Poster Presentation 95

Abstract Title:	**Altered Parvalbumin Cell Populations in Dorsolateral Prefrontal Cortex after Neonatal Hippocampal Damage in Macaques.**
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Abstract: The parvalbumin (PV) class of GABA interneurons is involved in sustaining the normal neuron signaling that supports proper functionality of the Dorsolateral Prefrontal Cortex (dlPFC) executive system. Because the dlPFC undergoes a protracted development, any disruption may play a role in working memory impairment and other cognitive deficits associated with neurodevelopmental disorders including schizophrenia (SCZ). Thus, we predicted that a neonatal hippocampal lesion would disrupt the normal PV-positive cell maturation within the dlPFC, consistent with an early limbic-prefrontal disconnection model of SCZ. We used tissue from four control and four experimental adult rhesus monkeys that sustained bilateral neonatal hippocampal lesions of varying degree to better understand the role of the hippocampus in dlPFC development. Specifically, we analyzed the relative density of PV-positive GABAergic interneurons in cortical layers IIIA and IIIB of Brodmann Area 46d of lesioned (Neo-H) and non-lesioned monkeys (Neo-C). We found a significantly higher density of PV-positive cells, specifically within layer IIIA of the dlPFC of Neo-H monkeys relative to the Neo-C monkeys, both between the left hemispheres of the two groups and across the groups when both hemispheres were considered together. These results were confirmed by estimations of total PV-positive cell populations in layer IIIA of area 46d. Moreover, layer IIIA PV densities of the Neo-H group were significantly positively correlated with the extent of hippocampal damage. Ultimately, these findings have implications for how neonatal lesions of the hippocampus may affect vulnerable structures and disrupt cognitive processing, eventually leading to deficits characteristic of neurodevelopmental disorders including schizophrenia.

Supported by: NIH award: MH-058846

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Poster Presentation 96

Abstract Title:	**Cortical Iron Accumulation Disrupts Brain Networks Supporting Working Memory in Older Adults**
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Abstract: Iron is a vital contributor to healthy brain function. However, iron accumulation in brain tissue can contribute to cognitive impairment and neurodegeneration. For instance, recent studies report a negative association between iron content in the brain and working memory performance. The mechanisms by which iron concentration affects memory, however, are poorly understood. Here, using Quantitative Susceptibility Mapping (QSM), an in vivo MRI technique for measuring iron content in the brain, in conjunction with task-based functional connectivity, we explored how cortical iron accumulation affects the neural networks that mediate visual working memory in healthy older adults (n = 28; age range: 67-85). Using whole-brain fMRI activity from an n-back visual working memory task, conducted inside a 3T MRI scanner, we identified four brain regions in which fMRI activity significantly predicted task performance as follows: the anterior cingulate gyrus (ACC), left dorsolateral prefrontal cortex (DLPFC) and bilateral inferior parietal lobules (IPL). Then, using each of these regions as a seed, the task-based functional connectivity of each region with every other region was calculated and subsequently correlated with QSM values (ppb) extracted from individually defined gray matter lobar masks (controlling for age and gender). We found that frontal and parietal lobe QSM negatively predicted the degree of task-based functional connectivity between all seed ROIs (frontal: p = 0.004, Beta = -0.56; parietal: p = 0.0001, Beta = -0.71). In contrast, QSM in the temporal and occipital lobes did not affect functional connectivity. Our results suggest that iron accumulation in the frontal and parietal lobes negatively impact neural networks that support working memory in older adults.

Supported by: NIH award: R01AG055449

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Poster Presentation 97

Abstract Title:	**Women Show Higher Cerebral Blood Flow than Men in Older Age**
Author(s):	E. R. Seago, Department of Neuroscience, U of Kentucky V. Zachariou, Department of Neuroscience, U of Kentucky C. E. Bauer, Department of Neuroscience, U of Kentucky B. T. Gold, Department of Neuroscience, U of Kentucky

Abstract: Adequate cerebral blood flow (CBF) is essential for proper delivery of oxygen and nutrients to brain tissue. Previous studies have linked age-related declines in CBF with neuropsychological deficits, lower brain volume, and larger volume of white matter hyperintensities (WMH) associated with vascular disease. In this study we tested for possible sex differences in these metrics of brain health in older adults. Thirty-one cognitively normal older adults (ages 67-85) were recruited from the UK Sanders Brown Center on Aging. CBF was quantified using MRI pseudo-continuous arterial spin labeling (PCASL) scans and WMH volume was identified using fluid attenuated inversion recovery (FLAIR). Then, using individually defined Freesurfer lobar and subcortical masks, we extracted cortical and subcortical CBF as well as cortical and subcortical structure volume (in mm3) for each participant and identified location of WMHs. Subsequently, in a multivariate ANOVA, we tested the main effect of sex on CBF, structure volume, and volume of WMHs. Sex had a significant main effect on CBF ($F(2,25)=4.138$, $p= .028$), with women showing higher CBF in both cortical and subcortical grey matter. Sex was also had a significant main effect on measures of brain volume ($F(2,25)=5.291$, $p=.012$) with women having both smaller ventricular volume and larger grey matter volume. However, sex did not have a significant main effect on WMH volume. Our results suggest that CBF may be a more sensitive measure of vascular health than WMHs. However, future research with a larger sample sizes will be required to confirm this conclusion.

Supported by: NIH award: RO1AG055449

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Poster Presentation 98

Abstract Title:	**Leisure Activities Improve the Functional Connectivity of the Neural Networks that Support Working Memory**
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Abstract: Cognitive reserve (CR) is the brain's ability to protect itself from cognitive impairment in the face of increasing brain pathology. Previous studies, using resting state functional connectivity have shown that higher CR correlates with increased resting-state functional connectivity and improved working memory performance. Few studies, however, have explored how CR impacts task-based functional connectivity when the neural networks that support working memory are engaged while participants execute working memory tasks. Here, we used task-based functional connectivity, in conjunction with an n-back visual working memory task, participants (n = 31) performed inside a 3T MRI scanner, to explore how CR, quantified using the CR index scale (CRI), affects the neural networks that support working memory. Using fMRI activity from the n-back task, we identified four brain regions where brain activity significantly predicted task performance: the anterior cingulate gyrus (ACC), left dorsolateral prefrontal cortex (DLPFC) and bilateral inferior parietal lobules (IPL). Using each region as a seed, the task-based functional connectivity of each region with every other region was calculated and correlated with the three subdivisions of CRI: CRI-Working, CRI-Education, and CRI-Leisure. We found that CRI-Leisure positively predicted the degree of task-based functional connectivity between the left IPL and the remaining seed ROIs. CRI-Working and CRI-Education did not predict functional connectivity. We conclude that CRI-Leisure, comprised of participation in activities such as reading, dancing, etc. is associated with the health of the frontoparietal neural network that supports working memory. The impact of CRI-Leisure appears to be focused on the posterior parietal brain regions of this network.

Supported by: NIH Award: R01AG055449

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Abstracts

Poster Presentation 99

Abstract Title:	**Wash In - Wash Out: Improving Hand Hygiene Compliance with the Use of a Visibility Board**
Author(s):	T. Kellenbarger, Nursing Practice Services, University of Kentucky

Abstract: Purpose: To improve both staff and overall hand hygiene compliance in the Transitional Units. Method: The visibility method was used for the hand hygiene compliance goal. The fiscal year 19 (FY19) goal was set for staff as a measure on their performance evaluation. Unit staff consists of Nurses, Nursing Care Techs and Patient Clerical Assistants. A visibility board was set up on the 2 Transitional Unit (2TU) to display monthly data and compliance for all staff who enter into or exit out of patient rooms. Compliance results are also sent to staff in weekly notes from the Patient Care Manager (PCM), reviewed in quarterly staff meetings, and discussed in daily safety huddles. Signs reinforcing the UK Healthcare "Threshold Rule" were hung on both units. Staff were also encouraged to advocate for their patients by reminding any university employee who failed to complete hand hygiene either going into or coming out of the patient room of the threshold rule. Results: The unit goal was set for a Threshold/Target/Max of 80%/90%/95%. As a result, the overall unit compliance improved from 70% in FY18 to 89% in FY19 to date. The unit staff compliance improved from 73% in FY18 to 92% in FY19 to date. Efforts will be made for the remaining 5 months to elevate staff compliance to the max goal of 95% or greater. Unit nursing leaders are also looking at individual group data with lower compliance to target for increased education and awareness to increase overall compliance.

Supported by: No Sources of Support

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Poster Presentation 100

Abstract Title:	**Using Plasma and Breath Measures to Detect APOE-dependent Changes in Glucose Metabolism**
Author(s):	R. Khanal, Department of Physiology G.Nation, Department of Physiology B. Farmer, Department of Physiology D. Carter, Department of Physiology L. A. Johnson, Department of Physiology

Abstract: Apolipoprotein E (APOE) is present in both the periphery and the brain, and is associated with circulating lipoproteins. APOE is well known for its connection to both Alzheimer's disease (AD) as well as cardiovascular diseases (CVD). In humans, there are three common isoforms of apoE: E2, E3, and E4. Compared to E2 and E3, E4 is associated with an increased risk of both AD and CVD. AD is associated with metabolic and vascular factors – both of which precede and may contribute to dementia. Interestingly, E4 is associated with deficiencies in both areas; there is both decreased cerebral glucose metabolism and lower cerebral blood flow in E4 individuals. However, the precise mechanism by which APOE alters metabolism is unknown. Therefore, we are conducting a human study in which we probe the effects of APOE on glucose and lipid utilization by measuring metabolic rate and respiratory exchange ratio (RER) – a reflection of energy substrate usage – using indirect calorimetry. Our preliminary findings in 60 subjects show measurable increases in RER during a cognitive challenge, as well APOE genotype specific effects on resting energy expenditure (REE). Additionally, a dietary glucose challenge resulted in an increase in RER only in E4 individuals. Plasma glucose levels also show an APOE-dependent change pre- and post- dietary challenge, with E4 individuals demonstrating larger increases. These findings are an important step toward elucidating the precise mechanism of APOE's effects on metabolism in order to better understand the role of this important genetic risk factor on vascular disease and dementia.

Supported by: NIH award: R01 AG060056 01 AHA award: 19PRE34380094

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Abstracts

Poster Presentation 101

Abstract Title:	**Developing and Testing a Smart Phone App to Enhance Voice Therapy Adherence**
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Abstract: Background: Maximizing effectiveness of evidence based voice therapies is the next step in the evolution of voice rehabilitation. Outcome studies of several voice therapy programs have demonstrated the effectiveness and efficiency of the programs. However, research has also demonstrated that of patients who initiate voice therapy, 47% do not complete the program, thus significantly reducing the effectiveness of treatment. An established barrier to therapeutic success is poor adherence to voice therapy. Objective: To investigate the influence of smartphone App delivery on adherence to voice therapy approach, specifically, Vocal function exercises (VFE) when compared to the traditional method of voice therapy delivery. The primary outcome measure was adherence, as calculated by the number of missed home-practice sessions. Methods: Thirty-three participants with normal voice were randomized to the traditional delivery or smartphone delivery. Both groups completed a 6-week VFE intervention. The traditional group recorded their data on a log sheet and were provided with audio files of the exercises. The App group video-recorded home practice sessions. Comparisons were made between the percentages of missed home practice tasks between the two groups. Significance was set at $p<0.05$. Results: Twenty six participants completed the study. On average, participants in the App group missed 202.09 (SD=79) tasks, and the traditional group missed 409.08 (SD=274) home practice tasks. Differences between the number of missed sessions between the two groups were statistically significant (p=0.04). Conclusions: Delivery of VFEs through a smartphone app was successful in improving adherence to home practice sessions of voice therapy.

Supported by: Myron and Elaine Jacobson Entrepreneurship Award (College of Health Sciences)

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Poster Presentation 102

Abstract Title:	**Cookbook Voice Therapy: A Recipe for Disaster?**
Author(s):	M.H. Bane, Department of Rehabilitation Sciences, U of Kentucky J.C. Stemple, Department of Rehabilitation Sciences, U of Kentucky

Abstract: Several voice therapies are supported by outcomes research demonstrating treatment efficacy. However, the active ingredients (AIs) responsible for efficacy have not been identified, and many are likely missing from voice therapy protocols. Our previous research dismantled a prescriptive, evidence-based program, Vocal Function Exercises (VFEs), to identify AIs by systematically modifying individual treatment aspects in a series of randomized trials. Dosage, mouth posture, goal-setting, and duration were identified as AIs which could be modified to an extent while preserving treatment efficacy. Our current research will identify AIs not described in the VFE protocol: 1) Clinicians routinely tailor treatments to individual patients. An online survey of clinical practice will identify the rationale for and deviations from the VFE protocol as potential AIs underlying treatment efficacy. Pilot data indicate all speech pathologists modify VFEs as a result of patient characteristics or clinical preference. 2) VFEs are employed by clinicians of various experience levels. Healthy volunteers randomized to an experienced or inexperienced clinician will complete six weeks of VFEs to determine the effect of clinician experience on the outcome measure of maximum phonation time (vocal efficiency). 3) Evidence-based therapies are delivered within an overarching therapeutic context. This grounded theory study will develop a theory of the process of using VFEs with individual patients.

Supported by: TL1TR001997

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Poster Presentation 103

Abstract Title:	**The Relationship Between Sex, Premorbid Function, and Comorbidity on Cognitive and Emotional Health in Survivirs of Critical Illness**
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Abstract: Introduction: Approximately 50% of patients surviving an admission to the intensive care unit (ICU) for critical illness develop long-term deficits in physical, emotional, and mental health, described as post-intensive care syndrome (PICS). Although older age, higher severity of illness, and longer times requiring mechanical ventilation increases risk of PICS, there is less known about the association between sex and premorbid health with PICS development. Purpose: The primary purpose of this study is to elucidate the relationship between sex, body-mass index, and premorbid function with cognitive and emotional health in patients surviving critical illness. Methods: A prospective observational study was performed on patients pending discharge from the hospital or at one-month follow-up visit in the ICU Recovery Clinic at an academic medical institution. Adult patients with admitting diagnosis of acute respiratory failure, sepsis, heart failure, or lung transplantation with an ICU stay > 4 days were eligible. A series of emotional and cognitive health assessments were performed. Descriptive statistics and linear regression will be performed to assess the association between the entire population with scores on outcome measures. Secondarily, we will perform independent t-tests (Wilcoxon 2-sample test) and chi-square (Fisher's Exact Test) to test for differences in outcomes scores based on the independent variables and co-variates. Results: 30 patients with a mean age of 52.5 years (15 female, 50%) participated in this study. Data collection of these patients is complete and pending statistical analysis. Final results and analyses on the HADS, MOCA, IES, and Eq-5D will be ready by time of presentation. Conclusion: We initially hypothesize that cognitive function will not differ between females and males. Secondarily, we believe that younger patients with unhealthy BMIs will have lower mental, emotional, and cognitive health scores.

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Abstracts

Poster Presentation 104

Abstract Title:	**The Bayesian Method for Confounding Adjustment as Applied to Personality and Substance Use Data to Estimate Average Causal Effect**
Author(s):	L. Su, MD/PhD program, University of Kentucky C. Wang, Department of Biostatistics, University of Kentucky C. Lee, Department of Psychology, University of Kentucky R. Milich, Department of Psychology, University of Kentucky D. Lynam, Department of Psychology, Purdue University

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.

Supported by: N/A

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Poster Presentation 105

Abstract Title:	**Using Random Forest Analysis to Improve Hospital's Implementation and Grouping of Transitional Care Strategies**
Author(s):	Gaixin Du, Center for Health Services Research, U of Kentucky Jing Li, Center for Health Services Research, U of Kentucky Arnold Stromberg, Department of Statistics, U of Kentucky Jessica Clouser, Center for Health Services Research, U of Kentucky Mark Williams, Center for Health Services Research, Department of Internal Medicine, U of Kentucky Glen Mays, Department of Health Management and Policy, U of Kentucky

Abstract: Objective . Transitional care (TC) is a critical factor in efforts to reduce hospital readmissions. TC strategies employed by hospitals are usually intercorrelated and administrated in groups. Our team have applied factor analysis (FA) and latent class analysis (LCA) to identify the combinations of TC strategies on the hospital characteristic pattern. However, the effectiveness the factors and classes on predicting readmission hasn't been fully investigated. We aim to use Random Forest (RF) to validate the combinations from two different methods. Procedures. Hospital characteristics were collected through a survey administered to 370 hospitals nationwide in 2015-2016. Readmission rates and patient characteristics were extracted from CMS inpatient claims data (2009-2014) for the associated hospitals. Community information is from Area Health Resource File. The Random Forest algorithm incorporated patient, hospital and community covariates in four models: 1) factors only, 2) TC strategies only, 3) latent classes only, and 4) all of the above. Results. RF validate that factors from the FA results and the latent class from the LCA have similar proportion of importance 0.72%&0.63%. They account 37.1% & 32.7% of the sum variance explained by individual TC strategies together. The relative importance of each variable in the full model and reduced model are similar. The combination of the TC strategies or the key TC strategies are taking more relative importance. Some key strategies work better individually than combination in predicting readmission. Conclusions. Results from RF provide guidance for efficiently regrouping TC strategies to maximize the efficiency and applicability.

Supported by: Funding Acknowledgement: This work was supported through a Patient-Centered Outcomes Research Institute (PCORI) award (Contract #TC-1403-14049).

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Poster Presentation 106

Abstract Title:	**White Matter Hyperintensity Regression is Associated with Decreased Brain Atrophy and Improvement in Memory Performance**
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Abstract: Background: Subcortical white matter hyperintensities (WMH) in the aging population frequently represent vascular injury that may lead to the cognitive sequelae. The dynamic nature of WMH have been well described in the literature, although the factors underlying WMH regression remain poorly understood. Methods: A sample of 377 participants from the Alzheimer's Disease Neuroimaging Initiative 2 (ADNI2) were included in the analysis. Inclusion criteria required available data regarding WMH volumetric quantification, structural brain measures (i.e., brain volume), and cognitive composite measures (memory and executive function) at baseline and after approximately 2 years, allowing changes in these measures (□) to be calculated. Subjects were categorized into three groups based on WMH change over time, including those that demonstrated regression (n=96; 25.5%), stability (n=72; 19.1%), and progression (n=209; 55.4%). Results: There were no significant differences in age, education, sex, or cognitive status between the three groups. ANOVA demonstrated significant differences in Δ atrophy composite between the progression and regression ($p = 0.004$) and the progression and stable groups ($p = 0.012$). Memory assessments improved over time in the regression and stable groups compared to those in the progression group in whom these measures declined ($p = 0.003$; $p = 0.018$). Conclusions: WMH regression is associated with decreased brain atrophy and improvement in memory performance over two years compared to those with WMH progression. These data suggest that WMH are dynamic and directly reflect both declines and improvements in cognitive performance depending on volumetric change over time. Further work elucidating the factors associated with WMH regression, stability, and or progression may help identify targets for therapeutic intervention for cSVD related cognitive decline and dementia.

Supported by: Data collection and sharing for this project was funded by the Alzheimer's Disease Neuroimaging Initiative (ADNI) (National Institutes of Health Grant U01 AG024904) and DOD ADNI (Department of Defense award number W81XWH-12-2-0012). ADNI is funded by the

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Poster Presentation 107

Abstract Title:	**Sex and Sport Differences in Baseline Neurocognitive Performance in Division-I Collegiate Athletes using the NIH-Toolbox Cognitive Battery**
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Abstract: Context: Neurocognitive testing is often performed following sport-related concussion to track recovery and make return to participation decisions. Understanding sex and sport-related differences in baseline neurocognitive scores aids in interpreting post-injury performance. Although available for some neurocognitive tests, sex and sport-related differences in neurocognitive performance for collegiate athletes have not been examined on the National Institutes of Health-Toolbox Cognitive Battery (NIHTB-CB). Objective: Determine if baseline NIHTB-CB scores differ between sex or sport in collegiate athletes. Participants: A total of 107 Division-I athletes (47 females, 60 males) that participated in soccer (n=45), football (n=30), or cheerleading (n=32) volunteered to participate. Methods: Participants completed tablet-based NIHTB-CB tests including the Flanker Inhibitory Control & Attention (FICA), Dimensional Change Card Sort (DCCS), Picture Sequence Memory (PSM), and Pattern Comparison Processing Speed (PCPS) tests. These assessments measured visual attention, cognitive flexibility, memory recall, and processing speed, respectively. Demographically-corrected scores were used for analyses. A combination of parametric and non-parametric tests compared scores based on sex and sport for each test. Results: Females demonstrated greater performance on the PCPS (p=0.006) while males exhibited better performance on the FICA (p=0.009). After controlling for sex, a significant difference across sports was identified in the FICA (p=0.007) with cheerleading exhibiting poorer performance than football (p=0.002) and soccer (p=0.047). No sex or sport differences were identified for the DCCS or PSM. Conclusion: Baseline differences in neurocognitive performance exist on the NIHTB-CB based on sex and sport suggesting these variables be taken into consideration when interpreting post-concussion scores in collegiate athletes.

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Poster Presentation 108

Abstract Title:	**Building on Appalachian Cultural Traditions to Support Rural Grandparent Caregivers**
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Abstract: Purpose: Poverty and poor health disproportionately affect older adults serving as primary caregivers to their grandchildren. Grandparent caregivers living in rural and underserved regions, including Appalachia, are especially vulnerable. However, Appalachian cultural traditions, including religious practices and spirituality, offer grandparents support when facing these challenges. Methods: To improve understanding of the role religion and spirituality play in coping, twenty-six grandparent caregivers, recruited through community organizations and snowball sampling, engaged in a series of four interviews. A coding team applied conventional content analysis to the transcripts, employing multiple approaches to ensure rigor and transferability. Results: Findings suggest that religion and spirituality help grandparent caregivers cope by (1) providing a sense of purpose and perspective; (2) fostering peace and perseverance; (3) encouraging forgiveness; and (4) strengthening social cohesion. Discussion/Conclusion: An improved understanding of the coping strategies employed by grandparent caregivers combined with a greater awareness of existing community assets can inform effective interventions for grandfamilies. Our findings suggest numerous opportunities for practitioners, policymakers, faith leaders, and social service administrators to leverage cultural traditions in Appalachian communities in order to support grandfamilies. For example, acknowledging the great solace grandparents find in attending church, religious and spiritual organizations may consider expanding programming for grandparents through developing programs that facilitate grandparents' development of a sense of purpose through good works, or programs that honor grandparents such as intergenerational scripture studies. Community leaders, local service providers and spiritual leaders may also consider seeking opportunities to locate programming for grandparents in religious and spiritual locations.

Supported by:	The University of Kentucky Center for Clinical Translational Sciences (Keller); the National Center for Advancing Translational Sciences: UL1TR000117/UL1TR001998; UKHealthCare; the Retirement Research Foundation (#2014-211: Schoenberg); Igniting Research

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Poster Presentation 109

Abstract Title:	**Risk Factors for Severe Maternal Morbidity in Kentucky Women**
Author(s):	Anna Hansen, Department of Sociology, University of Kentucky Dr. Svetla Slavova, Department of Biostatistics and Kentucky Injury Prevention Center, University of Kentucky

Abstract: Background. Women in the United States have face a steadily increasing risk of experiencing severe maternal morbidity (SMM) in pregnancy. The purpose of this study is to elucidate what factors increase Kentucky women's risk of experiencing SMM. Methods. We identified obstetric patients in state-wide inpatient hospital data in 2017. We used a logistic regression model to evaluate the association between experiencing SMM, women's demographic information, and common chronic disease states. Results. 2.12% of cases included within the study exhibited SMM. Risk factors significantly associated with SMM were race, state region, rurality and common disease states, namely hypertension, diabetes, and opioid use. When controlling for all other independent variables, the odds of black women experiencing SMM was nearly twice that of non-black women. The odds of Appalachian women experiencing SMM was 1.3 times the odds of non-Appalachian women, and the odds for women living in rural counties not adjacent to metropolitan counties was 1.5 the odds of women living in more populated areas. Common pre-pregnancy disease states associated with poor maternal outcomes in other populations were also determined to increase risk for SMM amongst Kentucky women. The odds of women with hypertension experiencing SMM was 20 times the odds of non-hypertensive women, the odds of a woman with type-II diabetes mellitus was 1.7 that of non-diabetic women, and the odds of women with a history of opioid use was twice that of women with no history of opioid use.

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Poster Presentation 110

Abstract Title:	**Self-Esteem Through Exercise: "Health & Fitness for All" Including Individuals with Intellectual and Developmental Disabilities**
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Abstract: Individuals with disabilities often suffer from health disparities, including obesity and depression. The purpose of this presentation is to describe Health & Fitness for All, a community-based program which incorporates exercise, universal design, and health coaching for individuals with intellectual and developmental disabilities to encourage a healthy lifestyle. Collaborating with the Human Development Institute at the University of Kentucky, the curriculum focus for the month of September was exercise. The overall goal was to develop weekly exercise activity for people with intellectual and developmental disabilities, their families, neighbors and friends. Objectives were threefold: introduce participants to varying forms of exercise, demonstrate these exercises and activities in public spaces, and initiate a health coaching dialogue. The following four sessions were implemented: 1) exercise scavenger hunt at the Kentucky Arboretum; 2) hiking and strength training at the Legacy Trail; 3) circuit training and yoga at a local park; and 4) cycling and basketball at a local YMCA. Universal design in the form of letters, numbers, images and stick figures were used for signage. Activities encouraged self-efficacy and relationship development. All sessions included a greeting and introduction from each participant, a warm-up, free choice exercise and partners when required, and a cool-down. Benefits of each exercise were discussed informally during the group activity. Health coaching questioning was posed to the group both pre- and post-activity. Questions included: How do you feel now (pre-activity)? How do you feel when you exercise? What is your favorite exercise? Would you do this type of exercise again? How do you feel now (post-activity)?

Supported by: Health and Fitness for All - Arc of Kentucky and Anthem

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Poster Presentation 111

Abstract Title:	**CD36, A Fatty Acid Translocase, Promotes Colorectal Cancer Cell Growth and Survival**
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Abstract: Altered fatty acid metabolism is a potential target for cancer therapy. Fatty Acid Translocase (CD36), a fatty acid transporter, and Fatty Acid Synthase (FASN), a key enzyme of de novo lipogenesis, are upregulated in colorectal cancer (CRC). However, the role of CD36 in CRC as well as its relation to de novo lipid synthesis is not understood. We show that CD36 is overexpressed in primary CRC as compared to normal colon mucosa and it positively correlates with FASN expression. shRNA-mediated knockdown of FASN leads to an induction of CD36 expression in CRC cells. Furthermore, CRC cells treated with TVB-3664, a FASN inhibitor, exhibit an upregulation of membrane-bound CD36. Treatment with SSO, a CD36 inhibitor, inhibits cellular proliferation which is further reduced when SSO treatment is combined with TVB-3664. Both knockdown and chemical inhibition of CD36 decrease expression of survivin, an oncogene implicated in cancer cell survival. In contrast, CD36 overexpression increases survivin in CRC cells. A higher level of survivin is observed in Pt2402 CD36+ cells as compared to Pt2402 CD36- cells. Finally, CD36 knockdown completely abolishes the ability of HCT116 cells to form xenograft tumors in vivo. In summary, CD36 upregulation is associated with an increase in tumorigenicity of CRC cells in vitro and in vivo. Data suggest that CD36 promotes tumor growth via upregulation of survivin and inhibition of pro-apoptotic proteins such as caspase-3 and PARP. A decrease in FASN expression is associated with CD36 induction, suggesting that it is a possible mechanism of resistance to FASN inhibitors.

Supported by: NIH award: T32ES07266 NIH award: P20GM121327 NIH award: R01CA208343

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Poster Presentation 112

Abstract Title:	**The Role of Androgens in Natural Killer Cell Attack of Urothelial Bladder Cancer Cells: Relevance to Bladder Cancer Gender Differences**
Author(s):	Lydia Livas, College of Medicine, U of Kentucky Charles T. Lutz, Department of Pathology, U of Kentucky

Abstract: In most organs, males are more likely than women to developing malignancy. This gender difference is especially striking in urothelial bladder cancer (UBC), a disease that is 3 to 4 times more prevalent in men than in women. Androgens are known to be immunosuppressive through a number of mechanisms. We investigated whether androgen induced immunosuppression may play a role in the male predominance of UBC. We focused specifically on NK cells due to their role in halting UBC in early stages and in the reduction of recurrence and metastasis of many cancers. We studied NK cell response to androgens by isolating NK and peripheral blood mononuclear cells (PBMCs) from donors and treating them with different concentrations of R1881. We used this a synthetic testosterone because it cannot be aromatized to estrogen. We then co-cultured UM-UC3 UBC cells with the treated and untreated lymphocyte preparations. Lymphocyte killing was analyzed using flow cytometry with a e-flour stain to identify dead cancer cells. We found that the NK cells and PBMCs treated with R1881 resulted in more live UM-UC3 events and therefore less cancer cell death. We also found that the killing achieved by PBMCs seemed to increase with lower doses of androgens, suggesting an inverse relationship between androgens and NK cell efficacy. In order to see if the androgen effect was due to endocrine effects on UM-UC3 cells, we treated UM-UC3s with R1881 and DMSO without exposure to NKs or PBMCs. We found no significant difference in live events between the two treatments, suggesting that androgens were not directly affecting the UM-UC3 cells. Based on our preliminary studies, we conclude that androgens suppress NK cell recognition and destruction of UBC cells.

Supported by: UK Department of Pathology PSMRF program

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Poster Presentation 113

Abstract Title:	**Optimization of Human Cancer Cell Xenografts into Zebrafish Larvae for High-Throughput Drug Screening**
Author(s):	B. Wilson, Department of Molecular and Cellular Biochemistry, U of Kentucky M. G. Haney, Department of Molecular and Cellular Biochemistry, U of Kentucky S. Dockins, Department of Molecular and Cellular Biochemistry, U of Kentucky J. S. Blackburn, Department of Molecular and Cellular Biochemistry, U of Kentucky

Abstract: The use of zebrafish in cancer xenograft models has grown rapidly with recent results showing that some zebrafish xenograft models can correctly predict which therapies a person's cancer will respond to in as little as four days. This growth is primarily due to the fact that this model takes advantage of the ease of in vivo imaging and the high-throughput screening capabilities of zebrafish compared to the more traditional mouse xenograft models. However, researchers have yet to come to a consensus on a standardized procedure for utilizing zebrafish for xenografts. This study aims to optimize a zebrafish xenografting protocol for various human cancers for high-throughput drug screening. We fluorescently labelled human cancer cell lines and injected them into 2-day-post-fertilization zebrafish larvae. We tested injections with different cell numbers and anatomical injection sites to find the cell number and site with the highest engraftment rate, best survival and most efficient injection time. We then performed RNAseq to compare expression profiles of cells xenografted into zebrafish versus cells in culture or mouse xenografts. Finally, we performed a high-throughput drug screen as proof-of-principle that these methods are useful in identifying novel anti-cancer compounds. This method of rapid drug screening may be useful for quickly determining which therapies may be effective on an individual basis, allowing for better clinical decision making and more efficient stratification of patients into clinical trials. In total, this work establishes standard operating procedures for the use of xenografts in zebrafish, providing new opportunities in personalized medicine and drug discovery.

Supported by: NIH awards: 5R00CA181500, R01CA227656, New Innovator Award 1DP2CA228043

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Poster Presentation 114

Abstract Title:	**Understanding the Role of ATR-774 Mutation in the Viability and Proliferation of Colorectal Cancer**
Author(s):	A. H. Overmann, MS (U of Kentucky College of Medicine) N. Holcomb, PhD (Markey Cancer Center, U of Kentucky) J. D'Orazio, MD, PhD (Department of Pediatrics and the Markey Cancer Center, U of Kentucky)

Abstract: Ataxia telangiectasia and Rad3-related (ATR) is a major regulator of the DNA damage response pathway responsible for sensing cell injury and integrating damage responses. Our group has identified a truncation mutation in ATR, I774Yfs*5, which is highly overrepresented in colorectal cancer, especially in the context of mismatch repair defects. Despite its prevalence, the impact of ATR-I774Yfs*5 on oncogenesis and tumor progression remains unknown. In this study, we sought to determine whether this mutation is driving carcinogenesis or metastasis by performing quantitative analyses of cell viability and proliferation. We measured cell viability using a spectrophotometric MTT assay in established colorectal cancer cell lines (DLD1 and HCT-116) and in benign colorectal epithelial cells (NCM-356) transfected with wild-type ATR compared to ATR-I774Yfs*5. Using flow cytometric analysis of cell division by dye dilution, we quantitated colorectal cancer cell proliferation in HCT-116 cells transfected with wild-type ATR compared to ATR-I774Yfs*5. MTT measurements of cell viability yielded no significant differences among WT-ATR and ATR-774 in any of the cell lines studied. Results of cellular proliferation assays in HCT-116 cells transfected with WT-ATR and ATR-774 did not detect significant differences in replicative rate. While it appears that the ATR-774 mutation does not increase proliferation in the colorectal cancer cell line studied, interestingly, this mutation has no deleterious effects on cell viability compared to WT-ATR. Our data suggest that truncated ATR may contribute to carcinogenesis through mechanisms other than by increasing replicative rate. Additional studies are needed to elucidate possible mechanisms by which the ATR-I774Yfs*5 mutation contributes to colorectal carcinogenesis.

Supported by:	UK Center for Clinical and Translational Science: Professional Student Mentored Research Fellowship Program (PSMRF) and NIH R01CA131075

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Poster Presentation 115

Abstract Title:	**Enhancing anti-tumor immunity and responses to immunotherapy by reversing interleukin-10 mediated immunosuppression in chronic lymphocytic leukemia**
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Abstract: B cell Chronic Lymphocytic Leukemia (CLL) is characterized by an accumulation of abnormal B cells, leading to serious immune dysfunction. This immune suppression is partially due to the production of mediators that downregulate T cell responses, and as a result many T-cell-based immunotherapies have experienced limited success in trials with CLL. CLL cells secrete the immunoregulatory cytokine Interleukin-10 (IL-10), and we previously found that eliminating IL-10 signaling in T cells reduced the growth of CLL. Therefore, we investigated the therapeutic potential for IL-10 blockade to enhance anti-tumor CD8+ T cells and increase the efficacy of immunotherapy in CLL. IL-10 production by human and Eμ-TCL1 mouse CLL cells depends on the transcription factor Sp1, and the Sp1 inhibitor mithramycin (MTM) suppresses CLL IL-10 production. However, MTM is not well tolerated in vivo, so we synthesized a novel analogue of MTM (MTM23), which similarly suppresses IL-10 and is tolerated at 12-fold higher doses. MTM23 enhances anti-CLL immunity in vivo by suppressing CLL growth and IL-10 production, allowing for increased CD8+ T cell proliferation and interferon-γ production. Furthermore, adding MTM23 to anti-PD-L1 immunotherapy greatly improved the control of CLL in vivo. CD8+ T cells were more prevalent in double treated mice than anti-PD-L1 alone, with an increase in CD8+ T cell functionality. This paradigm shifting approach is novel as current therapies for CLL do not target IL-10 and it may increase the efficacy of immunotherapies in human CLL. Moreover, this could be applicable to other cancers where T cell suppression plays a role.

Supported by: NIH award: T32CA165990 NIH award: UL1TR001998 NIH award: R01CA165469

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Poster Presentation 116

Abstract Title:	**A Protein Tyrosine Phosphatase 4A3 (PRL-3)/Wnt Signaling Axis as a Novel Therapeutic Target in Acute Lymphoblastic Leukemia (ALL) Relapse**
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Abstract: Acute Lymphoblastic Leukemia (ALL) is the most common pediatric malignancy and 15-20% of patients experience relapse, which is frequently more aggressive and treatment resistant than primary disease with unfavorable outcomes. Relapse occurs because conventional chemotherapies are unable to reliably and completely eliminate leukemia stem cells (LSCs), which have the ability to self-renew and form a leukemia from a single cell. The Wnt signaling pathway has emerged as having an important role in LSC self-renewal in T-ALL, but current Wnt inhibitors have unacceptable toxicity in the clinic. I have found the Protein Tyrosine Phosphatase 4A3 (PTP4A3 or PRL3) is highly expressed by ALL cells that also express Wnt pathways genes, and is not expressed by normal cells. In a zebrafish Myc-induced ALL model, PRL3 expression significantly enhanced LSC frequency, while inhibition of PRL3 reduced LSC numbers in vivo. In human cells, I found that PRL3 activates the expression of Wnt pathway genes. I have created transgenic zebrafish models of ALL that over-express both wild-type and mutant forms of PRL3 and constitutively active beta-catenin to define the role of PRL3 in Wnt signaling by assessing the effects of PRL3 and PRL3 mutants on LSC self-renewal and the phosphorylation status of Wnt pathway components in zebrafish models and human ALL cells. My research defines a novel role for the phosphatase PRL3 in self-renewal of cancer stem cells via activation of Wnt signaling, and targeting PRL3, which is expressed specifically by leukemia cells, represents a novel therapeutic strategy to inhibit WNT signaling in ALL.

Supported by: NIH Training Grant T32CA165990 NIH R01: R01CA227656 NIH New Innovator: 1DP2CA228043

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Poster Presentation 117

Abstract Title:	**The Regulation and Function of L-Type Amino Acid Transporter 1 in Response to Adipokines in Human Breast Cancer Cells**
Author(s):	T.B. Salisbury, Department of Biomedical Sciences, Marshall University, Huntington, WV

Abstract: One out of every three cancer deaths are linked to excess body weight and West Virginia has the highest rates of obesity in the country. Obese postmenopausal women have higher rates of breast cancer incidence, are less responsive to cancer therapy and have worse clinical outcomes than non-obese women have. The essential amino acid leucine is elevated in obesity, and it promotes cancer by functioning as an mTOR agonist. The uptake of extracellular leucine by breast cancer cells occurs through L-Type Amino Acid Transporter 1 (LAT1). We hypothesized that adipocytes secrete paracrine factors (termed adipokines) that induce LAT1-mTOR signaling in breast cancer cells. To investigate this hypothesis, we applied adipocyte-secreted factors (ASFs) to human MCF7 breast cancer cells. ASFs significantly ($P \leq 0.05$, N4) increased (~60%) the levels of LAT1 protein in MCF7 cells. Increases in LAT1 correlated with increases in mTOR activity, as measured by a 6-fold increase in the phosphorylation of the mTOR target protein p70 S6 Kinase ($P \leq 0.05$, N4). The LAT1 antagonist BCH has been shown to inhibit (>90%) leucine uptake by MCF7 cells. BCH (20 mM) treatment significantly ($P \leq 0.05$) reduced (by 70%) MCF7 colony formation. Supporting a role for leucine, was finding that its absence from cell culture medium suppressed (by 97%) MCF7 colony formation. Collectively, these data indicate that MCF7 cells are remarkably dependent on extracellular leucine, and support our hypothesis to suppress leucine-stimulated mTOR1 to inhibit breast cancer in obesity.

Supported by: National Institute Of General Medical Sciences of the National Institutes of Health under Award Number P20GM121299-01A1.

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Poster Presentation 118

Abstract Title:	**Non-Pungent Capsaicin Analogs: Potential applications in lung cancer therapy**
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Abstract: Capsaicin is the spicy pungent ingredient of chili peppers. Although traditionally associated with analgesic activity, recent studies have shown that capsaicin has profound anti-neoplastic effects in several types of human cancers. However, the applications of capsaicin as a clinically viable drug are limited by its unpleasant side effects, such as gastric irritation, stomach cramps and burning sensation. This has led to extensive research focused on the identification and rational design of second-generation capsaicin analogs, which possess greater bioactivity than capsaicin. Previous studies have shown that addition of long-chain unsaturated groups after the amide group of capsaicin were non-pungent and retained the bioactivity of capsaicin. These chemical nature of these compounds are unsaturated N-acylvanillamides (uN-AVAMs). However, a majority of these uN-AVAMs have been studied for their pain-relieving activity. We synthesized a panel of uN-AVAMs with 0-4 double bonds in the side chain of capsaicin. We investigated the growth-inhibitory activity of these compounds with an MTT-based screening assay. We selected our “hit compound” Arvanil for further studies. Next, we compared the apoptotic activity of arvanil and capsaicin in a panel of human small cell lung cancer (SCLC) cells. We observed that the non-pungent capsaicin-analog arvanil displayed greater magnitude of apoptosis than capsaicin. Most interestingly, arvanil did not display apoptotic activity in normal lung epithelial cells. The pro-apoptotic activity of arvanil and capsaicin was mediated by the intracellular calcium pathway. We measured the uN-AVAM-induced levels of intracellular calcium in SCLC cells. The pattern of uN-AVAM-induced intracellular calcium was analogous to the results obtained in the MTT assay. Therefore, the measurement of intracellular calcium may be used as a screening tool for capsaicin-mimetics with anti-cancer activity.

Supported by: Funding for our study was supported by a NIH R15-AREA Grant (2R15CA161491-02). Furthermore, this study was supported in part by an Institutional Development Award (IDeA) Grant number P20GM104932 from the National Institute of General Medical Sciences (NI

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Poster Presentation 119

Abstract Title:	**Capsaicin and natural capsaicin-like compounds suppress metastasis in lung adenocarcinoma**
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Abstract: Lung adenocarcinoma (LAC) accounts for the majority of all non-small cell lung cancer (NSCLC) cases. A substantial proportion of LAC patients present with local and distant metastasis at the time of their diagnosis. One of the earliest events of the metastatic process is the invasion of malignant cells through the surrounding extracellular basement membrane into the blood and lymph. The long-term goal of our laboratory is to identify nutrition-based agents which will suppress the growth and progression of human LACs. Capsaicin is the pungent ingredient of chili peppers. Published reports have revealed that capsaicin inhibits the invasion and metastasis of several types of human cancers including melanoma, prostate cancer, and cholangiosarcoma. However, the clinical application of capsaicin as an anti-cancer drug is limited by its unpleasant side-effect profile. This led us to compare the anti-metastatic activity of capsaicin with natural non-pungent capsaicin-like compounds, namely capsiate and capsiconiate. The structure and bioactivity of capsaicin closely resembles capsiate. There are no published reports involving the biological activity of capsiconiate. We measured the anti-invasive activity of these compounds by two independent invasion assays, namely the Boyden chamber assay and spherical invasion assay. We found that capsaicin and capsiate displayed anti-invasive activity in three human LAC cell lines. In contrast, capsiconiate did not suppress the invasion of any LAC cell lines. Furthermore, we tested the anti-metastatic activity of capsaicin in a syngeneic mouse model of metastasis. We observed that the daily dietary administration of capsaicin in AIN-76A diet (with 5% lipid level) robustly decreased the area metastatic foci (in the lung) relative to vehicle-treated mice. We investigated the signaling pathway underlying the anti-metastatic activity of capsaicin. Our results show that capsaicin directly interacts with Src and inhibits Src activation to suppress the metastasis of LAC. The results of our studies may foster the development of novel anti-metastatic therapies for human LAC.

Supported by: Funding for our study was supported by an NIH R15-AREA Grant (2R15CA161491-02) and a NASA Undergraduate Fellowship to NAN.

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Poster Presentation 120

Abstract Title:	**Choline Acetyltransferase: A novel molecular target in lung adenocarcinoma therapy**
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Abstract: The clinicopathological properties of lung adenocarcinoma (LAC) in smokers is divergent from LAC in non-smokers. One of the distinctive features of LAC in smokers is that the disease is relatively resistant to targeted molecular therapies. For example, targeted therapeutic agents like EGFR-inhibitors (erlotinib and gefitinib) are highly effective in LACs in non-smokers. However, these agents display much lower anti-tumor activity in LACs in patients who are active smokers. Similarly, lung cancer patients (who are active smokers) show a lower response to chemotherapy than those who are non-smokers. However, the majority of LAC patients are smokers. This underlines the need to identify viable drug targets for LAC therapy in patients who are exposed to cigarette smoke. A survey of literature reveals 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 the mitogenic activity of nicotine is that it promotes the production 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 analogous to their smoking history. Finally, the ChAT inhibitor BW813U causes robust apoptosis in human LAC cell lined and LAC cell lines isolated from patients. 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. The anti-tumor activity of BW813U is also observed in H838 cells (belonging to an 80 pack-year smoker) xenografted on athymic mice. Our studies show that antagonists of ChAT like BW813U may have therapeutic applications in the majority of the population of LAC who are smokers.

Supported by: Funding for our study was supported by a NIH R15-AREA Grant (2R15CA161491-02). Furthermore, this study was supported in part by an Institutional Development Award (IDeA) Grant number P20GM104932 from the National Institute of General Medical Sciences (NI

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Poster Presentation 121

Abstract Title:	**Overcoming Prostate Cancer Therapeutic Resistance with TGF-ß Signaling Inhibition**
Author(s):	N. Kyprianou, Departments of Urology, Molecular and Cellular Biochemistry, and Toxicology & Cancer Biology, University of Kentucky College of Medicine C.A. Wade, Department of Urology, University of Kentucky College of Medicine

Abstract: Prostate cancer is the most frequently diagnosed cancer in males and the second leading cause of cancer deaths in males in the United States, following only respiratory malignancies. The five-year survival for patients with non-metastatic prostate cancer is 98.9%, but patients with metastatic prostate cancer on initial diagnosis (4% of prostate cancer patients on diagnosis) had only a 28.2% five-year survival rate. 10-20% of prostate cancers progress to castration resistant prostate cancer (androgen-independent) within 5 years of diagnosis. Transforming Growth Factor-ß (TGF-ß) has opposing roles in prostate growth regulation. It serves as a tumor suppressor in normal prostate and early tumorigenesis by inducing apoptosis and inhibiting proliferation. However, TGF-ß promotes tumor progression in late tumorigenesis and metastatic disease by acting as a pro-proliferative, pro-metastatic effector by engaging tumor-associated protein kinases that block apoptosis and alter the transcriptome to confer epithelial to mesenchymal transition (EMT). Further, in progressive disease TGF-ß impacts actin cytoskeletal remodeling through cofilin upregulation and activity, an effector of metastasis. In our work, we demonstrate that that the use of TGF-ß Receptor I (TGFßRI) inhibitor (galunisertib) in combination with an androgen receptor blocker (enzalutamide) in a transgenic prostate cancer mouse model increased apoptosis, decreased proliferation, conferred a more differentiated phenotype, and reduced cofilin expression.

Supported by:	This project was supported by the CCTS Professional Student Mentored Research Fellowship. the NIH National Center for Advancing Translational Sciences, Grant No. UL1TR000117, Schwab Foundation Grant, and the James F. Hardymon Endowment.

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Poster Presentation 122

Abstract Title:	**Evaluation of pathological results of tomosynthesis guided vacuum assisted breast biopsy**
Author(s):	D. Chen, Undergraduate, U of Kentucky X. Wang, Department of Radiology, U of Kentucky

Abstract: OBJECTIVE: To evaluate the pathological results of tomosynthesis guided vacuum assisted breast biopsy (TVAB) in comparison to those of conventional stereotactic vacuum assisted biopsy (SVAB). MATERIALS AND METHODS: All women who underwent TVAB (from May 2013 to April 2015) or SVAB (from June 2015 to May 2017) procedure were included in this retrospective study. Patients' demographics, lesion radiologic appearance, and biopsy pathologic results were compared between these two groups. The significance level was accepted as $p<0.05$. RESULTS: 389 patients with 410 lesions underwent SVAB and 540 patients with 579 lesions underwent TVAB. The mean ages in SVAB and TVAB groups are 55.9±10.3 and 57.9±10.5, respectively. TVAB is found to have a higher biopsy rate of low contrast lesions than SVAB (26% vs 16%, $P < 0.05$). No statistically significant differences were found between the two groups with respect to histological results of lesions such as breast tissue, benign changes, high risk lesions, or malignant lesions ($p=0.161$). Among the malignant lesions, the rate of ductal carcinoma in situ (DCIS) is high in both SVAB group (88.6%) and TVAB group (77.9%), but no difference in the rate between these two groups is identified either ($p=0.26$). CONCLUSION: New biopsy technique-TVAB can biopsy more low contrast lesions with equivalent pathological results, including the malignancy and DCIS rate. Further analysis of the final results of lesions with high risk biopsy results between these two groups will be conducted.

Supported by: none

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Poster Presentation 123

Abstract Title:	**Modulation of Plasma Ceramide Levels by Dietary Fructans via Sphingomyelinase Pathway**
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Abstract: Ceramides are sphingolipids that are implicated in the development of cardiovascular and metabolic diseases. Increased levels of plasma ceramides are predictive of adverse cardiovascular events. Dietary fructans such as inulin have been suggested to promote cardiovascular and metabolic health by serving as prebiotics that promote beneficial changes in the gut microbiota. However, the biochemical mechanisms involved in these beneficial health effects are not well understood. We used metabolomic/lipidomic and transcriptomic approaches to investigate the effects of dietary inulin supplementation in an mouse model of atherosclerosis. Low density lipoprotein receptor knockout mice were fed an atherogenic diet supplemented with 8% inulin or cellulose as a control. The plasma lipidome was profiled using a UHPLC-Q Exactive Orbitrap mass spectrometer. Among the 923 assigned plasma lipid species, ceramides were significantly reduced 10 days after inulin treatment, and this effect persisted for up to 12 weeks. C16:0, C20:0 and C24:1 ceramide levels were decreased by dietary inulin supplementation. Interestingly, these are ceramide species that have been associated with cardiovascular disease risk in humans. These changes in plasma ceramides could result from alterations in de novo ceramide synthesis or production of ceramides by hydrolysis of sphingomyelins. The latter possibility is supported by our observation that the ceramide/sphingomyelin ratio in plasma was decreased after inulin treatment. This finding may result from our observed decrease in hepatic expression of the neutral sphingomyelinase gene Smpd3 in mice fed the inulin supplemented diet. These findings suggest that dietary fructans might be an effective way to reduce plasma ceramides which could have beneficial effects on the cardiovascular risks and metabolic diseases that have been associated with elevated plasma ceramide levels in humans.

Supported by: NIEHS/NIH grant P42ES007380

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Poster Presentation 124

Abstract Title:	**Photothrombotic microinfarct technique for chronic, in vivo imaging of mouse vasculature and astrocyte networks using multiphoton microscopy**
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Abstract: Vascular pathology contributes significantly to cognitive aging. Given the high incidence of cardiovascular disease in Kentucky and nationwide, vascular contributions to cognitive impairment and dementia (VCID) are a leading cause of dementia. The mechanisms by which vascular disease changes the brain are still largely unknown. Multiphoton microscopy helps by showing both the structure and the physiology of vessel-astrocyte interactions. Vascular pathology is modeled in our lab by delivering a precise infarct using LASER-activated thrombosis. Stereotaxic coordinates allow for precise placement of thrombosis, such as in the hippocampus or barrel cortex. Blood flow dynamics can then be measured at various time intervals, such as 30 minutes, one hour, six hours, and 48 hours after the insult. Ablation is directed and timed to minimize collateral damage to the surrounding tissue as well as potential vasogenic and cytotoxic edema formation. Adeno-associated virus injection of GCaMP6 allows for visualization of calcium signaling as astrocytes respond to infarction. Application of this technique in amyloidogenic APP/PS1 mice promises to illuminate the convergence of Alzheimer's disease (AD) and VCID related pathologies. Capillary flow stalls have also been observed with this technique in wild-type mice in the absence of infarction, sparking the question of the frequency and duration of stalls, as well as how that may be different in models of AD.

Supported by: NIH: RO1 AG027297 T32: AG000242-20 PSMRF: UL1TR001998

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Poster Presentation 125

Abstract Title:	**AT1a Receptor Deficiency Attenuates Thoracic Aortic Aneurysm Progression in FBN1 C1041G/+ Mice**
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Abstract: Angiotensin receptor type 1 (AT1 receptor) activation has been implicated in thoracic aortic aneurysms (TAAs). Losartan, an AT1 receptor antagonist, attenuates TAAs in multiple animals models. Recent studies concluded that losartan's attenuation of Marfan syndrome associated TAAs is unrelated to AT1 receptor antagonism. We determined the effects of AT1a receptor deletion on TAAs in the fibrillin-1 haploinsufficient (FBN1 C1041G/+) Marfan syndrome mouse model. Aortas from wild type and FBN1 C1041G/+ littermates, that were AT1a receptor +/+ or -/-, were imaged from 1 to 12 months of age using a rigorously standardized ultrasound protocol and verified by direct visualization at termination. Male FBN1 C1041G/+ mice had increased aortic diameters at 1 month compared to wild type littermates (Ascending: 1.39±0.06mm vs 1.16±0.07mm; p=0.04. Root: 1.63±0.05mm vs 1.35±0.06mm; p<0.001). Dilation at 1 month was not attenuated by AT1a receptor deletion. Subsequent expansion of both the ascending aorta and the aortic root in male FBN1 C1041G/+ mice was attenuated by AT1a receptor deletion. This difference in FBN1 C1041G/+ mice with AT1a receptor +/+ vs -/- could be detected at 3 months (Ascending: 1.51±0.04mm vs 1.28±0.06mm; p=0.002. Root: 2.05±0.06mm vs 1.79±0.08mm; p=0.03) and persisted to termination. Conversely, aortic diameters in 12 month old female FBN1 C1041G/+ mice compared to their wild type littermates were minimal (Ascending: 1.50±0.06mm vs 1.36±0.06mm. Root: 2.06±0.13mm vs 1.77±0.13mm). Deletion of AT1a receptors attenuates TAA progression but not initial development in male mice. Minimal aortic expansion in female FBN1 C1041G/+ mice highlights the need to perform sex-specific analyses of TAAs.

Supported by:	The project described was supported by the National Center for Research Resources and the National Center for Advancing Translational Sciences, National Institutes of Health, through Grant UL1TR001998. The content is solely the responsibility of the autho

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Poster Presentation 126

Abstract Title:	**Capsaicin-Induced Stimulation of Sensory Neurons in Adipose Tissue Promotes Increases in Blood Pressure in Mice Exposed to Early Life Stress**
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Abstract: Experimental stimulation of afferent signals from white adipose tissue (WAT) increase sympathetic activation in obesity-induced hypertension as part of the adipose afferent reflex (AAR). Male mice exposed to maternal separation and early weaning (MSEW) display increased sympathetic tone and mean arterial pressure (MAP) when fed high fat diet. We hypothesize that MSEW may influence AAR function and contribute to exacerbate obesity-induced hypertension. Therefore, we tested the subcutaneous WAT (scWAT, n=5) vs. gonadal WAT (gWAT, n=7) acute capsaicin-induced changes in MAP in male MSEW and control mice. MAP did not change after saline or capsaicin injections (0.5 nmol/ul) in scWAT. While saline in gWAT did not increase MAP, capsaicin stimulation increased it during 10 minutes ($p<0.05$). Furthermore, MSEW mice showed a greater change in capsaicin-induced MAP increases compared to controls ($p<0.05$). Fat from control mice was removed to measure capsaicin-induced calcitonin gene-related peptide (CGRP) release as a marker of sensory neurons activity. We found that CGRP release from scWAT was higher that from gWAT (n=4-6, $p<0.05$). These data suggest an increased sensory activation in scWAT. In another set of mice fed a high fat diet, selective afferent denervation of gWAT using resiniferatoxin (RTX; 20 pmol/ul) decreased MAP and HR. Thus, our data indicate that male mice show depot-specific afferent signals that influence acute and chronic MAP control. In addition, AAR could play an important role in the exacerbated response to high fat diet-induced increases in sympathetic tone and MAP observed in male MSEW mice.

Supported by: NIH award: R01 HL135158

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Center for Clinical and Translational Science **Abstracts**

Poster Presentation 127

Abstract Title:	**Sex Differences in a Mouse Model of Lipodystrophy-induced Hypertension**
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Abstract: Obesity rate is higher in women than in men and is more strongly associated with hypertension in extremely obese women. However, sex differences in the relative contribution of the adipose tissue to blood pressure control remained poorly understood. Therefore, in the present study, we investigated the mechanism involved in blood pressure elevation in male and female in adipose prorenin receptor (PRR) KO mice, a mouse model of lipodystrophy-induced hypertension. Male and female mice were fed a high fat (HF)-diet and implanted with a telemetry transmitter to measure blood pressure. The contribution of the renin angiotensin system was assessed by injection of Losartan, an AT1R blocker. The parasympathetic and sympathetic regulation of heart rate was assessed by the injection of atropine-methyl nitrate, propranolol or chlorisondamine. The decrease in systolic blood pressure induced by losartan was exacerbated in HF-fed adipose PRR KO female mice compared with control, but not in male mice. In contrast, the tachychardic response was significantly greater in HF-fed adipose PRR-KO male mice compared with control, but not in female mice. Together, our data indicated that SBP elevation in HF-fed adipose PRR-KO mice was primarily mediated by an AngII-dependent mechanism in female mice and by the para-sympathetic nervous system in male mice. One could speculate that the presence of an expanded adipose tissue decreased the ability of female to respond to ARBs whereas it decreased the ability of male to respond to sympathetic inhibitors. Together our data support the importance of personalized medicine for antihypertensive treatment choices.

Supported by:	National Institutes of Health Grants: R01-HL-130463 American Heart Association: 13SDG17230008 National Institute of General Medical Sciences: P30 GM127211 University of Kentucky, Center for Clinical and Translational Sciences: UL1TR000117

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Poster Presentation 128

Abstract Title:	**Renin-Angiotensin Inhibitors Do Not Improve Survival in Fibrillin-1 Hypomorphic Mice with Established Aortic Aneurysm**
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Abstract: Male and female fibrillin-1 hypomorphic (FBN1 mgR/mgR) mice (n=10-12/group) were stratified by aortic diameter at 6 weeks of age to ensure equivalent aortic diameter among groups. Osmotic mini pumps filled with PBS (vehicle), enalapril (2 mg/kg/d), or losartan (20 mg/kg/d) were implanted subcutaneously into mice after stratification. Mini pumps infusing drug or vehicle were replaced every 4 weeks for a duration of 12 weeks. Wild type littermates (n=10) were infused with PBS as a negative control to the Marfan mouse model. Ascending aortic diameters from male and female FBN1mgR/mgR mice and their wild type littermates were assessed by ultrasound every 4 weeks from 6 to 18 weeks of age. Aortic diameters were measured luminal edge to luminal edge during diastole. Baseline mortality of FBN1 mgR/mgR mice infused with PBS was 36% in male and 22% in female mice at the time of study termination. Within sex-matched mgR littermates, there was no significant difference in survival between groups treated with PBS, enalapril, or losartan after 12 weeks (p=0.224 for males, p=0.094 in females). In the same groups, no significant difference in maximum ascending aortic diameter was detected after treatment for 12 weeks (in males: PBS=2.69 +/- 0.19 mm, enalapril=2.04 +/- 0.27 mm, losartan=2.42 +/- 0.28 mm; p=0.24) (in females: PBS= 1.92 =/- 0.13, enalapril=1.89 +/- 0.31, losartan=1.98 +/- 0.17; p=0.86). Furthermore, aortic diameters in the FBN1mgR/mgR mice were found to demonstrate sexual dimorphism.

Supported by: This work was supported by the University of Kentucky Physician Pipeline Program as well as NIH 3R01HL133723. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH.

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Poster Presentation 129

Abstract Title:	**Mesenchymal stem cell derived exosome reduce cardiac fibroblast apoptosis and promote angiogenesis after ischemia/reperfusion injury**
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Abstract: Mesenchymal stem cells (MSC) transplantation is a promising approach for cardiac cellular therapy due to their cardiac protective effects in post-myocardial infarction (MI). Recent studies confirmed that MSC released paracrine factors, such as exosomes (EXs), are responsible for considerable part of their therapeutic benefits. However, the molecular mechanisms underlying MSC-derived exosome (MSC-EX) mediated cardiac protection are not fully understood. In this study, we explored the antiapoptotic effects of MSC-EX on H9C2 cardiac myofibroblast cell line and on primary cardiac fibroblast. We hypothesized that MSC mediated pro-survival and pro-angiogenic effects seen in vivo are in part due to the release of their secretory exosomes. Method and Results: To evaluate whether MSC derived-EXs may be used as an alternative MSC-based therapy for MI, we established an in vitro oxygen/glucose ischemic/reperfusion (I/R) injury model. Under control conditions, I/R injury was associated with significant H9C2 cell apoptosis. The effect of primary bone marrow derived MSC-EX on cell viability and metabolic activity was investigated. The effect of MSC-EX on blood vessel formation was evaluated through tube formation and migration of human umbilical vein endothelial cells (HUVECs). MSC-EX treatment was associated with reduction in H9C2 cell apoptosis compared to control conditions. Additionally, the supplementation of HUVEC cells with MSC-EX lead to significant increase in tube formation, a marker of enhanced angiogenesis. Conclusion: Our results indicated that MSC-EX protects myocardial cells from apoptosis and promotes angiogenesis. These results have significant translational aspects given the logistical advantages of exosomes in clinical practice and patients with acute myocardial infarction.

Supported by: NIH award: R01 HL124266 and University of Kentucky COBRE Early Career Program (P20 GM103527)

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Poster Presentation 130

Abstract Title:	**Mesenchymal Stem Cell Modulates Damage Associated Molecular Patterns (DAMPs) induced Macrophage Activation and Cytokine Release**
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Abstract: Myocardial infarction (MI) triggers a robust inflammatory response that promotes excessive tissue damage and fibrosis. Mesenchymal stem cell (MSC) transplantation has been shown to reduce this deleterious inflammatory response and are cardiac protective post-MI. However, the mechanisms that couple MSCs, inflammation and immune cell activation in damaged heart tissue are not well characterized. To elucidate the molecular mechanisms of MSC based immunomodulatory effects, we have developed an in vitro culture system that mimics the post-MI environment rich in damage associated molecular patterns (DAMPs). We hypothesize that DAMPs released from necrotic heart cells are sufficient to activate primary macrophage in vitro, and the extent of activation can be modulated by MSCs. Method and Results: Heart lysate (HL) was created by freeze-thaw technique to induce necrosis of the post-MI hearts. Presence of DAMPs (HMGB1, S100A8 and S100A9) in HL supernatants was evaluated using western blot. In culture, HL stimulation provoked a robust increase in primary bone-marrow derived macrophage (BMDM) cytokine production with a clear shift towards an inflammatory phenotype. This was obvious from their production of significantly higher amount of tumor necrosis factor-alpha (TNFa) compared to the anti-inflammatory cytokine, interleukin 10 (IL-10). Moreover, co-culture with MSCs reduced BMDM TNFa production while simultaneously increasing their IL-10 releases in vitro. Conclusion: Our study demonstrated that heart lysate enriched in DAMPs induce BMDM activation and cytokine release, an effect that is attenuated by MSCs. Moreover, this optimized heart lysate culture system can be utilized to test many molecular mechanisms and therapies for post-MI inflammation.

Supported by: NIH award: R01 HL124266 and University of Kentucky COBRE Early Career Program (P20 GM103527)

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Poster Presentation 131

Abstract Title:	**Anti-apolipoprotein A-I Antibody Profiles Correlate with Cardiovascular Disease Outcomes**
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Abstract: Apolipoprotein A-I (ApoA-I) is a target of IgG autoantibody induction in patients, but the role of these antibodies has not been fully elucidated. Anti-ApoA-I IgG antibodies targeting delipidated ApoA-I have been characterized as a biomarker of cardiovascular disease progression, but only moderate associations have been reported. We hypothesize that antibodies bound to ApoA-I as an immune complex are a critical and unexplored component of the antibody response to ApoA-I. An ELISA assay was used to screen plasma from 359 patients with coronary artery disease (CAD). Analysis of outcomes shows that patients in the lowest tertile for ApoA-I/IgG IC values have an increased risk for death and non-fatal myocardial infarction as compared to patients in the highest tertile with an hazard ratio of 1.89 (95% CI: 1.02-3.52; p = 0.04) after adjustment for 6 common cardiovascular risk factors. Pearson correlation analysis between ApoA-I/IgG ICs in the found no relationship between ApoA-I/IgG ICs and 26 common clinical measures. The antibody subclass composition of ApoA-I/IgG IC were then characterized in a second cohort of healthy blood donors and found to be enriched in IgG4. The ratio of pro-inflammatory IgG1 and anti-inflammatory IgG4 were compared between total plasma (9.9 IgG1/IgG4) and within the immune complex (0.30 IgG1/IgG4, p = 0.0003). The enrichment in the anti-inflammatory IgG4 provides a potential mechanisms of the protective effect of ApoA-I/IgG ICs in patients. The identification and further characterization of ApoA-I/IgG ICs has the potential to guide clinical diagnosis and intervention strategies in patients with atherosclerotic cardiovascular disease.

Supported by:	This work was supported through an Institutional Development Award (IDeA) from NIGMS of the NIH (P20GM103527) and a Scientist Development Grant from the American Heart Association (17SDG32670001). DH is supported by a training grant through the National C

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Poster Presentation 132

Abstract Title:	**Constant Light Exposure Increases Atherosclerosis in ApolipoproteinE-Deficient Mice**
Author(s):	J. M. Chalfant, Department of Biology, U of Kentucky D. A. Howatt, Saha Cardiovascular Research Center, U of Kentucky J. S. Pendergast, Department of Biology and Cardiovascular Research Center, U of Kentucky

Abstract: Circadian rhythms are 24-hour oscillations of almost every biological process in the body. The circadian system coordinates these rhythms of physiology and behavior with environmental cycles. Disruption of circadian rhythms increases the risk for cardiovascular disease (CVD). However, the mechanisms linking circadian disruption and CVD are largely unknown. In this study, we investigated the effects of constant light exposure, which chronically disrupts circadian rhythms, on atherosclerosis. We studied C57BL/6J ApolipoproteinE-deficient (ApoE-/-) mice because they spontaneously develop atherosclerotic lesions. At 7 weeks old, male ApoE-/- mice were singly housed in light-tight boxes in 12L:12D and fed low-fat diet. Locomotor activity and eating behavior rhythms were continuously monitored using passive infrared sensors and infrared video cameras, respectively. At 8 weeks old, mice were either kept in control 12L:12D or housed in constant light for 12 weeks. At 20 weeks old, atherosclerosis was quantified and serum lipids were measured. ApoE-/- mice housed in constant light had severely disrupted locomotor activity and eating behavior rhythms. Chronic exposure to constant light also increased atherosclerosis in male ApoE-/- mice compared to those in 12L:12D. Constant light exposure increased total serum cholesterol and the increased cholesterol was found on the atherogenic particles VLDL/LDL. In summary, chronic circadian disruption with constant light exposure increased atherosclerosis in male ApoE-/- mice via exacerbation of hypercholesteremia.

Supported by: This study was funded by National Institutes of Health grant P30 GM127211, the Gertude F. Ribble Trust, and the University of Kentucky.

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Poster Presentation 133

Abstract Title:	**Acute Phase Serum Amyloid A Potentiates Platelet Activation**
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Abstract: Platelets play a central role in sensing changes in the vasculature and responding to maintain hemostasis. Importantly, they also promote pathologic thrombosis and transmit important inflammatory cues with local and systemic impact. Indeed, a body of literature underscores the importance of platelets in a variety of inflammatory conditions. Despite detailed understanding of adhesive interactions mediated by platelets, much less is known about soluble inflammatory signals that serve as mechanistic links between tissue injury, inflammation, and platelet function. Serum amyloid A (SAA) is an acute phase reactant whose plasma levels can increase more than 1000-fold during a severe inflammatory response and can also be elevated during chronic inflammation. We have found that SAA potentiates platelet aggregation in response to low-dose thrombin (0.016 U/ml), likely by stimulating platelet secretion (cargo release) from dense granules, □ granules, and lysosomes. Additionally, SAA promotes platelet- leukocyte heterotypic interactions, which are downstream consequences of platelet secretory events. Ongoing work will identify the SAA receptor signaling pathway on platelets and their contribution to thromboinfammatory conditions.

Supported by: N/A

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Poster Presentation 134

Abstract Title:	**Gender, Comorbidities, and Outcomes in Cerebral Venous Thrombosis: KApSR Findings**
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Abstract: Introduction: Cerebral Venous Sinus Thrombosis (CVST) is a form of stroke involving the venous sinuses with an estimated incidence of 1.32-1.57/100,000/yr, with death or severe disability in less than 10%. The majority of reported epidemiologic and outcome data has been collected outside the United States (US). The objective of this study is to examine the gender characteristics of CVST patients in the United States, with representation of the Appalachian region. Methods: Data were collected using the Kentucky Appalachian Stroke Registry (KApSR), collected from admissions in a Comprehensive Stroke Center serving 554,300 from the central-eastern United States. All diagnosed CVST patients found in the database from 2010-2018 greater than 18 years of age were included in the data set. Descriptive data were computed using SPSS statistics. Results: 101 patients diagnosed with CVST were included. 58 patients were female (57.4%). Median age was 44 years. The National Institutes of Health Stoke Scale (NIHSS) was reported for 32 female and 21 male patients. Median NIHSS was .5 in females and 0 in males at admission. Median length of stay was 7 days in females vs. 4 days in males. Discharge data were available for 51 female and 33 Male patients. Of female patients, 28 (55%) were discharged to home, 17(33%) were transferred to continued care, 4(8%) were transferred to hospice and 2(4%) died within 48 hours of admission. Of male patients, 25(76%) were discharged to home, 7 (21%) were transferred to continued care, and 1 (3%) was transferred to hospice. Female patients had a higher burden or comorbidities and multimorbidity compared to male patients.

Supported by: CCTS Professional Student Mentored Research Fellowship (PSMRF) Program provided support for this project.

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Poster Presentation 135

Abstract Title:	**Gender Differences in Patients Undergoing Catheter Ablation of Atrioventricular Nodal Reentry Tachycardia**
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Abstract: Background: Atrioventricular nodal reentrant tachycardia (AVNRT) is the most common type of supraventricular tachycardia (SVT). Similar to other cardiac tests and interventions, gender bias may influence clinical decision making in providing appropriate care for AVNRT patients. We assessed for gender differences in the diagnosis and management of AVNRT patients that underwent catheter ablation. Methods: Patients that underwent catheter ablation for AVNRT were included. We explored the gender difference on various clinical parameters such as the time from SVT symptoms, SVT diagnosis and first electrophysiology consult to time of catheter ablation. Results: Among 140 patients screened, 116 patients met the inclusion criteria, including 67.2% women. Median time from symptoms onset to SVT diagnosis was 18.5 months [IQR 4.0-58.5] in women versus 4.0 months [0.75-34.7] in men, p=0.036. Once SVT was diagnosed, women took a median of 12.5 months [IQR 3.0-57.0] to proceed with ablation versus 3.0 months [1.0-7.0] for men, p=0.002. It also took a longer time from the first electrophysiology consultation to ablation: 54.5 days [20.75-144.75] for women versus 20.5 days [6.0-46.25] for men, p=0.008. Overall, it took 60.0 months [IQR 12.8-132.0] for women to have an ablation from initial symptoms onset versus 15 months [IQR 4.6-48.0] for men, p=0.001. Prior to ablation, women had 3.78±3.79 (mean ±SD) emergency department visits for SVT versus men 1.52±1.72 and women tried 1.28±0.82 medications versus men 0.76±0.68, P<0.001 for both comparisons. Conclusions: This study demonstrates significant and multifactorial gender-related disparities in AVNRT diagnosis and treatment. Larger studies are needed to confirm these results.

Supported by: N/A

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Poster Presentation 136

Abstract Title:	**Fat Mass, but Not Heart Rate Recovery, is Associated with Cardiorespiratory Fitness in Young, Sedentary Adults**
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Abstract: Peak oxygen uptake resulting from maximal graded exercise testing is considered a measure of cardiorespiratory fitness. Post-exercise heart rate recovery (HRRec) measures have been used as a clinical indicator of health and mortality in older adults. However, the relationship between HRRec and cardiorespiratory fitness in young, sedentary adults has not been fully elucidated. Purpose: To examine the association between peak oxygen uptake (VO2; ml·kg-1·min-1) and HRRec responses following a progressive maximal graded exercise test (MaxGXT; treadmill); and body composition measures in young, sedentary adults. Methods: We examined peak oxygen uptake (VO2; ml·kg-1·min-1) and absolute (beats·min-1) and relative (%) HRRec measures following a progressive MaxGXT; and body composition measures in 41 young, (mean ± SD, age = 26.7 ± 6.5) sedentary adults (27 females). Body composition measures including fat mass (kg), fat-free mass (kg), mineral-free lean mass (kg), and percentage body fat (%) were determined by total body DXA scans. Pearson's correlation analysis was used to determine if significant ($p < 0.05$) correlations were observed between peak VO2, absolute HRRec and relative HRRec, and body composition measures. Results: No significant correlations were observed between peak VO2 (36.0 ± 8.7) and absolute or relative HRRec at 1 min, 3 min or 5 min ($p>.05$). Peak VO2 was significantly correlated with percentage body fat (34.0 ± 8.7; $r = -0.77$; $p<.001$) and fat mass (26.0 ± 11.2; $r = -0.59$; $p<.001$). Conclusion: Heart rate recovery measures may not be a valid clinical indicator of cardiorespiratory fitness in sedentary, young adults.

Supported by:	NIH award: UL1TR001998 and TL1TR001997 from UK Center for Clinical and Translation Science; a Barnstable Brown Diabetes and Obesity Center Pilot Award; the University of Kentucky Pediatric Exercise Physiology Laboratory Endowment; and the University of Ke

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Poster Presentation 137

Abstract Title:	**Changes in Thromboinflammation following TAVR**
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Abstract: Transcatheter aortic valve replacement (TAVR) is a minimally invasive treatment option developed over two decades ago for patients with severe aortic stenosis who are poor surgical candidates. Despite the rapid increase in the utilization of this procedure, the optimal pharmacologic management of patients after TAVR is not completely understood. The current standard of care remains dual anti-platelet therapy, but there are several studies investigating the differences in anti-platelet only versus anti-coagulation regimens. One of the major complications post valve replacement is thrombosis of the new valve, leading to stroke, cardiogenic shock, and death. We sought to compare the thrombo-inflammatory changes following TAVR across several generations of valves in hopes of elucidating the mechanisms behind these complications. Prolonged thrombocytopenia typically occurring within 48 hours of valve placement has been associated with worse 8 week outcomes and 1 year mortality rate. No significant difference was detected in platelet decline between any of the valve types. In the newer generation of valves with smaller delivery systems, the overall inflammatory response to the procedure appeared to be decreased, in that both WBC and IL-6 levels were lower. Despite this decrease in general inflammation, levels of serum amyloid A, an acute phase reactant thought to be sensitive to myocardial injury, remained elevated with all of the valve types. Increased understanding of trends of thromboinflammation in patients undergoing TAVR has the potential to optimize standards of practice, thereby bringing new and important discoveries to the bedside.

Supported by: National Center for Advancing Translational Sciences, National Institutes of Health, Grant UL1TR001998.

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Poster Presentation 138

Abstract Title: **Thrombinflammatory and Endovascular Integrity Biomarkers in the Setting of Sepsis**

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Abstract: Background: Sepsis is an exaggerated response to an infection that results in systemic microvascular leakage and multiple-organ failure. Sepsis accounts for 10% of in-hospital mortality rates in the US. Current therapies do not properly tackle all aspects of this immune dysfunction; rather, they focus on aggressively treating the underlying infection or the resulting symptoms. Growing evidence indicates that platelets are key effectors in many inflammatory diseases, including sepsis. Thrombocytopenia - low platelet counts - is a common complication of sepsis and a biomarker for disease severity. The primary objective of this pilot study is to determine if platelet count and platelet function correlate with vascular integrity, changes in inflammation, sepsis sources, and patient outcomes. Methods: All hospitalized adult patients meeting the definition of severe sepsis using the Sepsis Related Organ Failure Assessment (SOFA) were eligible for enrollment in the registry / biobank. Blood samples at baseline and discharge were collected on enrolled patients as well as daily clinical information. Platelet activity was tested using Adenosine Diphosphate (ADP) and Thrombin Receptor Activating Peptide (TRAP) induced light transmission aggregation. Plasma was stored for subsequent biomarker analysis. Biomarkers to be analyzed include: IL-6, IL-1 beta, IL-10, MIP1-alpha, MIP1-beta, sCD40L, TNF-alpha, and endovascular integrity markers Angiopoietin 1 and 2. Follow up information was collected via electronic medical record or phone call. Results: A total of 86 patients have been recruited to this ongoing sepsis biobank. A preliminary biomarker analysis was performed and the results will be presented.

Supported by: NIH award: UL1TR001998

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Poster Presentation 139

Abstract Title:	**FND 4b Decreases Proliferation and Increases Apoptosis of Triple Negative Breast Cancer through AMPK Activation**
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Abstract: Purpose: Triple negative breast cancer (TNBC) is the most lethal and aggressive subtype of breast cancer. AMP-activated protein kinase (AMPK) is a major energy regulator that suppresses tumor growth, and 1-(3-chloro-4-((trifluoromethyl)thio)phenyl)-3-(4-(trifluoromethoxy)phenyl)urea (FND-4b) is a novel AMPK activator that inhibits growth and induces apoptosis in colon cancer. The hypothesis was that FND-4b would reduce growth and induce apoptosis of TNBC through AMPK activation. Methods: (i) Estrogen-receptor positive breast cancer (ER+BC; MCF-7 and T-47D), TNBC (MDA-MB-231 and HCC-1806), and breast cancer stem cells were treated with FND-4b for 24h. Immunoblot analysis assessed AMPK, acetyl-CoA carboxylase (ACC), ribosomal protein S6, cyclin D1, and cleaved PARP. (ii) Proliferation was assessed by performing sulforhodamine B growth assays and cell counting assays after 72h of FND-4b treatment. (iii) Cell death ELISA assays were performed after treating ER+BC and TNBC cells with FND-4b for 72h. Results: FND-4b increased AMPK activation with concomitant decreases in ACC activity, phosphorylated S6, and cyclin D1 in all subtypes. FND-4b decreased proliferation in all cells, while dose-dependent growth decreases were found in ER+BC and TNBC. Increases in apoptosis were observed in ER+BC and the MDA-MB-231 cell line with FND-4b treatment. Conclusions: Our findings indicate that FND-4b decreases proliferation for a variety of breast cancers by activating AMPK and has notable effects on TNBC. The growth reductions were mediated through decreases in fatty acid synthesis, mTOR signaling, and cell cycle flux. ER+BC cells were more susceptible to FND-4b-induced apoptosis, but MDA-MB-231 cells also underwent apoptosis with higher dose treatment.

Supported by: NIH award: T32 ES007266 (Daret St. Clair) NIH award: R01 CA195573 (BME)

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Poster Presentation 140

Abstract Title:	**The Axolotl as a Model for 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 juvenile and adult stages 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 show that axolotl (Ambystoma mexicanum) hatchlings can be used as a chemical screening model to investigate signaling pathways associated with tissue regeneration. As a proof of principle, we screened four compound collections: the Tocriscreen Stem CellToolbox (80 compounds), Selleckchem Epigenetics library (151 compounds), representative sets from the MicroSource Discovery Systems Spectrum Collection (2650 compounds) and 326 natural products from repository of the Center for Pharmaceutical Research and Innovation (CPRI). 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 new chemical screening model to investigate signaling pathways associated with tissue regeneration and also implicates utility for toxicology screening.

Supported by: NIH awards: R24 OD21479 and R24 OD010435 funding from UK Markey Cancer Center and the National Center for Advancing Translational Sciences (UL1TR000117)

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Poster Presentation 141

Abstract Title:	**Identifying the Pharmacogenetics of APOE-Dependent Response to Rapamycin as a potential Alzheimer's Disease Prevention**
Author(s):	M.F. Xia, Department of Pharmacology and Nutritional Sciences, U of Kentucky A.L. Lin, Sanders-Brown Center on Aging, Department of Pharmacology and Nutritional Sciences, Department of Biomedical Engineering, U of Kentucky

Abstract: Hypothesis: The APOE4 gene is the primary genetic risk factor of Alzheimer's disease (AD). Rapamycin has been shown to restore cerebrovascular functions in APOE4 mice, suggesting a potential AD prevention, but whether Rapamycin can be applied universally as preventative therapeutic remains unknown. The purpose of this study was to identify the APOE gene-dependent response to Rapamycin. Procedures: E3FAD and E4FAD mice co-express human Aβ via 5xFAD mutations on C57BL/6 homozygous APOE3/4 knock-in genotypes, they were presymptomatic of AD and fed with Control or Rapamycin supplemented diet for 16 weeks. Vascular neuroimaging, metabolic profiling, immunohistochemistry and behavior tests were recruited at the age of 7 months. Results: Rapamycin restored the low CBF and increased water content of pre-symptomatic E4FAD mice (n=6, p=0.007, Mean ± SEM = -0.7154 ± 0.4355, Mean ± SEM = 1.51 ± 0.412). The effects were more pronounced in female mice with FAD mutation. The restoration of CBF were associated with significantly reduced Aβ. In contrast, In E3FAD mice brains, glycolysis and carbohydrate pathways were significantly altered by Rapamycin. Specifically, the pentose phosphate pathway, nucleotide sugars, and aminosugars metabolism are consistently slowdown with decrease TCA cycle intermediates. Conclusions: Our results showed that Rapamycin restored CBF and facilitated A-beta clearance in APOE4 mice whereas altered brain metabolism in APOE3 mice. APOE3 mice displayed evidence of decreased glucose processing and many more changes than E4. These suggests energetics of the brain are subtly different in the two genotypes, and that they are affected differently by Rapamycin treatment.

Supported by: Funding: R01AG054459.

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Poster Presentation 142

Abstract Title:	**Characterizing unique regulatory sequences in sterol biosynthetic enzymes for the control of fungal pathogens**
Author(s):	K. B. Linscott, College of Medicine, U of Kentucky J. Chappell, Department of Pharmaceutical Sciences, U of Kentucky

Abstract: Invasive fungal infections are a significant cause of patient morbidity and mortality, indicating a need for the identification of new therapeutic targets. Squalene synthase is the first committed step in sterol biosynthesis, and while this enzyme plays a critical role in cell growth, the protein architecture is shared among eukaryotes and so is resistant to the design of fungal-specific growth inhibitors. It has been shown that there is a unique component of the fungal carboxy-terminal domain which allows the fungal squalene synthase, not the enzyme from plants or animals, to complement a knockout mutation in yeast. We hypothesize that there is a fungal-specific motif within this domain involved in regulation of the sterol pathway that can be mimicked for the development of an antifungal therapeutic. To identify this motif, we used the yeast Saccharomyces cerevisiae with a squalene synthase knockout mutation and expressed chimeric squalene synthases originating from multiple kingdoms of life. In contrast to previous observations, all enzymes tested were able to partially complement the knockout mutation when the genes were weakly expressed. Induction of non-fungal squalene synthases could not complement the yeast mutation and led to the accumulation of carboxy-sterol intermediates. These results suggest that the motif is involved in mediating an interaction between squalene synthase and the downstream C4-decarboxylase. Restoration of the complete complementation phenotype was mapped to a kingdom-specific 26-amino acid hinge motif, and over-expression of the C-terminal domain containing this hinge motif from a fungal squalene synthase led to growth inhibition of wild-type yeast.

Supported by:	The project described was supported by the Harold R. Burton and George A. Digenis endowed professorships.

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Poster Presentation 143

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. 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 (UK), 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 >1100 non-redundant bacterial strains and >390 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 (terpenes, macrolides, macrolactams, coumarins, indolocarbazoles, peptides, phenazines, piericidins, aromatic polyketides, glycosides, etc.). CPRI has enabled UK 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.

Supported by: This work was supported by National Institutes of Health grants R24 OD21479 (JST), the University of Kentucky College of Pharmacy, the University of Kentucky Markey Cancer Center and the National Center for Advancing Translational Sciences (UL1TR000117 an

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Poster Presentation 144

Abstract Title:	**Screening for Antimicrobial and Anticancer Drug Candidates from the Actinomycetes strains isolated from unique ecological niches in Pakistan**
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Abstract: The emerging antibiotics resistance especially the multidrug resistant (MDR) bacterial pathogens necessitates the continuous screening and search for new drug candidates from various sources. Pakistan is rich in biodiversity and there are diverse ecosystems in different regions of the country, including forests, saline lands, deserts, lakes and marine coasts. The interesting fact is most of these ecological niches are still unexplored and their microbial diversity is untapped with reference to the screening for new antibiotics and other chemotherapeutics. The actinomycetes are gram positive filamentous bacteria having high GC content in their genome and are the leading producers of most of the antibiotics and chemotherapeutics. In our search for new bioactive molecules we have isolated a large number of actinomycetes strains from different ecological niches in Pakistan. The isolated strains have been identified by microbiological, biochemical and genetic approaches (16S rRNA gene sequencing) etc. The laboratory scale cultivation of the selected strains and subsequent solvent extraction, purification and structure elucidation of the active molecules by mass spectrometry and NMR spectroscopy, yielded clinically useful known and new antibiotics and anticancer agents. Overall the study revealed that the actinomycetes flora of Pakistan is an untapped source and harbors the immense potential to produce novel bioactive molecules, and should continuously be explored to discover new drug candidates which can subsequently be developed as useful drugs.

Supported by: This work was supported by the grant from Higher Education Commission (HEC) Pakistan (HEC-NRPU Project 2121). This work was also supported by National Institutes of Health grants R24 OD21479 (JST), the University of Kentucky College of Pharmacy, the Unive

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Poster Presentation 145

Abstract Title:	**Biological and Chemical Screening of Actinomycete strains originated from Pakistan**
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Abstract: The development of the drug resistance among pathogens has reduced the therapeutic options for the treatment and we can no longer rely on the existing drugs. New drugs and new sources of drugs are needed. Due to the limitations of the chemotherapy, scientists are now focusing more for getting antimicrobial and anticancer drugs from natural sources. A collection of 60 actinomycete strains originated from different locations in Pakistan including deserts and lakes were investigated for their antimicrobial and in vitro anticancer activity against a set of 6 bacterial and fungal pathogens and 3 Human cancerous cell lines, including PC3, MCF7 and A549. The methanolic extracts obtained were also screened chemically by Thin Layer Chromatography, HPLC-UV and LC-MS techniques. The methanolic extracts exhibited promising antimicrobial activity against various gram positive and gram negative test strains. Among 60 strains screened, the extracts of about 15 strains exhibited significant in vitro anticancer activity against tested cell lines. The chemical screening results depicted the presence of active compounds with molecular masses in the range of 200 to 1000 Daltons. Consequently, 12 strains from this collection were selected as priority strains for scale-up studies, for the purification and identification of active compounds produced by these strains. The study revealed that the actinomycete strains originated from these sites are a promising source of clinically useful/new antimicrobials and various other chemotherapeutic agents.

Supported by:	This work was supported by the grant from Higher Education Commission, Pakistan (HEC-NRPU Project 2121). This work was also supported by National Institutes of Health grant R24 OD21479 (JST), The University of Kentucky, College of Pharmacy and the Nationa

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Poster Presentation 146

Abstract Title: **An ELISA Based Laforin Bio-Assay for the Treatment of Lafora Disease**

Author(s): Z. R. Simmons, Department of Molecular and Cellular Biochemistry M. S. Gentry, Department of Molecular and Cellular Biochemistry

Abstract: Lafora disease (LD), a fatal childhood epilepsy, is an autosomal recessive disease. 70% of LD patients carry mutations in the Epilepsy progressive myoclonus type 2A gene, (EPM2A) encoding the glycogen phosphatase laforin. Mutations in EPM2A lead to the accumulation of carbohydrate inclusion bodies called Lafora bodies (LBs) that result in neurodegeneration and death. 20% of LD patients have nonsense mutations/premature termination codons (PTCs). PTC readthrough therapy has shown to be effective in cells expressing PTC mutated EPM2A and can produce laforin that is full length and functional. The glucan phosphatase is necessary for normal glycogen metabolism. Laforin loss of function results in the accumulation of cytoplasmic glycogen-like aggregates called Lafora Bodies that are known to cause neurodegeneration and death. For the large subset of LD patients with PTC mutations, PTC readthrough therapy has the potential to rescue laforin's normal biological activity and the disease. In order to test whether the recovered protein possesses normal enzymatic activity, I have developed an Enzyme-Linked Immunosorbant Assay (ELISA) based laforin bio-assay to measure the activity of laforin readthrough products. Development of the laforin bio-assay is important so that it is suitable as a fully-automated biomarker for both mouse and patient laforin activity. Unique to this ELISA is the use of an anti-laforin single chain capture antibody, called a nanobody: a highly stable, highly specific, and easily reproducible antibody that originates from the camelid family. The newly developed anti-laforin nanobody is a key tool for establishing this assay as a high throughput method for determining the ability of small molecules to recover fully functional laforin in mice as well as humans.

Supported by: CCTS/NIH award: TL1

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Poster Presentation 147

Abstract Title: **Pharmacological Induction of Brown and Beige Adipose Tissue**

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Abstract: Brown adipose tissue (BAT) is associated with improved metabolic homeostasis in humans. Subcutaneous white adipose tissue (SC WAT) can acquire properties of BAT including increased uncoupling protein 1 (UCP1) expression in a process called beiging, and studies in rodents indicate that beige adipose tissue also improves glucose and lipid homeostasis. The goal of this study was to determine the ability of mirabegron (a β3AR agonist), pioglitazone (a thiazolidinedione), or a combination of the drugs to induce brown and beige adipose tissue and to determine the effects on glucose and lipid homeostasis. We randomized obese, insulin-resistant (IR) research participants to mirabegron (50 mg/day), pioglitazone (30 mg /day), or combination therapy treatment groups. Euglycemic clamping, oral glucose tolerance tests, adipose tissue biopsies, and PET-CT scans were performed at baseline and after 10 weeks of treatment. Mirabegron improved glucose homeostasis (reduced HbA1c and improved oral glucose tolerance) to a similar extent as pioglitazone without side effects or weight gain. Although mirabegron treatment increased insulin sensitivity, the effect size was much smaller than pioglitazone, yet mirabegron treatment significantly increased the insulinogenic and disposition indexes, suggesting that a major part of the mechanism of mirabegron action involved improving β-cell function. Mirabegron treatment consistently induced SC WAT beiging as evidenced by increased UCP1 expression (2.4 fold increase; $P<0.0001$), but did not induce BAT, suggesting that induction of beige adipose may be part of the mechanism responsible for improved glucose homeostasis. Pioglitazone also induced beiging (1.6 fold increase in UCP1; $P<0.01$), but not BAT. The combination of mirabegron plus pioglitazone was not additive, with similar effects on glucose tolerance as single drug. These results suggest that mirabegron treatment has significant beneficial metabolic effects in obese, IR subjects through a distinct mechanism involving SC WAT beiging and improved pancreatic beta cell function.

Supported by: NIH awards RO1 DK112282, CTSA grant UL1TR001998, and P20 GM103527-06.

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Poster Presentation 148

Abstract Title:	**A Phase 2 Study Evaluating a Proprietary Amino Acid Based Medical Food (enterade®) in patients with Quality of Life limiting Diarrhea due to Carcinoid Syndrome and other Neuroendocrine Tumors**
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Abstract: Background: Diarrhea in neuroendocrine tumor (NET) patients is a major symptom that presents chronically and severely affects their quality of life. Currently telotristat ethyl is the only FDA approved therapy for carcinoid syndrome diarrhea. Rationale: Enterade is an amino acid based oral rehydration solution which has been shown to restore intestinal villi and decrease secretory diarrhea in preclinical models. In a study of irradiated mice by Yin and colleagues, enterade®improved survival and improved body weight following irradiation (Yin et.al 2014). On electron microscopy of the ileum, there was loss of cell-to-cell contact after irradiation, which was restored after the introduction of enterade®. This study also suggested that the irradiated mice who received enterade®had lower levels of plasma endotoxin and IL-1β suggesting less bacterial translocation and inflammation as compared to the control population (Yin et. al 2014). Retrospective data presented at GI ASCO (2018) suggests antidiarrheal clinical activity in NET patients. Data needs to be validated in a prospective interventional trial. Method: This is an investigator initiated, single center, open label, phase II study involving well differentiated neuroendocrine tumors with quality of life limiting diarrhea (>4 stools/day). Two distinct subject cohorts (carcinoid syndrome diarrhea and non-carcinoid syndrome diarrhea) will be enrolled. The primary endpoint is reduction in frequency of diarrhea for individual subjects before and after enterade®. Subjects will maintain daily stool diary. Mean of daily stool frequency between Day 1 and 28 will be considered baseline. Diarrheal frequency of each patient will be compared to their own baseline during observation period. On day 29 (+/- 3 days), subjects will start enterade®BID for 28 days (D 29-D56). On Day 57 +/-3 days) subject will return to clinic for assessment of response.Based on a prior published study (Kulke et.al), we will assume that the mean daily reduction in Bowel Movements from baseline is equal to 1.5 (SD of change = 1.5) representing a large effect size = 1.0. A sample of 12 subjects in each cohort will provide over 90% power in detecting this effect size based on a two-sided paired t-test with 5% significance level. Additional 3 subjects will be added to each cohort to account for potential dropouts. Final sample size will be 15 subjects for each cohort. Trial is currently accruing. ClinicalTrials.gov Identifier: NCT03722511

Supported by: The project described was supported by Extrinsic Health Solution through a research grant.

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Poster Presentation 149

Abstract Title:	**Safety, feasible, and efficacy of early rehabilitation in patients requiring continuous renal replacement: A quality improvement initiative.**
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Abstract: Introduction: Early rehabilitation for critically ill patients is associated with improved outcomes. Historically, patients requiring continuous renal replacement therapy (CRRT) have been restricted to bed-rest. The purpose of this study was to develop an interdisciplinary protocol to increase early rehabilitation with focus on mobility in patients requiring CRRT. We assessed the safety, feasibility, and the limited efficacy associated with providing early rehabilitation to these patients. Methods: An interdisciplinary team developed the protocol with 2 main phases: 1)assessment of patient appropriateness to engage in rehabilitation, and 2) a 4-level progression of physical activity. Prospective data on major and minor adverse events were recorded to assess safety. Feasibility and efficacy was evaluated based on acceptability, implementation rates, integration of protocol into standard of care, and the association between levels of mobility and patient outcomes. Results: Over 12 months, 67 patients (54 ± 15 y/o, 44% female, BMI 29.2 ± 9.3 kg/m2) admitted to the MICU requiring CRRT received early rehabilitation under this protocol. The mean days of CRRT were 8.22 ± 5.8 days. 112 rehabilitation sessions were performed (112/152, 74%). No major untoward events occurred and only six minor adverse events were recorded (5.35%). There were no unintended CRRT interruptions. There was a significant correlation between higher mobility status and patient being alive at discharge (r=0.274, p = 0.025). Additionally, patients that had faster times to first rehabilitation were able to achieve higher rates of mobility (r=0.29, p=0.017) Conclusions: Implementation of an interdisciplinary protocol to increase early rehabilitation in critically ill patients requiring CRRT is safe and feasible. These data also suggest that early rehabilitation with focus on higher levels of mobility may lead to improved patient outcomes.

Supported by: No funding for this abstract

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Poster Presentation 150

Abstract Title:	**Barriers and Facilitators to Telemedicine Diabetic Retinopathy Screening Implementation in Primary Care**
Author(s):	F. Mehmeti, T. Belcher, C. William, A. Bastos de Carvalho. Department of Ophthalmology & Visual Sciences, U of Kentucky

Abstract: Background: Diabetic retinopathy (DR) is one of the leading causes of blindness in Kentucky. The Ophthalmology Department at the University of Kentucky (UK) runs a telemedicine diabetic retinopathy screening (TDRS) program that allows remote detection of DR, by conducting this exam in 45 primary care clinics (PCCs) across the state. After retina images are taken, they are sent to specialists at UK who interpret them and issue a report. The program allowed an increase in DR screening and diagnosis rates for underserved populations, but the rates remain below national target, suggesting that unidentified barriers exist. Methods: To assess barriers and enablers to TDRS, we conducted semi-structured interviews – guided by the Consolidated Framework for Implementation Research – with key informant subjects from six sites in our TDRS network. The interviews were transcribed and coded using a deductive codebook and ATLAS ti software. Inter-rater reliability of >0.85 was achieved in the first set of documents analyzed, through coding and re-coding, and confirmed by double coding of 20% of all transcripts. Results: Main barriers to TDRS were 1) time spent performing the exam, 2) technical ability and self-confidence in performing the exam, and 3) disruption of clinical workflow. Factors identified as enablers were 1) existence of organizational champion, 2) leadership positive pressure, and 3) exam performed by professional outside the clinical team. Discussion: Inner setting and Individual factors account for the major barriers and facilitators to TDRS in PCCs. Implementation strategies addressing these factors should lead to increased adoption of the exam and screening rates.

Supported by: The project described was supported by a UK CCTS Early Career Clinician-scientist award, the DRC at Washington University, Grant No. 2 P30 DK020579, the Cincinnati Eye Institute Ignite award, and (please add the scholarship you have through PSMRF (not sur

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Center for Clinical and Translational Science

Abstracts

Poster Presentation 151

Abstract Title:	**Examining the Clinical Dyadic Leadership Model: A Systematic Literature Review**
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Abstract: A recent trend in clinical leadership models involves a unit-based dyadic approach in which two individuals co-lead and share responsibilities. Health system administrators argue the dyadic model fosters a collaborative culture to share decision-making and emphasize patient care quality. However, little research exists on the benefits and disadvantages of the dyad leadership model. A systematic review was conducted to examine implementation and effectiveness of the dyad leadership model in healthcare systems. Databases were systematically searched for articles using medical subject heading (MeSH) terms relevant to dyads and leadership, such as co-lead, partner, and unit. Results yielded 52 articles. An abstract review resulted in 28 articles receiving full review by four authors. Ultimately, six articles met criteria for inclusion. Few studies addressed impact of the dyad leadership model on patient or hospital outcomes. The six articles reviewed provide (1) an assessment of perceptions toward teamwork and communication after dyad implementation, (2) a review of dyad model functionality within the system, (3) lessons learned from dyad model implementation, and/or (4) an assessment of dyad model fidelity. The findings indicate dyad models improve unit communication, increase employee satisfaction, and generate system alignment when supported by leadership with clearly defined roles, training, and dedicated time toward dyad duties. This review highlights benefits of employing dyadic leadership models and demonstrates why the dyad leadership model is growing in health systems. It also demonstrates a need for additional research to evaluate the impact of dyads on patient care, satisfaction, and key unit quality and performance indicators.

Supported by: This literature review has no external funding source. It was generated via research support by the Center for Health Services Research at the University of Kentucky.

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Poster Presentation 152

Abstract Title:	**Comparing Urban and Rural Evaluations of Medical Students by Attending Physicians**
Author(s):	H. Arnold, College of Medicine, University of Kentucky S. Keshtvarz, College of Medicine, University of Kentucky M. Lewis, College of Medicine, University of Kentucky R. Todd, MD, Department of Obstetrics and Gynecology, University of Kentucky J. Martin, MD, Department of Obstetrics and Gynecology, University of Kentucky K. McQuerry, PhD, Department of Statistics, University of Kentucky H. Bellamy, Department of Statistics, University of Kentucky

Abstract: Objective: To compare the quantity and rated quality of medical student narrative evaluations by attending physicians in rural community and urban university settings. Methods: This six-month cohort study included 45 physicians across various specialties from both urban and rural teaching hospitals. At the beginning of the study, a faculty development session was held where participants were familiarized with methods on improving their written narrative feedback. An interventional faculty development session was performed midway through the study. Narrative evaluations were collected and analyzed by 4 blinded raters for quality using both the Quality Improvement Instrument (QI) and the Completed Clinical Evaluation Report Rating (CCERR). A simple word count was used to analyze the quantity of comments. Baseline and post intervention scores were compared using paired t-tests. Results: Seventy-four evaluations were obtained from urban university faculty and 23 evaluations from rural community physicians. The median baseline scores were QI 2.0, CCERR 12, and word count 22 for the urban site and QI 2.75, CCERR 13.5, and word count 48.25 for the rural site. The post intervention scores were QI 1.75, CCERR 12.75, and word count 27.75 for urban faculty and QI 2.75, CCERR 16.25, and word count 69 for rural physicians. Conclusion: There was no statistical change in quantity or rated quality of narrative evaluation scores before and after the intervention for rural community or urban university faculty when $p<0.05$. However, a trend was identified that narrative evaluations by rural community physicians scored higher in all measures than urban university faculty.

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Poster Presentation 153

Abstract Title:	**LGBTQ* specific medical education at the University of Kentucky College of Medicine**
Author(s):	A. Hyder, S. Maela, University of Kentucky College of Medicine B. Fallin-Bennett, Keisa MD, University of Kentucky College of Medicine C. Adkins, Jessica, University of Kentucky College of Medicine D. Looff, Rachel, University of Kentucky College of Medicine

Abstract: Objectives: About 3.5% Americans identify themselves as lesbian, gay or bisexual and 0.3% as transgender. Some of the healthcare risks include STDs, anxiety, depression, suicide and cardiovascular disease, amongst many others. Lack of healthcare provider's awareness to the sensitive issues faced by this community and stigma towards them can lead to poor quality of care [1]. Goals of this study were to evaluate how students feel about the current training, what pre- clinical and clinical changes they would like to see. This year we added a qualitative analysis portion to the survey, to get any feeling/ideas students have towards the LGBTQ* training given to them at UKCOM. Overall goal is to prepare physicians so they have the skills needed to improve outcomes for this community. Methods: Over the course of July 2018, a survey was sent out to all medical students (M1-M4), 94 anonymous students responded. Students were asked about their demographics, to rate the quality and amount of education received. How prepared they feel handling a list of healthcare issues unique to LGBTQ* and what types of education they are interested in. They were asked to provide any ideas or comments about LGBTQ* health education at UKCOM. Results and conclusion: 61% of the M4s that answered, felt that the LGBTQ education was 'not enough' or 'enough but would appreciate more'. M4s felt 'not at all prepared or 'insufficiently prepared' for issues like sex reassignment surgery, transitioning and disorders of sexual development. Based on the data analysis, significant correlation was found between prior experience and comfort level of the students. Both M1s and M2s want LGBTQ* topics to be added to existing pre-clinical courses. In the open-ended section of the survey, students recommended adding an elective to learn more about LGBTQ* issues, standardized patient care in ICM, few days in LGBTQ* clinic during family medicine/internal medicine/psych rotations and using Salvation Army clinic as a resource to connect the LGBTQ* community to the students.

Supported by:	UK Population Medicine Summer Research Program (PM-SRP) grant of $1500 was given to me to do this project over summer of 2018.

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Abstracts

Poster Presentation 154

Abstract Title:	**Implementing Participant-Led Trauma-Informed Sexuality Education to Pregnant Teens and Teen Moms in Kentucky**
Author(s):	K. Haus, Department of Kinesiology and Health Promotion, U of Kentucky K. Michel, Department of Kinesiology and Health Promotion, U of Kentucky K. Mark, Department of Kinesiology and Health Promotion, U of Kentucky

Abstract: Students learn about a wide range of sexuality-related topics in from comprehensive sexuality education, but such programs are inconsistently delivered in the US school system, and even less so in Kentucky. Reports of unintended pregnancy for US women were 50% in 2017. Additionally, 19 in 1000 teens will get pregnant in the US. Rates in Kentucky are 54% higher, with 29 per 1000. We provide weekly sexuality education classes to high-risk students at the Family Care Center, a school for pregnant teens and teen moms from ages 13 to 18. Numerous students here have experienced some form of trauma, and by acknowledging the influence of context, our approach is intrinsically trauma-informed. Student involvement in course development is crucial for providing effective education in this group. This process empowers students to discuss the topics that are most important to them and ask questions about what they wish they knew before pregnancy, such as, “Why didn’t I know about an IUD?” or “How does birth control work – what does it actually DO?” or “I wish I knew that sometimes birth control fails and to use a backup!” All of these questions could have been answered through a comprehensive sexuality education class. Equipped with this information, we aim to empower these young women to become sources of accurate information for others in their communities. The purpose of this presentation is to highlight the process of developing and delivering participant-led trauma-informed sexuality education with these young women.

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Abstracts

Poster Presentation 155

Abstract Title:	**Laurel County Health in Motion: MAPP Community Assessment Implementation and Strategic Planning for Substance Use Disorder Interventions**
Author(s):	B. Gilley, Laurel County Health in Motion Coalition, Laurel County Health Department

Abstract: This project represents implementation of the MAPP Community Health Assessment Process by the Laurel County Health in Motion Coalition (HIM). Findings from the assessment and chosen strategic priority areas will be presented. Substance Use Disorder (SUD) and the affect Adverse Childhood Experiences (ACEs) have on addiction was also of interest to the coalition. The coalition hosted an ACEs Seminar for professionals who work in behavioral health, as well as, substance abuse prevention and treatment. The HIM Coalition conducted three different assessments. The three assessments included collection of secondary data on health indicators, a community survey and focus groups, a small workgroup event to that considered factors that could impact the health of the public, and a Gap Analysis of SUD resources. The data from the three assessments were analyzed using SurveyMonkey and Microsoft Excel. The findings of the three assessments indicated that Substance Use Disorder and Chronic Disease are top health indicators and important issues to members of the community. Other top health concerns included mental health, obesity, transportation, and infant mortality. The pre and post tests conducted as part of the ACE Seminar indicated a 35% increase in the participant's knowledge of ACEs after attending the seminar. The HIM Coalition has decided to choose two strategic priority areas: Substance Use Disorder and Chronic Disease Prevention and Management. The coalition will also continue to consider ACE's and family support within strategies to positively impact these priority areas.

Supported by:	"The project described was supported by the National Center for Research Resources and the National Center for Advancing Translational Sciences, National Institutes of Health, through Grant UL1TR001998. The content is solely the responsibility of the auth

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Poster Presentation 156

Abstract Title:	**Epithelial-Specific P85α KO Enhances Crypt Resilience to Radiation Injury**
Author(s):	E. B. Lynch, Departments of Internal Medicine and Microbiology, Immunology and Molecular Genetics, College of Medicine, University of Kentucky E. M. Bradford, Department of Internal Medicine, College of Medicine, University of Kentucky T. A. Goretsky, Department of Internal Medicine, College of Medicine, University of Kentucky C. Seibert, College of Medicine, University of Kentucky E. Pauw, College of Medicine, University of Kentucky T. Gao, Department of Biochemistry, University of Kentucky T. A. Barrett, Department of Internal Medicine, College of Medicine, University of Kentucky

Abstract: High-dose radiation targets highly proliferative compartments, making radiation an attractive option for aggressive cancers. However, radiation exerts stress on physiologically high cycling cells, including intestinal epithelial cells (IEC), where it causes significant toxicity (diarrhea, bleeding, etc). Here we examine the role of PI3-Kinase (PI3K) signaling in promoting epithelial repair after radiation injury. Previously, we found that reductions in class IA PI3K (pik3r1) (regulatory subunit p85α) induces the anti-apoptotic protein survivin and promotes IEC expansion in an ileocecal resection repair model. Preliminary data obtained in histopathologic sections from radiation proctitis patients reveal a 29.3% enhancement of survivin+ nuclei compared to normal colonic biopsies. To interrogate the role of IEC PI3K in radiation injury, we utilized VillinCre-p85fl//fl (p85KO) and VillinCre-p85+/+ subjected to high dose (12Gy) radiation. IEC Western blot (WB) data of unperturbed p85KO mice revealed a complete ablation of p85α, with subsequent increases in p-AktSer473 along with p-PTEN, p-GSK3βSer9, as well as p-p70S6K and survivin compared to WT controls, suggesting a deregulation of PI3K machinery. RT-PCR studies performed at baseline revealed increases in TA-enriched Wnt target genes, Axin2 (56%) and c-myc (39%) and reserve intestinal stem cell (ISC) markers HopX (33%), and Bmi1 (20%), at the expense of the active cycling Lgr5+ stem cells (-25%). Histopathologic sections highlight a distinct shift in the zone of proliferation with more than a 2-fold increase in BrdU+ cells at the reserve stem cell position 4 compared to controls (Fig 1). Following lethal radiation dosage, p85KO mice exhibited a 20% increase in survival as compared to wildtype (WT) littermates along with increased crypt survival (proportion of crypts with >5 BrdU+ cells/crypt, WT vs p85KO: 72% +/- 3 Vs 84% +/- 1, $p<0.004$). IEC markers of Akt activation (pGSK3β) increase from 24 to 84hr post radiation injury along with markers of activated stem cells (p-β-catSer552, p-PTEN). In p85KO mice, radiation induced lower levels of WB PUMA and cleaved caspase 3 compared to WT controls. Concomitantly, crypt lengths increased in p85KO (+9%) compared to WT (-20%). Taken together, our data suggest PI3K signaling enhances recovery from radiation injury through expansion of reserve ISC populations capable of creating proliferative Lgr5+ ISC and accelerating crypt IEC recovery from radiation-induced cell death. We posit this pathway limits apoptosis and enhances survival of proliferating progenitor populations which increases overall crypt survival. Given results suggesting p85α KO IEC increase PI3K signaling, we propose p85α as a potential drug-able target capable of enhancing recovery from radiation therapy.

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Abstracts

Poster Presentation 157

Abstract Title: **Diabetic Foot Exams: Effectiveness of Education and Improved Access**

Author(s): T.D. Collett RN, Director of Quality Services, Mountain Comprehensive Health Corporation

Abstract: In 2018, Mountain Comprehensive Health Corporation began a focused approach to diabetic care within our service area. Diabetic foot care, or the lack thereof, was identified as a concern within our patient population. MCHC, in collaboration with the University of Kentucky SEED grant, chose to tackle the problem by providing education regarding effective diabetic foot exams to providers and education for at-home foot care to patients. Training was given to providers on how to conduct a diabetic 3-minute foot exam and quick reference cards supplied for future guidance. Monofilaments were purchased and supplied to all providers to aid in completion of these exams. Staff were trained to prepare patients with diabetes upon “rooming” by removing his/her shoes and socks. Patients were also provided quick reference cards regarding at-home foot care and demonstration/teaching provided during office visits. Through this program MCHC identified a great need for access to Podiatric medicine. Consequently, Podiatry has since been added as a service available to MCHC patients in the Whitesburg Clinic daily, and 3 of 8 satellite clinics at least weekly. In 2017, approximately 156 diabetic foot exams were completed in MCHC clinics. In 2018, with the completion of provider education and ultimately, the addition of Podiatry, 353 diabetic foot exams were completed.

Supported by: The project included resources from the Centers for Disease Control and American Diabetes Association

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Poster Presentation 158

Abstract Title:	**Regulation of PI-3-Kinase Signaling Through p85α Drives Paneth Cell Fate Determination and Activity in the Intestinal Crypt**
Author(s):	C. M. Seibert, Departments of Internal Medicine-Digestive Disease and Microbiology Immunology and Molecular Genetics, U of Kentucky E. B. Lynch, Departments of Internal Medicine-Digestive Disease and Microbiology Immunology and Molecular Genetics, U of Kentucky T. A. Barrett, Departments of Internal Medicine-Digestive Disease and Microbiology Immunology and Molecular Genetics, U of Kentucky

Abstract: Paneth cells (PC) are specialized secretory epithelial cells found at the base of small intestinal (SI) crypts. PCs are the major source of Wnt ligands in the intestinal crypt and play a critical role in crypt homeostasis. PC disruption has been linked to significant pathology, including intestinal dysbiosis and Crohn's Disease. p85α is a negative regulator of the p110 subunit of the PI3-kinase (PI3K) signaling pathway which promotes crypt stem cell proliferation. Previous work by this laboratory has demonstrated that epithelial-specific p85KO (VillinCre-p85fl//fl) leads to increased stem cell expansion and accelerated healing from ileocecal resection, but the direct effect on PCs directly remains unclear. We hypothesized that the PCs of p85KO mice will be more numerous, larger in size, and have increased markers of PC activity compared to WT (VillinCre-p85+/+). Aperio software was used to quantify numbers and measure PC size. To determine PC activity, RNA transcripts of Wnt targets (MMP7 and EphB3) and PC antimicrobial peptides (Lyz1, Lyz2, and Ang4) were analyzed using RT-PCR. Preliminary data revealed a 44% increase in PC quantity (p85KO: 8.58±2.21, WT: 6.12±2.21) and a 30% increase in PC area (p85KO: 126.35 ±49.45mm2, WT: 97.84 ±39.38mm2). RNA analysis in p85KO mice demonstrated increased PC activity across transcripts measured (1.5-7-fold). This data suggests that removing the PI3K negative regulator p85α in epithelial cells is sufficient to drive stem cell fate decision toward secretory lineage cells. Future directions include increasing our statistical power by including more mice, and evaluating other important fate determination signaling pathways, including Notch.

Supported by:	The project described was supported by the VA Merit Grant and the National Center for Advancing Translational Sciences, through Grant UL1TR001998. The content is solely the responsibility of the authors and does not necessarily represent the official view

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Poster Presentation 159

Abstract Title:	**Case Series of Splenic Artery Embolization Using N-Butyl Cyanoacrylate for Blunt Splenic Trauma**
Author(s):	S. Sanampudi, U of Kentucky College of Medicine H. Kapoor, Department of Radiology, U of Kentucky D. Raissi, Department of Radiology, U of Kentucky

Abstract: Objectives: The purpose of this case series is to display our experience with the use of N-Butyl Cyanoacrylate (NBCA) for splenic artery embolization (SAE) in six patients with blunt abdominal trauma. Through this brief pictorial review, we aim to outline optimal patient selection, technical considerations for NBCA use, and procedural safety & efficacy. Background: Nonsurgical management of spleen is increasingly used in setting of blunt abdominal trauma since it allows for preservation of spleen. SAE using coils and plugs has been widely supported by literature showing high success and low complication rates. Use of other embolic materials such as ethanol, gel-foam particles, and NBCA has been reported but is less known. The advantages of NBCA include quick solidification, no end-organ damage, and feasibility of its use in setting of tortuous and/or small vessels where coils fail to anchor. Clinical Findings: Six patients with splenic injury secondary to blunt abdominal trauma and active extravasation on CT angiographic imaging were treated with SAE using a mixture of NBCA with Ethiodol. Four patients had grade-IV and one had grade III injuries. None of these patients had any procedure related complications necessitating re-imaging or inpatient admission (i.e. abscesses or recurrent bleeding) with follow-up ranging from 5months to 4years. One patient with grade-I laceration died two days post procedure from a worsening subdural hematoma. No splenectomies were recorded. Conclusion: SAE with NBCA for blunt splenic trauma is seen to be safe and effective on short to intermediate follow-up regardless of the patient's splenic injury grade.

Supported by: Not applicable

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Poster Presentation 160

Abstract Title:	**Noninvasive Biomarkers for Inflammatory Bowel Disease Monitoring: Drawbacks and Potential.**
Author(s):	C.Perry, Department of Internal Medicine, Division of Gastroenterology, U of Kentucky V. Patel, Department of Internal Medicine, Division of Gastroenterology, U of Kentucky S. Seif, Department of Internal Medicine, Division of Gastroenterology, U of Kentucky M. Hashim, Department of Internal Medicine, Division of Gastroenterology, U of Kentucky A. Yadav, Department of Internal Medicine, Division of Gastroenterology, U of Kentucky T. Barrett, Department of Internal Medicine, Division of Gastroenterology, U of Kentucky

Abstract: BACKGROUND: The recently published CALM study demonstrated that biomarkers such as CRP and fecal calprotectin (FC) are adequate surrogates for subclinical disease detection, and that fecal calprotectin can be used to escalate IBD therapy without repeat endoscopy when levels exceed 250 µg/g.1 Previous studies have indicated that fecal calprotectin levels elevated above 50 µg/g can be used as a screening tool, but are not specific enough to justify escalation of drug therapy without endoscopic confirmation of disease activity.4 We increasingly rely on biomarkers to drive our clinical decisions, and wish to evaluate the compliance rates and performance of these biomarkers in our practice. METHODS: We analyzed a database consisting of a prospective cohort of Inflammatory Bowel Disease patients who had undergone endoscopic evaluation between 2/1/2016-1/30/2019. Patients who underwent colonoscopy with biopsies for pathology and had a fecal calprotectin ordered within 1 month of endoscopy were eligible for inclusion in the analysis. 271 patients met eligibility criteria for inclusion. RESULTS: The overall fecal calprotectin compliance rate was 68.6% across all groups, compared to 99% compliance for CRP testing. Using a positive fecal calprotectin cutoff value of 100µg/g, the specificity among all IBD groups was 82.7%. When the cutoff value was increased to162µg/g, the specificity rose to 93.1%. CONCLUSION: Our results suggest that the specificity of fecal calprotectin is higher at lower positive cut off values than previously reported in the literature. Based on our results, we suggest considering escalation of therapy without endoscopy when fecal calprotectin values are ≥162 µg/g. Although fecal calprotectin is a highly sensitive/specific test for IBD inflammation, compliance still remains a major barrier to its utility.

Supported by:	The project described was supported by the National Center for Research Resources and the National Center for Advancing Translational Sciences, National Institutes of Health, through Grant UL1TR001998. The content is solely the responsibility of the autho

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Poster Presentation 161

Abstract Title:	**Effects of bacterial endotoxin LPS on the neuronal regulation of the heart, a sensory-CNS-motor nerve circuit as well as at neuromuscular junctions: Crustacean model**
Author(s):	C. Saelinger, Department of Biology, U of Kentucky M. McNabb, Department of Biology, U of Kentucky R. McNair, Department of Biology, William Paterson U S. Bierbower, Department of Biology, William Paterson U R. Cooper, Department of Biology, U of Kentucky

Abstract: Eatable crustaceans are susceptible to bacterial septicemia from injury or compromised defense by bacterial strains which can possibly have detrimental effects in mammals. Since many crustaceans (i.e., crabs, lobsters, crayfish) are used for animal food and human consumption, it is of interest to understand the effects potential bacterial infections can have on their and our health. The Red Swamp crayfish (Procambarus clarkii) was used as a model crustacean to investigate the effect of direct exposure to isolated endotoxin lipopolysaccharide (LPS) from gram-negative bacteria (Serratia marcescens). S. marcescens is a common strain identified to cause septicemia in mammals (500 µg/ml) and is prevalently found in nature. LPS injection into the hemolymph of crayfish revealed acute changes in heart rate and effects on survival. Direct LPS exposure on an in situ sensory-CNS-motor circuit produces a decrease in function at 500 µg/ml but has no significant effect at 100 µg/ml. At the isolated neuromuscular junction, the direct action of the LPS endotoxin (500 µg/ml) enhances evoked synaptic transmission and alters facilitation, while decreasing observable spontaneous vesicle fusion events. These direct actions on tissues appear to be independent of innate immune responses and suggests the LPS receptors on these tissues have a role in excitability of cellular function. In addition, we embarked on examining reproducibility in the data analysis with different participants.

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Poster Presentation 162

Abstract Title:	**Activity of Plazomicin in Comparison to other Aminoglycosides against Carbapenem-resistant Enterobacterales**
Author(s):	J. A. Clark, PharmD, MS, College of Pharmaceutical Sciences, U of Kentucky B. Kulengowski, PharmD, MS, PhD, Albert B. Chandler Hospital, UK Healthcare D. S. Burgess, PharmD, FCCP, FIDP, College of Pharmacy, U of Kentucky

Abstract: Background: Infections caused by carbapenem-resistant Enterobacterales (CRE) have become a serious health threat and lack therapeutic options. We evaluated a recently approved agent, plazomicin (PLZ), against other available aminoglycosides. Methods: Isolates were cultured from patients at an academic medical center. MICs were determined for these isolates against PLZ, amikacin (AMK), gentamicin (GEN), and tobramycin (TOB). Disk diffusion was utilized to characterize the phenotypic expression of carbapenem resistance: MBL, KPC, both, or other. Results: Overall, 140 clinical isolates were evaluated—81 produced KPC, 24 produced MBL, 8 produced both MBL and KPC, and 27 contained other resistant phenotypes. Table 1 shows the % of susceptible isolates (%S) to AMK and PLZ using CLSI, EUCAST, USCAST, and FDA breakpoints. The MIC50/90 values for AMK were 4/32 (Overall and KPC), 8/16 (MBL), 4/16 (Both), and 2/8 (Other). The MIC50/90 values for PLZ were 0.5/0.5 (Overall), 0.5/1 (KPC), 0.75/1 (MBL), 0.75/1 (Both), 0.5/1.5 (Other). Conclusions: Our study demonstrated that PLZ has excellent activity against clinical isolates possessing diverse carbapenem resistance phenotypes (i.e., KPC, MBL, both, or other). Ongoing research is necessary to further establish the role for PLZ in the treatment of CRE infections.

Supported by: Supported by partnership with Achaogen

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Poster Presentation 163

Abstract Title:	**The altered neonatal CD8 T cell immunodominance hierarchy to influenza virus antigens impacts peptide vaccination.**
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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. Vaccination continues to be the most important intervention for preventing Influenza disease, but current vaccines fall short of full protection and must be readministered every year. Work is underway to not only stimulate antibody responses to the virus but also promote CD8 T cell responses. CD8 T cells can provide heterosubtypic protection year to year as well as reducing morbidity for infections that do occur. This may be important for improving outcomes in vulnerable populations such as neonates, but neonatal T cells frequently respond differently than adult cells. We sought to understand CD8 T cell specificity and immunodominance during neonatal influenza infection and peptide vaccination as well as how any differences from the adult hierarchy might impact peptide vaccine effectiveness. We found that neonatal C57BL/6 mice display an altered CD8 T cell immunodominance hierarchy during influenza infection, preferentially responding to an epitope in the influenza protein PA rather than the co-dominant adult response to NP and PA. Similarly, pups respond to PA but not NP during peptide vaccination. These data suggest that vaccines targeting T cells should consider epitope usage if the intended patient population includes infants as well as adults.

Supported by: N/A

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Poster Presentation 164

Abstract Title:	**Leading Causes of Bacterial Keratitis: Not So Far from Home for Contact Wearers**
Author(s):	B. Goble, Senior in Agriculture and Medical Biotechnology, U of Kentucky M. Grady, Mechanical Engineering, U of Kentucky

Abstract: Bacterial keratitis is an eye infection that first exposes itself as eye redness and pain. Further progression results in tearing and puss-like secretions. If left untreated, as with those with poor healthcare access, will lead to permanent vision loss and blindness. Wearing contacts is the most common risk factor in keratitis incidents, it is also the only risk factor not related to trauma or disease. 74% of contact lens users do not replace lens cases on time and 79.3% of user's self-report not following all contact maintenance guidelines. 80% of keratitis infections are bacterial yet the literature suggests contact cleaning solutions may be partially to completely ineffective at destroying bacteria. As a result of the lack of sanitation, biofilms foster inside contact cases. In biofilm, bacteria have an increased ability to resist antimicrobial solutions and foster higher cell counts. One solution may be using the common household microwave to irradiate bacteria in contact cases as a convenient and effective way to sanitize biofilms. One of the two most common keratitis causing bacteria Staphylococcus aureus was chosen as it represents the highest rates of recurrent infection and corneal transplantation. To observe the effectiveness of treatment contact cases where swabbed, after various pre/post-treatment protocols and exposure times, to inoculate agar plates. Then, the number of colony's grown after 48 hours of incubation where enumerated. Success of this research project would offer eyecare professionals an easy alternative to greatly reduce their contact users' risk for bacterial keratitis without reliance on ineffective contact solutions.

Supported by: We would like to acknowledge NIH COBRE Phase III pilot funding under number 5P30GM110788-04 to carry out these experiments. We thank the Center for Pharmaceutical Research and Innovation (CPRI) for use of bacterial culture equipment. CPRI is supported, in

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Abstracts

Poster Presentation 165

Abstract Title:	**Toxoplasma cysts capable of persisting in the presence of the protective T cell immunity express increased levels of dense granule proteins 1, 2, 3, and 7 and rhoptry protein 35.**
Author(s):	R. Hannah, Department of Microbiology Immunology and Molecular Genetics, U of Kentucky E. Ochiai, Department of Microbiology Immunology and Molecular Genetics, U of Kentucky Q. Sa, Department of Microbiology Immunology and Molecular Genetics, U of Kentucky Y. Suzuki, Departments of Microbiology Immunology and Molecular Genetics, U of Kentucky and Department of Biomedical Sciences and Pathobiology, Virginia Polytechnic Institute and State U

Abstract: Toxoplasma gondii forms cysts preferentially in the brain and establishes chronic infection. One third of human population is estimated to be infected, but no drugs are currently available against the cysts. We recently uncovered that CD8+ T cells can eliminate the cysts. However, it is unknown why some cysts are able to persist in the presence of the CD8+ T cells in chronically infected hosts. To address this important point, we examined the expression levels of 17 proteins, which are know to be involved in formation of the cysts or the virulence of the acute stage form (tachyzoites), between the total cysts present in the absence of T cells and the cysts that persisted in the presence of T cells. Following a transfer of CD8+ immune T cells to infected T cell-deficient SCID mice, a small portion (4.3 %) of cysts with increased expression of five secretory molecules (dense granule protein 1, 2, 3, and 7, and rhoptry protein 35) among 17 molecules tested persisted for 7 days by avoiding elimination by the anti-cyst T cells. These changes did not occur in the presence of perforin-deficient CD8+ immune T cells or normal T cells from uninfected mice. Thus, these five molecules appear to be crucial for evading the perforin-mediated anti-cyst T cell immunity for persistence of T. gondii cysts. These data could provide the basis for developing novel therapeutic compounds to inhibit the immune evasion mechanism of the cysts for their eradication.

Supported by: Supported in part by NIH AI095032, AI134323, and AI136821

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Abstracts

Poster Presentation 166

Abstract Title:	**Deadly Pseudomonas aeruginosa: Have They Finally Met Their Match?**
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Abstract: Pseudomonas aeruginosa (PSA) cause severe healthcare-associated infections. The CDC reported in 2013 that 13% of these infections are due to multidrug-resistant PSA. We assessed the in vitro activity of new beta-lactam/beta-lactamase inhibitor combinations against extensively drug-resistant (XDR) PSA. In vitro susceptibility of 50 PSA isolates (49 XDR and one ATCC strain) to commonly utilized antipseudomonal agents plus the newer beta-lactam/beta-lactamase inhibitors was tested according to CLSI guidelines. These isolates were nonsusceptible to at least one antimicrobial in six of the seven following antipseudomonal agent categories: cephalosporins, carbapenems, monobactam, beta-lactam/beta-lactamase inhibitors, polymyxins, aminoglycosides, and fluoroquinolones. McNemar's test was utilized to determine statistical significance. All isolates were susceptible to polymyxin B and colistin. Apart from the polymyxins, ceftolozane-tazobactam had the highest susceptibility (94%) against these XDR-PSA (N=49) followed closely by ceftazidime-avibactam (88%) and amikacin (67%). Ceftolozane-tazobactam activity was not significantly different to ceftazidime-avibactam (p=0.45), but was significantly higher than amikacin (p=0.00195). All other beta-lactams tested demonstrated <8% susceptibility as well as gentamicin and tobramycin with 0%. Of the three isolates resistant to ceftolozane-tazobactam, one isolate was susceptible to aztreonam-avibactam. The second isolate was susceptible to ceftazidime-avibactam and amikacin, and the last isolate was susceptible to ceftazidime-avibactam. Activity of ceftazidime was restored with the addition of avibactam while activity of aztreonam was only enhanced. For this population of XDR-PSA, ceftolozane-tazobactam demonstrated the greatest in vitro activity followed by ceftazidime-avibactam. While ceftolozane-tazobactam had higher susceptibility rates than ceftazidime-avibactam, it is not a superior treatment option against these organisms and both agents can be considered.

Supported by: No financial support to disclose at this time

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Abstracts

Poster Presentation 167

Abstract Title:	**Assessing Rheumatology Patient Education Materials: Medical Complexity and Readability Perspectives**
Author(s):	S. Kim, Division of Biomedical Informatics, U of Kentucky A. Lenert, Division of Rheumatology, U of Kentucky M. Russell, Department of Communication, U of Kentucky

Abstract: Background/ Objective: Rheumatologists rely on patient education materials (PEM) to reinforce or supplement verbal instructions. However, the quantity and complexity of the materials delivered at the point of care has often been discredited. This study investigated associations between readability scores and disease complexity as rated by 16 practicing rheumatologists. Methods: We used readability and clinical natural language processing (cNLP) methods to assess textual levels of information quantity and complexity within 62 rheumatology PEMs obtained from the American College of Rheumatology (ACR) Website. A one-way analysis of variance was conducted to explore the impact of PEM type on complexity as measured by each model. Additionally, a Pearson product-moment correlation coefficient was computed to assess the relationships between the various scoring models. Results: The most serious complexity score assigned was for Vasculitis (Σ=48) which was rated 3 (high) by all 16 raters. The average readability grade level for the group of 42 diseases was slightly less than 12th grade (M=11.86), indicating easier materials than the 20 therapeutic materials (M=13.65). There was strong correlation between some readability scores and cNLP classes, but no relationships to medical complexity levels. Conclusions: Automatic extraction using text analytics has the potential to calculate the content complexity of PEMs to complement or replace readability scoring. Thus, future studies will require annotated corpora to develop and test PEMs specific to rheumatology. Based on these results, this study proposes a new scoring model for complexity that can be further refined and validated using cNLP.

Supported by:	The project described was partially supported by the NIH National Center for Advancing Translational Sciences, National Institutes of Health, through grant number UL1TR001998. The content is solely the responsibility of the authors and does not necessaril

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Poster Presentation 168

Abstract Title:	**Untargeted Lipidomics of NSCLC Shows Differentially Abundant Lipid Classes in Cancer vs Non-Cancer Tissue**
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Abstract: Lung cancer is the leading cause of cancer death worldwide and non-small cell lung cancer (NSCLC) represents 85% of newly diagnosed lung cancers. The high mortality rate of lung cancer is due in part to the lack of effective treatment options for advanced disease. A major limitation in the development of effective treatment options is our incomplete understanding of NSCLC metabolism at a molecular level. Improvements in mass spectrometry combined with our untargeted assignment tool SMIRFE enable the systematic and less biased examination of NSCLC metabolism. From 86 patients with suspected resectable stage I or IIa primary NSCLC, lipid extracts were prepared from paired disease and non-disease tissue samples and analyzed using ultra-high resolution Fourier transform mass spectrometry. Machine learning was employed to classify SMIRFE formula assignments into lipid categories with which differential abundance analysis was performed. Sterols and glycerolipids were consistently and significantly upchanged in disease versus control. This molecular phenotype suggests a possible therapeutic role for statins in the treatment of NSCLC. Additionally, several sterols belonging to the sterol ester subcategory are consistently and significantly upchanged, suggesting increased SCD1 activity. Although statin use and SCD1 expression have known effects on NSCLC prognosis, their metabolic effects are less understood. In our study, a large fraction of the NSCLC samples displayed this phenotype, suggesting that this metabolic phenotype may be shared across multiple genetic subtypes of NSCLC. Thus, pharmaceutical targeting of this metabolic subtype could have utility in the treatment of many genetic subtypes of NSCLC.

Supported by: This project was supported in part by NSF1419282 (PI Moseley), NIH P01CA163223-01A1 (PIs Andrew N. Lane and Teresa W.-M. Fan) and NIH UL1TR001998-01 (PI Kern).

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Poster Presentation 169

Abstract Title:	**Predicting Substance Use Disorder using Long-term ADHD Medication Records in Truven**
Author(s):	S. Fouladvand, Institute for Biomedical Informatics, University of Kentucky, Lexington, KY E. R. Hankosky, Department of Pharmaceutical Sciences, University of Kentucky, Lexington, KY H. Bush, Department of Biostatistics, University of Kentucky, Lexington, KY J. Chen, Institute for Biomedical Informatics, University of Kentucky, Lexington, KY L. P. Dwoskin, Department of Pharmaceutical Sciences, University of Kentucky, Lexington, KY P. R. Freeman, Department of Pharmacy Practice and Science, University of Kentucky, Lexington, KY D. W Henderson, Department of Pharmacy Practice and Science, University of Kentucky, Lexington, KY K. Kantak, Department of Psychological and Brain Sciences, Boston University, Boston, MA J. Talbert, Department of Pharmacy Practice and Science, University of Kentucky, Lexington, KY S. Tao, Department of Neurology, University of Texas Health Science Center, Houston, Texas G. Q. Zhang, Department of Neurology, University of Texas Health Science Center, Houston, Texas

Abstract: Purpose: About 20% of individuals with attention deficit hyperactivity disorder (ADHD) are first diagnosed during adolescence. While preclinical experiments suggest that adolescent-onset exposure to ADHD medication is an important factor in the development of substance use disorder (SUD) phenotypes in adulthood, the long-term impact of ADHD medication initiated during adolescence has been largely unexplored in humans. Methods: We presented a new framework with three components: 1) data pre-processing, 2) SUD prediction using Long-Short Term Memory (LSTM) networks, and 3) hypothesis exploration. We extracted 5,465,208 records from 118,063 Truven enrollees (Jan 2009 - Dec 2015) with an ICD-9 diagnosis of ADHD (314.X), and converted the Truven format into an enrollee time matrix. Among the enrollees with ADHD, 9,376 were SUD-Positive and 108,687 were SUD-Negative. This sequential medication record data was used to train the LSTM models and explore different hypotheses by varying the LSTM and inputs. Results: Our analysis indicates that temporal medication features, rather than stationary features, are the most important factors for predicting SUD among enrollees with ADHD that initiated ADHD medication during adolescence. We compared the LSTM with classical machine learning models regarding the SUD prediction performance. Compared to classical models, LSTM achieved 14% higher F1-Score for predicting SUD. Conclusion: We have systematically studied the long-term impact of ADHD medication initiated during adolescence using the LSTM model. We discovered that long-term temporal medication application patterns appear to be key factors that provide increased power to predict the development of subsequent SUD in adolescent ADHD enrollees.

Supported by: Start up grant

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Poster Presentation 170

Abstract Title:	**Moiety Modeling Framework for Deriving Pathway-Specific Relative Metabolic Flux from Mass Spectrometry Measured Isotopologues**
Author(s):	Huan Jin, Department of Toxicology and Cancer Biology, U of Kentucky Hunter N.B. Moseley, Department of Molecular & Cellular Biochemistry, U of Kentucky

Abstract: Many human diseases involve metabolic reprogramming that disturbs normal physiology and causes serious tissue dysfunction. Advances in analytical technologies, especially mass spectroscopy (MS) and nuclear magnetic resonance (NMR), have made metabolic analysis of human diseases a reality. Stable isotope tracing is a powerful technique that enables the tracing of individual atoms through metabolic pathways. Stable isotope-resolved metabolomics (SIRM) uses advanced MS and NMR instrumentation to analyze the fate of stable isotopes traced from enriched precursors to metabolites, providing richer metabolomics datasets for metabolic flux analysis. Both quantitative analysis as well as complex modeling are required to generate biologically meaningful interpretation of the complex isotopologue profiles of large composite metabolites. Here, we have developed a new moiety modeling framework for deconvoluting MS isotopologue profiles for both single and multiple-labeled SIRM MS datasets. This moiety modeling framework successfully integrates model representation, model optimization, and model selection together, not only solving the non-linear deconvolution problem, but also selecting the optimal model describing the relative fluxes of specific metabolite from a set of plausible models. By testing the moiety modeling framework on the timecourses of 13C isotopologue data for UDP-N-acetyl-D-glucosamine (UDP-GlcNAc), we were able to confirm its robust performance in isotopologue deconvolution and moiety model selection. Also, we found that different types of noise may exist in the datasets, complicating the model selection process. Over optimization of the non-linear inverse problem can hinder model selection due to the noise in the dataset, and combination of datasets can help prevent these effects of overfitting.

Supported by: NSF: 1419282 Moseley(PI) NIH: TR001998-01 Kern(PI)

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Poster Presentation 171

Abstract Title:	**Analyzing Temporal Omics Data using Hidden Markov Model**
Author(s):	Ayesha S Dina, Institute for Biomedical Informatics, University of Kentucky Donghee Hoh, Department of Energy Plant Research Lab, Michigan State University David M Kramer, Department of Energy Plant Research Lab, Michigan State University Jin Chen, Institute for Biomedical Informatics, University of Kentucky

Abstract: The cowpea, an annual herbaceous legume, is an important crop in the semi-arid regions across Africa. It is critical to identify quantitative trait loci (QTLs) for improving the robustness and efficiency of photosynthesis of cowpea, leading to the increased productivity. Improving the productivity and robustness of plant photosynthesis requires high-throughput phenotyping under environmental conditions that are relevant to the field. Three key photosynthetic parameters of 79 cowpea genotypes were measured periodically with the changes of temperature and light intensity in three days. Since the photosynthetic phenomics data are time and condition dependent, it is difficult to use them directly to identify QTLs for high yield and resistance to cold. We present a new probabilistic model to estimate the secondary phenotypes that describe how likely a plant responses to the change of environments. To do so, we adopt the Hidden Markov Model (HMM) to compute all of the transition probabilities between the stressed status and unstressed status. Our model has three steps. First, we identify plants with significant coherent phenotype patterns on specified continuous time periods. Second, for any given plant, we use bagging to prepare its training data and train a HMM model. Third, the transition probabilities of all genotypes learned in the previous step is used to identify the important QTLs. The experimental results on synthetic data show that our model is more accurate than the traditional probabilistic models. Applying our method on the cowpea phenomics data, important QTLs at chromosome 9 and 11 have been revealed.

Supported by: NSF ABI Innovation: A New Framework to Analyze Plant Energy-related Phenomics Data

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Abstracts

Poster Presentation 172

Abstract Title:	**Implementing Agglomerative Hierarchical Cluster Analysis for Fluid Biomarkers in Dementia Research**
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Abstract: Agglomerative hierarchical cluster analysis (HCA) is a commonly used unsupervised machine learning approach to find natural clusters of patients within a designated cohort. HCA is achieved by calculating a dissimilarity matrix between all points followed by clustering similar points together until eventually all points are grouped within the same cluster. Unfortunately, there is not a one-size-fits-all approach for this technique and key decisions must be made in order to best analyze the dataset at hand. Our goal in this study was to apply HCA methods to biofluid biomarker datasets to determine the optimal analytic procedure and to identify lead biomarker candidates for further clinical application. In this project we analyzed how different distance metrics, linkage types, and clustering techniques affect the produced HCA outputs. We focus on use of the Minkowski distance metric versus the traditional Euclidean distance metric using varied p parameters in calculating the dissimilarity matrix between points and their effect on the adjusted rand index in different distributions of simulated data. Our data suggest that on biofluid biomarker datasets both types of HCA are comparable and produce distinct profiles of disease within a population of patients with mild cognitive impairment due to cerebrovascular disease.

Supported by:	NIA award: 1UH2NS100606-01 and the National Center for Research Resources and the National Center for Advancing Translational Sciences, National Institutes of Health, through Grant UL1TR001998. The content is solely the responsibility of the authors and d

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Poster Presentation 173

Abstract Title:	**Information Technology and the U.S. Healthcare System: An Economic Perspective**
Author(s):	M.J. Russell, Department of Communication, U of Kentucky S. Kim, Division of Bioinformatics, U of Kentucky

Abstract: This literature review outlines the economic factors contributing to the high expenses and lack of quality inherent in each of the systems that comprise the U.S. healthcare industry: hospitals, Medicare and Medicaid, private health insurance, medications, and malpractice. As a unique nation with a unique health care system, it is imperative that we find a solution for these dual issues appropriate to our history and culture. Information technology provides tools that allow us one possible avenue to do so. The topic of this paper addresses an understudied and essential aspect of healthcare. Despite the growing body of literature on the benefits and barriers to the implementation and usage of health information technologies, studies often fail to consider healthcare as a complex system, instead focusing on individual component systems. After reviewing literature from the turn of the century to the present day, this paper argues that thoughtful implementation of health information technology can improve health care and stem rising costs by facilitating movement from a fee-for-services structure to a value-based reimbursement system, thereby enabling systemic change. Such change is not itself without barriers which are discussed with suggested directions for future research. Ultimately, this paper aims to shed new light on the state of modern healthcare and contribute to the exploration of new paths for improvement using a more comprehensive approach.

Supported by: N/A

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Poster Presentation 174

Abstract Title:	**Automated High-Content Analysis of Skeletal Muscle Immunohistology**
Author(s):	Y. Wen, MD/PhD Program, U of Kentucky K. Murach, College of Health Sciences, U of Kentucky I. Vechetti, Department of Physiology, U of Kentucky C. Vickery, Department of Physiology, U of Kentucky C. Peterson, College of Health Sciences, U of Kentucky J. McCarthy, Department of Physiology, U of Kentucky K. Campbell, Department of Physiology, U of Kentucky

Abstract: High volume analysis of skeletal muscle histological cross sections is often necessary for studying muscles 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 the 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.

Supported by: NIH award: AR061939

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Poster Presentation 175

Abstract Title:	**Relationship between Nutritional Support and Muscle Health in Survivors of Critical Illness**
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Abstract: Research Question: What is the relationship between nutritional support in the intensive care unit (ICU) and muscle health in patients surviving critical illness? Introduction/Research Hypothesis: In clinical practice, there is heterogeneity in the approach to nutritional support for patients with critical illness. Moreover, recent randomized control trials, fail to demonstrate benefit in providing early nutrition to these patients. Malnutrition has a negative impact on muscle health and physical functioning. We hypothesize that a lack of early nutritional support in critically ill patients will be associated with greater muscle dysfunction. Number of Subjects: 34 adult patients, median age of 53 (range 19-83) admitted to the medicine ICU were previously enrolled in a prospective study to assess muscle health. Proposed Methods: This project is a secondary retrospective analysis of a previously completed prospective muscle observational study. Participants previously performed a series of muscle assessments during admission to the ICU, hospital, and 1-month following hospital discharge. We are currently working with data analyst at CHSR to assess nutritional data such as delivery method, rate, and type as well as critical illness data e.g. ventilator days, ICU length of stay, and SOFA scores. Planned Statistical Analysis: Data will be assessed with descriptive statistics and histograms. To determine the relationship between nutrition and muscle, appropriate correlative test will be performed. A multi-variate logistic regression will be utilized to determine if the lack of nutrition in combination with clinical and demographic variables predicts muscle dysfunction at hospital discharge. Expected Results: We expect to demonstrate that patients who do not receive nutritional support early in the ICU will have a higher likelihood of developing muscle dysfunction. Career Development: As an undergraduate student planning for a career in medicine, the proposed provides many opportunities for learning and growth.

Supported by: NA

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Poster Presentation 176

Abstract Title:	**The Effects of Oxidative Stress on Lipid Droplet Formation in APOE Expressing Astrocytes**
Author(s):	J. C. Kluemper, College of Medicine Department of Physiology, U of Kentucky B. C. Farmer, College of Medicine Department of Physiology, MD/PhD Program, U of Kentucky L. A. Johnson, College of Medicine Department of Physiology, Sanders Brown Center on Aging, U of Kentucky

Abstract: The original report on Alzheimer's Disease (AD) in 1906 described a phenotype of glial lipid droplet (LD) formation. However, unlike plaques and tangles, this observation has received little attention, and the potential role LDs play in the development of AD remains undetermined. Apolipoprotein E (apoE) is involved in shuttling lipids in the central nervous system, and the e4 allele of APOE is the strongest genetic risk factor in the development of AD. Humans express three main isoforms of apoE: E2, E3, and E4. E4 has been linked to a 15 fold increase in developing AD. Our recent studies have found that E4 astrocytes display increased LD content compared to E3 astrocytes. Oxidative stress has been linked to LD accumulation in glia in Drosophila models. The current study explores the role of oxidative stress in LD formation in E3 and E4 astrocytes. We induced oxidative stress by incubating astrocytes with varying concentrations of rotenone or hydrogen peroxide. Lipid droplets are concurrently stained with the neutral lipid stain BODIPY and analyzed using fluorescent-based methods. Glutathione is a cellular defense against oxidative stress. Thus, APOE effects on expression of glutathione in astrocytes is also explored. Finally, sectioning and imaging of human apoE expressing mouse brains is conducted to determine in vivo concentrations of LDs between E3 and E4 mice. We hope these findings will provide better understanding of the cause of LD formation in astrocytes, the role of APOE in this process, and eventually serve as the basis for future AD treatments.

Supported by: NIH award: R01 AG060056 01 AHA award: 19PRE34380094

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Poster Presentation 177

Abstract Title:	**Developing Zebrafish Models to Study the Link Between SoxC Transcription Factors and CHARGE Syndrome**
Author(s):	L.A. Krueger, Department of Biology, U of Kentucky A.C. Morris, Department of Biology, U of Kentucky

Abstract: The molecular mechanisms underlying the ocular birth defects observed in CHARGE patients are poorly understood. Our laboratory studies the development of the vertebrate visual system using zebrafish. Previous work from our lab has shown that knockdown of Sox11, a member of the SoxC family of transcription factors, in zebrafish results in microphthalmia, coloboma, brain, trunk, and heart defects, all phenotypes observed in CHARGE syndrome. Furthermore, a duplication of Sox11 has been identified in a patient clinically diagnosed with CHARGE syndrome, and CHD7 has been shown to directly interact with Sox11 and Sox4 in neural stem cells. Taken together, these data strongly suggest that loss of SoxC expression contributes to the ocular and other phenotypes observed in Chd7-associated CHARGE syndrome. In this study, we begin to further investigate the role that Sox11 plays in the phenotypes seen in CHARGE syndrome by generating Sox11-mutant zebrafish using the CRISPR-Cas system. The resulting Sox11 mutant lines will be characterized for phenotypes related to CHARGE and will be compared to an established CHD7 mutant line. These experiments will provide a better understanding of the potential role of Sox11 in the pathogenesis of CHARGE.

Supported by: Funding from CHARGE Syndrome Foundation NIH Award R01 TL1 Trainee Grant

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Poster Presentation 178

Abstract Title:	**Neuro-Avatar: A Reverse Translational Model of an Ongoing Cell Therapy Clinical Trial for Parkinson's Disease**
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Abstract: Currently two clinical trials (NCT01833364 and NCT02369003) are underway which feature the implantation of autologous peripheral nerve grafts to the brain (targeted to the Substantia Nigra, Nucleus Basalis of Meynert, or Putamen) 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 cutaneous sensory nerve located in the lateral ankle, of patients undergoing DBS surgery. The nerve receives a conditioning injury 14 days before grafting, and samples are collected from the pre-conditioned and post-conditioned nerve. RNA sequencing of these nerve samples shows transcriptome changes consistent with the expected pro-regenerative changes of transdifferentiated repair phenotype Schwann cells. However, the neurobiology of the graft within the brain, the regenerative activity of the pre vs post-lesioned nerve, and the survival of grafted tissue have not been examined. In order to address these questions, this study aimed to develop an animal model of the grafting procedure using the same human tissue grafted into patients with Parkinson's disease. Athymic nude (Hsd:RH-Foxn1rnu) rats were stereotaxically implanted with segments of human peripheral nerve (pre-conditioned or post-conditioned) into the dorsal striatum. Each animal received a unilateral graft with a contralateral sham insertion. Two weeks or six months post-implant the brains of these animals were processed for histopathological analyses. Assessment of graft cell survival, graft morphology, and host tissue response will be reported. In summary, this study uses clinical trial samples to answer basic science questions that will guide future clinical trial design.

Supported by: Grant/Other Support: Gifts to the Brain Restoration Center Grant/Other Support: Tom Dupree for Parkinson's Disease Research Grant/Other Support: University of Kentucky start-up funds Grant/Other Support: National Center for Advancing Translational Scie

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Poster Presentation 179

Abstract Title:	**"See Blue. See Through." CLARITY for 3-D In Vivo Imaging of the Neurovascular Unit**
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Abstract: CLARITY is a newly developed tissue clearing method used for the transformation of biological tissue into a tissue-hydrogel hybrid, enabling highly detailed images of the brain's cellular structure. Historically, imaging studies have been limited to small regions of the brain or do not allow for staining of relevant proteins or genes. CLARITY uses an acrylamide hydrogel to maintain the structural organization of proteins and nucleic acids and surfactant-assisted delipidation to render the tissue permeable to immunostaining and suitable for detailed microscopic analysis. For our studies, we used the X-CLARITY™ System from Logos Biosystems. Male CD-1 mice were anesthetized; the thorax was opened; and an infusion needle was placed into the left cardiac ventricle to perfuse the brain with PBS and paraformaldehyde. Whole brain was collected and fixed in paraformaldehyde. After washing with PBS, brains were either processed as a whole or sliced into sections. Brain tissue was placed in hydrogel solution and hybridized utilizing the X-CLARITY™ Polymerization System. Once hybridized, lipids from the tissue were removed through electrophoresis with ionic detergents using the X-CLARITY™ Tissue Clearing System. After clearing, the neurovasculature was stained with collagen IV primary antibody followed by incubation with Cy3-conjugated secondary antibody. In addition, we cleared the brains of mice with YFP-labeled neurons. Cleared brain tissue was imaged using a Nikon A1R inverted confocal microscope. We are currently using CLARITY with single- and two-photon microscopy imaging to examine the spatial relationship between cells of the neurovascular unit in animal models of neurodegenerative and neurological disorders.

Supported by:	This research was funded by a UK Equipment Competition award (to BB) with matching funds from the Department of Pharmaceutical Sciences, the Sanders-Brown Center on Aging, the Spinal Cord and Brain Injury Research Center, and the Epilepsy Center. Addition

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Poster Presentation 180

Abstract Title:	**Phenotype of MitoNEET Null Mice, a Known Regulator of Mitochondrial Function and Target for Neuroprotection**
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Abstract: The functional and cognitive deficits that manifest from traumatic brain injury (TBI) are the results of complex mechanisms. After primary injury to the brain, a secondary injury cascade occurs which encompasses increases in oxidative stress, changes in Ca2+ homeostasis, and mitochondrial dysfunction. mitoNEET, an outer mitochondrial membrane protein, has been shown to be critical to mitochondrial function after TBI and may be a promising therapeutic target. Previous studies show that pioglitazone, an FDA-approved drug used to treat diabetes, interacts with mitoNEET to impact neuroprotection after TBI and spinal cord injury, independent of peroxisome proliferator activated receptor (PPARγ). Furthermore, NL-1, a pioglitazone derivative lacking PPARγ binding, increases cortical tissue sparing following TBI and improves cognitive outcome, an effect lost in mitoNEET knock-out (KO) mice. To develop a better understanding of baseline, phenotypic differences between mitoNEET KO mice and wildtype mice, we compared body composition and cognitive function. We hypothesized that mitoNEET KO mice would show cognitive and mitochondrial deficits compared to wildtype littermates that will be exacerbated with age. Body composition analysis, using magnetic resonance imaging, revealed mitoNEET KO mice had reduced fat mass compared to heterozygotes and WT littermates, where as the lean mass composition and total body weight remained unchanged. Novel object recognition indicated a decrease in cognitive function in mitoNEET KO mice compared to heterozygous and WT littermates. Results show unique mitochondrial-mediated phenotyping of mitoNEET KO mice, supporting the role of mitoNEET as a central modulator of mitochondrial bioenergetics and a novel target for intervention following CNS injury.

Supported by: Kentucky Spinal Cord and Head Injury Research Trust #15-14A National Center for Research Resources and the National Center for Advancing Translational Sciences, National Institutes of Health, through Grant UL1TR000117 Merit Review Award # I01BX003405 t

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Poster Presentation 181

Abstract Title:	**Experimental Internal Carotid Artery Stenosis Models Pathogenic Features of Moyamoya Syndrome**
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Abstract: Moyamoya is an arteriopathy defined by the progressive stenosis of the intracranial internal carotid arteries accompanied by the formation of abnormal vascular networks. To address the paucity of research on the adult-onset Moyamoya Syndrome, which completely lacks any animal model for evaluation, our lab created a novel surgical technique, termed internal carotid artery stenosis (ICAS), that attempts to model the cerebrovascular changes seen in the human Moyamoya Syndrome. We hypothesized that the ICAS model would mimic the key proposed pathogenic features of Moyamoya Syndrome; namely, intimal hyperplasia of the major vessels of the cerebrovasculature leading to vessel stenosis and the formation of compensatory collateral arteries. ICAS (n=9) and sham (n=6) surgeries were performed in a randomized fashion on male C57Bl/6 mice (age = 16 weeks). RNA was collected 28-days post-surgery. Expression of previously identified genes associated with human Moyamoya Syndrome (VEGF, SDF-1a, MMP-9, bFGF, VCAM-1, and MCP-1) was quantified by qPCR. PRISM software was used for data analysis. ICAS increases genetic expression of VEGF in the whole brain (fold change=0.60, p=0.050) and SDF-1a in the striatum (fold change=0.59, p=0.016), and decreases genetic expression of MMP-9 in the ipsilateral cortex (fold change=0.39, p=0.044). The upregulation of VEGF and SDF-1avis indicative of hypoxia-induced angiogenesis and ischemia-induced inflammation, and the downregulation of MMP-9 may indicate decreased extracellular remodeling in the cortex. Taken together with the previous discovery that ICAS induces stenosis of the major vessels of the cerebrovasculature, these findings support ICAS as a relevant model of the proposed pathology of Moyamoya Syndrome.

Supported by: NIH 1 R01 NS089515-01 awarded to GJB and a PSMRF grant from UK Center for Clinical and Translational Science awarded to APKW

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Poster Presentation 182

Abstract Title:	**Network-Dependent Effects of Alzheimer's and Cerebrovascular Pathology on White Matter Decline**
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Abstract: White matter (WM) is affected by both Alzheimer's disease (AD) and cerebrovascular disease (CVD) pathology. Recent work has suggested that CVD and AD pathology independently contribute to white matter in spatially distinct brain regions cross-sectionally. However, it is unknown how AD and CVD pathology differentially impact longitudinal change in WM connections within large-scale brain networks underlying human cognition. Eighty-three non-demented individuals were recruited to investigate how AD and CVD pathology predicted change in baseline and 1-year follow-up diffusion tensor imaging (DTI) data within major brain networks: the default mode network (DMN), executive control network (ECN), dorsal attention network (DAN), and the hippocampal network (fornix). Cerebrospinal fluid (CSF) β-amyloid (Aβ) concentration was used to measure AD pathology and hypertension (HTN) diagnosis was used as a marker of CVD risk. Multiple linear regression analyses that included Aβ and HTN as simultaneous predictors of WM decline in each network indicated that Aβ alone predicted decline in fornix WM, HTN alone predicted decline in ECN WM, both Aβ and HTN predicted decline in DMN WM, and neither Aβ nor HTN predicted decline in DAN WM. These results indicate that AD and CVD pathology differentially affect WM connections in a way that mirrors their predominant cognitive changes. AD pathology preferentially affects fornix and DMN WM, which are both involved in memory. In contrast CVD pathology affects ECN and DMN WM, which are both involved in executive function. Therefore, breakdown in WM connections may be an important mechanism by which these pathologies influences cognition.

Supported by: This study was supported by the National Institute on Aging and National Center for Advancing Translational Sciences of the National Institutes of Health (grant numbers: R01AG033036, R01AG055449, P30AG028383, P01AG030128, TL1TR001997, NR014189, R01AG04241

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Poster Presentation 183

Abstract Title:	**Plasma and CSF IL-6 Concentration Profiles Are Different in Aneurysmal Subarachnoid Hemorrhage Patients With and Without Cerebral Vasospasm**
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Abstract: Introduction: Recovery from aneurysmal subarachnoid hemorrhage (aSAH) is frequently complicated by cerebral vasospasm (CV). Although the cause of CV is unknown, inflammation may play a role. We designed a small pilot study to evaluate IL-6 concentration temporal profiles in plasma and CSF in aSAH patients. Methods: Following IRB approval, we analyzed plasma and CSF samples from 5 subjects to determine IL-6 concentrations at 4 time points. All samples were obtained, processed, stored, and analyzed according to standard procedures. Results: Prospectively collected plasma and CSF samples were analyzed for all selected patients. In plasma, the mean IL-6 concentration decreased over the first 5 days in both aSAH cohorts but increased on PBD7 and PBD10 in aSAH patients with CV but not in aSAH patients without CV. In CSF, the mean IL-6 concentration increased over the first 7 days in both aSAH cohorts; however, the mean IL-6 concentration decreased on PBD10 in aSAH patients without CV, whereas, in aSAH patients with CV, the mean IL-6 concentration was still elevated on PBD10. Discussion: This pilot study demonstrated differences in IL-6 concentration profiles in both plasma and CSF in aSAH patients with and without CV. Plasma profile differences may be attributed to a delayed burst of inflammation in aSAH patients on or about PBD5 that is protective against CV through some undefined mechanism and should be further studied. In CSF, this delayed burst of inflammation was not seen; however, secondary brain injury from CV may confound our analysis.

Supported by:	The project described was supported by the National Center for Research Resources and the National Center for Advancing Translational Sciences, National Institutes of Health, through Grant UL1TR001998. The content is solely the responsibility of the autho

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Poster Presentation 184

Abstract Title:	**V2a Neurons are Critical to Restore Breathing Following Spinal Cord Injury**
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Abstract: Respiratory failure is the leading cause of death in spinal cord injury patients. We hypothesize that ipsilaterally projecting glutamatergic V2a neurons in the brainstem and ventral spinal cord contribute to recovery of diaphragm function following injury by activating latent respiratory pathways that cross below the site of injury (termed the crossed phrenic phenomenon). To test our hypothesis, we used a transgenic mouse line that expresses DREADDs in V2a neurons in order to increase their excitability via activation of Gq signaling pathways following injection of the drug-like molecule clozapine-N-oxide (CNO). We performed a high level C2 hemisection (C2Hx) spinal cord injury to paralyze the diaphragm ipsilateral to injury. Electromyography (EMG) recordings of the ipsilateral diaphragm confirmed paralysis. However, increasing V2a neuron excitability by intraperitoneal injection of CNO restored rhythmic burst activity to the paralyzed diaphragm within hours or days after injury. Moreover, the contralateral (uninjured side) diaphragm is able to maintain regular rhythmic breathing when V2a neuron activity is altered. Finally, we show that silencing V2a neurons prevents induction of the crossed phrenic phenomenon to restore breathing two weeks following spinal cord injury. These results indicate that targeting Gq signaling pathways in V2a neurons has the potential to restore function to respiratory muscles following spinal cord injury without significant adverse side effects on respiratory rhythm generation.

Supported by:	UK Center for Clinical and Translational Science and Training Pilot Grant (SAC and WA) (Grant UL1TR001998) Albert J. Ryan Fellowship Division of Neurosurgery, Cincinnati Children's Hospital Medical Center

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Poster Presentation 185

Abstract Title:	**The Effect of Sex, Sport Participation and Concussion History on Gaze Stabilization in Division I Collegiate Athletes**
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Abstract: Context: The Gaze Stabilization Test (GST) quantifies rotational head velocity while an individual maintains visual acuity through the vestibular-ocular reflex (VOR). The VOR is often affected following concussion, suggesting the GST may be a valuable assessment for concussion management. Objective: Create normative GST values in collegiate athletes and explore the effect of sport, sex, and concussion history on performance. We hypothesized that differences in GST performance would be identified based on sex, sport, and concussion history. Participants: A total of 121 Division-I football, soccer and cheer athletes (70 males, 51 females), participated. Methods: The GST was completed in the yaw plane (leftward and rightward). Gaze stabilization was identified as the fastest rotational head velocity with accurate visual acuity in each direction. Normative GST values were expressed as median and interquartile range. Kruskal-Wallis tests with post-hoc Mann-Whitney U tests examined differences between sports. Mann-Whitney U tests compared GST performance based on sex and concussion history. Alpha was set a-priori at 0.05. Results: The median GST values were 145 and 150 deg/sec for GST in the leftward and rightward direction. A main effect for sport was detected for rightward gaze stabilization ($p=0.017$). Cheer (173.82±43.88 deg/s) demonstrated faster rotational velocities than soccer (147.89±25.33 deg/s; $p=0.004$). No significant differences were identified in any GST measures based on sex ($p\geq0.24$) or concussion history ($p\geq0.97$). Conclusions: Normative estimates for GST may enhance concussion evaluation for collegiate athletes with suspected VOR involvement. GST performance is influenced by sport which may reflect VOR adaptations based on sport-specific demands.

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Poster Presentation 186

Abstract Title:	**Deficits in Postural Control and Neurocognitive Performance Following Return to Participation from Sport-Related Concussion: A Preliminary Study**
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Abstract: Context: Sport-related concussion (SRC) increases the risk of musculoskeletal injury for at least 12 months after return to athletic participation. Residual deficiencies in neurocognitive performance or postural control following SRC may contribute to this relationship. Objective: Determine if collegiate athletes with a recent SRC have poorer neurocognitive performance and postural control compared to healthy control athletes. Participants: Fourteen Division-I collegiate athletes (9 male, 5 female) who recently returned to unrestricted participation following SRC were compared to fourteen healthy Division-I athletes matched by sport, sex, and age. Methods: Neurocognitive function was assessed using three validated tablet-based tests that examined executive function, processing speed, and episodic memory. Demographically-corrected (age, sex, education, race, ethnicity) standard scores (T-score) were calculated for all neurocognitive tests. Postural control was assessed with a series of double-limb balance tests on firm and foam surfaces while performing a side-to-side headshake with eyes closed or standing with hands clasped, elbows extended, and thumbs up while rotating their trunk side-to-side visually focusing on their thumbs. Sway velocity (°/s) and performance errors were examined for analysis. Independent t-tests with effect sizes (ES) were used for group comparisons with an alpha level of 0.10. Results: The SRC group exhibited poorer executive function (SRC:45.75±7.15, Control:52.83±11.00, ES=0.78; p=0.02) and greater sway velocity (SRC:1.30±0.49°/s, Control:1.07±0.32°/s, ES=0.56; p=0.06) and balance errors (SRC:4.23±3.72, Control:1.84±2.41, ES=0.78; p=0.10) on the foam surface with a headshake. Conclusions: Collegiate athletes with a recent SRC may experience poorer executive function and postural control despite passing standard clinical exams and returning to unrestricted participation.

Supported by:	The project described is supported by the National Center for Research Resources and the National Center for Advancing Translational Sciences, National Institutes of Health, through Grant UL1TR001998. The content is solely the responsibility of the author

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Poster Presentation 187

Abstract Title:	**Improvements in gait deficits with peripheral nerve grafts implanted into the substantia nigra in patients with Parkinson's disease during deep brain stimulation surgery: 2-year follow-up study**
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Abstract: OBJECTIVE: Our goal was to determine the effects of deep brain stimulation (DBS) plus on gait parameters and to see if DBS plus has long-term (two-year follow-up) benefits on disease severity and mobility in patients with Parkinson's disease (PD). METHODS: We evaluated the effects of DBS-plus on gait and disease severity at the baseline and at the 2-year follow-up after surgery for 8 participants. Various gait parameters (gait velocity, step length, cadence, single support and double support) were measured with Gaitrite along with UPDRS and H&Y scores, before and after DBS plus, during the OFF (medication OFF/stimulation OFF) stage. RESULTS: More severely affected individuals with Hoehn and Yahr (H&Y) of >/=3 (N=5) showed improvements in both spatial (step length, gait velocity) and temporal measures (cadence) of gait, whereas less severely affected individuals (H&Y) of <3 (N=3) did not show these improvements. Changes in gait parameters persisted even after 2 years of DBS-plus implantation. More severely affected compared to less affected group also showed reduction in H&Y and UPDSR (Part III) scores. Unlike previous studies, changes in temporal (cadence) measures were observed for gait over the two years. CONCLUSIONS: With the preliminary data, we observed improvement in gait and disease severity parameters, especially for individuals who were most severely affected in the group. Interestingly, the observed changes persisted two years post-surgery. DBS Plus might prove to be an effective intervention in long-term changes of disease and gait symptoms in PD patients.

Supported by:	Supported by gifts from the Brain Restoration Center, Ann Hanley Parkinson's Research Fund, and the Werner F. Schmitt Endowment for Neurobehavior and Aging, and by the National Center for Advancing Translational Sciences through National Institutes of Hea

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Poster Presentation 188

Abstract Title:	**Regional Variations in Aneurysm Morphology in Appalachia**
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Abstract: Background and Purpose: Intracranial aneurysms (IA) are not an uncommon finding in the general population, and subarachnoid hemorrhage is a feared consequence of IA rupture. The morphology of aneurysms contributes to the risk of treatment and complexity of those treatments. Our aim was to evaluate morphological characteristics of aneurysms and risk factors in a cohort of Appalachian patients to provide insight into the regional variation in aneurysm complexity. Methods: A retrospective chart review was performed of patients undergoing 3D angiograms for IAs at a Comprehensive Stroke Center serving Appalachian communities between 01/01/2012 and 01/01/2018. Data collected included patient demographic information, comorbidities and aneurysm characteristics evaluated by 3D angiogram. All statistical analyses were completed in SAS 9.4. Results: The study included 276 patients (203 female and 73 male) with 404 IAs. Of the 276 patients, 113 had ruptured IAs. Irregular shape was determined by smallest to largest dome diameter ratio less than 0.8, presence of secondary aneurysmal sacs, branch incorporation or multi-lobulated status. At least one irregular aneurysm was present in 85.7% of patients. Notably, the cohort of patients native to Appalachian counties had a statistically significant increased frequency of family history of IA ($p < 0.05$) and posterior circulation aneurysms ($p < 0.02$). On univariate analysis, secondary aneurysmal sac presence, largest dome diameter to largest neck ratio and anterior communicating and posterior communicating artery location posed increased risk of rupture. Conclusion: Patients native to Appalachian counties did not have an elevated risk of rupture relative to patients of non-Appalachian counties but did have different aneurysm characteristics and genetic risk factors. Other findings further highlight the importance of known morphological risk factors. Importantly, our findings show unique characteristics about IAs in the Appalachian population that could enhance the quality of care provided to this population.

Supported by: Professional Student Mentored Research Fellowship Program

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Poster Presentation 189

Abstract Title:	**A Brain-Computer Interface for Motor Rehabilitation after Spinal Cord Injury**
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Abstract: Development of increasingly efficient motor rehabilitative techniques for spinal cord injury (SCI) patients would add to the ease and quality of motor rehabilitation available. Experiments pairing transcranial magnetic stimulation (TMS) with peripheral nerve stimulation (PNS) have shown a timing-dependent effect on motor evoked potential (MEP) amplitude. This suggests that PNS applied in a closed-loop manner could improve motor function through positive reinforcement. A brain-computer interface (BCI) was developed to apply afferent PNS in response to electroencephalogram (EEG) features related to motor intent. In this study, twelve subjects with cervical spinal cord injuries participated in 4 weeks of BCI-driven PNS while engaged in an interactive cue-driven hand grip task. Nine subjects repeated the intervention and received PNS applied at random. Maximum voluntary contraction force (MVC) and TMS-evoked motor map volume (MMV) were used as outcome measures. Outcomes were analyzed separately for the less affected hand (LA) and more affected hand (MA). Subjects that received PNS closely timed with movement (n=10) had mean MMV outcome ratios (post/pre) of 1.6 ± 0.2 (LA) and 0.9 ± 0.1 (MA) and mean MVC outcome ratios of 1.7 ± 0.3 (LA) and 2.0 ± 0.4 (MA). For matched interventions (n=9), there was a significant difference in the MVC outcome ratios between groups for both hands (LA: p=0.039, MA: p=0.049). While these results come from a relatively small cohort, they suggest that BCI-driven closed-loop protocols with fine control of PNS timing could be a valuable adjunct to physiotherapy in patients with SCI.

Supported by: This work was supported in part by National Institute of Child Health and Human Development grant 1R21HD079747 and National Science Foundation grant 1539068.

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Poster Presentation 190

Abstract Title:	**Mice Exposed to Early Life Stress Display Sex-Specific Upregulation of Leptin Gene Expression in Adipose Tissue**
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Abstract: Early life stress (ELS) is an independent risk factor for increased BMI and cardio-metabolic disease risk later in life. We have previously shown that a mouse model of ELS, Maternal Separation and Early Weaning (MSEW), increases adiposity in weanlings and exacerbates high fat diet (HFD)-induced fat expansion only in adult female MSEW mice. Therefore, the aim of this study was to investigate the sex-specific effects of MSEW on fat-derived hormones implicated on body weight homeostasis. After 12 weeks of HFD, female MSEW mice showed increased BW, fat mass and leptin mRNA expression in gonadal white adipose tissue (gWAT), but not subcutaneous WAT, compared with controls. Males, however, only displayed increases in adiponectin mRNA expression with no effect due to MSEW. To begin to address the mechanism by which MSEW increases leptin expression in female mice, we analyzed 16 methylation sites of the leptin promoter in gWAT from mice fed a HFD. The methylation landscape in the leptin promoter was different between male and female mice. However, we found that CpG sites 3 and 15 were significantly hypomethylated only in fat from female MSEW mice comparted to controls ($p<0.05$). Both sites in the leptin promoter are strong areas for transcription factor binding. In addition, DNMT3A was upregulated in MSEW mice ($p<0.05$). Taken together, our current working hypothesis is focused on elucidating whether exposure to MSEW may promote the binding of specific transcription factors that upregulate leptin gene expression in a depot and sex-specific manner.

Supported by: R01 HL135158

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Poster Presentation 191

Abstract Title:	**Establishing the Relationship between Aging and Gamma Delta T Cells in Human Visceral Adipose Tissue**
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Abstract: Chronic inflammation in adipose tissue is strongly linked to the development of cardiometabolic disorders which occur at high frequency in old age. Although most research related to chronic inflammation in adipose tissue focuses on the obese state, recent evidence suggests that age-associated adipose tissue inflammation is governed by different mechanisms from those attributed to obesity. Identification of age-specific mechanisms that promote adipose tissue inflammation is a critical next step in developing therapies to reduce the burden of cardiometabolic disorders in the growing aging population. Previously, our lab demonstrated that an expanded population of γδ-T cells in visceral adipose tissue of aged mice contributes to age-related chronic inflammation. The objective of this study was to validate that human adipose tissue undergoes an age-associated expansion of γδ-T cells like that observed in mice. Using flow cytometry, we found that the γδ-T cell population (expressed as a percentage of total leukocytes in the sample) in non-obese (BMI <30) individuals significantly increased with aging (R2=0.5068). In contrast, obese (BMI>30) individuals showed no significant correlation between age and γδ-T cell population (R2=0.0351). Most of the γδ-T cells had an effector memory phenotype (~85-88%), but the proportion of those effector memory γδ-T cells expressing CD69 activation marker increased by age in both BMI groups, suggesting an age-dependent increase in activation and tissue-resident status. Overall, our results suggest that γδ-T cells accumulate in visceral adipose tissue of both mice and humans and may have an important role in the development of chronic inflammation underlying multiple age-associated diseases.

Supported by: NIH award: R01AG039732 and pilot funding from UK Center for Clinical and Translational Science

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Center for Clinical and Translational Science

Abstracts

Poster Presentation 192

Abstract Title:	**A Comparison of Bioavailable Vitamin D and 25(OH)D to Intramyocellular Lipid and Skeletal Muscle Hemodynamics**
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Abstract: Introduction: 25(OH)D is the primary and most commonly used measure to assess vitamin D status; however, some researchers suggest that bioavailable (25(OH)DBIO) better represents vitamin D physiology. Recent publications have suggested that low 25(OH)D status is linked to impaired muscle metabolic function. We have shown that 25(OH)D is a predictor of intramyocellular lipid (IMCL) and may increase mitochondrial lipid availability. This study examined the correlation of both biomarkers with local muscle lipid and hemodynamics in aged, active adults. Objective: Determine if 25(OH)DBIO is more strongly associated with IMCL and skeletal muscle hemodynamics than 25(OH)D in healthy, aged individuals. Methods: Healthy, aged individuals received 13 weeks of vitamin D supplementation in a double-blinded, placebo-controlled manner. Serum 25(OH)D was measured and 25(OH)DBIO calculated using a previously developed equation. Gastrocnemius IMCL was measured through magnetic resonance spectroscopy. Tissue-level VO2 was calculated using near-infrared spectroscopy/diffuse correlation spectroscopy. Statistical analyses were conducted using JMP 12. Results: Correlations of change in 25(OH)D were similar to those of 25(OH)DBIO for all comparisons. Correlation coefficients of 25(OH)DBIO were not substantially improved compared to those of 25(OH)D for IMCL ($p=0.150$, $r=0.237$; $p=0.007$, $r=0.415$, respectively), rVO2 ($p=0.809$, $r=0.042$; $p=0.813$, $r=0.040$, respectively), or any other factors. These results were independent of exercise, BMI, age, and sex ($p>0.05$). Conclusion: Our data show that 25(OH)DBIO and 25(OH)D are similarly associated with skeletal muscle outcomes. Because of the increased cost and burden associated with calculating 25(OH)DBIO, 25(OH)D may remain the most practical biomarker to assess when examining muscle health in aged, healthy adults.

Supported by: NIH award: R21AG046762-02

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Poster Presentation 193

Abstract Title:	**Chemerin is a Biomarker of Aging in Mice**
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Abstract: Chronological age is the time an organism has been alive, whereas biological age is how (un)healthy that organism is or how old it seems. Currently, research efforts are being devoted to developing biomarkers of aging which can accurately determine an organism's biological age and overall mortality risk. Chemerin is an adipokine secreted by white adipose tissue. Physiologically, chemerin is involved in adipogenesis and inflammation, and chemerin levels are elevated in patients with type 2 diabetes, obesity, and cardiovascular disease. Due to the tendency for adipose tissue to become fibrotic in later ages, the secretory phenotypes observed in senescent cells, and the observation that other cytokines are correlated with aging, we hypothesized that serum chemerin levels would increase with age in mice. We measured serum chemerin levels via enzyme linked immunosorbent assay (ELISA) in a longitudinal cohort of both male and female C57BL/6 mice. We discovered that serum chemerin levels significantly increased with age in both sexes; further, we found no correlation between chemerin and body fat mass or other adipokines such as leptin or adiponectin. Therefore, we propose that chemerin is a novel and independent biomarker of aging in mice. In the future, we will determine whether the chemerin levels we measured are correlated with survival and lifespan in the same mice. Moreover, we will examine serum chemerin levels in aging populations of nonhuman primates and humans from the CCTS biospecimens core. Further research will elucidate the role of chemerin in biological aging and could eventually establish chemerin as a clinical biomarker of life expectancy and biological age.

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Poster Presentation 194

Abstract Title:	**Mitochondrial changes synergize with long chain fatty acid derivatives to support Th17 inflammation in diabetes**
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Abstract: Mechanisms that regulate metabolites and downstream energy generation pathways are key determinants of T cell cytokine production, but the processes underlying the Th17 profile that predicts the metabolic status of people with obesity are untested. Th17 function requires fatty acid uptake, and our new data show that blockade of mitochondrial fatty-acid uptake catalyzing protein CPT1A with etomoxir inhibits Th17 profile production by cells from people with type 2 diabetes (T2D). A low CACT:CPT1A ratio in immune cells from T2D subjects indicates altered mitochondrial function and coincides with the preference of these cells to generate ATP through anaerobic glycolysis rather than fatty acid oxidation. However, glycolysis was not critical for the Th17 profile. Instead, □ oxidation blockade through CACT knockdown in T cells to mimic characteristics of T2D promotes cells from lean subjects to utilize 16C-fatty acylcarnitine to support a Th17 profile. 16C-fatty acyl-carnitine alone had no effect. These data show that long chain acylcarnitine combines with reduced □ oxidation to promote disease-predictive inflammation in human T2D. Because glycemic control is the goal of classical T2D interventions, the demonstration that glucose is not the dominant activator of Th17-mediated inflammation in T2D raises concerns that fatty acid metabolites will continue to drive systemic and/or tissue inflammation even after glycemic control is optimized. The newly appreciated disconnect between glucose as a fuel and T2D inflammation may also explain the modest impacts of anti-hyperglycemic drugs on T2D inflammation in T2D clinical trials, given that hyperglycemia and inflammation are only secondarily linked.

Supported by: R01DK108056, W911NF-09-0001, UL1TR001998, Boston University Flow Cytometry Core Facility, T32AI089673, T32AI08967, T32DK007201, University of Kentucky College of Medicine

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Poster Presentation 195

Abstract Title:	**Evaluating the Experiences of FCS Cooperative Extension Agents Use of Policy, System and Environmental Strategies to Reduce Obesity in Rural Counties**
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Abstract: High rates of obesity are seen across the country with rural areas disproportionately affected. Based on the socio-ecological model, policy, system, and environmental approaches targeted at the population level have the potential to create more sustainable health behavior change than individual level approaches. Historically, the Cooperative Extension Service (CES) has provided direct education related to healthy eating and active living in response to high obesity rates. Utilizing the resources and infrastructure of the CES, the Centers for Disease Control challenged CESs across the country to implement PSE strategies in counties with obesity rates greater than 40% through the CDC 1416 High Obesity Project. This qualitative study examined the experiences of Family and Consumer Science (FCS) Cooperative Extension Agents in conducting PSE strategies in addition to their direct education roles within their rural counties in an effort to reduce the high prevalence of obesity. Semi-structured, in-depth interviews with ten FCS Extension agents from Kentucky and Tennessee were conducted upon completion of the project and were analyzed thematically. These FCS agents encountered several barriers while implementing PSE strategies including inadequate training and poor communication regarding responsibilities and available resources. In addition, FCS agents found PSE work to be overwhelming and time consuming. Agents felt that support from project staff and their community partners allowed them to be successful. Findings from this study will be used to better prepare FCS agents in other rural counties across the country to conduct PSE work in an effort to reduce obesity prevalence in their communities.

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Poster Presentation 196

Abstract Title:	**Dry Needling Improves Static and Dynamic Balance in Individuals with Chronic Ankle Instability**
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Abstract: Individuals with chronic ankle instability (CAI) commonly exhibit balance deficits that are associated with dysfunction of the fibularis longus (FL) muscle. Dry needling (DN) is a treatment that targets muscular trigger points and is hypothesized to improve neurophysiological function of treated muscles. The ability of FL DN to improve dynamic and static balance in patients with CAI is unknown. Purpose: Examine the effect of FL DN on dynamic and static balance in individuals with CAI. Methods: Twenty-five adults with CAI (9 males, 16 females; 26±9.42 years; 173.12±9.85cm; 79.27±18kg) volunteered to participate. Participants completed the Star Excursion Balance Test (SEBT) and postural control measures before and immediately after a single DN treatment to the FL. The anterior, posterolateral, and posteromedial directions of the SEBT were tested in a random order and reach distances were normalized to a percent of leg length. A composite SEBT score was calculated by dividing the normalized, average scores in each direction by three. Postural control was assessed in single-limb stance on a forceplate through time to boundary (TTB) measurements and calculated in the mediolateral and anteroposterior directions under eyes open and eyes closed conditions. A single DN treatment was performed on the FL using a “pistoning” technique. Descriptive statistics (mean change ± SD), paired t-tests, and standardized response mean effect sizes were calculated to compare balance measures before and immediately after the FL DN intervention ($p \leq 0.05$). Results: Following DN, significant improvements were identified in the composite (3.98± 4.45%, $p<0.001$, ES=0.89), posteromedial (4.85±5.75%, $p <0.001$, ES=0.84) and posterolateral reach directions (4.96±5.49%, $p<0.001$, ES=0.90) but not in the anterior reach direction (2.11±5.77%, $p=0.08$, ES=0.37). Under eyes-open conditions, TTB improved in the mediolateral (0.27±0.43, $p=0.004$, ES=0.63) and anteroposterior (0.84±1.43, $p=0.007$, ES=0.59) directions., However, no significant changes were identified in any TTB measures with eyes closed ($p \leq 0.20$). Conclusions: FL DN created immediate improvements in dynamic and static balance in individuals with CAI. Future studies should examine the effects of multiple DN treatments and the mechanism behind this therapeutic effect.

Supported by: Pilot funding from the UK Department of Rehabilitation Sciences

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Poster Presentation 197

Abstract Title:	**Is Regional Anesthesia Associated with More Complications and Readmissions after Ankle Fracture Surgery in the Inpatient and Outpatient Setting?**
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Abstract: Importance: There is concern that regional anesthesia is associated with an increased risk of complications. The most concerning complication is hospital readmission for uncontrollable pain once the regional anesthetic wears off. Objective: To determine if complications and/or readmission rates are greater in patients who received supplemental regional anesthesia after open reduction and internal fixation (ORIF) of their ankle fracture when compared to those that underwent general anesthesia alone. Design: Retrospective review of The National Surgical Quality Improvement Program (NSQIP) Participant Use Data Files (PUF) from January 1, 2014 to December 31, 2016. Results: A total of 9,459 patients met inclusion criteria. There was not a significant difference in postoperative complications between patients in the RA and GA groups in both inpatient and outpatient setting ($p=0.021$). Patients in the RA group had significantly longer operative duration in both inpatient (79 vs. 71 minutes; $p=0.0024$) and outpatient setting (72 vs. 66 minutes; $p<0.0001$), significantly shorter mean LOS overall (GA=1.7 days vs. RA=1.1 days, $p<0.001$) and in the outpatient setting ($p<0.001$). Readmission rate for pain was significantly higher in the outpatient RA group ($p=0.004$). Conclusions and Relevance: Patients who received supplemental regional anesthesia had shorter LOS, increased operative time, and increased readmission rates for pain. Our study highlights rebound pain as a significant occurrence after regional anesthesia leading to hospital readmission. Future studies and better patient education is required to minimize rebound pain and decrease its consequential effect of representations and/or readmissions.

Supported by: There were no sources of support for this abstract.

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Poster Presentation 198

Abstract Title:	**Surgical Outcomes in the Frequency, Etiology, Direction, Severity (FEDS) Classification System for Shoulder Instability**
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Abstract: Background: The Frequency Etiology Direction Severity (FEDS) system was developed as a simple but reliable method for classifying shoulder instability based on four factors attainable by history and physical examination (Frequency: Solitary, Occasional, Frequent; Etiology: Traumatic, Atraumatic; Direction: Anterior, Posterior, Inferior; Severity: Subluxation, Dislocation). This study investigated epidemiology and two-year surgical outcomes for the most common FEDS categories in the Multicenter Orthopaedic Outcomes Network (MOON) Shoulder Instability Cohort. Methods: 1204 prospectively enrolled patients undergoing surgery in the MOON Shoulder Instability cohort were assigned to FEDS categories. Two-year follow-up was available for 610 patients (83.1% of eligible). Categories with at least 5% of patients were further analyzed by patient reported outcomes (ASES, WOSI, SANE) and rates of recurrent subluxation, dislocation, and revision surgery. Results: Nineteen categories represented at least 1% of patients. Occasional traumatic anterior dislocation (OTAD) was the most common category with 16.4% of patients. Five other anterior categories (STAS, OTAS, FTAS, STAD, FTAD) and one posterior category (STPS) represented at least 5%. Patient reported outcomes improved significantly for each category but by varying amounts. The highest rates of recurrent subluxation occurred in FTAS, OTAS, and OTAD; dislocation in OTAS and FTAS; and further surgery in OTAD. The lowest rates of failure occurred in STPS. Conclusion: While overall success was good, different FEDS categories showed varying degrees of improvement and failure rates, indicating that the system can be used to provide prognostic insight for presurgical education. Overall, outcomes decreased with higher initial frequency suggesting benefit of earlier surgical intervention.

Supported by: Orthopaedic Research and Education Foundation NIH Grant UL1TR001998

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Poster Presentation 199

Abstract Title:	**The Effect of Acute Sleep Restriction on Running Mechanics During an Exhaustive Treadmill Run**
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Abstract: Purpose: Inadequate sleep is a risk factor for injury, yet the mechanisms by which sleep restriction increases injury risk during running remain unknown. The purpose of this study was to determine if running mechanics would be altered following one night of sleep restriction. Methods: Nine subjects (21 ±3yrs, 55 ±10kg) completed an exhaustive treadmill run following either 8 hours (well-rested, WR) or 3 hours of sleep (sleep-restricted, SR). Right tibia peak impact accelerations (RtPk), head peak impact accelerations (HdPk), and shock attenuation were measured for 3 minutes during the first 2-5 minutes and final 3 minutes. Results: Time to exhaustion during the exhaustive treadmill test was not significantly different between the WR and SR conditions respectively (38.5 ±15.3 minutes, 40.0 ±14.7 minutes, p = 0.69). There were no significant differences in shock attenuation between conditions during the first 2-5 minutes (WR: 58.96 ±7.09, SR: 57.72 ±7.33, p = 0.55) and final 3 minutes (WR: 58.00 ±8.73, SR: 57.53 ±7.58, p = 0.84). No significant differences were found between conditions for RtPk (WR: 5.19 ±0.73g, SR: 5.07 ±0.92g, p = 0.49, WR: 5.38 ±0.87g, SR: 5.29 ±0.96g, p = 0.64) and HdPk (WR: 2.12 ±0.44g, SR: 2.11 ±0.37g, p = 0.79, WR: 2.22 ±0.45g, SR: 2.20 ± 0.36g, p = 0.76) during the first 2-5 minutes and final 3 minutes respectively. Conclusion: Running mechanics were not altered following one night of sleep restriction, however more research is needed to understand the effects of chronic sleep restriction on injury risk during running.

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Poster Presentation 200

Abstract Title:	**Factors Affecting Sensory Organization Test Scores in Division-I Collegiate Athletes**
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Abstract: Context: The Sensory Organization Test (SOT) provides an objective measurement of postural stability following sport-related injury that challenges the visual, vestibular, and somatosensory systems during double-limb quiet stance. Understanding factors that affect pre-injury SOT performance is essential for interpreting scores in athletes that are evaluated following sport-related musculoskeletal injury or concussion. Objective: Determine the effect of sex, sport, concussion history, and lower extremity injury history on SOT performance in collegiate athletes. Participants: Seventy-six Division-I soccer players and cheerleaders (37 females, 39 males) who were injury-free at the time of testing. Methods: All subjects completed the SOT and an injury history survey. The SOT is a 6-condition assessment that incorporates sway and visual referencing with eyes opened and closed conditions using an immersive virtual reality computerized dynamic posturography system. Scores for each SOT condition along with composite and sensory preference scores were analyzed. Independent t-tests compared SOT scores based on sex (males, females), sport (soccer, cheer), concussion history (yes, no), or lower extremity injury history (yes, no). Results: Females had significantly better postural stability on SOT Condition 3 (visual referencing, fixed support) compared to males ($p=0.04$). No other differences were identified for the SOT conditions, composite scores, or sensory preference scores based on sex, sport, concussion history, or lower extremity injury history ($p<0.05$). Conclusions: Despite previous studies finding postural stability differences based on sex, sport, or injury history, SOT performance was not affected by these factors in Division-I athletes. These findings can assist with interpreting SOT scores during clinical evaluation.

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Poster Presentation 201

Abstract Title: **Time to Return to Functional Activities Post Shoulder Surgery: A Case Study**

Author(s): K. J. Wilson, , U of Kentucky Healthcare Sports Rehabilitation T. L. Uhl, Department of Rehabilitation Sciences, College of Health Sciences, U of Kentucky

Abstract: Background: In physical therapy, self-reported function is commonly assessed. However, patient self-report has not been paired with objective capabilities. The purpose of this study is to compare objective time to return to function to subjective patient-reported function in patients following shoulder surgery. Methods: Two patients, one undergoing an anterior capsulolabral repair (age =19) and one undergoing a subacromial decompression with distal clavicle excision (age= 46), were included, so far. We asked patients to complete a valid self-reported outcome measure called the PENN Shoulder Score which is a subjective score. Patients were measured through a series of shoulder objective functional tests (SOFT) across the duration of rehabilitation. Four functional tasks have been completed for both subjects. Differences were compared between their subjective reporting and objective capabilities. Results: Patient undergoing capsulolabral repair demonstrated they could perform the four functional tasks 29 ±11 days prior to reporting no difficulty with same tasks subjectively. The patient following decompression demonstrated that they could perform the four tasks 16±14 days prior to reporting no difficulty with these same tasks. Conclusion: Limited findings from our first two patients suggest performance of a functional task precedes perception of performance of daily functional tasks such as combing hair, placing cups on shelves or pushing and pulling doors open with their affected shoulder. This difference could be attributed to fear of re-injury, not performing the activity regularly, or the time the PENN Shoulder score was administered.

Supported by: College of Health Sciences- Dr. Tim Uhl

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Abstracts

Poster Presentation 202

Abstract Title:	**Patient Reported Outcomes after Anterior Cruciate Ligament Reconstruction Predict Isometric Quadriceps Torque**
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Abstract: The purpose of this study is to determine if inflammation and patient reported outcomes one month post-anterior cruciate ligament reconstruction (ACLR) predict muscle function six months post-surgery. Nineteen patients who underwent ACLR (82.8±20.3kgs, 1.7±0.1m, 18.4±2.8yrs, 8M, 11F) completed this study. One month post-surgery (1.1±0.3months) individuals completed the Knee Osteoarthritis Outcomes Score (KOOS), and visual analog scale (VAS) for pain. Patients were aspirated one month post-ACLR, commercially available ELISA kits were used to determine concentrations of interleukin-1β (IL-1β) in synovial fluid. At six months (6.1±0.3months) patients completed maximal involved limb isometric contractions. Rate of torque development (RTD) was calculated as the slope of the time-torque curve taken from onset of torque to peak torque. Linear regressions were run to determine if levels of IL-1β, KOOS scores, and VAS scores, controlling for height and weight, one month post-ACLR would better predict peak torque or RTD six months post-ACLR. The model with the highest adjusted R2 was identified as the best model. Levels of IL-1β and patient reported outcomes one month post-surgery did not significantly contribute to the variance of RTD (86.8±68.0Nm/kg). Height, mass, KOOS-pain (73.3±19.2), KOOS-sport (41.9±40.2), and VAS (30.6±28.8) were included in the final model predicting 50.6% of the variance of peak isometric torque (151.3±49.1Nm; p=0.038). IL-1β (-4.75±1.3pg/mL) did not significantly contribute to predicting the variance of peak torque. Although levels of inflammation after surgery may not explain muscle function six months after surgery, patient reported outcomes for pain and sport performance can, suggesting early clinical use to aid targeted rehabilitation.

Supported by: This research was supported by the NIH National Center for Advancing Translational Sciences through grant number UL1TR001998 and by the Multidisciplinary Value Program Initiative at the University of Kentucky. The content is solely the responsibility of t

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Poster Presentation 203

Abstract Title: **Immune profiling of CD8+ T cell-mediated removal of Toxoplasma gondii cysts**

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Abstract: Chronic infection with Toxoplasma gondii is estimated to affect one third of human population. The basis of this chronic infection is the formation of cysts preferentially in the brain. There is no drug to eradicate cysts. Recent studies demonstrated increased incidence of brain cancers in infected individuals. We recently demonstrated that CD8+ immune T cells are able to remove cysts from the brain through a perforin-dependent mechanism in collaboration with phagocytes. To obtain a landscape view of the CD8+ T cell-mediated remove the cysts, we compared mRNA levels for 750 genes involved in the anti-cyst immune process using NanoString nCounter mouse myeloid innate immunity panel. Infected nude mice received CD8+ immune T cells from either infected BALB/c or perforin knouckout mice. Another group received no T cells. At 7 days after the cell transfer, the total RNA purified from their brains were applied for the analysis. We found mRNA levels for the following 6 genes were significantly increased specifically in the presence of perforin-sufficient CD8+ immune T cells; C-X-C motif chemokine receptor 3 (CXCR3) and 6 (CXCR6), chitinase-like 3 (Chil3), inducible T cell costimulator receptor (Icos) and its ligand (IcosL) and interleukin 18 receptor 1 (IL18r1). Icos-IcosL system is one of the costimulatory pathways in T cell activation, suggesting an involvement of this pathway in activation of CD8+ cytotoxic T cells for cyst removal. CXCR3 and CXCR6 could mediate the recruitment of the T cells and microgial/macrophages for cyst destruction and removal.

Supported by: NIH award: AI095032, AI134323 and AI136821

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Poster Presentation 204

Abstract Title:	**Providers' Attitudes toward Implementation of Evidence-Based Practices in Patients with Syncope**
Author(s):	A. M. Cowley, Center for Health Services Research, University of Kentucky M. O. Sirrine, Center for Health Services Research, University of Kentucky H. Yuan, CHSR Data and Statistical Core, University of Kentucky J. Li, Center for Health Services Research, University of Kentucky

Abstract: Aiming to provide guidance on the evaluation and management of syncope, a collaboration of leading healthcare and heart associations issued the Guideline for the Evaluation and Management of Patients with Syncope in 2017. Adopting a standardized guideline-based approach to syncope offers an opportunity for delivering optimal care to patients suffering from syncope. Guided by the Consolidated Framework of Implementation Research (CFIR), Project MISSION seeks to implement evidence-based practices from the syncope guidelines. We examine differences and gaps in providers' attitudes toward evidence-based practices with syncope, as these attitudes often influence implementation success. We distributed the Evidence Based Practice Attitudes Scale and Organizational Readiness to Change Assessment to over 400 specialists in cardiology, hospital medicine, and emergency medicine at four sites. Survey analysis demonstrates significant differences in attitudes between specialties (n=110). When considering a project champion, 31 and 35% of cardiologists and emergency specialists, respectively, feel as though a champion in their organization has the authority to carry out an implementation, while 52% of hospitalists feel this way. 73% of Hospitalists and Cardiologists agreed that opinion leaders in their organization are willing to try new clinical protocols, while only 62% of Emergency specialists agreed. When presented with the guidelines of focus, 79% of Emergency specialists and Hospitalists agreed that the guidelines are supported by their individual clinical experience in their field, while only 62% of cardiologists agreed. We present the overall gaps and differences in attitudes among the specialties and organizations and how these differences could affect the success of implementation.

Supported by: NIH Award: 1U01HL143508-01

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Poster Presentation 205

Abstract Title:	**Post injury mu-opioid receptor (mOR) expression in the oculo-trigeminal axis: Is Less mOR?**
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Abstract: Ocular surface injury results in ocular hypersensitivity behavior that peaks 10 days after corneal injury and returns to baseline thereafter. This apparent recovery is mediated the activation of mu-opioid receptors (mOR) in peripheral nerves also known as latent sensitization. Latent sensitization is therefore a positive adaptive response to injury, but it also represents a state of pain susceptibility. Here, we aim at improving our understanding of peripheral latent sensitization by studying the changes in mOR expression along the cornea-trigeminal axis after ocular injury. We analyzed mOR expression with ex vivo quantification (Western Blot and qPCR) and confocal microscopy. Ex vivo analysis suggests decreased expression of corneal mOR at 4 and 8 weeks after corneal injury; on the other hand, mOR expression is not significantly different in the trigeminal ganglia. Under microscopy, MOR-mCherry mice (that express fluorescent tags on mOR) expressed mOR in cornea and TG. In the cornea, the highest density of mOR were present in the terminal ends of the epithelial layer—compared to stromal and subbasal layers. In the TG, the majority of V1 neuron cell bodies expressed mOR. After CSI a decrease in density of mOR in the ophthalmic division of the TG was seen.

Supported by: University of Kentucky Department of Ophthalmology funds. UK CCTS Pre-Doctoral Fellowship TL1 sponsorship.

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Poster Presentation 206

Abstract Title:	**Analyzing the Statistical Properties of the Basso Mouse Scale for Injured Mice Populations in Order to Determine Normality**
Author(s):	K.Richards, College of Health Sciences, U of Kentucky J. C. Gensel, Spinal Cord and Brain Injury Research Center, Department of Physiology, College of Medicine, U of Kentucky

Abstract: The Basso Mouse Scale (BMS) is frequently utilized in Spinal Cord Injury Labs in order to measure the locomotor outcome of injured mice based on a 0-9 scale. More specifically, the BMS scale measures the locomotor function of mice on days 1, 3, 7, 14, 21, and 28 post injury. Throughout the years, the BMS scale has been used extensively, in turn generating a significant amount of data. The goal of the experiment is to determine the statistical population properties of the compiled BMS scores, focusing on 75 kdyn (severe) injuries. It is hypothesized, that through compiled data, the normality of the population can be determined, and in turn generate many statistical tests including: 95% and 75% confidence intervals, median based on categorical deviation, score frequency, etc. for each day post injury (dpi). Once determined, this data will better assist future studies by establishing exclusion criteria. In the future, it would be ideal to apply a more refined statistical analysis of this data in order to further the understanding and quantification through the use of the BMS. By doing so, a baseline for the control population will be determined.

Supported by:	NIH NINDS, Spinal Cord and Brain Injury Research Center, members of NERO: Neuroinflammation and Endogenous Repair (Lab), Oh yeah!

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Poster Presentation 207

Abstract Title:	**Changes in Lumbo-Pelvic Coordination following an Eight-Week Postpartum Physical Therapy Intervention**
Author(s):	Frederick Zachman, MD, Department of Obstetrics and Gynecology, Good Samaritan Hospital Sara Haynes, PT, Department of Physical Therapy, Good Samaritan Hospital Lauren Carney, PT, Department of Physical Therapy, Good Samaritan Hospital Korbin Jackson, Department of Biomedical Engineering, University of Kentucky Colin Drury, Department of Biomedical Engineering, University of Kentucky Tiara Harris, Department of Biomedical Engineering, University of Kentucky

Abstract: Prevalence of low back pain (LBP) among pregnant women is high. Abnormalities in lower back mechanics can impose excessive stress and strain on lower back tissues leading to development of LBP. Pregnancy-related changes in musculoskeletal system of pregnant females influence their lower back mechanics and are likely to have a role in LBP during pregnancy and postpartum. The objective of this study is to determine the effects of an 8-week physical therapy session on the lumbopelvic coordination of post-partum females. Twenty women who have post-partum pelvic floor disorders will be selected from the University of Kentucky Health Care system. The patients will complete two data collection sessions (i.e. before and after their 8-week therapy treatment) including trunk forward bending and backward return, a manual material handling task, a walking test, and a sit-to-stand and stand-to-sit tests. Thoracic and pelvic rotations will continuously be recorded using wireless inertial measurement units and magnitude and timing aspects of lumbo-pelvic coordination will be analyzed and compared between pre- and post-therapy sessions. The physical therapy intervention will focus on strengthening the pelvic floor muscles. We expect to observe distinct differences in lumbo-pelvic coordination between the different data collection sessions due to the therapy treatments. Any pre-therapy data collection sessions performed will be reported during the Biomedical Research Day.

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Poster Presentation 208

Abstract Title:	**Pain Assessment and Analgesic Delivery in Mechanically Ventilated Patients: Can We Do It Better?**
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Abstract: Introduction: Pain is identified as one of the greatest discomforts during intensive care unit (ICU) stay. Although Critical Care Pain Observation Tool (CPOT) score was extensively validated to assess pain, practitioners' interpretations of individual components may remain heterogeneous. As well, we sought to determine the frequency with which there was an administration of pain medication with a change in CPOT score to 2 or greater. Methods: Retrospective chart review of mechanically ventilated medical ICU patients ≥18 years was performed from July 2016 to June 2018. CPOT scores, along with scored individual components and medication delivery, were abstracted. Results: 3,265 distinct ICU admissions were analyzed, median age was 57-years and 53% were male. A total of 162,240 CPOT scores were abstracted; 18,910 of which were identified as an increase in CPOT score. Increases in CPOT components scores were as follows: change in facial expression score occurred 62% of the time, followed by 55% for body movements, 53% for ventilator compliance and 47% for muscle tension. Within 30 minutes following an increase in CPOT score, a pain medication was administered as follows: for an increase in CPOT score by ≥2 lead to pharmacologic intervention 22% of the time; 24% with increase by ≥3, 27% with increase by ≥4 and 31% with increase by ≥5. Conclusions: Multiple components were responsible for increase in CPOT score. Continued standardized training in assessing CPOT components remains important. These data indicate that the potential for shortened delivery time of pain medications when CPOT scores increase, does exist.

Supported by: None

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Poster Presentation 209

Abstract Title:	**Analysis of Hydroxyurea Efficacy in Kentucky Pediatric Sickle Cell Disease Patients**
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Abstract: Sickle cell disease (SCD) is the most common hemoglobin disorder in the United States, with severe disease complications that have historically resulted in lifespans shortened by decades. Children with the more severe genotypes still experience survival rates to adulthood that linger below 95%. In this study we assess pediatric SCD management in Kentucky from 2012- 2018, aiming to evaluate improvements in care resulting from the 2014 release of an Expert Panel Report by the National Heart, Lung, and Blood Institute (NHLBI). In the pediatric population, these new guidelines most importantly suggest expanding utilization of hydroxyurea, an effective disease-modifying medication. This study examines longitudinal data from both the University of Kentucky and the University of Louisville regarding the efficacy of hydroxyurea treatment. Markers of disease severity were chosen to reflect the most common and distressing clinical manifestation of SCD—recurrent acute pain. These markers include hospitalizations and emergency room visits for vaso-occlusive crises as well as pain-related events. Laboratory data was also collected to assess appropriate therapeutic range as well as medication adherence. Our early findings suggest that use of hydroxyurea in all patients over 9 months of age, regardless of clinical severity has led to an overall improvement in the morbidity and mortality associated with this disease. However, the goal of our project is not only to answer the question of care improvement, but also to quantify these results and use them to refine our management of this vulnerable population.

Supported by: NIH award: UL1TR001998 and pilot funding from UK Center for Clinical and Translational Science

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Poster Presentation 210

Abstract Title:	**Pilot Psychiatric Screening for Patients with Type 1 Diabetes**
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Abstract: Objectives: Youth with type 1 diabetes (T1D) are at high risk for developing psychiatric disorders, including depression and anxiety, which have been associated with nonadherence and poor outcomes. The current study assessed the feasibility and acceptability of screening for psychiatric concerns in a pediatric diabetes clinic. Methods: Over the course of a 4 week pilot, families in a university-affiliated pediatric diabetes clinic were asked to participate in a standardized psychiatric screening using REDCap. Eligible participants had T1D and were between 7-21 years of age. Patient and caregiver filled out validated measures of depression, anxiety, life stressors, and post-traumatic symptom disorder. Chart review provided demographic information. University of Kentucky Medical IRB Approved, Protocol #17-0790-P1G. Results: Of the 15 eligible caregiver-patient dyads, 7 completed the screening, with an acceptance rate of 46.7%. Of those who did not participate, most reported a lack of time or interest in participation. In screening for trauma, 5/7 (71.4%) patients reported exposure to a traumatic event during their lifetime. Based on questions about anxiety disorders, 3/7 (42.8%) had a possible anxiety disorder. On depression screening, 2/7 (28.6%) parents rated their children as depressed although 0/7 patients reported clinically significant levels of depression. However, 2/7 (28.6%) of patients indicated that they had contemplated suicide within the past 2 weeks. Conclusion: Screening was accepted by about half of families and was feasible to complete during an outpatient clinic appointment. Traumatic exposures and post-traumatic symptoms were identified in a significant number of patients. Out of 7 patients, 2 patient with suicidality were identified even though they did not endorse clinically significant depressive symptoms on MFQ. Neither had disclosed suicidality to their provider or parent. Routine suicide screening should be a part of all outpatient appointments.

Supported by:	The project described was supported by the National Center for Research Resources and the National Center for Advancing Translational Sciences, National Institutes of Health, through Grant UL1TR001998. The content is solely the responsibility of the autho

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Poster Presentation 211

Abstract Title:	**Impact of azithromycin on human macrophage gene expression**
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Abstract: Background: Pseudomonas aeruginosa (PA) colonizes the lungs of up to 90% of patients in the end-stages of cystic fibrosis (CF) and accelerates pulmonary functional decline through induction of an excessive, dysregulated inflammatory response. Long-term anti-inflammatory therapy with the azalide antimicrobial agent azithromycin (AZM) has been established in a series of randomized clinical trials as a beneficial intervention in these patients. We have demonstrated that AZM polarizes macrophages to a regulatory, alternatively-activated phenotype in a murine cell line and in a mouse model of PA infection. Here we hypothesized that AZM can induce similar gene expression patterns in human peripheral blood mononuclear cells (PBMCs) as those observed in mouse models and human sputum samples. Methods/Procedures: PBMCs were isolated from leukoreduction filters obtained from the Central Kentucky Blood Center. Cells were cultured in the presence of growth factors that induce macrophage differentiation, and then stimulated with LPS in the presence of activating cytokines and AZM. The impact of AZM on macrophage gene expression was evaluated using custom-designed gene array cards that include specific macrophage genes that characterize activation, phenotype, and autophagy. Results: AZM blunted expression of pro-inflammatory genes in the presence of IFN-γ and LPS (TNF, IL-6, IL-1b). AZM showed little to no effect on key regulatory macrophage genes (except ARG2 and IKBKB). AZM blunted expression of autophagy-associated genes including ATG5, MTOR, and AKT1. Conclusions: The gene expression signature induced by AZM in human peripheral blood monocytes is similar to that observed in mice and in cells isolated from human sputum.

Supported by:	Igniting Research Collaborations Pilot Funding Program University of Kentucky Colleges of Pharmacy and Medicine Sinai A, Feola DJ. "Toxoplasma modulation of human macrophage polarization: potential involvement of secreted parasite deubiquitinases." N

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Poster Presentation 212

Abstract Title:	**Roles of ASIC and TRPV1 Channels in the Stimulatory Effect of Inhaled SO2 on Vagal Bronchopulmonary C-fibers**
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Abstract: Chronic exposure to sulfur dioxide (SO2), an air pollutant, causes airway injury and results in debilitating airway diseases. Transient exposure to SO2 triggers coughs and reflex bronchoconstriction, indicating a stimulatory effect of SO2 on airway afferents. Indeed, a recent study in our lab has demonstrated that vagal bronchopulmonary C-fibers are the primary target of inhaled SO2. However, the mechanisms of SO2-caused stimulatory effect still unknown. This study aimed to investigate underlying mechanism of this stimulatory effect of SO2 on pulmonary sensory nerves. Single-unit fiber activities of pulmonary C-fibers were recorded to SO2 exposure in anesthetized rats. Our results showed the following. First, SO2 caused a stimulatory effect on pulmonary C-fibers. Second, sodium bicarbonate alleviated the systemic acidosis and SO2-induced pulmonary C-fibers stimulation. Third, this stimulatory effect of SO2 was blocked by pretreatment with amiloride (an acid-sensing ion channels blocker, ASICs) or combined with AMG8910 (a transient receptor potential vanilloid subtype-1 antagonist, TRPV1). To investigate if this stimulatory effect is generated by SO2 on sensory nerves, the change in F340/F380 ratio was measured in isolated rat vagal pulmonary sensory neurons. Pretreatment with amiloride and AMG8910 reduced SO2-increased F340/F380 ratio in these neurons. To explore the role of ASICs and TRPV1, used awake C57/BL6 and TRPV1-/- mice to measure cough responses. TRPV1-/- mice exposed to SO2 showed little cough responses after amiloride aerosol treatment compared to C57/BL6. In conclusion, inhaled SO2 lowered the pH in airway/lung tissues, which generated the stimulatory effect on pulmonary C-fibers by activation of ASICs and TRPV1 channels.

Supported by: NIH grant: U01 (AI123832-01)

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Abstracts

Poster Presentation 213

Abstract Title:	**Driving pressure and Mortality in Medical & Surgical ICU Patients following Paralytic administration**
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Abstract: Methods: A retrospective analysis of electronic medical records was performed. Patients included Medical and Surgical ICU admissions from 9-1-15 to 6-30-18. In addition to Driving Pressure, data were collected for age, BMI, acute kidney injury, cirrhosis, active dialysis, Elixhauser Co-morbidity score, gender, race, P/F ratio, heart rate, mean arterial pressure, respiratory rate before and after cisatricurium, mortality, hospital LOS, ICU LOS, daily SOFA, Vent days, pressor agent days, and discharge destination. Multiple logistic regression modeling was examined with Hospital Mortality as the outcome. Results: 196 ICU admissions were identified, & average age was 49. Driving pressure groups were examined as <10 cm H2O, 10-14, 15-19, 20-24, and 25 or greater. The percent of females in each subgroup of DP increased with increasing DP (20%, 33%, 41%, 63% and 57% respectively). Mortality increased with increasing DP (27%, 33%, 47%, 51%, and 52% respectively). The logistic regression model (without assigning the DP subgroups) was based on Driving Pressure as a continuous variable, Age, Gender, AKI, and a DP*Gender interaction term as predictors. The values for the variables (model coefficient, p value) were DP: 0.0121, 0.752; AKI: 0.7206, 0.044; Age: 0.04, 0.001; Gender (F vs M): -2.58, 0.025; DP * Gender: 0.128, 0.042, respectively. Conclusion: Despite an interpretation that gender's statistically significant coefficient in conjunction with the insignificant DP coefficient, suggests that Driving Pressure was more strongly associated with mortality for females compared to males. Further prospective analyses may be necessary to more accurately determine an associated between female gender and driving pressure.

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Poster Presentation 214

Abstract Title:	**Not Easy, Being Wheezy : A retrospective comparison of outcomes in massive pulmonary embolism patients between treatment modalities**
Author(s):	Jiawen Liu, College of Pharmacy, U of Kentucky George Davis, Department of Pharmacy Practice & Science, U of Kentucky Susan Smyth, Gill Heart Institute, U of Kentucky Jeffery Talbert, Department of Pharmacy Practice and Science, U of Kentucky

Abstract: Hypothesis: Pulmonary embolism (PE) is a leading cause of cardiovascular death in the US, however, the optimal care of patients remains unclear. The current advanced therapy options for acute massive PE are systemic thrombolysis, ultrasound-assisted catheter-directed thrombolysis, embolectomy and extracorporeal membrane oxygenation (ECMO). Recently ECMO utilization in this setting is gaining popularity, however routine use is prevented by limited data. Our institution expanded the role of ECMO as an initial management of acute massive PE. The aim of this project was to evaluate ECMO-treated patients to other modalities and report mortality and other clinical outcomes. Number of subjects: n=33 Procedures: Retrospective chart review for all patients underwent PERT activation and is risk stratified to massive PE from 09/2015 to 09/2018 were conducted. Results: Ongoing research. Baseline characteristics: Approximately 58% of the patient present initially as a transfer from OSH. Average age ~61 years old, ranging between 15 to 88. There was 2 pediatric patient and 17 elderly, which is about 52% of the overall patient cohort. Gender is distributed evenly among male and female. Tobacco use is found in 45%(n=13/29) of the patient for which smoking history can be obtained. The overall mortality is about 64% and highest in the anti-coagulation only group(33%) and lowest in ECMO group(14%). Major bleeding in is reported in 33% of all patients and highest seen in the tPA gtroup. Overall average LOS is ~9 days and 7.4 days for average ICU LOS. Longest seen in the EKOS+ECMO treatment group with 19 days overall and 14.8 days in ICU.

Supported by: NA

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Poster Presentation 215

Abstract Title:	**The ASTERS study: Assessing the Role of Sphingolipids in AcuTE Respiratory Distress Syndrome (ARDS)**
Author(s):	JL Sturgill, Department of Internal Medicine, Pulmonary Critical Care, U of Kentucky PE Morris, Department of Internal Medicine, Pulmonary Critical Care, U of Kentucky

Abstract: Acute lung injury (ALI) and the more severe manifestation, acute respiratory distress syndrome (ARDS) describe syndromes of acute onset, bilateral, inflammatory pulmonary infiltrates and impaired oxygenation. ARDS/ALI are a continuum of disease which results in a life threatening, rapidly progressive illness and occurs in critically ill patients. Recent reports in JAMA highlight the significant public health impact ARDS/ALI has on the critically ill population in that despite robust research efforts, these illnesses continue to be underdiagnosed, undertreated, and continue to have a high mortality rate (≥ 40% of all confirmed diagnoses). The estimates for ARDS/ALI incidence vary due to inconsistencies with proper diagnosis and lack of valid biomarkers of disease; however, it is expected that anywhere from 20-50% of patients on mechanical ventilation will develop this disease. Previous work by our group has shown that sphingolipids play a multifaceted role in lung inflammation. Sphingolipid are a class of bioactive lipids that play a role in cellular processes such as apoptosis, cell migration, and adhesion. Ceramide is one species of sphingolipid we have investigated in both man and mouse. Our laboratory has shown that ceramide is upregulated in pulmonary inflammation in mouse models of pneumonitis and is elevated in the exhaled breath condensate of mechanically ventilated patients at risk for ARDS/ALI. Our work coupled with the work of others highlighting a role for ceramide in COPD, surfactant dysfunction, and infectious disease make ceramide a logical candidate biomarker that warrants further investigation. To our knowledge, there are no studies examining the role of ceramide as a biomarker in ARDS/ALI. Thus, our overarching hypothesis is that ceramide is elevated in the lungs of patients who develop ARDS/ALI. This lipid dysregulation accounts for the pathophysiology seen in this disease and may be a potential pharmacologic target for clinical treatment. Thus the purpose of this exploratory research is to maximize existing specimens to further evaluate ceramide as a biomarker for acute lung injury.

Supported by:	The project described was supported by the National Center for Research Resources and the National Center for Advancing Translational Sciences, National Institutes of Health, through Grant UL1TR001998. The content is solely the responsibility of the autho

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Poster Presentation 216

Abstract Title: **Automatic Monitoring of Potential Drug Abuse on Twitter via Machine Learning**

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Abstract: The National Center on Addiction and Substance Abuse (NCASA) reported that 70% of teens are checking social media accounts on a daily basis. The prevalence of social media is constantly growing and its influence on teens today is only growing and drug use is no exception to this. In fact, teens on social media are five times more likely to buy cigarettes, three times more likely to drink, and two times as likely to smoke cannabis. The purpose of this project is to analyze tweets using a semi supervised learning method and co-training algorithm to determine if they can be good indicators of drug abuse. This is necessary due to the fact that millions of tweets are made every minute, and it is impossible to humans to screen every single one to determine who might be at risk of drug abuse. Eventually, tweets and posts from social media can be used to establish an automatic on-line monitoring system to detect potential drug use through the application of these machine learning algorithms and thus, provide a way of intervention. For this particular study, the classification method for both views of the co-training part was Random Forest; in preliminary studies, this method proved both the slowest yet most accurate. On average, this method of classification and learning yielded a maximum average accuracy of 72.81% which is fair but far from optimal. However, many paths can be taken to go about testing and increasing the accuracy rating in the future.

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Poster Presentation 217

Abstract Title:	**Assessing Behavior Changes Following In Utero Opioid Exposure in Rodents**
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Abstract: Background: Opioid dependence is at epidemic levels and thus opioid exposure in pregnancy has led to the increase in neonatal abstinence syndrome (NAS). The effects on memory and behavior in babies born with NAS are unclear and warrants further research. Using a novel mouse model with an extended gestational period, we aim to study the effects of in utero opioid exposure on memory. Study hypothesis: We hypothesize that mice exposed to morphine in utero will result in behavioral changes including increased withdrawal behavior and decreased performance in memory assessments. Methods: Beginning on G18 dams were treated daily with saline, morphine 10 mg/kg or morphine 30 mg/kg via subcutaneous injection until day of birth. Pups were evaluated daily for the first seven days to measure signs and symptoms of withdrawal that included wet dog shakes, jumps, body temperature, and ultrasonic vocalizations. Differences in memory were measured using Y-maze and novel object recognition tests starting at one month of age. Results: Preliminary data from 3 month-old spiny mice born exposed to morphine were found to exhibit increased withdrawal behavior and altered memory compared to saline treated mice. Conclusions: These data suggests that in utero morphine exposure results in decreased memory performance in 3 month old spiny mice. Further studies are needed to determine any underlying molecular changes responsible for these differences. We are hopeful this novel mouse model will further our understanding of the long term consequences of in utero opioid exposure.

Supported by: N/A

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Abstracts

Poster Presentation 218

Abstract Title:	**Tobacco use in Pregnancy Intervention for Cessation (ToPIC)**
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Abstract: Background: Smoking in pregnancy is a modifiable cause of adverse birth and maternal outcomes, yet nearly one-third of pregnant Medicaid patients in Kentucky use tobacco. This pilot study evaluates the effectiveness of prenatal tobacco cessation counseling by a non-physician Certified Tobacco Treatment Specialist (CTTS). Methods: Participants were pregnant (<20 weeks gestation) smokers at participating UK or Baptist Health Lexington clinics and randomized to intervention or control groups. Women completed tobacco use surveys, urine cotinine tests, and CO2 levels at 4 time points (two prenatal and two postpartum). Additionally, participants in the intervention were contacted by the CTTS at least once monthly. Changes in tobacco use from baseline to the third trimester and 2-8 weeks postpartum, within and between the intervention and control groups, were compared using generalized estimating equations and two-factor mixed models. Results: Sixty-six eligible women enrolled (34 intervention, 32 control). Groups were similar at baseline. Intervention participants reported smoking significantly fewer cigarettes per day (CPD) (p=0.049), had lower cotinine levels (p=0.003), and higher CO2 levels (p=0.042) at the 3rd trimester, and lower cotinine (p=0.003) and fewer CPD (p=0.004) at 2-8 weeks postpartum, compared to baseline and control groups. There were no changes observed among women in the control group. No women in either group achieved tobacco cessation. Discussion: Use of a CTTS resulted in reduced tobacco use in the third trimester and in the early postpartum period. More data are needed to assess the impacts of prenatal tobacco cessation counseling by a CTTS on long term tobacco use.

Supported by: Value of Innovation to Implementation Program (VI2P) award from the UK Center for Health Services Research

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Poster Presentation 219

Abstract Title:	**Characteristics of opioid using mothers from the Addiction Severity Index (ASI).**
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Abstract: Background: The lifetime history of women with opioid use disorder (OUD) is important in addressing the multifaceted issues in the management of infants with Neonatal Abstinence Syndrome (NAS). NAS refers to a constellation of withdrawal signs in infants after prenatal opioid exposure. ASI provides a measure the severity of potential issues in seven domains (medical, employment, alcohol, drug, legal, family, and psychiatric history). Objective: This study's objective is to examine environmental and maternal factors that may have an effect on the treatment and development of infants with NAS. Design/methods: As part of a prospective randomized clinical trial (NCT03396588) for treatment of NAS, ASI was administered to mothers with OUD or in Medication Assisted Treatment. The ASI addresses 7 areas potentially affected by substance abuse in those with OUD. Results: To date, 45 mother-infant dyads are participating in the clinical trial. 35/45 completed the ASI. All mothers except for one (who is multiracial) are white, non-Hispanic and mean age of 26.98 years (range 19-38). Conclusions: Characteristics of women with OUD reflect lifelong stresses including, economic hardship and low education achievement, involvement in the criminal justice system, family histories of alcohol and/or drug abuse, family conflict, and psychiatric disorders. Characteristics of this vulnerable population are considered when designing interventions to address substance use and recovery in pregnant and parenting women with OUD. The ASI provides researchers with a better understanding of the environment of the babies with NAS and the factors that may influence mothers to abuse opiates while pregnant.

Supported by: NIH/NIDA award: 3R01DA043519-02S1 "The project described was supported by the National Center for Research Resources and the National Center for Advancing Translational Sciences, National Institutes of Health, through Grant UL1TR001998. The content is

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Poster Presentation 220

Abstract Title:	**Overcoming Barriers to a Randomized Clinical Trial: Understanding Opioid Exposed Infants and their Mothers**
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Abstract: Background and Objective: Neonatal Abstinence Syndrome (NAS) is the diagnosis given to infants experiencing withdrawal from opiate exposure in utero. This problem is on the rise, and it remains unclear how opiate treatment of NAS affects children's long-term developmental outcomes. The study goal is to determine whether clonidine treatment of NAS would result in a better neurobehavioral performance compared to morphine. Methods: This prospective randomized clinical trial (NCT03396588) is currently enrolling infants that are ≥ 35 weeks' gestational age, exposed to opioids, and admitted for treatment of NAS. Informed consent comes from the participants' mothers. Infants are scored using the Finnegan Neonatal Abstinence Scoring System1 and then randomized to receive morphine or clonidine if scores indicate need for treatment. Masked examiners will complete validated neurodevelopmental and neurobehavioral assessments throughout the first two years of life. A set of maternal surveys will further inform researchers on environmental and maternal factors that may influence childhood outcomes. Discussion: Barriers to any randomized, pharmacological clinical trial have potential to affect the outcomes if they are not properly addressed. Some of the barriers encountered in this study were anticipated and accounted for, while others have required adaptation along the way. These include but are not limited to the characteristics of patient population and systems issues. The research team remains intentional in its efforts to complete this ongoing study while maintaining fidelity.

Supported by: NIH award: R01DA043519 University of Kentucky CCTS for providing DSMB and RedCap database (NIH CTSA UL1TR001998)

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Center for Clinical and Translational Science

Abstracts

Poster Presentation 221

Abstract Title:	**Characterization of Abuse-Deterrent Formulation Opioid Prescribing through the Kentucky All Schedule Prescription Electronic Reporting System**
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Abstract: The development of abuse-deterrent formulations (ADFs) of opioid analgesics has been proposed as a means to decrease the abuse potential of these medications. The U.S. Food and Drug Administration (FDA) has approved labeling for ten brand name opioids which describe abuse-deterrent properties, five of which are currently marketed in the U.S. Utilization of ADFs in clinical practice is not well described within the literature. As such, this study seeks to characterize prescribing of ADFs in Kentucky as identified through the Kentucky All Schedule Prescription Electronic Reporting (KASPER) System. Data were extracted for all prescriptions for ADF opioids reported to KASPER during the study period (2015-2018). Rates of ADF use were calculated according to age, sex, and region and were standardized per 1,000 persons. Utilization of currently marketed ADFs was expressed as number of distinct patients and number of prescriptions per year. In 2017, the rate of ADF use in Kentucky was 1.93/1,000 and was highest among persons aged 55-64 years (4.91/1,000). Use rates were equal between males and females (1.93/1,000). The prevalence of ADF use was significantly higher in Western Kentucky counties (Delta region) than in the Appalachian region [rate ratio (RR): 1.66; 95% confidence interval (CI): 1.55-1.77] and Central region [RR: 1.65; 95% CI: 1.56-1.75]. Among the five currently marketed products, utilization was greatest for OxyContin® for all years. These data suggest that there is geographic variability in the prescribing of ADF opioids. Further research is necessary to understand what factors may be associated with differences in prescribing patterns.

Supported by: The project described was supported by funding from the U.S. Food and Drug Administration (BAA-17-00123).

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Poster Presentation 222

Abstract Title:	**Application of a Continuum of Care Model for Claims-Based Analyses of Substance Use Disorder in the Kentucky Medicaid Database**
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Abstract: We sought to establish a method for applying a simple continuum of care for substance use disorder (SUD) to claims-based analyses and to identify intervention points for the Kentucky Medicaid population based on the established continuum of care. A case series study was developed using administrative claims data from Kentucky Medicaid from July 1, 2016 to December 31, 2017. Patients aged 18 to 64 with incident SUD were considered to ascertain whether they progressed in treatment for SUD. Frequency analyses were conducted to describe the population in terms of the level of care at each visit and chi-square analyses were utilized to check for significant differences. 55,583 SUD patients were included in the analysis after the application of the inclusion criteria. This population was majority male (53.9%), White (79.4%), non-Hispanic (87.3%), and rural-dwelling (51.7%). Patients were most frequently diagnosed at emergency (29.3%) or low (30.8%) levels of care. Patients who did not receive follow-up care were more frequently diagnosed at an emergency level than patients who did receive follow-up care (49.1% vs 19.7%). The largest percentage of patients had a diagnosed opioid use disorder (41.3%). There was evidence of downward filtration to lower levels of care among patients diagnosed in emergent conditions at their second and final follow-up visits. A continuum of care for administrative claims-based analyses to ascertain patient progress in SUD treatment can be utilized to analyze populations at an organizational level. These results highlight potential interventional points at an administrative level for other healthcare organizations.

Supported by: N/A

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Poster Presentation 223

Abstract Title:	**Agreement in Top Diagnoses Among Children With and Without NAS: Truven MarketScan Commercial Database, 2009 to 2015**
Author(s):	K. L. Conner, Department of Pharmacy Practice & Science, U of Kentucky J. Talbert, Department of Pharmacy Practice & Science, U of Kentucky

Abstract: As rates of neonatal abstinence syndrome (NAS) rise across the United States, there is an urgent need to assess the health outcomes of children who were diagnosed with NAS as infants. The objective of this analysis was to ascertain differences in top diagnoses for children with and without NAS. We hypothesize that differences in diagnoses will become more extreme in later childhood. Using the Truven MarketScan Commercial Database, 2,483 children aged 10 and under were identified as having a NAS diagnosis between January 1, 2009 and September 30, 2015. These children were categorized into three separate categories for analysis: up to age 1, ages 1 to 5, and ages 6 to 10. The top 50 diagnoses of these children were compared against the top 50 diagnoses for children under age 10 without NAS, categorized into similar categories (22,688,750 children). Observed and expected probabilities of agreement were calculated from the list of diagnoses. Among children up to age 1, the observed probability of agreement between the top 50 diagnoses was 0.528 (expected probability of 0.51). In children age 1 to 5, the observed probability of agreement was 0.754 (expected probability of 0.785). In children age 6 to 10, the observed probability was 0.493 (expected probability of 0.621). These results indicate that differences exist in these populations, but larger differences arise in later childhood beyond what is expected. This indicates an urgent need for further research in health outcomes for children with a history of NAS in later childhood.

Supported by: N/A

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Poster Presentation 224

Abstract Title:	**Impact of Local Smoke-free Workplace Laws on Youth Tobacco Use in Kentucky**
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Abstract: Purpose: Smoke-free ordinances are associated with decreased adult smoking rates, but the impact on youth tobacco use has been less studied. The purpose was to determine whether presence and strength of a local smoke-free policy was associated with use prevalence of cigarettes and smokeless tobacco among 10th graders in Kentucky, and whether use rate differed by urban/rural location, controlling for demographic and social factors. Methods: Data were from the Kentucky Incentives for Prevention survey, administered biennially by REACH Evaluation for the Kentucky Department of Behavioral Health. Data were collected in 2004-2016 from 366,593 10th grade students in 173 school districts representing 119 of 120 counties in Kentucky. Logistic regression assessed the impact of law status and urban/rural location on use prevalence, controlling for demographics, other ATOD use, social factors, and year. Results: Compared to those in counties without smoke-free laws, those living in a county with a comprehensive ordinance were 15% less likely to smoke cigarettes (p=.002), and those living in a county with moderate or weak law were 9% less likely to smoke (p=.03). For smokeless, compared to those living in a county without a smoke-free law, those living in a county with a comprehensive law were 16% less likely to use smokeless tobacco (p=.02); there was no difference in smokeless use prevalence between counties with moderate/weak laws and those with no laws. Urban/rural status was unrelated to use prevalence in either models. Conclusions: These findings demonstrate the protective effect of comprehensive smoke-free policies on youth tobacco use prevalence.

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Poster Presentation 225

Abstract Title:	**Regulating Gabapentin as a Drug of Abuse: A Survey Study of Kentucky Community Pharmacists**
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Abstract: OBJECTIVES: As the number of gabapentin prescriptions has increased, so have reports of its misuse and diversion. This has led some states to utilize prescription drug monitoring programs (PDMPs) to more closely monitor gabapentin. The objective of this study was to describe Kentucky community pharmacists' perceptions of gabapentin misuse and diversion, as well as their stance on reclassifying the drug as a controlled substance (CS). METHODS: Responses were collected using an online survey sent to all pharmacists practicing in Kentucky in August 2016. The survey collected demographic characteristics and pharmacists' experience with gabapentin dispensing. Pearson's chi-squared statistics were calculated to examine the distribution of support for gabapentin as a CS in Kentucky across each of the categories of individual variables. Logistic regression was used to estimate the effects of pharmacist demographics and experiences with gabapentin on their support of gabapentin reclassification. RESULTS: Responding community pharmacists (n=1084) believe that the abuse and diversion of gabapentin is a problem in their communities, with 9 in 10 (89.6%) indicating they agree or strongly agree. Over three-fourths (87.5%) indicated support for reclassifying gabapentin as a CS. Common reasons for opposition were that they would not reduce or eliminate abuse (45.8%) and they would be an inconvenience to patients (17.0%). Pharmacists practicing in independent pharmacies and pharmacists practicing for over 20 years were less likely to support gabapentin reclassification. CONCLUSION: Kentucky community pharmacists express considerable concern over the possible misuse and diversion of gabapentin and widely support regulatory changes reclassifying gabapentin as a CS.

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Abstracts

Poster Presentation 226

Abstract Title:	**Voices of Hope: A Process Evaluation of a Recovery Community Center**
Author(s):	A. Elswick, Department of Family Science, U of Kentucky A. Fallin-Bennett, College of Nursing, U of Kentucky

Abstract: Substance use disorders (SUDs) are chronic disorders that have traditionally been managed acutely. More recently, SUD treatment has undergone a paradigmatic shift toward a recovery management model which focuses on long-term SUD management and the delivery of peer-based services. Within this model, recovery community centers (RCCs) are peer-operated centers that function as a hub for the delivery of peer-based services, whose aim is to increase the recovery capital of its participants. This study evaluated the formation of Voices of Hope (VOH), the first RCC in the state of Kentucky. Methods: Qualitative interviews were conducted during the formative phase of development to identify needed programs and services. Next, quantitative data was collected and analyzed to reflect the current usage of the RCC by the recovery community. Results: Among its peer-based services, VOH offers the following programs and has served the following number of people: telephone recovery support (n=626), a social support for people in recovery, recovery coaching (n=52), whereupon certified peer support specialists help people in recovery set and achieve goals, an Employment Readiness Program (n=4), which employs people in recovery part-time and seeks to help them develop marketable skills, and various peer-based recovery support groups including yoga (n=27), family groups such as SMART Friends and Family and Parents of Addicted Loved Ones (n=42), and individual support meetings (n=114) such as Refuge Recovery, All Recovery Meetings, and Women's All Recovery Meetings. Currently, VOH's RCC has 253 members. Discussion/Conclusion: RCC's play a unique role in the delivery of peer-based recovery support services.

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Poster Presentation 227

Abstract Title:	**Substance Use and Related Issues Among the LGBT Population**
Author(s):	M. Riffe, College of Social Work, U of Kentucky M. Staton, Department of Behavioral Science, U of Kentucky M. Tillson, Center on Drug and Alcohol Research, U of Kentucky T. Acree, Center on Drug and Alcohol Research , U of Kentucky

Abstract: Substance use (SU) is an important public health problem that disproportionately affects a number of individuals in Kentucky. Kentucky is one of the top states dealing with a SU crisis and currently ranks among the highest in the country in mortality rates due to drug overdoses. However, one group within the state that has been neglected in substance abuse research is the lesbian, gay, bisexual, and transgender (LGBT) community. The purpose of this study is to explore SU patterns among LGBT individuals, as well as other co-occurring health issues, in an effort to promote continued research, policy, and programs which are LGBT specific. A review of literature was conducted using scholarly databases such as EBSCOhost, PsycINFO, and Academic Search Complete. Key terms included LBGT, drug use, addiction, Kentucky, gay, and substance treatment. Results show LGBT individuals have an elevated risk for SU due to internalized homophobia, victimization, and limited/discriminatory treatment services. Additionally, they were found to have initiated earlier than heterosexuals, have a faster introduction to intravenous administration, and were more likely to have experienced overdose. LGBT individuals are also at risk for high rates of infectious disease, co-occurring disorders, and participation in high-risk behaviors. LGBT communities represent a unique population in terms of substance use patterns and behaviors. Research must be conducted to see if identified trends of SU relating to sexual orientation are relevant in Kentucky to better inform treatment services. Such research has the potential to promote LGBT substance use programs, thereby bridging a gap in services.

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Abstracts

Poster Presentation 228

Abstract Title:	**Reducing Stigma Associated with Substance Use Disorders in Rural-Based Medical Students Through a Community Engagement Program**
Author(s):	M. H. Koenig, UKCOM Rural Physician Leadership Program, U of Kentucky R. Todd, UKCOM Rural Physician Leadership Program and Department of Ob/Gyn, U of Kentucky

Abstract: Research has demonstrated that healthcare providers generally have negative attitudes towards patients with substance use disorders (SUDs). It has also been shown that the stigma associated with SUDs can adversely impact the care of these patients. Often, medical students' only exposure to patients with SUDs is after an overdose or when these patients exhibit drug-seeking behaviors. These limited and biased experiences may be the reason for or help perpetuate stigma towards this patient population. To address these negative beliefs towards patients with SUDs in a rural community, the University of Kentucky College of Medicine Rural Physician Leadership Program formed a partnership with a local addiction treatment center. Once a month, one third- or fourth-year medical student researches and prepares a 1-hour lecture on a topic related to SUDs. The student then delivers this presentation to and interacts with a group of approximately 100 men at the addiction treatment center. The goals are that students will develop positive impressions of individuals with SUDs as well as a deeper understanding of issues that affect this patient population. Students were given a pre- and post-intervention questionnaire (Modified Perceived Stigmatization Questionnaire) as well as reflective questions in order to assess for changes in attitude towards individuals with SUDs. Preliminary data indicates that students developed a more positive attitude towards this population after the experience.

Supported by: None

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Poster Presentation 229

Abstract Title:	**Endobronchial Ultrasound with Transbronchial Needle Aspiration in the Diagnosis of Thoracic Diseases; A Single Center Experience**
Author(s):	D. Harris, College of Medicine, University of Kentucky, Lexington, KY, S. Saha, Department of Surgery, Division of Cardiothoracic Surgery, University of Kentucky, Lexington, KY

Abstract: Purpose: Historically mediastinoscopy has been the gold standard for lung cancer diagnosis and staging, but mediastinoscopy has many limitations including: sensitivity, limited number of lymph node levels that can be sampled, and safety. Endobronchial ultrasound with real-time guided transbronchial needle aspiration (EBUS-TBNA) is a relatively new and less invasive technique being used for lung cancer staging. Many studies have reported that EBUS-TBNA has similar sensitivity and specificity when compared to mediastinoscopy with a significantly lower complication rate. We preformed this review to determine our institutions experience with EBUS-TBNA in lung cancer diagnosis and staging. Methods: We reviewed the last 150 EBUS-TBNA procedures preformed at our institution from May 26, 2016 - August 31, 2017 for lung mass evaluation. Results: We reviewed the charts of 150 patients. Ninety-seven of the 150 patients had a confirmed diagnosis of malignancy. Forty patients had a diagnosis other than cancer, and 13 patients had incomplete information or were lost to follow-up. EBUS-TBNA was correct in diagnosing malignancy or excluding malignant lymph nodes in 92 of the patients with malignancy. Over all the sensitivity, specificity, positive predictive value, and negative predictive values of EBUS where 94.0, 100.0, 100.0 and 91.5 percent respectively. Only three complications were reported intraoperative or at the first follow-up appointment. Two patients suffered minor bleeding, and one suffered major bleeding that resulted in cardiac arrest. Conclusions: EBUS-TBNA has a similar sensitivity and specificity to mediastinoscopy, with fewer complications. Because of its reliability, cost effectiveness, and safety, EBUS-TBNA is gradually replacing mediastinoscopy.

Supported by: The project described was supported by the National Center for Advancing Translational Sciences, UL1TR001998,and the Dean of the College of Medicine, University of Kentucky. The content is solely the responsibility of the authors and does not necessarily

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Abstracts

Poster Presentation 230

Abstract Title:	**Lateral Axillary Exposure for Antegrade Access during Endovascular Repair of Complex Abdominal Aortic, and Thoracoabdominal Aneurysms**
Author(s):	Jeremy Miller, Medical Student, U of Kentucky Roberto Aru, MD, General Surgery Resident, U of Kentucky Michael Bounds, MD, Department of Vascular Surgery, U of Kentucky Nathan Orr, MD, Department of Vascular Surgery, U of Kentucky David Minion, MD, Department of Vascular Surgery, U of Kentucky Sam Tyagi, MD, Department of Vascular Surgery, U of Kentucky

Abstract: Radial, brachial, and axillary approaches for device delivery for the treatment of complex Abdominal Aortic Aneurysms (AAA) and Throacoabdominal Aortic Aneurysm (TAAA) have been described, but there remains a paucity of literature on the efficacy and safety of such approaches. Our approach has been a lateral axillary exposure (LAE) with direct multiple sheath access for antegrade delivery of devices followed by primary closure of the axillary artery. The aim of this study is to describe our technique and report our results of this approach. This study is a retrospective review of fifty-three patients who were treated with parallel grafts for endovascular repair of complex AAA and TAAA using stent grafts. The axillary artery was exposed with a vertical axillary skin incision and retraction of the lateral border of the pectoralis major to expose the axillary artery distal to the pectoralis minor. Multiple 5 through 12-French sheaths were used to directly access the axillary artery for delivery of endovascular devices. The aortic repairs requiring LAE included: 9 cases of endoleaks from prior endovascular repair, 24 para-renal AAAs, and 20 TAAAs. LAE was used to delivery 151 stents from 114 axillary sheaths into 114 arteries with 100% technical success. There were two postoperative complications: one hematoma treated conservatively with observation (1.9%), one left brachial vein DVT treated with anticoagulation (1.9%). There were no peripheral neurologic, cerebrovascular, arm ischemic complications, and no need for access related reoperation. LAE is a safe and effective technique to deliver endovascular devices in the repair of complex AAA and TAAA. LAE provides antegrade access for the simultaneous delivery of multiple renovisceral devices without neurologic or ischemic complications without the use of prosthetic conduits or tunneling.

Supported by:	The project described was supported by the National Center for Research Resources and the National Center for Advancing Translational Sciences, National Institutes of Health, through Grant UL1TR001998. The content is solely the responsibility of the autho

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Poster Presentation 231

Abstract Title:	**Sustained Bupivacaine Analgesia Following Facial Reconstructive Surgery: A Study of Release Kinetics and Injectability of an In situ Forming Implant (ISI)**
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Abstract: Introduction: Post-operative analgesia for facial reconstructive surgery often relies on opioids. The heightened risk for dependence and other adverse outcomes suggests a need for an alternative method of analgesia. The purpose of this study is to formulate a sustained-release In situ forming implant (ISI) that will provide a prolonged nerve block with the use of the local anesthetic bupivacaine. Methods: A drug delivery system was synthesized with drug-loaded poly(β-amino ester) (PBAE) microparticles inside in situ forming poly (lactic-co-glycolic acid) (PLGA). Release kinetics of different combinations of PBAE macromer were compared to calculate bupivacaine concentration at several time points. A compression apparatus was used to calculate time needed to inject 0.5mL of the different ISIs at various applications of force with different needle gauges available in the operating room. Results: The ISI made with AH6 3:1 PBAE microparticles demonstrated release kinetics most closely approaching the goal, maintaining a steady release of ~115 hours (goal 168 hours), though release plateau was less than the therapeutic dose (<0.15mg/ml). This ISI also demonstrated the most promising injection profile, overall requiring the least time to inject 0.5mL at 25N with a 20G needle. Conclusion: An ISI made with AH6 3:1 PBAE microparticles demonstrated improved release kinetics compared to those previously described in the literature and had a promising injection profile. Further studies are warranted to demonstrate sustained release of bupivacaine at therapeutic concentration and with smaller needle gauges.

Supported by: National Science Foundation REU Program, University of Kentucky (#1757354)

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Poster Presentation 232

Abstract Title:	**The Contribution of Specific Enhanced Recovery After Surgery (ERAS) Protocol Elements to Reduced Length of Hospital Stay After Ventral Hernia Repair**
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Abstract: Introduction: VHR is a commonly-performed procedure that may be associated with prolonged hospitalization. ERAS protocols are intended to decrease hospital LOS. This study aims to evaluate the impact of compliance with individual VHR ERAS protocol elements on LOS. Methods: With IRB approval, medical record review was conducted for consecutive cases of open VHR performed between August 2013 and July 2017, with ERAS protocol implementation in August 2015. Clinical predictors of LOS were determined through forward regression of log-transformed LOS. The effects of specific ERAS elements on LOS were assessed after adjusting for clinical predictors. Results: 234 patients underwent VHR (109 ERAS, 125 pre-ERAS). Across all patients, the geometric mean LOS was 4.8 days (95% CI 4.5 – 5.1). Independent predictors (p's < .05) of increased LOS were CDC Wound Class III or IV, COPD, prior infected mesh, concomitant procedure, mesh size, and age. ERAS implementation was associated with a 15% or 0.7 day (95% CI 6% – 24%) reduction in mean LOS after adjustment. ERAS element compliance associated with reduced LOS are shown in the Table. Compliance with acceleration of intestinal recovery was low (25.6%) as many patients were not eligible for alvimopan due to preoperative opioids, yet when achieved, provided the greatest reduction in LOS (-37%). Conclusions: Implementation of a VHR ERAS protocol results in decreased LOS. Evaluation of the impact of specific ERAS element compliance to LOS is unique to this study. Compliance with acceleration of intestinal recovery, early postoperative mobilization, and multimodal pain management provided the greatest LOS reduction.

Supported by: CCTS PSMRF Medical Student Research Award, 2018 SAGES Medical Student Research Award, 2019

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Poster Presentation 233

Abstract Title:	**Management of Enteroatmospheric Fistulae Using Patient-matched 3D-printed Devices**
Author(s):	J. W. Warwick, College of Medicine, U of Kentucky A. C. Bernard, Trauma and Acute Care Surgery, U of Kentucky

Abstract: Background: An enteroatmosperic fistula (EAF) is an abnormal connection between the intestinal lumen and the outside environment. EAFs typically arise in the setting of open abdomen surgery (OA), and greatly complicate patient care. No optimal approach to EAF/OA wound care exists. Current techniques such as Negative Pressure Wound Therapy (NPWT) are extremely labor intensive, restrict patient mobility, and can be very expensive, often limiting outpatient management. As the wound management interval for EAF/OA patients can persist for 6-12 months, EAFs place a significant burden on the healthcare providers and can severely impact patient quality of life. Therefore, we sought to develop an easier, less intensive alternative that patients could potentially use to manage their EAF/OA wound at home. Methods: This study investigates the efficacy of a 3D-printed device to isolate fistula effluent and manage EAF wound care. The device acts as a shunt, diverting intestinal contents away from the OA wound bed and into an ostomy bag, independent of NPWT. Results: Data points will include dressing change frequency and duration, supplies used, patient comfort, and mobility. Study participant and provider (nurse) experiences using the device will be evaluated using a modified technology acceptance model (TAM). This data will be collected as a compilation of (5) individual case studies over the next 6-8 months. Discussion: This device is being studied under an abbreviated investigational device exemption (IDE) and is not currently approved for commercial use. Results will be analyzed to determine if this device can offer an effective, affordable, and simple solution to EAF/OA wound management.

Supported by: UK CCTS PSMRF

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Poster Presentation 234

Abstract Title:	**Comparison of In-Person Versus Telemedicine Cochlear Implant Evaluation: A Pilot Study**
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Abstract: Objectives: Cochlear implantation delays have been correlated to distance from the CI center. Telemedicine could connect CI specialists with patients in remote locations to address this issue. The objective of this study is to assess the feasibility, acceptability, and dependability of remote cochlear implantation candidacy evaluations. Methods: A prospective, randomized study was conducted at the University of Kentucky between August 2015 and January 2018. Three groups were examined: normal hearing volunteers, hearing aid candidates, and cochlear implant candidates. The CI evaluation was performed twice in succession: in-person (traditional booth conditions) and using teleaudiology technology (OTOsphere® comprehensive remote audiology setup). Testing involved routine audiometry, word recognition testing, AzBio and CNC testing. Subjects served as their own controls. Primary outcome was percent difference in AzBio between methods and we hypothesized that we would find a less than 5% mean difference. RESULTS: Thirteen subjects were tested. Mean percent difference in AzBio between in-person and remote testing was 1.6% (±2.06%). PTA, SRT, word recognition and CNC testing was similar between methods. Testing conditions were acceptable to audiologists and subjects. CONCLUSION: This pilot study displays that remote cochlear implant evaluations using telemedicine technology are feasible to perform without loss of fidelity compared to in-person evaluation. Further study to validate this method in a larger population is warranted.

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Poster Presentation 235

Abstract Title:	**Variation in the Quality of Thyroid Nodule Evaluation Prior to Surgical Referral**
Author(s):	Lan Jiang BS, College of Medicine, University of Kentucky Cortney Y. Lee MD, Department of General Surgery, University of Kentucky David A. Sloan MD, Department of General Surgery, University of Kentucky Reese W. Randle MD, Department of General Surgery, University of Kentucky

Abstract: Background: Thyroid nodules are highly prevalent, and due to their malignant potential, proper evaluation is imperative. The objective of this study was to characterize variation in thyroid nodule evaluations. Materials and Methods: This retrospective review included all consecutive surgical referrals for thyroid nodules from October to December 2017 at a single institution. We determined the proportion of evaluations that contained a thyroid-stimulating hormone (TSH) level and a high-quality ultrasound, because these components of thyroid nodule evaluations are common to several evidence-based guidelines. Results: The study cohort included 64 patients, with a median age of 51.5 years. Primary care providers referred most patients (51.6%), followed by endocrinologists (40.6%), and other specialists (7.8%). In total, 35.9% of evaluations did not include a TSH value, which is vital to any thyroid nodule evaluation. The majority of evaluations (95.3%) included a dedicated ultrasound, but only 12.3% of ultrasound reports commented on nodule size in 3-dimensions, structure, echogenicity, and lymph nodes, which we considered the minimum commentary indicative of a high-quality ultrasound. Only 51.5% of evaluations included a TSH and appropriate imaging. If patients receiving low-quality ultrasound reports were excluded, 9.4% of the entire cohort received a guideline-concordant, high-quality evaluation. Conclusions: Great variation exists in the quality of thyroid nodule evaluations prior to surgical referral. Two necessary components of thyroid nodule evaluations that contribute most to the observed deviation from guidelines are obtaining a TSH value and obtaining an ultrasound with enough information to risk stratify the nodule.

Supported by:	"The project described was supported by the National Center for Research Resources and the National Center for Advancing Translational Sciences, National Institutes of Health, through Grant UL1TR001998. The content is solely the responsibility of the auth

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Poster Presentation 236

Abstract Title:	**Discrepancies in Adrenal Tumor Size Measured on Preoperative Imaging and Surgical Specimens and Implications for Outcomes and Management**
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Abstract: Background: Tumor size plays a major role in the recommended treatment approach for adrenal incidentalomas. We hypothesized that cross sectional imaging underestimates pathologic size for adrenal tumors and aimed to evaluate the ability of CT to accurately predict tumor size. Methods: We reviewed 114 consecutive adrenalectomies performed between 6/1/2011 and 5/31/2018 at a single institution. We excluded tumors >10cm, cases without preoperative CT imaging, and those without accurate pathologic tumor measurements. A single abdominal radiologist independently reviewed all images and provided measurements of the adrenal mass in axial, coronal, and sagittal planes. Adrenal sizes noted on the original radiology report were recorded. Results: 75 patients formed the final cohort. The mean tumor size noted on final pathology was 4.4cm. The greatest CT diameter overestimated the final tumor size in 61.3% (n=46) and underestimated the final tumor size in 34.7% (n=26) with an average variation between the two measurements of 0.8cm. The longest CT diameter was most often measured in the axial plane (44%), followed by the sagittal plane (33.3%), and the coronal plane (26.7%). While the largest CT diameter overestimated the final specimen size (mean 4.7 +/- 1.7cm vs 4.4 +/- 2.0cm, p=0.02), the tumor diameter in the sagittal plane generally provided an accurate approximation of the final specimen size (4.4 +/- 2.0cm vs 4.4 +/- 1.7cm, p=0.96). Of the 44 cases with available original radiology, the mean size noted on the report was significantly less than the largest mean size identified on independent review (4.2 +/- 1.7cm vs 4.6 +/- 1.7cm, p<0.001).

Supported by:	The project described was supported by the National Center for Research Resources and the National Center for Advancing Translational Sciences, National Institutes of Health, through Grant UL1TR001998. The content is solely the responsibility of the autho

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Poster Presentation 237

Abstract Title:	**Identifying Barriers to the Surgical Treatment of Colon Cancer in Appalachian Kentuckians**
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Abstract: Background: Kentucky has the highest incidence of cancer in the country, and it ranks highest in the incidence of colon cancer (49.4 per 100,000, compared to nationwide at 38.4 per 100,000). [1] Appalachian Kentuckians also have a higher mortality from colon cancers, compared to non-Appalachian populations. [2] However, colon cancers are treatable with surgical intervention, which offers the greatest likelihood of survival if identified early. Advanced cancers become less amenable to surgical options and are associated with low 5-year survival rates. There are significant health disparities for people living in Appalachia. Notable barriers to surgical care in low-resourced environments include financial constraints, environmental delays, lack of knowledge about the implications of disease and treatment options. [3] The barriers faced by this community to surgical care is unknown. Methods and Expected Results: To better understand the barriers to surgical treatment faced by Appalachian Kentuckians with colon cancer, an exploratory mixed methods approach will be used in this study. Focus groups will be conducted to generate an index of barriers to surgical care. The focus groups will be conducted in Morehead and Hazard, Kentucky. The index will be developed into a questionnaire and administered to Appalachian Kentuckians with resectable colon cancer to understand the barriers from a quantitative perspective. Career Development: Through the course of this study, I will develop an understanding of the application of key research methodologies (focus groups and surveys) in health equity research.

Supported by:	This project is supported by the CCTS Small Grants. Dr. Madabhushi is supported by University of Kentucky, Center for Clinical and Translational Science TL1 Grant (NIH: TL1TR001997)

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Poster Presentation 238

Abstract Title:	**Comparing effects of CDK inhibition and E2F1/2 ablation on neuronal cell death pathways in vitro and after traumatic brain injury**
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Abstract: Traumatic brain injury (TBI) activates multiple neuronal cell death mechanisms, leading to post-traumatic neuronal loss and neurological deficits. TBI-induced cell cycle activation (CCA) in post-mitotic neurons causes regulated cell death involving cyclin-dependent kinase (CDK) activation and initiation of an E2F transcription factor-mediated pro-apoptotic program. Here we examine the mechanisms of CCA-dependent neuronal apoptosis in primary neurons in vitro and in mice exposed to controlled cortical impact (CCI). In contrast to our prior work demonstrating neuroprotective effects by CDK inhibitors after TBI, examination of neuronal apoptotic mechanisms in E2F1-/-/E2F2-/- or E2F2-/- transgenic mice following CCI suggests that E2F1 and/or E2F2 likely play only a modest role in neuronal cell loss after brain trauma. To elucidate more critical CCA molecular pathways involved in post-traumatic neuronal cell death, we investigated the neuroprotective effects and mechanisms of the potent CDK inhibitor CR8 in a DNA damage model of cell death in primary cortical neurons. CR8 treatment significantly reduced caspase activation and cleavage of caspase substrates, attenuating neuronal cell death. CR8 neuroprotective effects appeared to reflect inhibition of multiple pathways converging on the mitochondrion, including injury-induced elevation of pro-apoptotic Bcl-2 homology region 3 (BH3)-only proteins Puma and Noxa, thereby attenuating mitochondrial permeabilization and release of cytochrome c and AIF, with reduction of both caspase-dependent and -independent apoptosis. CR8 administration also limited injury-induced deficits in mitochondrial respiration. These neuroprotective effects may be explained by CR8-mediated inhibition of key upstream injury responses, including attenuation of c-Jun phosphorylation/activation as well as inhibition of p53 transactivation of BH3-only targets.

Supported by: NIH award: 4R01NS052568-10 ROLE OF CELL CYCLE PATHWAYS IN TRAUMATIC BRAIN INJURY (TBI)

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Poster Presentation 239

Abstract Title:	**Phenelzine, Pargyline, and Hydralazine: The effects of Lipid Peroxidation-Derived Aldehyde Scavenging and Monoamine Oxidase Inhibition on Learning and Memory and Cortical Tissue Sparing Following Experimental TBI**
Author(s):	J. R. Kulbe, Department of Neuroscience and Spinal Cord and Brain Injury Research Center, U of Kentucky J. A. Dunkerson, Department of Neuroscience and Spinal Cord and Brain Injury Research Center, U of Kentucky P. F. Huettl, Department of Neuroscience and Center for Microelectrode Technology, U of Kentucky J. A. Wang, Spinal Cord and Brain Injury Research Center, U of Kentucky R. Smith, Spinal Cord and Brain Injury Research Center, U of Kentucky E. D. Hall, Department of Neuroscience and Spinal Cord and Brain Injury Research Center, U of Kentucky

Abstract: In the US, over 5 million people suffer from a traumatic brain injury (TBI)-related disability. There are no neuroprotective FDA-approved pharmacotherapies for TBI. Lipid peroxidation-derived neurotoxic aldehydes contribute to neuronal death and neurologic dysfunction after TBI. Phenelzine (PZ) contains a hydrazine moiety capable of scavenging aldehydes. Therefore, PZ can improve mitochondrial bioenergetics and reduce aldehyde load following experimental TBI. However, PZ is an FDA-approved monoamine oxidase inhibitor (MAOI)-class anti-depressant and the effect MAO inhibition has on TBI is unknown. The goal of this study was to compare the ability of PZ (aldehyde scavenger, MAOI), hydralazine (HZ, aldehyde scavenger, non-MAOI) and pargyline (PG, non-aldehyde scavenger, MAOI) to improve learning and memory and cortical tissue sparing following severe CCI in 3mo male Sprague-Dawley rats. PZ (15mg/kg), HZ (5mg/kg), PG (15mg/kg), or vehicle (saline) were administered intraperitoneal 15min, 24h, and 48h post-CCI. Morris Water Maze (MWM) was conducted post-injury D3-7. Animals were euthanized and perfused post-CCI D8. The same dosing paradigm was utilized in uninjured animals and cortical tissue was sent for HPLC analysis of monoamines and their metabolites. The results indicate that neither PZ, HZ, nor PG improved CCI-induced deficits to retention memory or cortical tissue sparing. However, HZ performed the best, improving cortical tissue sparing compared to vehicle by 10%. Concerningly, PZ was the only group to not show significant improvement during the MWM acquisition phase, and lost significantly more weight than all other groups, possibly due to an increase in norepinephrine or serotonin as was seen in uninjured cortical tissue.

Supported by: NIH-NINDS 5R01 NS083405, 5R01 NS084857, and NRSA F30 NS096876.

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Poster Presentation 240

Abstract Title: **Aged astrocytes maladaptively contribute to the neuroinflammatory milieu following TBI**

Author(s): J. M. Morganti, Sanders-Brown Center on Aging and Deptarment of Neuroscience, U of Kentucky

Abstract: Advanced aging is one of the most powerful predictors for the incidence and vulnerability to a traumatic brain injury (TBI). Problematically, aged survivors of TBI are almost 40% more likely to develop progressive neurodegenerative disorders compared to young. Moreover, aged survivors of TBI exhibit significant impairments in functional recovery as well as increased comorbidities following TBI. Despite the increased risk and poorer outcomes, strikingly little is known about how TBI differentially affects the brain in the aged, compared to young. In the current study, we examined how and when aged astrocytes differ from young astrocytes following TBI as a function of neuroinflammatory gene expression and time after injury. TBI was reproduced using the focal controlled cortical impact method on young (3m) and aged (18m) C57BL6 mice. Three post-injury intervals spanned acute and subacute injury timeframes (1, 3, and 7 days). At the prescribed interval, astrocytes were isolated from the injured brain parenchyma. RNA from enriched astrocytes was analyzed using gene arrays to model the multivariate inflammatory response as a function of age and post-injury interval. In parallel cohort of mice, we quantified glial reactivity at these time points using standard immunohistochemistry techniques. Our results indicate that aged astrocytes exhibit an exaggerated neuroinflammatory response to TBI, compared to young astrocytes.

Supported by: The project described was supported by the National Institute on Aging, through R21AG058006, and National Center for Research Resources and the National Center for Advancing Translational Sciences, National Institutes of Health, through Grant UL1TR001998.

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Poster Presentation 241

Abstract Title:	**Informing Ethical Research: Understanding Experiences of Trauma-Exposed Research Participants**
Author(s):	M. Berexa, Department of Psychology, U of Kentucky A. C. Jones, Department of Psychology, U of Kentucky C. L. Badour, Department of Psychology, U of Kentucky

Abstract: Research on the safety and psychological well-being of participants engaging in trauma-related research is critical. Existing research, which is limited primarily to the use of questionnaires and interviews, indicates that participant experiences are often positive. The present study examined participant reactions to a trauma-related challenge study in the laboratory. 54 adult women (Mage=35.78, SD=13.73) with a history of interpersonal violence (IPV) completed questionnaires and a diagnostic interview for posttraumatic stress disorder (PTSD). Session 2 involved an imagery task; participants recalled the details of a neutral life event or an IPV event out loud for 5 minutes. The recording was played for participants to listen to. Following two weeks of daily assessments, participants provided feedback about whether they enjoyed participating (ENJOY), would recommend the study to a friend (FRIEND), and were glad they participated (GLAD). Questions were rated on a scale of 0 (Not at all) to 5 (Very much so). Overall, participants highly rated all outcomes (ENJOY: M=3.91, SD=1.09; FRIEND: M=4.24, SD=0.91; GLAD: M=4.57, SD=0.74). There were no differences in ratings as a function of condition, PTSD symptom severity or by the condition by PTSD symptom interaction, suggesting that participants viewed the study positively regardless of PTSD symptom severity or condition. Findings indicate that the study was not a negative experience for participants; they were overall glad to have participated. Results were not different for those with elevated PTSD symptoms or in the trauma condition. These findings are important in light of concerns about the safety of trauma-related research.

Supported by:	The project was supported by the National Center for Advancing Translational Sciences, National Institutes of Health, through Grant UL1TR001998. The content is solely the responsibility of the authors and does not necessarily represent the official views

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