitive decline. However, the relationship between metabolic syndrome, altered brain structure and cognition is multifactorial and has only been demonstrated after chronic disease has clinically manifested. We investigated the five individual components of metabolic syndrome in association with cognitive function and the primary marker of cerebrovascular disease, white matter hyperintensities (WMH). This allowed us to explore the existence of any subclinical brain abnormalities and/or cognitive decline in cognitively and otherwise healthy adults. Thirty-seven healthy subjects (age 63.2 +/- 2.9, 12 male) underwent a series of cognitive tests, a blood draw, and magnetic resonance imaging (MRI). Blood samples were used to measure non-fasting triglycerides, non-fasting glucose and cholesterol. In addition, resting systolic blood pressure and body mass index were also measured. These five metrics were used to generate an average and assessed both as a composite and separately. As part of the MRI protocol, FLAIR imaging was collected and analyzed in order to quantify WMH volume. After adjusting for age and sex, there was a significant positive correlation between WMH and the combined metabolic syndrome components ($r = 0.41$, $p = .02$). When explored separately, there was a significant positive correlation between WMH and both non-fasting glucose ($r = 0.46$, $p = .02$) and non-fasting triglycerides ($r = 0.40$, $p = .03$). However, there was no significant negative correlation between the combined metabolic syndrome components and cognitive function. These findings suggest that alterations in the brain may occur prior to the clinical manifestation of metabolic syndrome.

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POSTER PRESENTATION #96

Abstract Title: **White Matter Microstructure in the Default Mode Network Mediates Executive Function Declines Associated with Aging, Alzheimer's, and Cerebrovascular Pathology**

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Abstract: Objective: This study investigated whether white matter (WM) microstructure in the default mode network (DMN) may serve as a common marker of executive function decline due to age, Alzheimer's disease (AD), and cerebrovascular disease (CVD). Methods: 32 older adults underwent diffusion tensor imaging (DTI), FLAIR imaging, cerebrospinal fluid (CSF) sampling, and neuropsychological assessment. Fractional anisotropy (FA) was measured in WM pathways connecting DMN regions. WM lesion (WML) volume in DMN-WM was quantified using FLAIR images, and CSF was analyzed for levels of A β 42. Cross-sectional relationships between variables were explored with additional longitudinal follow-up underway. Results: Partial correlations controlling for sex and education revealed relationships between measures of age, WML volume, and CSF A β 42 with both executive function ($r = -.39, -.32, .37$) and FA in DMN-WM ($r = -.38, -.39, .44$), which was also associated with executive function ($r = .65$). Separate mediation analyses found that FA in DMN-WM mediated the effect of age (58% mediation, indirect effect (ab) = -0.16, 95% CI: [-0.36, -0.04]), CSF A β 42 (72% mediation, $ab = 0.17$ [0.04, 0.34]), and WML volume (76% mediation, $ab = -0.16$ [-0.43, -0.03]) on executive function. Conclusion: These results point to alterations in WM microstructure as an underlying mechanism of executive declines associated with aging, AD, and CVD. Further, interventions preserving WM microstructure may protect against the negative impact of multiple pathologies.

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POSTER PRESENTATION #97

Abstract Title: **Novel Applications of MRI Techniques in the Detection of Neuronal Dysfunction before Tangle Pathology in Tau Transgenic Mice.**

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Abstract: Background: Tauopathic patients have significant cognitive decline accompanied by severe, irreversible brain atrophy. Neuronal dysfunction is thought to occur years before diagnosis. A major obstacle in the treatment of tauopathies is that current diagnostic tools are ineffective at detecting pre-pathological changes. We previously developed a MEMRI (manganese-enhanced magnetic resonance imaging) protocol coupled with R1-mapping to measure the extent of neuronal dysfunction that occurs before appearance of cognitive deficits and tau pathology associated with the rTg4510 tau model. In this study, we performed MEMRI with mangafodipir, an FDA-approved contrast. Methods: We used MEMRI to measure neuronal dysfunction in rTg4510 mice tau transgenic mice at 2 months (no pathology/cognitive deficits), and 3 months (presymptomatic pre-tangle pathology detectable). We measured MEMRI R1 changes before (baseline) and after (time-course) injecting mangafodipir (50mg/kg) intraperitoneally. We focused on the superior cortex and hippocampal sub-regions. Results: We found mangafodipir to be an effective contrast for MEMRI of mouse brains. Optimal enhancement of the cortex and hippocampus occurs 12-24 hours post-injection. Conclusions: This study builds upon our previous work showing that MEMRI (with MnCl₂) reveals important functional differences between tau transgenic and non-transgenic mice. Here we found that mangafodipir is as effective as MnCl₂ in performing MEMRI. Mangafodipir exhibits less toxicity than MnCl₂ due to structural similarity to EDTA (used to treat manganese toxicity), making mangafodipir a target for translation of MEMRI for tauopathy into human subjects.

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POSTER PRESENTATION #98

Abstract Title: **Using Wide-Field Fluorescent Angiography and Fundus Autofluorescent to Identify High-Risk Features of Patients with Acute Onset Posterior Vitreous Detachments for Progression to Retinal Detachment.**

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Abstract: BACKGROUND: Posterior vitreous detachment (PVD) is a condition in which the vitreous of the posterior eye begins to liquefy and separate the vitreous hyaloid from the retina. The major risk with acute PVD is a retinal tear, which occurs in over 10% of patients and is often located in the far periphery of the retina requiring visualization by dilated ophthalmoscopy with scleral depression. Ultra-widefield (UWF) retinal cameras allow for color and fluorescein imaging of over 200 degrees of the retina and may be useful in revealing high-risk features of the peripheral retina that predispose to the development of tears. OBJECTIVES: This is a prospective study to utilize UWF imaging to visualize the peripheral retina during natural progression of acute PVD and identify areas susceptible to retinal tears. METHODS: Patients (n=100, >18 years of age, not child bearing, no pre-existing retinal disease) with acute PVD and controls (n=10) with chronic PVD without evidence of retinal tears are being enrolled (UK IRB 16-1048-F6A). UWF imaging (d0/7/28) will assess the integrity of the retinal tissues, and fluorescein angiography will visualize peripheral retinal vascular features. Standard of care treatment with dilated exam and scleral depression is performed as well. Abnormal features in eyes that progress to retinal tears will be further studied by qualitative assessment. CONCLUSION: UWF may aid in the detection of high-risk features of the peripheral retina during natural progression of acute PVD. We have established feasibility of this technique and are currently recruiting for this study.

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POSTER PRESENTATION #99

Abstract Title: **Eulerian Video Magnification: A Novel Approach to Assess Choroidal Blood Flow**

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Abstract: Diabetic retinopathy is an increasingly prevalent disease, and a leading contributor to the burden of all-cause blindness worldwide. In addition to retinal changes, choroidal abnormalities are common in patients with diabetes. Indocyanine green (ICG) angiography, which can be seen through the RPE layer, has been used to visualize choroidal vessels filling abnormalities in eyes of patients with retinopathy, such as diabetics. Although this technique can detect gross vascular defects, it does not provide much information concerning anatomic or structural features of the choroid and it requires static images taken over sequentially over minutes. Additionally, the ICG contrast dye is known to cause allergic reactions, and requires venipuncture. We aim to investigate the application of Eulerian Video Magnification (EVM) to assess choroid vasculature perfusion quickly and noninvasively. The EVM algorithm, developed at Massachusetts Institute of Technology, amplifies small changes from seemingly static video, and has been demonstrated to rapidly visualize the human pulse. Preliminary studies from our laboratory have shown the ability of this novel technique to visualize choroidal perfusion using a standard short video of the retina, which can be accomplished noninvasively. We will build upon our preliminary data and establish this technique as a noninvasive choroidal imaging modality with the long-term goal of using it to improve our understanding of the role of the choroid in retinal pathologies that involve alterations of choroidal perfusion, such as diabetic choroidopathy, macular degeneration and central-serous chorioretinopathy.

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POSTER PRESENTATION #100

Abstract Title: **Pol Versus Env Genetics in SHIV-Infected Macaques Highlights Importance of Phylogenetic Signal**

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Abstract: Previously we investigated HIV pol populations in SHIV-infected macaques by single-genome sequencing to determine if low-level replication was a source of residual viremia during ART and to investigate viral compartmentalization across tissues. Using this approach, we found no evidence for evolution during suppressive ART and little evidence of viral compartmentalization. To investigate the possibility that the low diversity in pol masked the emergence of new viral variants and/or compartmentalization, we applied the same methods to the more diverse env gene in the infected macaques. Two macaques (M03250 and K02396) received 20 weeks of ART (TNF, FTC, EFV) and one macaque (6760) was untreated. Longitudinal plasma samples (N=11) from treated macaques were analyzed by single-genome sequencing of a 1 kb pol fragment and a 2.5 kb env fragment. Tissues were collected at necropsy after infection for 30 weeks of infection and single-genome sequences were obtained from a plethora of tissues. The entire 2.5kb env fragment and the 101 nucleotide V3 region alone were evaluated separately for population diversity, divergence, and compartmentalization using phylogenetic and panmixia analyses, and compared to results from pol. Phylogenetic and panmixia analyses of 2.5kb env sequences in plasma did not reveal the emergence of new variants during ART, showing that the lack of evolution in pol was not due to low phylogenetic signal in this region. Env populations analyzed in tissues from 6760 were highly diverse but showed similar population structures to pol and a lack of tissue compartmentalization. By contrast, phylogenetic analyses of only the V3 env region showed very weak phylogenetic signals and little diversity, indicating that the V3 region is not appropriate to evaluate intra-individual populations for diversity, evolution, and phylogenetic structure. These findings highlight the importance of performing single-genome and deep sequencing on regions of the viral genome with strong phylogenetic signal.

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POSTER PRESENTATION #101

Abstract Title: **CD8+ T cells remove *Toxoplasma gondii* cysts by recognizing common or cross-reactive epitopes expressed in both genotypes II and III of the parasite**

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Abstract: *Toxoplasma gondii*, an obligate intracellular parasite, establishes a chronic infection by forming tissue cysts preferentially in the brain. This chronic infection is ubiquitous worldwide, and up to one third of human population is estimated to be infected with this parasite. It is well recognized that this chronic infection can reactivate and develop life-threatening toxoplasmic encephalitis in immunocompromised individuals. Even in immunocompetent individuals, *T. gondii* infection is associated with increased risk and mortality of brain cancers. However, there are currently no drugs effective on the cysts of the parasite. Therefore, to improve public health, it is critical to develop a new method to eliminate *T. gondii* cysts from chronically infected individuals. Our previous study demonstrated that CD8+ T cells of mice genetically resistant to the infection have a capability to remove *T. gondii* cysts from the brain. The majority of *T. gondii* isolates from infected people in North America and Europe are one of three genotypes, types I, II, and III; type II is predominant and type III is also common in the isolates from immunocompromised individuals. We here show that a transfer of CD8+ immune T cells primed with a type II or a type III strain of *T. gondii* both efficiently removed cysts of a type II strain from infected SCID mice, although the former tended to be slightly more efficient than the latter. Similarly, a transfer of type II-primed CD8+ T cells removed cysts of a type III strain. Therefore, CD8+ T cells are capable of removing *T. gondii* cysts by recognizing epitopes commonly expressed in types II and III strains or cross-reactive between these two genotypes.

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POSTER PRESENTATION #102

Abstract Title: **Examining Incidence and Cost Related to Acute Kidney Injury in Hospitalized Patients with Infective Endocarditis**

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Abstract: Introduction: Infective endocarditis (IE) is a detrimental condition associated with high morbidity and mortality. Patients with IE can develop distinct forms of acute kidney injury (AKI) related to the infection or the antimicrobials used for treatment. We aim to examine the incidence, timeline occurrence and cost of AKI in hospitalized patients with IE. Methods: A retrospective cohort study of hospitalized patients with IE admitted to UK hospital from 2013 to 2015. IE was defined by modified Duke criteria. AKI was defined utilizing serum creatinine-KDIGO criteria. AKI was classified as early if it occurs within the first 72 h of admission and late if it occurs after 72 h of admission. Patients with diagnosis of end-stage renal disease or kidney transplant before the indexed admission were excluded. Results: A total of 303 patients were included in the study. Of these, 59% were men and 95% were white. Mean age (SD) was 45.5 (16) years and the median length of hospital stay (IQR) was 19 (8–42) days. AKI occurred in 190 (63%) of patients. Of these, 56 (29.5%) developed early AKI and 134 (70.5%) had late AKI. Hospital mortality was significantly higher in patients that develop early AKI (30.4% vs 14.2% in those with no AKI, $p=0.01$; and 30.4% vs 15.7% in those with late AKI, $p=0.02$). The median (IQR) total direct hospitalization cost was \$14,801 (6,758–30,526) for no AKI; \$25,755 (10,336–70,409) for early AKI and \$55,956 (32,943–74,356) for late AKI (p -trend <0.01). Conclusion: Two out of three hospitalized patients with IE develop AKI. Most episodes of AKI occur after 72 h of hospital admission. The occurrence of early AKI is associated with higher hospital mortality. The occurrence of late AKI, which is likely related to nephrotoxicity from antimicrobials, is associated with higher total direct cost.

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POSTER PRESENTATION #103

Abstract Title: **Making a Difference in Staphylococcus aureus Bacteremia**

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Abstract: While data exists to support a reduction in mortality from Staphylococcus aureus bacteremias with treatment guideline adherence, compliance in practice is suboptimal. To encourage evidence-based practices, a S. aureus bacteremia institutional guideline was developed and the adherence results were evaluated in a previous study. Pre- and post-guideline data demonstrated a significant increase in appropriateness of therapy with no difference in total guideline adherence or mortality, likely due to small sample size. The primary objective of the current study is to evaluate associations between an antimicrobial stewardship consult and all-cause mortality in S. aureus bacteremia patients within 30 days of diagnosis. Secondary objectives include analysis of total guideline adherence and appropriateness of therapy. A quasi-experimental approach evaluated a pre-implementation period from 2014-2015 and a post-implementation period from 2015-2017 for a S. aureus bacteremia institutional guideline. An antimicrobial stewardship consult note was utilized to provide guideline-based. Inclusion criteria consisted of patients 18 years or older with first time S. aureus bacteremia diagnosis identified by the Verigene® Nanosphere rapid diagnostic system. Patients were excluded if receiving comfort care, if transferred to another facility or if the patient expired within 48 hours of the first positive blood culture. Medical record notes were written at 48-72 hours and 5-7 days after collection of the first positive blood culture, and on the last day of therapy or day of discharge, whichever came first. Data collection and analysis is ongoing. Thus far, 175 patients in the pre-protocol and 175 patients in the post-protocol implementation groups are included.

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POSTER PRESENTATION #104

Abstract Title: **Detection and Handling of Spectral Artefacts in Fourier Transform Mass Spectra of Metabolomics Experiments**

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Abstract: Fourier-transform mass spectrometry (FTMS) allows for the high-throughput detection of thousands of metabolites. Conservatively, over 90% of the observed spectral features do not correspond to known metabolites and cannot be placed into existing metabolic networks. Without accurate assignment of these features, discerning their roles within living systems is effectively impossible. Assignment remains difficult due to the low concentrations of some detected metabolites, the volume of data produced by FTMS and the small m/z differences between isotopologues. Additional phenomena producing large numbers of spectral artefacts further complicate FTMS assignment. Assignments made to these artefact peaks can create large interpretative errors. We have observed three types of artefacts unique to FTMS that often result in regions of abnormally high peak density which we collectively refer to as high peak density artefacts. 1 - Fuzzy sites: small regions of m/z space with a 'fuzzy' appearance due to the extremely high number of peaks. 2 - Ringing: where a very intense peak produces side bands of decreasing intensity that are symmetrically distributed around the main peak. 3 - Partial ringing: where only a subset of the side bands are observed for an intense peak. Fuzzy sites and partial ringing appear to be novel artefacts previously unreported in the literature and we hypothesize that all three artefact types derive from Fourier transformation defects. We have developed a set of tools to detect these artefacts and are developing new methods to mitigate or eliminate their effects on spectra and downstream analyses.

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POSTER PRESENTATION #105

Abstract Title: **Automated High-Content Analysis of Skeletal Muscle Immunohistology**

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Abstract: High volume analysis of skeletal muscle histological cross sections is often necessary for studying muscle physiology. As automation improves for immunohistochemistry and fluorescence microscopy, preparation and imaging of muscle sections is performed with ever increasing speed and efficiency. As such, high content image data analysis represents the most significant bottleneck in workflow, especially for large-scale studies. To date, no fully automated, accurate, and reliable software is yet available to muscle researchers. Therefore, we introduce FiberVision, a software that 1) improves upon previously reported algorithms, 2) achieves > 94% accuracy for myofiber detection, size measurement, type classification, and myonuclear counting without human input, and 3) is available with a readily usable interface. FiberVision is the most robust, intuitive and free software available for muscle histological analysis, and will greatly improve analysis efficiency for the spectrum of muscle researchers.

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POSTER PRESENTATION #106

Abstract Title: **Genetics of RIN3 Expression in Alzheimer's Disease**

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Abstract: A recent meta-analysis compiling GWAS data from 74,046 individuals identified 19 statistically significant Alzheimer's Disease (AD) susceptibility loci. One of these loci, rs10498633, was protective to the disease and in linkage with the genes SLC24A4 and RIN3. Although the former is expressed in the brain and potentially involved in neuronal development, the latter, RIN3, encodes a protein that is involved in endocytic vesicular trafficking and directly interacts with BIN1 (linked to tau-pathology in AD) and CD2AP (linked to late onset AD). Our lab maintains a library of cDNAs reverse transcribed from RNA isolated from 61 brain samples acquired from individuals who were longitudinally followed prior to death. These cDNA samples include those from 30 AD brains and 31 non-AD brains. To begin to determine the mechanism of the AD-associated SNP action, we determined the absolute amounts of alternatively spliced isoforms of RIN3 transcripts by using primers designed to selectively amplify specific isoforms by qPCR. The amounts of RIN3 isoform transcripts were compared to each other as well as with other relevant genes. Immunostaining was also performed with a RIN3 antibody on human brain sections of temporal cortex. In qPCR evaluation, we observed a significant increase in RIN3 expression in AD and significant variations in alternative splicing associated with rs10498633, implying these changes may contribute to the protective mechanisms of the SNP in reducing AD risk. Strikingly one alternatively spliced isoform with a pre-mature stop codon appears to evade nonsense-mediated decay, perhaps through translation re-initiation. Finally, we provide evidence which suggests RIN3 is expressed in numerous central nervous system cell types including endothelial cells, neurons, and astrocytes, potentially indicating that alterations in RIN3 may have a role in endothelial dysfunction, neuronal tau pathology, or modifications to blood brain barrier permeability.

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POSTER PRESENTATION #107

Abstract Title: **'Keeping Active': Comparison of Active Learning Techniques in Teaching Neuroanatomy to First-Year Medical Students**

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Abstract: Purpose: To compare the effectiveness, as measured by student's test scores, of two active learning strategies used to teach imaging anatomy in a first-year neuroanatomy course: audience response incorporated into a traditional didactic lecture versus audience response in the context of a "flipped classroom" approach. Methods: A retrospective review of student test performance was performed on ten multiple choice imaging-specific questions, comparing students taught with audience response alone (n=256) to those taught with audience response in the context of a flipped classroom approach (n=274). A test question had to be administered at least once to each group to be included in the analysis. Population test score variance was determined via an F-test, and the Satterthwaite method was used for variance estimation. The mean test scores were compared using a t-test. Results: There was no significant difference in the mean test scores for students taught using audience response in the context of a didactic lecture (mean 0.9385 ± 0.005) and those taught with audience response incorporated into the flipped classroom method (mean 0.9362 ± 0.004). Conclusion: Regarding test performance, the flipped classroom approach may not offer any advantage over other active learning strategies in teaching imaging anatomy to medical students.

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POSTER PRESENTATION #108

Abstract Title: **Body Composition Affects NK Cells in the Elderly: Adipose Tissue Correlates with Plasma IL-15**

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Abstract: NK-mediated cytotoxicity and cytokine secretion decline with aging. With this decline, infections, cancers, and deaths increase. NK cells require IL-15 for development and homeostasis. The main sources of immune system IL-15 are macrophages and dendritic cells. We postulated that muscle and adipose tissues also provide a significant source of IL-15, especially in aging, when immune cell functions decline. We tested 50 healthy adults aged >70 years old and correlated their body composition to IL-15 level, and NK cell function. Adipose and skeletal muscle cross-sectional areas (cm²) were measured by CT scanning of the mid-thigh and abdomen. Plasma IL-15 was measured by ELISA. NK cell phenotyping and function were analyzed by flow cytometry. Subcutaneous adipose tissue significantly correlated with NK cell expression of the immune regulatory molecule, CD38. Abdominal visceral fat mass significantly correlated with IL-15 level. This correlation proved even stronger in non-obese subjects. Plasma IL-15 level did not correlate with mid-thigh skeletal muscle, but significantly correlated inversely with muscle strength. We tested muscle and adipose tissue biopsies from a separate cohort; these tissues had similar IL-15 RNA levels, but adipose tissue expressed more of the IL-15 chaperone, IL-15R α . NK cells were stimulated in vitro with K562 leukemia cells and with immobilized anti-NKp46 antibody. Plasma IL-15 significantly correlated with NK cell cytotoxic activity and with CCL4 (MIP-1 β) production in response both to K562 cells and to NKp46-crosslinking. Visceral fat produces harmful inflammatory cytokines. We propose that visceral fat in elderly humans also produces IL-15 and supports NK cells.

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POSTER PRESENTATION #109

Abstract Title: **Antibody binding differences in alpha-synuclein derived from Parkinson's disease and multiple system atrophy brain tissue**

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Abstract: Hypothesis: Abnormally aggregated alpha-synuclein found in Parkinson's disease (PD) and multiple system atrophy (MSA) brains has different conformations and thus will exhibit different antibody-binding abilities. Background: In synucleinopathies such as PD and MSA there is growing support for the idea that different conformations of alpha-synuclein underlie the clinical and pathologic differences seen in these two diseases. In prior studies we found alpha-synuclein seeding ability present in both PD and MSA brain extracts using a cell-based FRET assay. Here we test biochemical and antibody-binding between alpha-synuclein in these two diseases. Procedures: Brain tissue from patients with PD (n=3) and MSA (n=3) was serially extracted to yield detergent-insoluble fractions. We used commercial antibodies and novel antibodies generated to alpha-synuclein to test MSA and PD fractions for binding of alpha-synuclein by immunoprecipitation. The forms of alpha-synuclein bound to the antibodies were assessed by fluorescence microscopy for ability to induce aggregates in cells overexpressing alpha-synuclein. Results: There were distinct differences in the ability of various antibodies to bind to alpha-synuclein from PD vs MSA. Both commercial and novel antibodies were able to bind a form of alpha-synuclein which was capable of seeding synuclein aggregation in the cell-based assay from MSA samples, but not from PD samples. Conclusions: Differential antibody binding implies that different epitopes are available for binding in the aggregated state. This supports the idea that conformational differences exist in alpha-synuclein in MSA and PD and may underlie the diverse clinical and pathologic characteristics seen in these two synucleinopathies.

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POSTER PRESENTATION #110

Abstract Title: **Pathological Role of Visceral White Adipose Tissue in Development of Severe Acute Pancreatitis**

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Abstract: Elderly patients with acute pancreatitis (AP) often develop a severe life-threatening condition with necrotizing pancreas, multi-organ dysfunction, and high mortality. Our previous studies point to the cytokine interleukin 6 (IL-6) as playing a major role in AP progression. The objective of this study was to identify the origin of IL-6 and elucidate mechanisms contributing to severe AP (sAP) in the aged. AP was induced in mice (aged, 23-24 months). A subgroup of mice was subjected to surgical removal of visceral adipose tissues. Approximately 50% of mice developed sAP determined by high plasma creatinine. Plasma levels of IL-6 in mice with sAP were significantly higher than in those with mild AP ($p < 0.01$). Mice with sAP exhibited strong expression of IL-6 in visceral adipose tissue, far stronger than in any other organ examined. Compared to mice with mild AP, mice with sAP showed elevated peritoneal lipase activity at 1h and plasma free fatty acid levels at 24h ($p = 0.05$), which correlated strongly with plasma IL-6 levels ($R^2 = 0.89$ and 0.77 , respectively). AP was significantly milder in mice with surgical removal of fat compared to sham, evidenced by lower plasma levels of IL-6 ($p < 0.01$), free fatty acids ($p < 0.05$), and creatinine. There was no difference in peritoneal lipase activity between the groups indicating that initial pancreatic damage was equivalent. These data support our hypothesis that: (1) lipase released from the damaged pancreas injures visceral adipose tissue and causes severe inflammation, and (2) IL-6 and free fatty acids released from damaged adipose tissues contribute to the development of sAP.

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POSTER PRESENTATION #111

Abstract Title: **Regulation of intestinal villus cell brush border membrane bile acid co-transport in obesity**

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Abstract: Altered lipid homeostasis causes many of the morbidities of obesity. However, how intestinal bile acid (BA) absorption, perhaps the most important component of lipid homeostasis, may be altered during obesity is poorly understood. Intestinal lipid absorption requires BAs, which are reabsorbed in the terminal ileum via Na-dependent co-transport (ASBT/SLC10A2) on the brush border membrane (BBM) of villus cells. Inhibition of ASBT activity has been shown to reduce lipid and lipid soluble vitamin absorption resulting in malnutrition. However, while lipid absorption has shown to increase in obesity, how ASBT may be altered is not known. In this study, BBM Na-BA co-transport in Obese Zucker rats (OZR) was significantly increased compared to that from leans (LZR). Since Na/K-ATPase affects ASBT function at the intact cell level, it was measured and interestingly, found to be reduced. ASBT protein expression increased three-fold in the BBM of the intestinal cells from OZR. There was also a 3-fold increase in ASBT expression in protein preparations from whole intestinal cells from OZR, suggesting ASBT stimulation likely to be secondary to increased transcription of the protein. The levels of BA activated transcription factor, farnesoid-X-receptor, known to increase ASBT gene expression, was also increased two-fold in OZR. Therefore, Na-bile acid co-transport increase in obesity is not secondary to altered Na-extruding capacity of villus cells. The mechanism of stimulation of ASBT is likely secondary to increased synthesis of the BBM co-transporter. Better understanding of the regulation of BA absorption which directly affects lipid absorption may result in novel and efficacious treatment modalities for obesity.

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POSTER PRESENTATION #112

Abstract Title: **PGRMC1/S2R: A Targetable Mechanism for Insulin Receptor Signaling**

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Abstract: Background: As of 2014, 29.1 million Americans suffer from diabetes, creating a severe socioeconomic and medical burden on society. Impaired insulin signaling is central in the development of type 2 diabetes, presenting a unique therapeutic challenge. Insulin resistance is associated with a reduction in Insulin Receptor (IR) kinase activity and activation of the PI3K (phosphatidylinositol 3-kinase) pathway. Additionally, obese individuals show decreased insulin binding due to a reduction in IR levels without an alteration in ligand-receptor binding affinity. The progesterone receptor membrane component 1 (PGRMC1), also known as sigma-2 receptor (S2R), is an endosomal protein that promotes cellular signaling via receptor trafficking. A recent translational study determined that PGRMC1 was decreased in patients with insulin-resistant disease, suggesting a role in insulin signaling. Methods: Human subcutaneous adipose tissue was obtained from human patients with BMI ranging from 28-35 courtesy of Dr. Philip Kern. Tissue samples were maintained at -80C until digestion with RIPA buffer and immunological analysis. Fully differentiated human subcutaneous adipocytes were purchased from Zenbio, Inc., and maintained according to the manufacturer's protocol. Differentiated subcutaneous adipocytes were treated with the PGRMC1/S2R ligands, AG205 (10 μ M) and PB28 (1 μ M), and analyzed via western blot. Results: Both Insulin Receptor β (IR β) and PGRMC1 protein levels decreased with increasing BMI in human subcutaneous adipose tissue. Treatment with AG205 and PB28 significantly increased IR β levels in fully differentiated human subcutaneous adipocytes from pooled donors (p=0.004 and p=0.027 respectively). Additionally, AG205 treatment increased IR β significantly (p=0.013) in differentiated adipocytes derived from a single female donor with a BMI of 38. Conclusion: Treatment with PGRMC1/S2R ligands increases IR β protein levels significantly in human adipocytes and plays a critical role in IR signaling after insulin stimulation.

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POSTER PRESENTATION #113

Abstract Title: **Effect of Neurotensin on Hepatic Fatty Acid Synthesis**

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Abstract: Neurotensin (NT) is a gut peptide that is released from enteroendocrine cells of the small intestine after fat ingestion. Our hypothesis is that NT deficiency protects hepatocytes from high fat diet (HFD)-induced hepatic steatosis by: (1) decreasing fatty acid (FA), triglyceride (TG), and cholesterol synthesis via activation of AMP-activated protein kinase (AMPK) and (2) increasing FA oxidation by enhancing mitochondrial activity. Primary mouse hepatocytes were isolated from murine livers and were treated with 0, 10, 100, 1000, 2000, and 4000 nM of NT. Western blots will be run to determine the effect on levels of phosphorylated AMPK (p-AMPK) and phosphorylated extracellular signal-regulated kinases 1 and 2 (p-ERK 1/2). Increases in p-ERK 1/2 and decreases in p-AMPK will indicate that these hepatocytes contain NT receptors. Future work will determine which NT receptor (NTR)—NTR1 or NTR3—plays a more significant role. Additionally, wild type (WT) and NT knockout (KO) mice were fed a low fat diet (LFD) or HFD for 24 weeks. After sacrifice, the average liver mass of the NT-KO mice on a HFD was significantly less than the average liver mass of the WT mice. Western blots and real time polymerase chain reactions (RT-PCR) of the liver tissue will be conducted for the following enzymes: p-AMPK, steroid response element binding protein 1-c (SREBP-1c), fatty acid synthase (FASN), and HMG-CoA reductase. If liver tissues from NT KO mice fed a HFD have increases in p-AMPK and SREBP-1c and decreases in FASN and HMG-CoA reductase, then this will suggest that NT deficiency protects the liver from HFD-induced obesity through inhibition of FA synthesis.

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POSTER PRESENTATION #114

Abstract Title: **Age-Dependent Expansion of Gamma Delta ($\gamma\delta$)-T Cells in Visceral Adipose Tissue**

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Abstract: Adipose tissue has become well-known for its role in chronic metabolic diseases such as diabetes and cardiovascular disease. Inflammation originating from the adipose tissue appears to be an underlying contributor to these chronic conditions. To date, the majority of research in this field has focused on obesity without regard for aging, despite the fact that aging often poses a larger risk. The objective of this study was to identify age-specific alterations in adipose tissue physiology which may underlie chronic inflammation. Our previous microarray analyses of visceral adipose tissue from young (4-mo) and aged (24-mo) mice showed evidence of increased T cell populations in the aged including a 6-fold increase in gene expression of T cell receptor gamma. Using flow cytometry we found that gamma delta ($\gamma\delta$)-T cells are abundant in visceral adipose tissue of aged mice comprising up to 30% of the immune cell population and showing a 5-fold increase in number by aging ($p < 0.01$). This expansion was unique to visceral adipose tissue, not being observed in subcutaneous fat, spleen, blood, or skin. Using TCR δ knockout mice, we found that genetic deficiency of $\gamma\delta$ -T cells significantly diminished the inflammatory response of aged adipose tissues to ex vivo stimulation with IL-1 β ($p < 0.01$). These findings support our hypothesis that expansion of $\gamma\delta$ -T cells in adipose tissue contribute to chronic inflammation which is characteristic of aging. Future studies investigating the potential role of IL-17, a cytokine largely produced by $\gamma\delta$ -T cells, in mediating adipose tissue inflammation are being planned by our laboratory.

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POSTER PRESENTATION #115

Abstract Title: **Immune Cells Implicated in the Induction of White Adipose Beiging by Acute Cold Exposure**

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Abstract: White adipose primarily serves to store energy, whereas brown fat expresses uncoupling protein 1 (UCP1) and is highly metabolically active. Beige adipocytes are induced in response to cold in white adipose depots and also express UCP1. The ability of UCP1 to dissipate energy is thought to protect against obesity and improve glucose homeostasis. To determine whether humans accumulate beige cells, we stimulated the thigh with an ice pack 30 minutes a day for 10-days and measured UCP1 by immunohistochemistry. UCP1 expression increased almost 2-fold ($p=0.0005$) by the icing protocol. Previous work from our lab identified mast cells as important immune cells in the seasonal induction of UCP1; in response to cold, mast cells degranulate and release histamine, which stimulates PKA to induce UCP1. In order to identify mechanisms regulating beige fat induction by 10-day icing, we measured gene expression in our adipose tissue samples using the nCounter System. The panel of genes consisted of immune cell markers, cytokines, beige and brown fat markers, angiogenic genes, extracellular matrix genes, and genes involved in lipid metabolism. We performed a correlation analysis on the change in gene expression and change in UCP1 detected by immunohistochemistry. There were very high correlations between the change in UCP1 and the mast cell protein tryptase, the eosinophil marker Siglec8, and the eosinophil chemokine CCL26 in both the iced leg and the contralateral leg. The results of this study provide further evidence that mast cells are important for beiging in humans, and suggest that part of the mechanism may involve eosinophil recruitment.

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POSTER PRESENTATION #116

Abstract Title: **The Influence of Cold Exposure on Angiogenesis in Human Adipocytes**

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Abstract: Obesity, diabetes, and hyperlipidemia contribute to the leading causes of mortality globally. As such, it is essential to explore novel avenues for therapeutics. Adipose beiging is the induction of multilocular adipocytes expressing uncoupling protein 1 (UCP1) in subcutaneous white adipose tissue. UCP1 uncouples oxidative respiration in the mitochondria, dissipating energy as heat. In rodents, beige adipose tissue not only protects against obesity but also takes up glucose and free fatty acids, rendering it protective against diabetes and hyperlipidemia. Induction of the beiging of white adipose tissue is therefore being evaluated as a potential therapy for obesity, diabetes, and hyperlipidemia. To investigate the role of cold exposure in the beiging of adipose tissue in humans, subjects were treated with an ice pack on the anterior mid-thigh for thirty minutes daily for ten days. Subjects underwent a pre- and post-treatment subcutaneous adipose tissue biopsy. Immunohistochemistry revealed that UCP1 increased in the iced and contralateral legs after icing. The RNA for the endothelial cell marker TIE1 increased in both legs after icing, and there were changes in angiopoietins, the ligands of TIE1. Since angiogenesis is linked to beige adipose formation and function, we stained with lectin and quantified vessels and capillaries. Upregulation of angiogenesis could provide a mechanism for how cold exposure and the beiging of adipose tissue improves insulin sensitivity and reduces inflammation. However, we were unable to detect a change in capillary or vessel density after this ten day treatment. It is possible that more time is required to reveal an angiogenic response in adipose tissue, and we are evaluating seasonal responses in these subjects.

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POSTER PRESENTATION #117

Abstract Title: **Cold-Induced Changes in Human Subcutaneous White Adipose Tissue: Evidence of Immune System Activation**

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Abstract: Mammals use the highly thermogenic brown adipose tissue (BAT) to defend against cold temperatures. Lean humans have BAT, and its activity increases in a cold environment; however, little is known about the response of white adipose tissue (WAT) to cold, a process called beiging. Studies in rodents have demonstrated that WAT beiges in response to cold, a process dependent on alternatively activated (M2) macrophages. It was hypothesized that repeated exposure to cold temperatures would stimulate human subcutaneous (SC) WAT beiging through recruitment of M2 macrophages, and that this would be inhibited in obese individuals. Lean (BMI < 27) and obese (BMI 27-45) subjects, male and female, between the ages of 21-65 were recruited in the summer. Adipose biopsies were performed before and after treatment with an ice pack on the thigh for 30 minutes daily over 10 days. Uncoupling protein 1 (UCP1) and macrophage expression was measured by real time RT-PCR and immunohistochemistry (IHC). UCP1 RNA increased in response to cold in lean but not obese subjects. IHC demonstrated a significant increase in CD68/206 positive macrophages as well as UCP1 expression in adipose of both the iced and non-iced thigh in response to cold in lean but not obese subjects. In conclusion, human SC WAT upregulates UCP1 in response to cold stimulus, and this response is inhibited by obesity. The induction of UCP1 is linked to M2 macrophages, explaining in part why obese subjects, who have low-grade inflammation, have an impaired beiging response. This could potentially be exploited to treat metabolic diseases.

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POSTER PRESENTATION #118

Abstract Title: **Heme Oxygenase Induction Suppresses Hepatic Hepcidin and Rescues Ferroportin and Ferritin Expression in Obese Mice**

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Abstract: Hepcidin, a phase II reactant secreted by hepatocytes, regulates cellular iron levels by increasing internalization of ferroportin- a transmembrane protein facilitating egress of cellular iron. Chronic low-grade inflammatory states, such as obesity, have been shown to increase oxidative stress and enhance hepcidin secretion from hepatocytes and macrophages. Heme-heme oxygenase (HO) is a stress response system, the induction of which reduces oxidative stress thereby abating patho-physiological conditions such as obesity and metabolic syndrome. 8 weeks old male obese (ob) mice and their age- and sex-matched lean mice were used as controls. CoPP was administered intraperitoneally once a week (3 mg/kg) for 6 weeks to obese mice. CoPP plus stannous mesoporphyrin (SnMP) was administered intraperitoneally three times a week (20 mg/kg) for 6 weeks. We investigated the effects of HO-1 induction on hepatic hepcidin levels and on iron homeostasis in tissues from lean and obese mice. Obese mice exhibited hyperglycemia along with increased levels of pro-inflammatory cytokines (MCP-1, IL-6, $p < 0.05$), oxidative stress and increased hepatic hepcidin levels ($p < 0.05$). Enhancement of hepcidin was reflected in the reduced expression of ferroportin in obese mice ($p < 0.05$). Further our results showed attenuation of insulin receptor phosphorylation and attenuation of metabolic regulators including pAMPK, pAKT and pLKB1. Cobalt protoporphyrin (CoPP)-induced HO-1 up-regulation in obese mice and reversed these pathophysiological alterations ($p < 0.05$) while attenuating hepatic hepcidin levels and enhancing ferritin expression. These effects of CoPP were prevented in obese mice concurrently exposed to an inhibitor of HO (SnMP) ($p < 0.05$). Taken together, our results highlight a modulatory effect of HO on iron homeostasis mediated through the suppression of hepatic hepcidin in conjunction with the rescue of cellular ferritin levels. Therefore these findings may prove an effective strategy in treating the metabolic consequences of obesity including alteration of liver iron homeostasis.

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POSTER PRESENTATION #119

Abstract Title: **Popliteus Avulsions**

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Abstract: Isolated popliteal tendon (PT) avulsions, which occur more predominantly in the pediatric population, represent a small subset of posterior lateral corner injuries. Isolated avulsion of the popliteal tendon was first described in 1985 and since then there have been a limited number of case reports describing this injury. Though operative and non-operative treatment have been described, little has been done to evaluate which method, if any, is superior. Diagnosis has been confirmed by x-ray, arthroscopy, and MRI yet no clear preference exists between these modalities. All documented case reports of popliteal tendon avulsions were reviewed with regards to mode of injury, diagnosis, type of treatment, and outcome at last reported follow up. Pooled data showed x-ray was proficient in diagnosing an isolated avulsion injury, while MRI was more sensitive in determining concomitant ligamentous injuries. Concomitant ligamentous injuries represented a higher chance of negative outcome with conservative treatment. As such, x-ray followed by MRI was determined to be the gold standard for diagnosis of this injury. Reported outcomes of both non-operative and operative isolated PT avulsions are favorable. Due to the low incidence of popliteal avulsions a prospective randomized trial is not feasible to differentiate what treatment protocol is best. To date there has been no reported difference between the two groups. The majority of patients were not followed into skeletal maturity and were only monitored for a short period of time. Longer follow-up, especially in pediatric patients, for isolated PT avulsion injuries may yield better information concerning potential outcomes of different treatment groups.

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POSTER PRESENTATION #120

Abstract Title: **Return to Sport Significantly Worse Following Patellofemoral Articular Cartilage Procedures than Tibiofemoral Procedures: A Systematic Review**

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Abstract: Objective: The purpose of this systematic review was to compare return to sport (RTS) between patients undergoing isolated tibiofemoral (TF) cartilage procedures and those with patellofemoral involvement (PF). We hypothesized that ability to RTS would be significantly lower for those with patellofemoral lesions. Design: We performed a search according to the PRISMA guidelines of the PubMed, CINAHL, Cochrane Center Register of Controlled Trials, and SportDiscus electronic databases to identify articles that analyzed RTS in athletes following articular cartilage procedures. RTS was defined as the self-reported ability to participate at the patient's preoperative level of competition. Surgical procedures included microfracture, osteochondral autograft, autologous chondrocyte implantation, and osteochondral allograft transplantation. A Fisher Exact test was utilized to compare RTS between patients with TF or PF lesions. Results: A total of eight studies (n=266 patients; 240 TF and 26 PF) met the criteria for inclusion. Only 9/26 (35%) of the PF patients returned to sport compared to 171/240 (71%) with isolated TF lesions (p<0.001). Overall, patients with isolated tibiofemoral lesions were 4.7 times more likely to return to pre-injury sports activity level compared to patients with patellofemoral involvement (Odds Ratio=4.7, [95% CI: 1.99 to 11.00], p<0.001). Conclusion: Patellofemoral patients were 4.7 times less likely to return to their preoperative level of sports activity compared to those with tibiofemoral lesions. While future studies are necessary to elucidate whether this effect is primarily due to the large contact stresses borne by the patellofemoral joint during dynamic activity or other patient-related factors, the current results may be used to create realistic postoperative expectations.

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POSTER PRESENTATION #121

Abstract Title: **Lower Preoperative VR-12 Mental Component Scores Are Associated with Longer Return-to-Work Delays after MPFL Reconstruction**

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Abstract: Introduction: Medial patellofemoral ligament (MPFL) reconstruction is often performed as definitive treatment for recurrent patellofemoral instability. While the effect of mental health on outcomes has been well-described for other orthopaedic injuries, the role of mental health in treating patients with patellofemoral instability has yet to be reported. This study investigated the effect of preoperative mental health on postoperative outcomes after MPFL reconstruction. We hypothesized that patients with lower preoperative mental health scores would demonstrate inferior postoperative outcomes. Methods: From our IRB-approved prospective outcomes registry, we identified consecutive MPFL reconstruction patients with complete preoperative and minimum 1-year follow-up data. Relationships between preoperative VR-12 Mental Component (MC) scores and postoperative patient-reported outcomes were assessed using Pearson correlation coefficients for continuous variables and chi-square tests for categorical variables. Postoperative outcomes included Lysholm and IKDC scores, subjective patient satisfaction, and return-to-work data. Results: We identified 30 patients (mean age=21.5 years, range=15-37 years; 20 females, 10 males; mean follow-up 22 months, range=12-60 months). Twenty-three patients (77%) had MC scores in the bottom quartile of normative data. Preoperative MC scores were inversely correlated with weeks before return to work ($r=-0.50$, mean = 30 ± 12.133 , $p=0.004$) but not ultimate return-to-work rates ($p=0.12$), improvements in Lysholm or IKDC ($p=0.9$, $p=0.92$), or patient satisfaction ($p=0.75$). Conclusions: Lower preoperative VR-12 Mental Component scores were associated with longer duration before returning to work post-surgery, despite improved postoperative patient-reported outcomes and high levels of patient-reported satisfaction with MPFL reconstruction. While causes for lower mental health in this unique patient population hasn't been elucidated, surgeons should consider quantifying preoperative mental health and adjusting expectations accordingly.

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POSTER PRESENTATION #122

Abstract Title: **Degree of Structural Pathology in the Female Femoroacetabular Impingement Patient is Related to Changes in Sexual Activity**

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Abstract: Introduction: Patients with femoroacetabular impingement (FAI) of the hip often report alterations in the ability to perform activities of daily living. The relationship between structural pathology and preoperative symptoms affecting sexual activity has yet to be illuminated in FAI patients. As such, the purpose of this study was to compare the relationship between structural pathology and patient reported sexual activity status in a series of FAI patients. We hypothesized that greater structural pathology would be associated with significant modification of activity related to their hip pain. Methods: From our prospective outcomes registry, we identified 72 female FAI patients with complete clinical and radiographic data. Preoperatively, patients completed a survey which included questions on sexual activity related to their hip pain. In addition, the magnitude of so-called “cam” or “pincer” deformities were assessed by radiographically measuring the alpha angle and lateral center edge angle (LCEA), respectively. To determine if there was threshold value of LCEA or alpha angle associated with frequent pain during intercourse, receiver operating characteristic (ROC) curves were calculated. Patients were grouped based on the ROC curve results, range of motion (ROM), radiographic measures, and how frequently patients were aware of their hip during intercourse and how often activities were modified to avoid hip pain. Results: LCEA>31.4° was associated with frequent pain during intercourse (AUC=0.73, p=0.01); however, alpha angles were not associated with hip pain during sex (p=0.97). When grouped using the 31.4° threshold, patients with greater LCEA had significantly worse hip flexion (101±9 vs. 107±10, p=0.02), internal rotation ROM (15±8 vs. 21±10, p=0.005), and adduction ROM (10±2 vs. 12±5, p=0.002). Furthermore, a significantly greater prevalence of patients with greater LCEA reported being frequently aware of their hip during sex (p=0.01), and more frequently reported modifying activities to avoid damaging the hip (p=0.05). Conclusion: Larger structural pathology in female FAI patients, specifically the pincer-type deformity, was associated with a greater effect on patient-reported sexual activity status.

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POSTER PRESENTATION #123

Abstract Title: **Pain and the Positivity Effect: How Acute Pain Influences Recall, Recognition, and Response Time toward Positive Images in Older and Younger Adults**

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Abstract: The positivity effect refers to the tendency to favor positive over negative stimuli, and can be assessed by measuring how well people recall, recognize, and quickly respond to stimuli of varying valence. Socioemotional selectivity theory posits that as people age, they become increasingly likely to demonstrate the positivity effect because they become more motivated to maximize positive emotions and minimize negative ones. Yet, pain can threaten positivity. The threat is particularly relevant for older adults, as approximately 70% of older adults report experiencing physical pain within the previous month. The goal of the current study was to test whether older adults recall, recognize, and respond faster to positive images following pain compared to younger adults. It was hypothesized that older adults would recall, recognize, and respond faster to positive images following pain than younger adults. Forty-eight older and 48 younger pain-free adults participated in a lab study where they underwent a pain-free and a pain task and were then asked to recall, recognize, and respond to previously-seen neutral, negative, and positive images. With regard to recall, results revealed that older adults remembered significantly less negative pictures than younger adults ($t(98) = 3.18, p = .002$), but did not differ from younger adults in recall of positive ($t(98) = -0.73, p = .46$) or neutral pictures ($t(98) = 0.46, p = .65$). With regard to recognition, results revealed that after experiencing pain, both older and younger adults were marginally more willing to judge a negative picture as having been previously seen, $t(97) = 1.79, p = .08$. With regard to latency, an age x valence interaction revealed that older adults took significantly longer than younger adults to recognize negative images ($t(97) = 7.40, p < .001$). The hypothesized three-way interaction of age group x pain condition x picture valence was not found for any of the three positivity outcomes. Results suggest that the strategies older and younger adults use to maintain positivity in the face of pain may be similar in nature. Future research should investigate whether older adults have additional strategies that allow them to counteract the negativity of frequent pain, and if so, test whether those strategies can be applied to others experiencing acute pain.

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POSTER PRESENTATION #124

Abstract Title: **Gender Specific Inflammasome Activation in the Trigeminal Ganglion**

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Abstract: The effect of gender on pain and analgesia has been the subject of important studies for decades. It is widely known that common forms of painful conditions, such as neuropathic pain, are more prevalent in females. Determining the cellular and molecular mechanisms underlying such differences will enhance our basic understanding of pain biology, and will also help target therapy that addresses these gender discrepancies. Recently our lab detected unprecedented gender dependent differences in inflammasome activation in satellite glial cells (SGCs) cultured from the trigeminal ganglion (TG). The TG houses the cell bodies of corneal sensory fibers and SGCs and represents an important relay station for corneal sensory input. We hypothesize that activation of the NLRP3 inflammasome in trigeminal SGCs is gender specific. To test this, trigeminal ganglia were harvested from male and female mice and grown in cell culture. Alu-like RNAs (B1 and B2 RNAs), known to activate the inflammasome, were administered to the cultured SGCs. Twenty-two hours after B1/B2 RNA stimulation, quantitative PCR was performed to evaluate changes in inflammasome activation markers in male versus female cells. Notably in B1-treated TG SGCs, males showed a significant increase in inflammasome effector protein known as ASC compared to females while females showed a significant increase in IL-18 compared to males ($p < 0.05$). In B2 treated TG SGCs, female mice showed significantly higher levels of IL-18 and Dicer-1 ($p < 0.05$). These findings suggest that there may be intrinsic cellular mechanisms that modulate inflammasome activation in male versus female SGCs. Future studies should build upon these findings and further investigate these cellular pathways as a potential mechanism of gender specific differences in pain behavior.

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POSTER PRESENTATION #125

Abstract Title: **Macrophage Migration Inhibitory Factor (MIF) in mouse visceral and somatic sensation**

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Abstract: MIF is a soluble lymphokine mediating immune response as a pro-inflammatory factor. It is also recognized as a mediator in pain during inflammation and nervous tissue trauma. We previously showed that MIF antagonism prevented bladder pain and bladder inflammation. Therefore, we investigated whether global deletion of MIF could block abdominal mechanical hypersensitivity (referred pain), micturition and histological changes in a rodent model of cyclophosphamide (CYP) induced cystitis. After administration of CYP to MIF knockout mice (MIF KO) and C57 (wild-type; wt) mice, we measured changes in: a) abdominal mechanical sensitivity; b) micturition volume and frequency; c) bladder histology. MIF KO mice were less responsive to abdominal mechanical stimulation than wild type mice at baseline. Responses were markedly increased after CYP in wild type mice but not in MIF KO mice. MIF knockout mice had significantly larger micturition volumes at baseline than wt mice, yet both strains had a similar percent decrease in micturition volume and increase in micturition frequency after CYP. Bladder histology scores were similar in both strains. In addition, body weight was greater in MIF knockout mice. Therefore, while MIF knockout has no effect on micturition changes or bladder inflammation in cyclophosphamide-induced cystitis, MIF mediates somatic and visceral sensation at rest. MIF deletion reduced abdominal mechanical hypersensitivity caused by cyclophosphamide, indicating a role for MIF in mediating referred bladder pain. These are novel findings implicating MIF in normal and pathological sensation. The exact locus of these effects (organ level; peripheral vs central nervous system) remains to be determined.

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POSTER PRESENTATION #126

Abstract Title: **Role of Interleukin-1 Receptor (IL-1R) in Morphine-mediated Analgesia Using a Mouse Model of Incisional Pain**

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Abstract: Background: Opioids are commonly prescribed for pain, in 2012, 259 million prescriptions for opioid pain medications were written (CDC.org). Most people who are prescribed opioid pain relievers take them due to a genuine medical needs, e.g. post-op. pain. Patients can experience tolerance and loss of effectiveness of opioids over time and this may have contributed to the current opioid addiction epidemic. Interleukin-1 β (IL-1 β) plays a major role in host defense and inflammation and is associated with inflammation, opioid analgesia and pain sensitivity. The aim of this study was to determine the role of IL-1R1, the receptor activated by IL-1 β in morphine tolerance using a mice model of incisional pain. Methods: WT and IL-R1 $^{-/-}$ C57BL/6 mice (n=5/trt., group) were subjected to a 0.5mm incision on the right hind-paw and were administered morphine (10mg/kg, s.c.) or saline daily from post-op., day 0 to 3. During the post-op days, nociception was assessed by recording the paw-withdrawal latency (PWL) (sec.) in response to thermal stimuli, mechanical stimuli and motor coordination measured using a rotarod assay. Results: Compared to WT mice treated with morphine, IL-R1 $^{-/-}$ mice showed greater PWL times in response to heat and mechanical stimuli. A similar trend was also recorded when mice were placed onto the rotarod to measure coordination. Conclusion: This study suggests that IL-1 β and its cognate receptor might be involved in incisional pain and may be potential therapeutic for the treatment of acute inflammatory pain. Further studies are being conducted to determine the role of IL-1R1 in morphine tolerance.

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POSTER PRESENTATION #127

Abstract Title: **Maternal Nicotine Exposure Prior to and during Pregnancy and Nursing Increases Offspring Obesity Risk**

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Abstract: Research shows that babies born to mothers who smoked during pregnancy are at increased risk for obesity later in life. Nicotine is considered one of the most deleterious chemicals in cigarette smoke. Thus, we examined the potential mechanisms of offspring obesity susceptibility following perinatal nicotine exposure in a mouse model. Dams were exposed to vehicle or nicotine before and during pregnancy and nursing. At 7 weeks of age, male offspring of nicotine-exposed dams showed a trend towards greater body fat percentage ($p=0.079$) compared to vehicle-exposed offspring, and at 12 weeks of age, nicotine-exposed offspring displayed significantly impaired glucose tolerance ($p<0.05$) as compared to vehicle offspring. Additionally, skin fibroblasts were isolated from the offspring after weaning (3 weeks), grown in culture, and incubated in media that stimulated the cells to accumulate lipid droplets. Lipid levels and mRNA markers related to obesity (chemerin and adiponectin) were quantified. Strong trends toward greater lipid staining ($p=0.053$) and adiponectin ($p=0.067$) expression levels were observed, as well as significantly increased chemerin expression levels ($p<0.05$) in cells collected from nicotine versus vehicle-exposed offspring. Thus, we found that cells isolated from offspring born to nicotine-exposed dams are programmed for increased lipid storage shortly after birth, which proposes a mechanism for the increased body fat percentage observed in offspring born to nicotine-exposed dams. Future studies will increase sample size, evaluate protein expression in offspring, and examine the effects of maternal smoking versus maternal nicotine exposure. This study is relevant due to the rise of e-cigarettes and nicotine replacement therapies.

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POSTER PRESENTATION #128

Abstract Title: **The Role of MCP-1/CCR2 in Ethanol Neurotoxicity in the Developing Brain**

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Abstract: Fetal ethanol exposure may result in fetal alcohol spectrum disorder (FASD) and one of the most devastating effects of developmental exposure to ethanol is the loss of CNS neurons. The underlying molecular mechanisms, however, are unclear. Ethanol-induced neuronal death is accompanied by neuroinflammation. Monocyte chemoattractant protein 1 (MCP-1), also called chemokine (CC motif) ligand 2 (CCL2), is a chemokine which is involved in neuroinflammation. The current study was designed to determine the role of MCP-1 in ethanol-induced damage to the developing brain. Ethanol exposure (2.5 g/kg) by subcutaneous injection causes neuronal death, microglial activation, and an increase in the expression of MCP-1 and its high affinity receptor CCR2 in the brain of postnatal 4 day-old mice. To block MCP-1 signaling, we performed two subcutaneous injections of either a MCP-1 synthesis inhibitor (bindarit; 100 mg /kg), or a CCR2 antagonist (RS504393; 1 mg/kg) at 24 and 0.5 hours prior to ethanol exposure. These inhibitors decreased ethanol-induced apoptosis and microglial activation which was evaluated by caspase-3 immunoblotting (IB) and Iba1 immunohistochemistry (IHC), respectively. Further studies using gene knock out mice confirmed that the deficiency in MCP-1 or CCR2 made mice more resistant to ethanol-induced neurodegeneration which was demonstrated by caspase-3 IB and Fluoro-Jade C staining. These mice were also less sensitive to ethanol-induced microglial activation. It appeared that deletion of MCP-1 was more effective than CCR2 in terms of protective effects. In summary, our data suggest that MCP-1/CCR2 signaling may be involved in ethanol-induced neuroinflammation and neurodegeneration, and inhibition of MCP-1/CCR2 signaling may offer protection against ethanol-induced damage to the developing CNS.

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POSTER PRESENTATION #129

Abstract Title: **Neonatal dendritic cells alter the immunodominance hierarchy of the CD8 T cell response during influenza infection**

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Abstract: Neonates are more susceptible to influenza virus infection than adults, resulting in increased morbidity and mortality as well as delayed clearance of the virus. Multiple differences between the adult and neonatal immune response to influenza help explain this vulnerability. Dendritic cells are of particular interest in this process as their decreased function in neonates results in the poor T cell activation observed during neonatal influenza infections. We sought to understand how differences in neonatal dendritic cells shape CD8 T cell specificity and immunodominance during influenza infection as well as how this may affect memory formation and viral clearance. We found that neonatal C57/B6 mice display an altered CD8 T cell immunodominance hierarchy, preferentially responding to the influenza protein PA rather than the dominant adult epitope in the NP protein. Additionally, upon secondary infection, mice first infected as pups suffered increased morbidity compared to mice infected previously as adults. Finally, transfer of influenza infected adult dendritic cells to pups resulted in increased T cell activation and enhanced viral clearance. Taken together, these data suggest that neonatal dendritic cells alter CD8 immunodominance, and this may compromise viral clearance and memory formation.

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POSTER PRESENTATION #130

Abstract Title: **Exposure to PCB126 during the Nursing Period Significantly Impairs Early-Life Glucose Tolerance**

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Abstract: Polychlorinated Biphenyls (PCBs) are persistent environmental organic pollutants that are known to have detrimental health effects. In a mouse model in our lab, PCB126 exposure during pregnancy and nursing alters offspring body composition and glucose tolerance. The purpose of this study was to expose dams to PCB126 during the nursing period only. Female ICR mice were bred and half of the dams were exposed to either vehicle (safflower oil) or 1 μ mole PCB126 per kg of body weight via oral gavage on postnatal days 3, 10, and 17 (n = 9/group). Offspring body weight, lean and fat mass, and glucose tolerance were measured. Both male and female offspring displayed normal body weights as well as body composition (p > 0.05). However, both male and female offspring that were exposed to PCBs during the nursing period had significantly impaired glucose tolerance at 3 weeks of age (p < 0.05). This persisted until 9 weeks of age in the female offspring (p < 0.05), but the difference disappeared as the male offspring aged (p > 0.05). Our earlier work suggests that in utero and postnatal PCB126 exposure predisposes offspring to having lower lean mass and impaired glucose tolerance later in life. However, our current study shows that exposure to PCB126 through the mother's milk impairs glucose tolerance in the short-term and is likely caused by impairments in insulin receptor signaling in the periphery as others have shown with direct PCB exposures in adult mice. Future experiments will investigate the mechanisms of dysfunction caused by in utero PCB126 exposure, which may be driving the increased risk of obesity and insulin resistance in adult offspring.

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POSTER PRESENTATION #131

Abstract Title: **Measurement of Intermittent Hypoxemia (IH) Events in Preterm Infants: Development of a Validated Method**

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Abstract: Background: Due to cardiorespiratory immaturity preterm infants are at increased risk for Intermittent Hypoxemia (IH); episodic drops in oxygen saturation (SpO₂). Evidence suggests IH events in early postnatal life may have acute and/or long-term consequences. A key element to investigations of the prevalence and the significance of IH in preterm infants is the requirement of reliable and reproducible measurement of the individual events at various 'thresholds' of hypoxemia. We report our efforts to develop/validate a digital data collection and analysis system that can record and report the frequency/severity of hypoxemic events in preterm infants. Objective: Determine the accuracy and reliability of digital capture and software-defined approach to identification of IH events in preterm infants. Design/Methods: A total of 20 infants were studied at 3 independent hourly intervals, providing 60 patient-hrs. We recorded SpO₂ via streamed data and analyzed off-line by software designed and developed by our research team. Three independent investigators blinded to patient status determined IH events for each patient-hr; these 'true values' were compared to the IH defined by the prototype software program. Additional studies evaluated the impact of signal averaging during data capture with respect to software accuracy. Standard ANOVA and Pearson's correlation analyses were used. Results: Investigator-analyses of streamed SpO₂ data from 60 individual-hr-intervals (2s averaging time) required more than 20 total hrs of personnel effort. Inter-observer variability was less than 2% across a wide range of IH incidence (SpO₂<80). The developed software method provided results very similar to the observer measures at 3 thresholds (Fig 1), R²=0.98. Using longer intervals of signal averaging in the data stream (2s vs. 8s interval) reduced the ability to detect prolonged IH events, suggesting that signal averaging should be minimized for most accurate results (Fig 2). Conclusion: IH events are important contributors to morbidities in preterm infants and accurate recording of these events is paramount in determining their impact. We have developed an automated, convenient, and time efficient strategy to record such events, with 98% accuracy when compared to human measurements. This approach is sensitive to signal averaging artifact but can be used reliably in future studies of IH in preterm infants.

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POSTER PRESENTATION #132

Abstract Title: **Aromatherapy as an Adjunctive Therapy for Neonatal Abstinence Syndrome: A Pilot Study.**

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Abstract: Neonatal Abstinence Syndrome (NAS) is a condition that produces gastrointestinal and autonomic neurologic dysfunction. To date there have been no studies examining the use of aromatherapy in the treatment of infants with NAS. A non-blinded, randomized controlled trial was conducted at a level 4 NICU. Infants were randomized to a standard treatment or standard treatment + aromatherapy group. Aromatherapy was applied using an inhalation patch containing 80:20 mixture of Lavender and Chamomile placed in the infant's bassinet. Standard demographic data, length of stay, duration of morphine therapy, and Finnegan scores were collected. Each group had equal numbers of single and multidrug exposures and did not differ with regard to basic demographics. Infants who received aromatherapy had shorter lengths of stay than infants who received only standard therapy (11.4 days vs. 17.8 days, $p < 0.05$). The average length of morphine treatment was shorter in the aromatherapy group as compared to the standard therapy group (7.4 days vs 12.7 days, $p < 0.05$). Our results showed the use of these oils on infants with NAS in addition to standard therapy reduced time spent in the NICU by 6.4 days as compared to standard therapy alone. Additionally, the duration of morphine treatment was shorter in the aromatherapy group by 4.6 days. This is an important reduction given the high cost associated with NAS admissions. A reduction of hospital stay length by 6.4 days yields a savings to the health care system of \$20,678.40. We feel that further study of the incorporation of aromatherapy into a NAS treatment algorithm is warranted.

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POSTER PRESENTATION #133

Abstract Title: **Neurodevelopmental Outcomes of Infants with Neonatal Abstinence Syndrome**

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Abstract: Because of the current opiate-dependence/abuse epidemic, there is an increasing number of babies with a diagnosis of Neonatal Abstinence Syndrome (NAS). Little is known about the neurodevelopmental outcomes of these infants. The objective of this study is to determine the developmental outcomes of infants treated for NAS at one and two years of age. This is a retrospective chart review of 50 children seen at the NICU follow-up clinic between 2011 and 2014. The Bayley Scales of Infant and Toddler Development edition III were administered at one year and two years, assessing motor and cognitive development. Language assessment was performed using the Bayley III or Preschool Language Scale 4 (PLS-4). There was a significant decrease in cognitive scores from first year to second year ($p < 0.0001$). Motor scores did not differ between the two age groups ($p = 0.4881$). There was also a significant decrease in language scores between the two age groups ($p = 0.0027$). The mean weights at one year and two years were 10.0 (1.7) kg, 45th percentile; and 13.9 (3.8) kg, 57th percentile on the growth curve, respectively. The children with NAS demonstrated good weight gain postnatally. However, in spite of neurodevelopmental scores being close to the standard score at one year, there was a concerning decrease found in cognitive and language scores at two years of age. This calls for an early intervention and close follow-up of these children with NAS. Future studies should include longer follow-up to determine the long-term developmental impact of in utero opiate exposure.

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POSTER PRESENTATION #134

Abstract Title: **Assessing pain in neonates with in-utero opiate and tobacco exposure**

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Abstract: Neonatal withdrawal from opiate exposures in-utero is of growing importance in Kentucky and throughout the U.S., while tobacco exposure remains high in Appalachian states. Neonatal pain assessment scores are tools used routinely in NICUs to assess this “fifth vital sign.” We sought to determine if pain scores differ between 3 groups: neonates with tobacco exposure, opiate exposure, and the lack of exposures to those substances. (A fourth group, opiate-no-tobacco yielded only 2 subjects that fit inclusion criteria). We tested the hypothesis that pain scores of infants with fetal exposure to tobacco or opiates are not different from scores of those with no exposure. Methods: This is a retrospective review using data from a sample of convenience obtained over a 3-month timeframe. Infants of gestational age between 34 0/7 and 41 6/7 weeks were identified and data were collected associated with a standardized procedure for the metabolic screening, to which all babies are required to be exposed. Groups were compared descriptively by Chi-squared (gender), ANOVA (gestational age, birth weight, age at time of screen), and Kruskal-Wallis test (pain score). Results: Neonates, divided into 3 groups based on exposure: 1. No exposure to tobacco, opioids, or opiates, 2. exposure to tobacco but not opioids-or-opiates, 3. exposure to both tobacco and opioids-or-opiates. There were no significant differences among groups as to birth weight, gestational age, and post-natal age at time of metabolic screening. Pain scores (N-PASS) for the selected population of neonates of 34 weeks gestational age and greater theoretically range from 0 to 11, while individuals’ scores in our study ranged from 0 to 4. Median pain scores were 0 for each of the 3 groups. The null hypothesis is not rejected (χ^2 of .055 < χ^2 4.605; p-value .9728); the 3 groups may have no significant difference in pain scores following heel stick. Our study was limited by small sample size.

PSMRF program, U of Kentucky College of Medicine, U of Kentucky Department of Pediatrics.
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POSTER PRESENTATION #135

Abstract Title: **Relationship between Postnatal Weight Gain and Intermittent Hypoxemia (IH) in Preterm Infants.**

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Abstract: Background: Sustained hypoxia impairs weight gain; supported by both human and animal data. Brief episodic drops in oxygen saturation (IH) occur almost invariably in extreme preterm infants and may have a cumulative effect on neonatal morbidities. Rat pups exposed to IH had impaired growth compared to unexposed. Objective: Test the hypothesis that chronic IH is associated with impaired growth in preterm infants; as reflected by lower weight Z-score at 8 wks of life. Design/Methods: Preterm infants ≤ 29 wks gestational age (GA) were prospectively enrolled. Oxygen saturation (SpO₂) was continuously monitored using high-resolution (2s averaging, 1Hz sampling) pulse oximeters upon admission until 8 wks of life. Weight measures, at birth and 8 wks postnatal age, were retrospectively collected from medical records. Z-scores were calculated based on Fenton 2013 growth curves. Novel software was used to analyze SpO₂ data. IH measures were defined as: Primary, %time-SpO₂<80: percent time spent with SpO₂<80%/week; Secondary, IH-SpO₂<80: Number of events/week with SpO₂<80% (duration 4-180s). We adjusted for birth weight Z-score, GA, sex, and inborn vs. outborn status. Summary of results: Weight measures at 8 wks of age were present for 49 infants. There was no statistically significant correlation between primary outcome measure of cumulative IH (%time-SpO₂<80%) and weight Z-score at 8 wks of life (adjusted $r=-0.02$, $p=0.84$). There was a negative correlation between birth weight Z-score and cumulative chronic IH for the first 8 weeks of life that was not statistically significant (adjusted $r=-0.19$, $p=0.09$). Similarly, no significant correlations between secondary outcome measure (IH-SpO₂<80) and growth were noted. There was a strong positive correlation between birth weight Z-score and Z-score at 8 wks of age (adjusted $r=0.8$, $p<0.0001$). Conclusion: Our results do not show a statistically significant correlation between chronic cumulative IH and growth at 8 wks of life in preterm infants ≤ 29 wks GA. Findings might be primarily due to small study size. However, current analyses do not take caloric intake into account. Given close monitoring of preterm infants in the NICU, we speculate increased caloric needs in setting of high cumulative IH may have been corrected for by immediate nutritional adjustments during the study period. A larger prospective study adjusting for caloric intake is imperative.

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POSTER PRESENTATION #136

Abstract Title: **Relationship Between Acute Kidney Injury and Intermittent Hypoxemia in Extremely Preterm Infants**

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Abstract: BACKGROUND: Intermittent Hypoxemia (IH), episodic oxygen desaturation events, is common in preterm infants and generally attributed to apnea of prematurity often superimposed upon suboptimal lung function/structure. Acute Kidney Injury (AKI) is associated with increased morbidity and mortality in neonates. Premature infants typically have immature renal structure and function at birth and are at high risk of AKI in the perinatal period. It has been proposed that sleep apnea and nocturnal hypoxemia may contribute to kidney injury, the development of chronic kidney disease (CKD), and the progression to kidney failure. We wanted to assess the relationship between IH and AKI in preterm infants. OBJECTIVE: Test the hypothesis that intermittent hypoxia is associated with acute kidney injury in preterm infants, as reflected by a rise in serum creatinine. DESIGN/METHODS: A total of 18 infants <28wks gestational age (GA) admitted to the Kentucky Children's Hospital neonatal intensive care unit were enrolled in a prospective cohort. Oxygen saturation (SpO₂) was continuously monitored using high-resolution (2s averaging, 1Hz sampling rate) pulse oximeters upon admission until 8 wks of life. IH measures were defined as: %time-SpO₂<80: percent time spent with SpO₂<80%; IH-SpO₂<80: events/day with SpO₂<80% (duration 4-180s). Creatinine levels were measured daily as standard of care. AKI was defined per the modified Kidney Disease Improving Global Outcomes (KDIGO) definition. Mean IH measures in the AKI and No AKI groups were compared accounting for repeated measures, then adjusted for GA. RESULTS: AKI was present in 9 of the 18 infants enrolled. Baseline characteristics were as follows (Mean±SD): Birth weight, AKI 760.7± 176 g vs. No AKI 788.6 ± 138.8 g, p=NS; GA, AKI 25.1 ± 1.21 wks vs. No AKI; 26.4 ± 1.09 wks; p<0.05. Infants with AKI demonstrated a trend towards more frequent IH and more time spent with SpO₂<80% (figure 1). Due to the low sample size and the amount of variability in the data, no statistically significant differences were found. CONCLUSIONS: IH is common in preterm infants in the first 4 weeks of life. In the AKI group, infants had more frequent IH events that did not reach statistical significance. Further investigation of the mechanistic association of IH and AKI in preterm infants is necessary to improve the care of this vulnerable population. A large prospective study testing urinary biomarkers of AKI to assess associations with IH is currently ongoing.

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POSTER PRESENTATION #137

Abstract Title: **Exercise Regulates Energy Metabolism in a Novel 'Stress-Less' Mouse**

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Abstract: Oxidative stress (OS) plays a key role in obesity by altering skeletal muscle fiber type, myokine levels and alters adipose tissue adipokine expression. These changes can negatively impact energy metabolism creating an obese phenotype. Exercise paradoxically increases redox stress which in-turn signals antioxidant protection. Therefore, we hypothesized reducing OS would lower fat mass, improve skeletal muscle and adipocyte function, and enhance energy metabolism. Two 'stress-less' mouse models were used that overexpress antioxidant: (i) catalase transgenic (Cat-tg), that overexpress catalase 3-4 fold higher than wild type littermates and (ii) a hybrid between Cat-tg and obese mice (Ob/Ob), Bob-Cat. These "stress-less" models and their wild type controls were subjected to a moderate exercise (8 weeks of treadmill, 15m/min for 30 min) or sedentary regimen. Body weight, food intake, fat and lean mass (ECHO-MRI), metabolic parameters (CLAMS), and adipose and skeletal muscle function were determined. Results showed Bob-Cat and Cat-tg groups on exercise lost weight and fat mass compared to the wild type, C57BL6, sedentary group. CLAMS revealed increased energy expenditure and food intake within all exercise groups except Bob-Cats. Exercise also trended toward increased plasma insulin and HDL levels. Within adipose tissue, exercise trended to increase the mRNA expression of adiponectin and catalase and catalase activity in C57 and Cat-tg groups. Exercised groups trended toward higher ratios of Type1/Type2 muscle fibers. Our results reveal exercise positively impacted energy metabolism and obesogenic pathways in the novel "stress-less" mouse.

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POSTER PRESENTATION #138

Abstract Title: **Nucleoside Reverse Transcriptase Inhibitors Suppress Laser-Induced Choroidal Neovascularization in Mice**

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Abstract: Nucleoside reverse transcriptase inhibitors (NRTIs), widely used to treat HIV infection, have been shown to be therapeutic in a mouse model of dry AMD, through their intrinsic anti-inflammatory activity that targeted the purinergic receptor P2X7 and the NLRP3 inflammasome pathway. One NRTI, stavudine (d4T) was found to suppress laser-induced choroidal neovascularization (CNV) in mice in a P2X7-dependent fashion. Here we evaluate the efficacy of three other NRTIs in the laser-induced mouse model of CNV. We evaluated the NRTIs lamivudine (3TC), zidovudine (AZT), and abacavir (ABC), and the P2X7 antagonist A438079. CNV was induced by laser injury in C57BL/6J wild-type, Nlrp3^{-/-}, and P2rx7^{-/-} mice, and CNV volume was measured after 7 days by confocal microscopy. Drugs were administered by intravitreal injection immediately after the laser injury. VEGF-A in RPE-choroid lysates was measured three days after laser injury by ELISA. HEK293 cells expressing human and mouse P2X7 were exposed to the selective P2X7 receptor agonist, 2', 3'-(benzoyl-4-benzoyl)-ATP (Bz-ATP) with or without 3TC, and VEGF-A levels in media were measured by ELISA. Intravitreal injection of 3TC, AZT, and ABC significantly suppressed laser-induced CNV in C57BL/6J wild-type and Nlrp3^{-/-} mice ($P < 0.05$), but not in P2rx7^{-/-} mice. Intravitreal injection of A438079 also suppressed the laser-induced CNV ($P < 0.05$). 3TC, AZT and ABC blocked VEGF-A levels in the RPE/choroid after laser injury in wild-type ($P < 0.05$) but not P2rx7^{-/-} mice. Moreover, there was no additive effect of 3TC on CNV inhibition when co-administered with a neutralizing VEGF-A antibody. Stimulation of human and mouse P2X7-expressing HEK293 cells with Bz-ATP increased VEGF secretion ($P < 0.001$), which was abrogated by 3TC ($P < 0.001$). Stimulation of primary human RPE cells with Bz-ATP increased VEGFA and IL6 mRNA levels, which was abrogated by 3TC. Concluding, multiple clinically relevant NRTIs suppressed laser-induced CNV, and down-regulated VEGF-A, via P2X7.

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POSTER PRESENTATION #139

Abstract Title: **Ethanol Induces ER-Stress and the Expression of Mesencephalic Astrocyte-Derived Neurotrophic Factor in Neuroblastoma Cells**

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Abstract: Objectives: Ethanol exposure can lead to significant neurodegeneration in the developing brain due to elevated endoplasmic reticulum (ER)-stress. Mesencephalic astrocyte-derived neurotrophic factor (MANF) is an ER-stress inducible protein expressed in many cell types including neurons. Previous studies have shown that MANF can protect cells from ER-stress induced apoptosis, yet the mechanism is still to be elucidated. In this study, we will examine whether ethanol exposure can induce ER-stress and MANF expression in neurons in vitro, and also develop neuron-specific MANF knockout mice models for the long-term goal to test whether MANF can protect neurons from ethanol-induced neurodegeneration and explore potential mechanisms of its neurotrophic role. Methods: Neuroblastoma cells N2a (mice) and SH-SY5Y (human) were treated with EtOH at the pharmacologically relevant concentration of 400 mg/dl. Gene expression was analyzed by immunohistochemistry and western blot. Purkinje cell-specific MANF-deficient mice will be generated using the Cre/loxP system. Mice homozygous for the Manf-floxed allele will be crossed with Purkinje cell-specific Cre lines: B6.Cg-Tg(Pcp2-cre)3555Jdhu/J and B6.129-Tg(Pcp2-cre)2Mpin/J. Mice will be genotyped by PCR. Results: Ethanol exposure to neuroblastoma cells induced the expression of unfolded protein response (UPR) genes including GRP78, activated-ATF6, CHOP, and XBP1s. MANF was also upregulated. MANF was expressed in both the developing and mature Purkinje cells in the wild type mice brain. Both the Manf-floxed and pcp2-Cre mice are viable and the breeding process is undergoing as planned. Conclusion: Ethanol exposure leads to ER-stress in neuroblastoma cells, which activates unfolded protein response and upregulates the expression of MANF. MANF-deficient mice will offer a powerful tool for the investigation of ER-stress in ethanol neurotoxicity.

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POSTER PRESENTATION #140

Abstract Title: **ESwab vs Scalpel Blade Scraping for the Corneal Ulcer**

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Abstract: Background: Dozens of patients are referred yearly to the cornea service with corneal ulcers. Ideally, empiric antibiotic should be initiated following corneal ulcer scrapings and then tailored following culture sensitivities. This is difficult given that many patients from rural communities are initially seen by an eye care provider who may lack the experience and lab supplies necessary for corneal scrapings. The present study assessed the non-inferiority of a less-invasive collection method (ESwab; Copan Diagnostics, Inc) in comparison to the current standard of care. Methods: Consenting patients (n= 30) with suspected bacterial keratitis were enrolled. Each participant received the standard 2 scrapings for gram stains and KOH, followed by collection with the ESwab, after which the remaining traditional scrapings were performed. All collections were sent for culture and analysis. The primary outcome measure was concordance of culture growth between the two collection methods. The opportunity cost related to the treatment of each patient was also calculated, based on the distance the patient traveled to reach the Ophthalmology clinic. Results: 26 eyes from 26 patients have been sampled thus far. The concordance between the ESwab and scrapings was 100% (11/11) when no antibiotics had been given and 57% (8/14) when antibiotics had been given. However, the concordance between the ESwab at 4hours and the scrapings was 100% (12/12), while the ESwab at 24hours was positive 86% of the time when scrapings were negative and antibiotics were given. The concordance between the ESwab and scrapings was 100% when the scrapings were positive (15/15) and 30% (3/10) when the scrapings were negative. Results will change as more subjects are enrolled and the opportunity cost is calculated. Conclusion: The ESwab collection method is a more accessible, more cost effective, less invasive alternative to the current standard of care for corneal microbiological specimen collection. It is particularly effective in antibiotic naïve patients. The ESwab is not inferior in collection capabilities and can be used to increase organism specific treatment of bacterial keratitis.

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POSTER PRESENTATION #141

Abstract Title: **Adipose-Derived PAI-1 Correlates with Systemic Levels, Kidney Injury and Severity of Intra-Abdominal Sepsis**

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Abstract: Adipose tissue is recognized as an important contributor to chronic inflammatory diseases. Using a murine model, we previously reported that visceral adipose tissue is also highly active during acute inflammation and is a major source of cytokines and coagulant factors during experimental sepsis. The purpose of this study was to evaluate the clinical significance of adipose-derived inflammatory cytokines and pro-coagulant factors during sepsis. Surgical patients (n=76, Age: 24-88, BMI: 19-34, 52% female) undergoing an abdominal procedure were enrolled and categorized into four groups: Control (non-inflammatory), Local Inflammation (e.g. appendicitis), Sepsis (abdominal source of infection), and Severe Sepsis (sepsis with organ failure). Visceral adipose tissues (mesenteric, epiploic, and omentum) and blood were collected. All sources of adipose tissue from sepsis and severe sepsis groups showed trends of increased mRNA levels of IL-6, IL-1 β , PAI-1, PAI-2, and Thbs-1. Among these, PAI-1 was consistently and significantly upregulated more than 20-fold in the severe sepsis group compared to controls ($p < 0.05$). Plasma concentration of PAI-1 in patients with severe sepsis strongly correlated with PAI-1 mRNA levels in each of the adipose depots sampled ($r = 0.9$: mesenteric, $r = 0.7$: epiploic, $r = 0.8$: omentum), serum creatinine levels ($r = 0.92$, kidney injury marker), and plasma procalcitonin ($r = 0.8$, sepsis severity marker). Histologically, adipose tissue samples from patients with sepsis were absent of marked inflammatory cell infiltration. Collectively, these data indicate that high plasma levels of PAI-1 are strongly associated with the development of kidney injury and the severity of intra-abdominal sepsis, and are likely derived from upregulated PAI-1 production by resident cells within visceral adipose tissues.

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POSTER PRESENTATION #142

Abstract Title: **Incidence of Clostridium difficile Infection in Patients Undergoing Ileostomy Closure**

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Abstract: Recognized by the CDC for resulting in over 250,000 cases and 14,000 deaths of both hospitalized patients and patients in acute care hospitals, Clostridium difficile infection (CDI) is a major cause of morbidity and mortality in the hospital environment. As an enteric pathogen Clostridium difficile poses a particular risk to patients undergoing colorectal surgery, and previous studies have found higher rates of CDI in these patients. One such common colorectal procedure that has been understudied with regards to CDI incidence is ileostomy reversal, which is performed to close openings made in the small intestine and abdominal wall resulting from initial ileostomy surgery. The aim of this retrospective study is to characterize the rate of CDI among patients undergoing ileostomy closure by examining patient data from the University of Kentucky Medical Center (UKMC). CDI incidence data and patient demographic information was collected from a review of all patients who underwent colorectal resection, colostomy or ileostomy stoma creation, and colostomy or ileostomy closure procedures at the UKMC from January, 2014 to April, 2016. 1,585 patients undergoing the aforementioned colorectal surgeries were identified during this time period with 75 patients having a history of CDI. Of these 75 cases, 39 occurred within 40 days of the patient's surgery—13 cases occurring post ileostomy or colostomy reversal surgery and 26 cases occurring post colostomy, ileostomy or another colorectal resection procedure. Overall, postoperative CDI incidence in patients undergoing ileostomy or colostomy reversal at the UKMC from January, 2014 to April, 2016 appeared to be lower (0.8%) compared to patients undergoing stoma creation or other intestinal tract resection surgeries (1.8%). However, further analysis of CDI detection protocols and other surgical groups is needed for full comparison to the variety of published studies.

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POSTER PRESENTATION #143

Abstract Title: **ACS-NSQIP-based risk score predicts readmission after gastrectomy**

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Abstract: Introduction: No quantitative method exists to predict readmissions after gastrectomy. Unplanned readmissions are an economically and clinically significant problem. This study used a national database to examine predictors of early readmission and to create a scoring system to direct resource allocation and discharge planning. Methods: We identified gastrectomy patients with readmission data from the 2012-2014 ACS-NSQIP database. A cox-regression model identified the readmission predictors used to create a readmission risk score (RRS). Thirty-day readmission rates were compared to the RRS. Results: 475/4064 (11.7%) patients were readmitted within thirty days (median 6 days). Resection extent, cancer diagnosis, operative time, age, and sex did not affect readmission rates (all $p > 0.05$). 174 of the readmissions were for gastrointestinal/failure-to-thrive (FTT) issues (147 from partial vs. 27 from total, $p = 0.025$). 163 readmissions were due to infection (121 from partial vs. 42 from total, $p = 0.035$). Independent factors in the RRS included organ site infection (OR-4.61), deep surgical site infection (OR-4.33), myocardial infarction (OR-3.09), superficial surgical site infection (OR-2.39), venous thromboembolism (OR-2.46), sepsis (OR 1.86), and diabetes (OR 1.29), all $p \leq 0.025$. Only 8.3% of RRS=0 patients were readmitted, compared to 12.3% of RRS=1, 25.1% of RRS=2, 34.1% of RRS=3, and 41.3% of RRS ≥ 4 ($p < 0.001$). Conclusions: RRS 2, 3, and ≥ 4 , nearly doubled, tripled, and quadrupled readmission rates from baseline, respectively. In the current healthcare climate, which requires reducing readmissions using limited resources, this novel scoring system can focus post-discharge care on higher-risk gastrectomy patients with RRS ≥ 2 .

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POSTER PRESENTATION #144

Abstract Title: **DBS Plus: A Platform for Cell Therapy Delivery in Patients with Parkinson's Disease**

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Abstract: Clinical trials focusing on neurodegenerative diseases with cell therapy face many hurdles. Issues from regulatory approval to patient well-being may short-circuit the trial even before questions related to efficacy can be addressed. We have developed a strategy to address many of these issues and are in the process of carrying out two Phase I studies examining the safety and feasibility of autologous peripheral nerve grafts delivered to target brain areas at the time of deep brain stimulation (DBS) surgery as well as how the grafts may alter the progression of Parkinson's disease (PD). DBS therapy is FDA approved for the treatment of several conditions including PD. However, many PD-related symptoms are not relieved with DBS. In addition, PD is constantly progressing with no current therapy to halt or reverse the progression of the disease. We deployed nerve grafts containing Schwann cells from the sural nerve; Schwann cells, after injury, transdifferentiate to become "repair cells" and release a host of factors including GDNF, NGF, BDNF, and NT-3. Here we describe how our cell therapy delivery strategy has helped us clear many of the hurdles encountered in early-stage clinical trials. Three key advantages of our design are 1) because participants have their own sural nerve removed and transplanted at the time of DBS surgery, without any significant modifications, the delivery of the grafts does not require FDA oversight; 2) because DBS surgery is an insurance reimbursable procedure, trial costs are greatly reduced, and 3) because DBS is a standard of care for Parkinson's disease, patients do not have to forego the therapeutic benefits of DBS to participate in the trial. We have transplanted grafts into the substantia nigra and/or nucleus basalis of Meynert in 37 participants without any severe adverse events related to the study. For the 17 individuals who have had the surgery at least more than a year ago, 11 have shown clinically important improvements in their movements when we tested their underlying responses while temporarily off their therapy. Although more time is needed to follow all individuals to assess overall efficacy, we are finding that this approach of combining cell therapy at the time of DBS surgery provides a useful benefit when designing clinical trials examining neurological disorders.

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POSTER PRESENTATION #145

Abstract Title: **Implementation and Outcomes of an ERAS Protocol for Open Repair of Ventral Hernia**

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Abstract: Background: Enhanced Recovery after Surgery (ERAS) protocols are evidence-based quality improvement pathways reported to be associated with improved patient outcomes. The purpose of this study was to compare short-term outcomes for open ventral hernia repair (VHR) before and after implementation of an ERAS protocol. Materials and Methods: After obtaining IRB approval, surgical databases were searched for VHR cases for two-years prior and eleven months after protocol implementation. Groups were compared on perioperative characteristics and clinical outcomes using chi square, Fisher's exact or Mann Whitney U test, as appropriate. Process evaluation determined the level of adherence to protocol details. Results: 171 patients underwent VHR (46 patients with ERAS protocol in place and 125 controls). Preoperative characteristics of age, gender, ASA Class, comorbidities, and smoking status were similar between the two groups. Body mass index was lower among ERAS patients ($p = .038$). ERAS patients had earlier return of bowel function (median 3 days vs. 4 days) ($p = .003$) and decreased incidence of superficial surgical site infection (SSI) (7% vs. 25%) ($p = .008$) than controls. Protocol adherence by ERAS component ranged from a low of 54% (acceleration of intestinal recovery) to 100 % (postoperative glucose control). Protocol adherence by case varied from 55% (1 patient) to 94% (4 patients). Conclusions: A comprehensive ERAS protocol for VHR demonstrated improved patient outcomes. Process evaluation provided important information about our successes and opportunities for improvement. A system-wide culture focused on enhanced recovery is needed to improve protocol adherence and subsequent patient outcomes.

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POSTER PRESENTATION #146

Abstract Title: **Peripheral Nerve Grafts to the Brain of Patients With Parkinson's Disease: Microscopic, Biochemical, and Immunohistochemical Characterization**

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Abstract: Currently two clinical trials (NCT01833364 and NCT02369003) are underway which feature the implantation of a peripheral nerve autograft to the brain (targeted either to the Substantia Nigra or the Nucleus Basalis of Meynert) in combination with Deep Brain Stimulation (DBS) for the treatment of patients with Parkinson's disease. This nerve tissue is harvested from the sural nerve (a sensory nerve located in the ankle) of patients undergoing DBS surgery. Two tissue samples per patient are collected for study (one during the Stage I surgery, another during the Stage II surgery 5-14 days later) in addition to the tissue used for the graft. As of 2/27/16, 40 patients have received a graft. This study examines several aspects of the peripheral nerve tissue; including microscopic appearance, levels of neurotrophic factors, morphology of Schwann Cells, and presence of macrophages. Techniques used include H&E and MCOLL histological staining, immunohistochemistry, and ELISA. These results are supplemented by immunohistochemical analysis of the brain of non-human primates that have undergone an analogous procedure. The results of this model show growth of tyrosine hydroxylase-containing nerve fibers, which are a marker of dopamine-producing neurons, into the area of the peripheral nerve graft. In addition, results in this model show the presence of S100beta-containing cells as well as GFAP-containing cells within and surrounding the graft, which is a marker of peripheral nerve regeneration. These findings suggest that the nerve graft in human patients may also display a regenerative phenotype which has the potential to alter the course of neurodegeneration in the brain.

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