

CCTS Poster Presentation Abstracts

25 Abstract Title: **Assessing the Relationship between Sports Participation and Self-Esteem among Middle-School Students**

Author(s): E.A. Whitney, College of Education, Dept. of Kinesiology & Health Promotion, U of Kentucky
M. Kidd, College of Education, Dept. of Kinesiology & Health Promotion, U of Kentucky

Abstract: Adolescents experience many changes physically, emotionally, and socially as they transition from youth to adulthood. Participation in extracurricular activities (EAP) has been shown to provide a positive outlet for self-discovery, as well as promote self-esteem during this developmental period. EAP has also previously been associated with lower dropout rates, problem behaviors, and improved social skills among adolescents. Finally, EAP can aid and promote self-esteem in adolescents. Given this background, the purpose of this study was to analyze the relationship between participation in school or community sponsored sports as one facet of EAP and self-esteem in early adolescence. Data were collected from N = 35 middle-school students ranging in age from 12-14 years old. Ironically, the results of this study revealed there to be no significant relationship between adolescents who participate in sports (school or community) and self-esteem. The limitations of this study will be discussed.

Supported by:

Primary Presenter / email: **Kidd, M.** / mldi226@uky.edu
Basic Science
Behavior

Mentor / e-mail: Whitney, E.A. / liz.fettrow@uky.edu



CCTS Poster Presentation Abstracts

26 Abstract Title: **Impact Evaluation of 'College CHEF,' a Campus-based, Culinary Nutrition Education Program**

Author(s): J. McMullen, Department of Kinesiology and Health Promotion, U of Kentucky
M.J. Ickes, Department of Kinesiology and Health Promotion, U of Kentucky

Abstract: Objective: Evaluate the impact of the College CHEF program, a campus-based culinary nutrition education program, to determine if there were significant differences from pre- to post-intervention with participants' attitudes, behaviors, self-efficacy, and knowledge as they pertained to healthy eating and cooking. Participants: College students who were members of various campus-based Living Learning Programs (LLPs) who completed the pre- and -post- measures comprised the control group (N = 17) and those who completed the measures and attended three or more sessions made up the intervention group (N = 15). Methods: Programming consisted of four 2-hour sessions held weekly over the course of a month. Participants were actively engaged in nutrition education and hands-on cooking classes. The study was quasi-experimental pre-, post- design with surveys administered to both groups at baseline and -post- intervention. Results: Intervention participants reported significant improvements as compared to the control group for the following subscales: Fruit and Vegetable Consumption ($p = 0.001$), Self-Efficacy for using Fruits, Vegetables, and Seasonings ($p = 0.015$), and Knowledge of Cooking Terms and Techniques ($p = 0.000$). Conclusions: Campus-based, culinary nutrition education programming has the potential to impact college students' self-efficacy for using fruits and vegetables, fruit and vegetable consumption, and cooking knowledge. Future research should incorporate additional strategies to further improve outcomes, such as through operationalization of social cognitive theory constructs, and should include follow-up measures to determine the long-term impact and sustainability of programming.

Supported by:

Primary Presenter / email: **McMullen, J.** / jennifer.e.mcmullen@uky.edu
Basic Science
Behavior

Mentor / e-mail: Ickes, M.J. / melinda.ickes@uky.edu



CCTS Poster Presentation Abstracts

27 Abstract Title: **Doing the Most Good: Promoting Healthy Eating among Central Kentucky's Youth**
Author(s): E. A. Whitney, Department of Kinesiology & Health Promotion, U of Kentucky

Abstract: Afterschool and summer programs, either affiliated through the school or community, have been demonstrated to improve the lives of children and families. Studies have continuously shown that such programs can improve social and behavioral outcomes, bolster academic performance (in the form of test scores and grades in school), and increase school attendance. In addition to these benefits, these programs have the potential to support health outcomes of children and youth. With regard to promoting healthy eating, evidence-based nutrition education is one pathway to improving the knowledge and eating habits of children. While schools remain a critical focal point for introducing and reinforcing health habits of youth, a considerable number of youth attend afterschool and summer programs in their communities. Thus, community agencies are uniquely positioned to provide programming for children/adolescents to improve health outcomes. Children ages 8 – 11 at one community agency in Central Kentucky participated in a nutrition education program on two days per week during a four-week period during the summer. Pre and post-test data were collected from participants prior to and after the program, and measured participants knowledge and behaviors related to healthy eating. Results revealed some statistically significant differences on the study outcomes. Limitations will be discussed.

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Primary Presenter / email: **Whitney, E. A.** / liz.fettrow@uky.edu
Basic Science
Behavior

Mentor / e-mail: Whitney, E.A. / liz.fettrow@uky.edu



CCTS Poster Presentation Abstracts

28 Abstract Title:	Neuroimaging correlates of sensation-seeking and disinhibition in healthy subjects
Author(s):	H. S. Chaudhry, U of Kentucky D. K. Powell, Department of Anatomy and Neurobiology, U of Kentucky T. H. Kelly, Department of Behavioral Science, U of Kentucky

Abstract: Background: Impulsivity, a multidimensional biologically-based construct associated with drug use, serves as an effective targeting variable to improve prevention interventions. White matter structure is altered in drug dependent subjects and among healthy impulsive subjects. However, the differential effects of dimensions of impulsivity, such as disinhibition (Dis) and sensation seeking (SS), have not been explored. In this study, we used diffusion tensor imaging (DTI) and diffusion kurtosis imaging (DKI) to examine the associations between these dimensions and white matter structure. Methods: 40 healthy young adults were recruited based on Dis and SS scores on the Zuckerman-Kuhlman Personality Questionnaire (ZKPQ). Diffusion-weighted MRI scans of these subjects underwent voxel-wise analysis of fractional anisotropy (FA), mean diffusivity (MD), and mean kurtosis (MK) via tract-based spatial statistics (TBSS). These measures were then correlated with SS and Dis scores on the ZKPQ. Results: TBSS revealed a positive correlation between SS on the ZKPQ and FA in multiple white matter tracts, including the right cingulum, bilateral inferior fronto-occipital fasciculus (IFOF), bilateral inferior longitudinal fasciculus and right superior longitudinal fasciculus (SLF). Disinhibition was positively correlated with FA in the right SLF. Conclusions: In individuals without substance abuse history, SS is associated with sensitivity to the reinforcing effects of both novelty and stimulant drugs. In this study, SS was associated with right cingulum structure, suggestive of increased integrity of limbic and memory-associated connections within the brain, and bilateral IFOF, suggestive of more robust integration of auditory and visual association cortices with prefrontal regions of the brain. These findings suggest biologically-based mechanisms by which SS may be linked to drug and novel stimulus reinforcement.

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Primary Presenter / email:	Chaudhry, H.S. / hsch222@uky.edu Basic Science Behavior
Mentor / e-mail:	Powell, D.K. / david.k.powell@uky.edu



CCTS Poster Presentation Abstracts

29 Abstract	Cerebrovascular Disease Risk Factors and Arteriolar Sclerosis in the Kentucky Appalachian 'Stroke-belt.'
Title:	
Author(s):	O.M. Al-Janabi, Dept. of Behavioral Sciences & Sanders-Brown Center on Aging, U of Kentucky A.A. Bahrani, Dept. of Biomedical Engineering, U of Kentucky E.L. Abner, Sanders-Brown Center on Aging & Dept. of Epidemiology, U of Kentucky C.D. Smith, Dept. of Neurology, U of Kentucky P.T. Nelson, Sanders-Brown Center on Aging & Dept. of Pathology, Div. of Neuropathology, U of Kentucky D. Moser, College of Nursing, U of Kentucky G.A. Jicha, Depts. of Neurology & Behavioral Sciences & Sanders-Brown Center on Aging, U of Kentucky

Abstract: Background: The relationship between cerebrovascular disease (CVD) risk factors and arteriolar sclerosis has been widely studied with significant variability in finding among groups. We hypothesized that chronic small vessel injury in the form of arteriolar sclerosis, measured quantitatively using MRI T2 volumetric to measure total white matter hyperintensity (WMH) volumes, will identify specific CVD risk factors responsible for the development of cerebral arteriolar sclerotic changes in our Kentucky "stroke-belt" population. Methods: A Cross-sectional analysis of clinical and quantitative MRI data on 114 subjects with normal cognitive function (n=52) and mild cognitive impairment (MCI; n=62) was performed. Quantitative total WMH volumes were examined in relation to potentially causative CVD risk factors using linear regression models adjusted for age, education, and gender. Results: Among CVD risk factors analyzed, age ($p < 0.001$), education ($p = 0.003$), hypertension ($p = 0.012$), and hyperlipidemia ($p = 0.008$) demonstrated the strongest associations with WMH volumes. Conversely, CVD risk factors such as a history of diabetes, smoking, heart attacks, atrial fibrillation, and stroke that have shown associations with CVD pathology on imaging in other studies were not statistically associated with increased WMH in this cohort. Conclusion: Our findings suggest similarities and yet differences in the impact of CVD risks on the development of CVD pathology measured by WMH on MRI. Hypertension and hyperlipidemia appear to represent common shared risks across geographically disparate groups.

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Primary Presenter / email: **Al-Janabi, O.M.** / omar.aljanabi@uky.edu
Clinical Science
Behavior

Mentor / e-mail: Jicha, G.A. / gregory.jicha@uky.edu



CCTS Poster Presentation Abstracts

30 Abstract Title: **Distinguishing Motives of Physical Activity in Military Conditioning Courses**

Author(s): L. Buenrostro, Department of Kinesiology & Health Promotion, U of Kentucky
 R. LaCoe, Department of Kinesiology & Health Promotion, U of Kentucky
 J. Pedescleaux, Department of Kinesiology & Health Promotion, U of Kentucky

Abstract: Developing an understanding of motivational factors is essential for understanding the physical activity practices of college students in the Reserve Officer Training Corps (ROTC). Purpose: This study was designed to determine the motivational factors influencing the participation of college-aged men and women enrolled in ROTC lead military conditioning classes. We hypothesized that 1) the highest motivation in males and females would be fitness, 2) there would be no differences when comparing the mean scores by sex, and 3) there would be no difference when comparing motives between classifications (sophomore, senior, etc.). Methods: Male (n=51) and female (n=14) ROTC students, 20.34 ±2.35 yrs., enrolled in a military conditioning course were invited to participate. The Motives for Physical Activities Measure-Revised (MPAM-R) questionnaire was used to assess the strength of five motives for participation in physical activities; (1) Fitness, (2) Appearance, (3) Competence, (4) Social, and (5) Interest. A one-way ANOVA was used to determine differences in motives by grade classification, and an independent samples t-test was used to determine the difference in motives by sex. Results: Our data showed that the highest mean score motive for males (5.98 ±0.88) and females (5.76 ±1.47) was fitness. There were no differences when comparing motives between sex and classification. However, junior females highest mean score (6.08 ±0.57) was appearance. Conclusion: Our analysis suggested that the main motive for ROTC student's participation was fitness. Fitness is an important aspect of ROTC conditioning that prepares cadets for the physical rigors of military service.

Supported by:

Primary Presenter / email: **Buenrostro, L.** / lbu233@g.uky.edu
Clinical Science
Behavior

Mentor / e-mail: Pedescleaux, J. & LaCoe, R. / jonell.pedescleaux@uky.edu



CCTS Poster Presentation Abstracts

31 Abstract Title: **Affordable Care Act: Changes in insurance coverage and service utilization among high-risk female injection users who are HCV positive**

Author(s): B. Douglas, College of Social Work, U of Kentucky
M. Staton-Tindall, College of Social Work, U of Kentucky

Abstract: Background and Purpose: In October, 2013, the Affordable Care Act (ACA) was established and open enrollment began. This policy established healthcare insurance eligibility to low income citizens. ACA had particularly important implications for increasing access to healthcare for Americans living in rural communities, particularly those diagnosed with chronic diseases who were unable to receive treatment services because of insurance coverage status. The proposed study examines insurance coverage before and after ACA implementation among a sample of high risk rural women drug users in Appalachia. Specific research questions include: 1) Did ACA lead to increased health insurance coverage among high-risk rural women drug users? 2) Were there changes in utilization of medical services for individuals testing positive for HCV among high risk-rural women drug users after ACA implementation? Methods: This study involved random selection, screening, and face-to-face baseline interviews with 400 women in rural jails in one Appalachian state. Follow-up interviews were conducted 3 months post-release. Analysis will focus on insurance coverage during the 3-month follow-up occurring before ACA (before January 1, 2014) and or after ACA implementation (after January 1, 2014). Results: Preliminary findings indicated that a significantly higher proportion of rural women reported having insurance coverage after the initiation of ACA open enrollment (31.1% vs. 2.6%, $p < 0.001$). Multivariate models showed that having health insurance was a robust predictor of service utilization in the follow-up period, along with days experiencing illness. Conclusions: Findings will be discussed with specific attention to intervention development for increasing access to insurance and health care for high-risk rural women.

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Primary Presenter / email: **Douglas, B.** / breonna.douglas@uky.edu
Clinical Science
Behavior

Mentor / e-mail: Tindall, M. / mstindall@uky.edu



CCTS Poster Presentation Abstracts

32 Abstract Title: **The relationship between drug use and happiness among high- risk female inmates in Appalachia**

Author(s): K. Frost, College of social Work, University of Kentucky
M. Tindall, College of Social Work, University of Kentucky

Abstract: Background and purpose: Research suggests the search for happiness is among the top reasons individuals report for initially using drugs, as well as continually using. Drug use gives short term effects of euphoria and happiness, while continual drug abuse can lead to feelings of shame and vulnerability. There is limited research among drug users on their overall perceptions of happiness – particularly among their lifestyle and culture in Appalachia. The proposed study examines happiness among a sample of high- risk rural female drug users, and its impact on their perceptions of success following community re-entry from jail. Methods: This study involved random selection, screening, and face- to- face baseline interviews with 400 women in rural jails in one Appalachian state. Analysis will focus on the relationship between drug use severity and subjective ratings of happiness, as well as how ratings of happiness are associated with perceptions of strengths at community re-entry. Conclusions: The search for happiness is one of the most important goals one has in life. Happiness adds quality to life, and gives meaning to everything we do. Happiness helps to focus on the positive aspects of oneself and allows overlooking the negatives. If findings from this study suggest that happiness is associated with re-entry strengths, there will be important implications for clinical translation for intervention development for rural women.

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Primary Presenter / email: **Frost, K.** / kathy.frost@uky.edu

Clinical Science

Behavior

Mentor / e-mail: Tindall, M.S. / mstindall@uky.edu



CCTS Poster Presentation Abstracts

33 Abstract Title: **Impulsive Behavior as a Predictor of Outcomes for Adolescents Enrolled in an Online Contingency Management Program for Smoking Cessation**

Author(s): A.M. Harvanko, Departments of Behavioral Science and Psychology, U of Kentucky
 J.C. Strickland, Department of Psychology, U of Kentucky
 B.A. Reynolds, Department of Behavioral Science and Markey Cancer Center, U of Kentucky

Abstract: Aim: The current study examined self-report and performance measures of impulsive behavior as predictors of online contingency management smoking cessation therapy outcomes among adolescents. Methods: Data from two adolescent online contingency management smoking cessation therapy studies were examined. Participants were randomized to either an active or control form of the therapy. Breath carbon monoxide (CO) levels were assessed 3x/day during five separate phases: baseline, shaping, abstinence, thinning, and return to baseline. Preceding and following contingency management therapy, impulsive behavior was assessed with the Barratt Impulsivity Scale, a measure of delay discounting, a continuous performance task, and a Go/Stop task. Outcomes of interest were reductions in breath CO by group (i.e. active and control condition) and reductions in CO as a function of impulsive behavior. Results: Compared to control condition, individuals in the active condition had significantly lower CO levels following baseline treatment phase. Mixed modeling analysis indicated that delay discounting was associated with a decrease in smoking and average treatment phase CO from baseline to return to baseline for participants in the active but not the control condition. No significant associations were found between the other measures of impulsive behavior and change in average treatment phase CO. Conclusions: Online contingency management therapy is effective in decreasing CO levels in adolescent smokers. Adolescents who discount less (i.e., who are less impulsive on this measure) have greater reductions in smoking and breath CO during contingency management therapy. Delay discounting may allow clinicians to tailor treatment recommendations for greater treatment efficacy.

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Primary Presenter / email: **Harvanko, A.M.** / Arit.H@uky.edu
Clinical Science
Behavior

Mentor / e-mail: Reynolds, B.A. / brady.reynolds@uky.edu



CCTS Poster Presentation Abstracts

34 Abstract Title: **Assessing Behavioral Problems in Children with Hearing Loss**

Author(s): V. Rashidi, College of Medicine, U of Kentucky
 C.E. Fiorillo, Department of Otolaryngology-Head & Neck Surgery, U of Kentucky
 J.A. Jacobs, Department of Health Behavior, U of Kentucky
 C.R. Studts, Department of Health Behavior, U of Kentucky
 M.L. Bush, Department of Otolaryngology-Head & Neck Surgery, U of Kentucky

Abstract: HYPOTHESIS: Observations from clinical practice and several studies suggest that children with hearing loss (HL) may be at risk for developing disruptive behavior problems. The hypothesis of this study was that preschool-aged children with HL have a higher prevalence of disruptive behavior problems than those with normal hearing (NH). PARTICIPANTS: Parents of children (ages 2-5 years) with HL using hearing aids or cochlear implants were recruited from the University of Kentucky Department of Otolaryngology and several partnering sites. Parents of same-aged children with NH were recruited as a comparison group. PROCEDURES: Eligible participants completed a one-time assessment session using a standardized parent-report behavioral assessment instrument (Child Behavior Checklist/1.5-5) and a set of questionnaires targeting related constructs, mental health history, and sociodemographic characteristics. RESULTS: 71 participants have been recruited to date (35 HL, 36 NH). When controlling for household income, children with HL have a higher prevalence of disruptive behavior problems (aOR=3.52, 95% CI=1.13-10.97) than NH children. Similarly, parents of children with HL had higher odds of subjectively reporting concerns about their child's behavior (aOR=4.62, 95% CI=1.22-17.48). Compared with children with NH, those with HL had higher odds of having others express concern to the parent regarding their behavior (p=0.04). While not statistically significant, 3 of 37 children with NH versus 0 of 36 children with HL had ever received mental health services (p=0.08). CONCLUSIONS: Hearing loss in childhood has profound effects on language development but may also impact behavior. Children with hearing loss demonstrate disruptive behavior problems yet may be less likely to receive intervention. Further research is warranted to identify and address behavioral problems in this population.

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Primary Presenter / email: **Rashidi, V.** / vaniarashidi@uky.edu
Clinical Science
Behavior

Mentor / e-mail: Bush, M.L. / matthew.bush@uky.edu



CCTS Poster Presentation Abstracts

35 Abstract Title: **Effects of acute buspirone administration on impulsive choice and inhibitory control in cocaine users**

Author(s): M.R. Romanelli, College of Medicine, U of Kentucky
J.C. Strickland, Pshchology, U of Kerntucky
B.L. Bolin, Behavioral Science, U of Kentucky
C.R. Rush, Psychology, Behavioral Science and Psychiatry, U of Kentucky
W.W. Stoops, Medicine, Psychology, Behavioral Science and Psychiatry, U of Kentucky

Abstract: Cocaine users display increases in impulsive choice as well as deficits in inhibitory control that may increase the likelihood of injury, risky behavior (e.g., unprotected sex), and/or escalation of current drug use. Although behavioral strategies to ameliorate these maladaptive behaviors may have promising short-term outcomes, it is not known whether pharmacological interventions might further improve long-term efficacy. Recent evidence suggests that buspirone maintenance may decrease impulsive choice. The current study evaluated the acute effects of buspirone on behavioral measures of impulsivity. Eleven subjects with a recent history of cocaine use completed this within-subject, double blind, placebo-controlled outpatient protocol. Subjects completed measures of inhibitory control (i.e., cued go-no/go task) and impulsive choice (i.e., sexual risk delay-discounting task) following acute oral administration of buspirone (10 and 30 mg), triazolam (0.375 mg; positive control), and placebo (negative control) across four sessions. Physiological and subject-rated drug effects were also measured. Data were analyzed using repeated measures ANOVAs. Buspirone did not change ratings on positive subject-rated measures (e.g., Like Drug; Take Again) although dose-dependent decreases in diastolic blood pressure were also observed following buspirone administration. Buspirone also did not change performance on measures of impulsive choice or inhibitory control; however, slower reaction times were observed at the 30 mg buspirone on the cued go/no-go task. Triazolam produced increases in positive subject-rated measures and robust decreases in response time. These findings suggest that acute buspirone had little impact on behavioral measures of impulsive choice and inhibitory control and highlight the importance of examining acute versus chronic dosing.

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Primary Presenter / email: **Romanelli, M.R.** / mromanelli@uky.edu
Clinical Science
Behavior

Mentor / e-mail: Stoops, W.W. / william.stoops@uky.edu



CCTS Poster Presentation Abstracts

36 Abstract Title: **Systematic Adaptation of Parenting Intervention Delivery in Underserved Communities: Appalachia and ADAPT-ITT**

Author(s): C. Studts, Department of Health Behavior, U of Kentucky
 H. Bundy, Department of Anthropology, U of Kentucky
 S. Bardach, Graduate Center for Gerontology, U of Kentucky
 J. Jacobs, Department of Health Behavior, U of Kentucky
 F. Feltner, Center of Excellence in Rural Health, U of Kentucky

Abstract: Background: The efficacy of behavioral parent-training (BPT) interventions in reducing child disruptive behavior problems is well-established. However, in many underserved communities, the combination of cultural barriers and poor access to mental health services poses a substantial challenge to BPT's "delivery-as-usual." We are applying the 8-phase ADAPT-ITT model to systematically adapt BPT intervention delivery to fit community preferences in rural central Appalachia, a region with disproportionate poverty levels, low educational attainment, and mental health professional shortages. Results from the first two ADAPT-ITT phases are reported: (1) assessing community perspectives in order to (2) decide which intervention to implement. Methods: Guided by our Community Advisory Board, we completed and analyzed (a) semi-structured key informant interviews with 21 parents and (b) three focus groups with 12 local child service providers. We explored perceptions of behavior problems in young children; awareness of relevant interventions/programs; and preferences regarding four aspects of intervention delivery: interventionist, location, modality, and dose. Findings: All participants noted the need for local programs targeting early childhood behavioral problems. Parents recommended against services located in medical, mental health, or educational settings, describing labeling, stigma, and privacy concerns. Service providers identified additional barriers, including challenges in engaging parents. Most participants preferred local, trusted interventionists and recommended fewer than 6 intervention sessions. Modality and location preferences varied. Consideration of these preferences led to selection of (a) the Family Check-Up intervention; (b) local community health workers as interventionists; and (c) flexibility regarding modality and location of intervention delivery. The final six ADAPT-ITT phases will involve systematic adaptations of the Family Check-Up and a pilot implementation trial of the adapted delivery model.

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Primary Presenter / email: **Jacobs, J.** / julie.jacobs@uky.edu
Community Science
Behavior

Mentor / e-mail: Studts, C. / tina.studts@uky.edu



CCTS Poster Presentation Abstracts

37 Abstract Title: **Center of Pressure Excursion During a Single Leg Standing Test in Ambulatory Children with Cerebral Palsy**

Author(s): R.T. Callahan, Department of Kinesiology and Health Promotion, U of Kentucky
 H. White, Motion Analysis Laboratory, Shriners Hospital for Children, Lexington, KY
 J.J. Wallace, Department of Kinesiology and Health Promotion, U of Kentucky
 M.B. Pohl, Department of Kinesiology and Health Promotion, U of Kentucky
 R. Shapiro, Department of Kinesiology and Health Promotion, U of Kentucky
 H. Iwinski, Department of Orthopaedic Surgery, Shriners Hospital for Children, Lexington, KY

Abstract: Cerebral Palsy (CP) is the most common disabling motor disorder of childhood. 70% of children with CP ambulate, but most demonstrate gait patterns different from those of a typical developing (TD) child. Three-dimensional gait analysis has shown to be helpful in clinical assessment, however not every setting has the space or equipment to perform this testing and clinicians instead rely on the Gross Motor Function Measure (GMFM). The GMFM is an 88-part questionnaire designed to screen, diagnose and guide treatment for patients with CP. Administration is time consuming and it would be valuable for clinicians to have a quick and efficient method to evaluate gross motor ability without sacrificing testing sensitivity. Research has shown stability measurements to be highly correlated to gross motor function and testing can be completed in a shorter time than seen with a three-dimensional gait test or GMFM questionnaire. Single leg standing testing (SLST) has been used to evaluate postural stability and one's ability to maintain equilibrium of their center of mass, but more recently force plates have been used to collect center of pressure excursion (COPE) data as well. COPE is a measure of the total deviations of the center of pressure (COP) under the foot. Trials have demonstrated increased COPE for affected subjects and smaller variances in COP for TD populations. This testing has not yet been performed with children who have CP. The goal of this trial is to determine if relationships are present between a SLST, three-dimensional gait testing outcomes and GMFM score in ambulatory children with CP.

Supported by:

Primary Presenter / email: **Callahan, R.T.** / ryan.callahan@uky.edu
Clinical Science
Other

Mentor / e-mail: Pohl, M.B. / mbpo223@uky.edu



CCTS Poster Presentation Abstracts

38 Abstract Title: **Body Mass Index, Exercise, and Weight Perception: Impact on School Performance in Teens**

Author(s): M. Rajagopal, College of Medicine, U of Kentucky
 A. Briggs, Adolescent Medicine, U of Kentucky
 H. Omar, Adolescent Medicine, U of Kentucky

Abstract: 1. Purpose: Childhood obesity continues to increase in the United States and is a significant problem in Kentucky. It also has effects on school performance. The purpose of this paper is to determine the relationship between grade point average and other factors, including: body mass index, living situation, exercise habits, and weight perception. 2. Methods: Data from School-Based Health Promotion Centers (SBHC) in one middle school in Central Kentucky was used for this study. Students in sixth, seventh, and eighth grades were screened at the SBHC for a variety of behaviors and lifestyle characteristics, including interviewing the students using the Perkins Adolescent Risk Screen (PARS). Students are excluded if their parents do not give consent for the screening. Body Mass Index was calculated by dividing the student weight in kilograms by the height in square meters. Later, student grade point averages were obtained from the school and matched to the student's ID number. 3. Data/Results: Data from a total 579 students: 278 sixth graders, 151 seventh graders, and 150 eighth graders. 145 were underweight, with a BMI less than 18.5; 241 were normal weight, with a BMI between 18.5 and 24.9; 100 were overweight, with a BMI between 25 and 29.9; and 93 were obese, with a BMI over 30. 281 males and 298 females. To see if differences in average GPAs were significant, t-test analysis was used. There were significant ($p < 0.05$) difference in GPA between the following groups: BMI under 25 vs BMI 25+, normal BMI vs abnormal BMI, good living situation vs poor living situation, exercise vs no exercise, and good weight perception compared to poor weight perception. These significant differences also existed when comparing males and females separately. Correlation coefficients were calculated and show that GPA is negatively correlated with BMI in both males and females as well as negatively correlated with an increasingly poor living situation, fewer hours of exercise, and poor weight perception. 4. Conclusions: Overall, a higher BMI tends to be associated with a lower GPA. In addition, poor living situations, not exercising, and poor weight perception also seem to be associated with lower academic performance.

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Primary Presenter / email: **Rajagopal, M.** / megan.rajagopal@uky.edu
Clinical Science
Other

Mentor / e-mail: Omar, H. / Hatim.Omar@uky.edu



CCTS Poster Presentation Abstracts

39 Abstract Title:	Neurocognitive Measures in an Adolescent Sports Concussion Sample
Author(s):	L. M. Koehl, Department of Psychology, U of Kentucky H.L. Combs, Department of Psychology, U of Kentucky D.T.R. Berry, Department of Psychology, U of Kentucky D.Y. Han, Departments of Neurology, Neurosurgery, & Physical Medicine & Rehabilitation, U of Kentucky

Abstract: Documented incidence rates of sport-related concussions have increased in recent years. Concern regarding potential cognitive consequences has driven researchers and clinicians to seek measures that detect difficulties post-concussion. As computerized measures are introduced to identify baseline abilities and to track cognitive changes, there is a need to determine comparability between computerized and traditional neurocognitive testing. Twenty-nine athletes (Mage = 14.41, SD = 1.32) experiencing persistent concussion symptoms were compared to 25 healthy athlete controls (Mage = 14.08, SD = 1.32). Participants were administered neuropsychological screenings, including ImPACT and several paper and pencil measures. No significant differences were found in age, ethnicity, sex, or education. Differences were examined using one-way ANOVAs. Significant differences were found between groups on three ImPACT domains (Verbal Memory $F = 13.93$, $p < .001$; Visual Memory $F = 15.54$, $p < .001$; Visuomotor Speed ($F = 16.91$, $p < .001$) and on seven paper and pencil measures: CMS Dots Learning ($F = 4.15$, $p = .047$), CMS Dots Delay (visual memory; $F = 5.74$, $p = .02$), Trails A ($F = 23.63$, $p < .001$), Trails B ($F = 12.62$, $p < .001$), D-KEFS Design Fluency ($F = 17.03$, $p < .001$), phonemic fluency ($F = 9.22$, $p = .004$), semantic fluency ($F = 7.60$, $p = .008$), and Beery Visuomotor Index ($F = 41.08$, $p < .001$). These findings suggest ImPACT effectively detects prolonged cognitive symptoms following concussion. When compared to paper-and-pencil measures, convergent scores in most domains suggest comparability between this computerized measure and traditional measures.

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Primary Presenter / email: **Combs, H.L.** / hannah.combs@uky.edu

Clinical Science
Trauma/Injury/Rehabilitation

Mentor / e-mail: Han, D.Y. / d.han@uky.edu



CCTS Poster Presentation Abstracts

40 Abstract **Reduction of Cervical Cancer and Other Papilloma Virus Pathology by Improving Immunization Rates in Kentucky**

Title: N. Udechukwu, College of Medicine, U of Kentucky
 P. Duffin, Department of Biology, Transylvania U
Author(s): A. Briggs, Dept. of Pediatrics, Div. of Adolescent Medicine & Young Parents Program, U of Kentucky
 H. Omar, Dept. of Pediatrics, Div. of Adolescent Medicine & Young Parents Program, U of Kentucky

Abstract: Human Papillomavirus (HPV) is the most common sexually transmitted infection in the United States. Pathological presentation range from cervical cancer, genital warts, ano-genital cancer, and oro-pharyngeal cancer. Although, there are ways to manage these diseases, there is no absolute treatment for an active HPV infection. As such, care must be taken to emphasize the importance of HPV vaccine administration. In Kentucky, there is a low inclination for uptake or adherence to HPV vaccine, even in free instances, despite the higher than national average rate of cervical cancer. Studies from health care providers detailed the vaccination schedule and poor communication in clinics as barriers to adequate vaccine uptake in Kentucky. Based on these studies, a comprehensive strategy including targeted educational efforts focused on patients and their parents as well as reminder systems were employed by our clinic facility. We applied a retrospective study approach to evaluate our efforts in newly admitted adolescent patients between ages 9-26 seen in our facility from 10/2006-09/2015. We observed higher rates of HPV vaccination in our clinic compared to that of the state as we reached 99.16% of patients who at least received their first shot of HPV Vaccine compared to <53% receiving one dose in the state of Kentucky. Additionally, more of our patients were completing vaccinations, including 55.64% females in our study compared to 26.8% females in Kentucky and 39.65% males in our study compared to negligible data recorded for Kentucky by the CDC statistics in 2013. We envision that our efforts, if implemented within the state as a whole, will lead to increasing HPV vaccination and a corresponding decline in the prevalence of the HPV related pathology in Kentucky.

Supported by: Supported by Division of Adolescent Medicine
 Primary Presenter / email: **Udechukwu, N.S.** / nsud222@uky.edu
Community Science
Other
 Mentor / e-mail: Omar, H. / hatim.omar@uky.edu



CCTS Poster Presentation Abstracts

41 Abstract Title: **High Risk Substance Use and Sexual Behavior in Girls with Early Justice System Involvement: A Systematic Review**

Author(s): M. Tillson, College of Social Work, U of Kentucky
M. Staton-Tindall, College of Social Work, U of Kentucky

Abstract: Background: Individuals with substance abuse issues are often involved in the criminal justice system, which can provide an important opportunity for intervention and treatment. Limited research has focused on substance-abusing youth involved in the juvenile justice system, particularly girls. As proportional arrest rates of adolescent females have increased in recent years, this area of research is important for intervention. The purpose of this research project is to conduct a systematic literature review to describe patterns of risky substance use behaviors among girls involved with the justice system, to explore the intersection of these behaviors with risky sexual practices, and to assess outcomes related to gender-specific systems of intervention and care. Methods: A search of scholarly articles focused on sexual behaviors, substance use patterns, and the intersection of these two constructs among incarcerated adolescent females was conducted. Results from studies discussing female-targeted interventions were also reviewed. Results: Themes from the literature suggest that girls with juvenile justice involvement display riskier and more ubiquitous patterns of both substance use and sexual activity, with earlier ages of initiation for many behaviors compared to their non-incarcerated cohort. Gender-specific programming addressing substance abuse is currently a growing field with promising results, but interventions and care related to reproductive and relational health are still lacking coherence. Implications: Considering the association of risky sexual activity and substance use in juvenile girls, as well as the high prevalence of both conditions among incarcerated female youth, recommendations are made for juvenile justice treatment frameworks to address both needs interrelatedly and comprehensively.

Supported by:

Primary Presenter / email: **Tillson, M.** / mdti223@uky.edu

Basic Science

Other

Mentor / e-mail: Staton-Tindall, M. / mstindall@uky.edu



CCTS Poster Presentation Abstracts

42 Abstract Title: **Central Appalachia Inter-Professional Pain Education Collaborative (CAIPEC)**

Author(s): R. Cardarelli, Family and Community Medicine, U of Kentucky
 W. Elder, Family and Community Medicine, U of Kentucky
 D. King, West Virginia Clinical and Translational Science Institute
 J. Schilling, Family and Community Medicine, U of Kentucky
 S. Weatherford, Family and Community Medicine, U of Kentucky

Abstract: CAIPEC is a multi-faceted CE approach targeted at health professionals in Kentucky and West Virginia (areas that suffer from opioid overuse and inappropriate prescribing practices). CAIPEC brings state organizations, academic institutions, and targeted stakeholders together to deliver evidence-based chronic pain education and delivery interventions. This project reaches across a spectrum of interdisciplinary and inter-professional audiences. CE activities (with culminating resources available at participating AHECs) include webcasts, live round-table community meetings, web-based enduring material, and a “Chronic Pain Practice Toolkit”. CAIPEC also partnered to present at the state-required interprofessional chronic pain CME conferences in both KY and WV hosted by the KY/WV Academies of Family Physicians. CAIPEC effectiveness will be evidenced by measured changes in practitioner knowledge and attitudes plus impact on implementation and practice performance will be evaluated in a controlled study of (patient-level) pain evaluation and (population-level) opioid prescriptions rates.

Supported by: Funding for this project (\$350,000) is provided by the Pfizer Consortium. The start date for this project was December 2014, and will conclude in March 2016.

Primary Presenter / email: **Weatherford, S.** / sarah.weatherford@uky.edu
Basic Science
Other

Mentor / e-mail: Cardarelli, R. / roberto.cardarelli@uky.edu



CCTS Poster Presentation Abstracts

43 Abstract Title: **Emotional Support and Psychological Health of Low-Income Populations**
 Author(s): K. Namkoong, Department of Community and Leadership Development, U of Kentucky

Abstract: BACKGROUND: Socioeconomic status has been linked a wide range of health problems. Especially, low-income is one of major obstacles in enhancing health outcomes, because it limits the access to valuable health resources. Although there have been diverse health enhancement programs, relatively few focus on the roles of emotional support, which has positive impacts on physical and psychological health outcomes. Therefore, this study examines the effect of emotional support on overall health status and psychological well-being of low-income population. METHODS: Secondary data was collected from the Health Information National Trends Survey Cycle 4 (HINT, 2014). The sample of this study was restricted to 1,704 respondents consisted of 852 SNAP-Ed eligible recipients (i.e., low-income adults) and 853 SNAP-Ed ineligible selected by the propensity matching technique. Univariate ANCOVA was conducted to test the main and the interaction effects. RESULTS: Results showed that there were not significant differences in psychological well-being between: 1) SNAP-Ed eligible recipients and the ineligible ($F=3.07$, $p=.278$); and 2) those who had emotional support and those who had not ($F=13.83$, $p=.167$). However, there was a significant interaction effect between SNAP-Ed eligibility and emotional support on psychological health outcomes ($F=6.76$; $p=.009$). Similarly, there was a marginally significant interaction effect on overall health status ($F=3.50$; $p=.062$), although there were no main effects of SNAP-Ed eligibility ($F=1.65$; $p=.345$) and social support ($F=6.38$; $p=.239$). CONCLUSION: This study shows the lack of emotional support has more negative impacts on psychological health outcomes of low-income adults. These findings suggest the need for health programs that can enhance the access to emotional support for low-income population.

Supported by: This study used the Health Information National Trends Survey - Cycle 4 (2014) collected by National Cancer Institute (NCI).

Primary Presenter / email: **Namkoong, K.** / kang.namkoong@uky.edu
Community Science
Other

Mentor / e-mail: /



CCTS Poster Presentation Abstracts

44 Abstract

Title:

Profile of synthetic drug-users in corrections-based substance abuse program

Author(s):

K.S. Smith, Center on Drug and Alcohol Research, U of Kentucky
 S. Shalash, Center on Drug and Alcohol Research, U of Kentucky
 E.M. Winston, Center on Drug and Alcohol Research, U of Kentucky
 M. Staton-Tindall, College of Social Work & Center on Drug and Alcohol Research, U of Kentucky
 K. Pangburn, Kentucky Department of Corrections
 E. Litton, Center on Drug and Alcohol Research, U of Kentucky

Abstract: There has been a significant increase within the past decade in the use of synthetic cannabinoids and cathinones. Emerging use of synthetic drugs raises concerns among treatment providers and criminal justice authorities due to the fact that synthetic drugs are associated with adverse effects yet are more difficult to detect with standard drug tests. This presentation describes the characteristics of individuals involved in the criminal justice system who have reported synthetic drug use within the 12-month period prior to incarceration. This analysis includes secondary data collected as part of the Criminal Justice Kentucky Treatment Outcome Study. Data was collected during the baseline for individuals entering Kentucky Department of Corrections substance abuse treatment programs from May 2013 to June 2015 (N=17,199). Analysis focused on differences in demographic characteristics, drug use patterns, and criminal history between individuals who reported synthetic use (n=1,899) and those without any reported use (n=15,300) in the year prior to incarceration. Synthetic users were predominately male (81.4%), white (84.1%), and unmarried (57.3%). Compared to non-synthetic users, synthetic users were more likely to be younger (30.2 vs. 34.3, $p < .001$), have higher rates of anxiety (55.1 vs 40.3, $p < .001$), spent significantly more nights incarcerated in the 12-months prior to their current incarceration (55 vs 39.4, $p < .001$), and reported using other categories of illicit drugs at considerably higher rates. Findings suggest that synthetic users could be considered higher risk than non-synthetic users in myriad ways. Further research should focus on long-term outcomes for synthetic users such as recidivism, relapse, and overall health status.

Supported

by:

Kentucky Department of Corrections

Primary Presenter / email:

Smith, K.E. / kirstenelins@uky.edu**Community Science****Other**

Mentor / e-mail:

Staton-Tindall, M. / mstindall@uky.edu



CCTS Poster Presentation Abstracts

45 Abstract	Evaluation of Methodology Used in Risk Network Research Among Populations Engaging in Sexual and Drug-Related Risk Behavior
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Title:	
Author(s):	A.E. Su, College of Medicine, U of Kentucky A.M. Young, Department of Epidemiology and Center on Drug and Alcohol Research, U of Kentucky A.E. Rudolph, Department of Epidemiology, Boston U School of Public Health, Boston, MA L. King, Center on Drug and Alcohol Research, U of Kentucky S. Jent, Center on Drug and Alcohol Research, U of Kentucky J.R. Havens, Center on Drug and Alcohol Research and College of Medicine, U of Kentucky

Abstract: Background: Social network analysis (SNA) seeks to understand how people are connected in a population and can be a powerful tool that can yield insights into disease transmission. To map risk networks, researchers collect information (name, age, gender, etc) and behavioral data about participants and their partners (i.e., 'alters'). To construct valid and reliable networks, accuracy in reported data is critical. Objective: This study evaluates the accuracy with which participants report alters' identifying demographic data. Methods: Data were collected from 2008 to 2010 from 503 rural drug users. Network ties (n=897) involved recent (past 6 months) sex, drug co-usage, and/or social support. Study staff cross-reference the data provided about alters with the data that participants provide about themselves to construct a risk network that represents all direct and indirect connections among participants (i.e., a sociometric network). Analyses were conducted to determine the accuracy of reported ages (years) and names (binary). Results: Participants gave alters' exact names and ages within two years in 75% and 79% of relationships, respectively. Name reporting was more accurate in reciprocally reported ties and those involving social support and a male alter. Age was more accurate in reciprocal ties and those characterized by kinship, sexual partnership, frequent communication, recruitment referral, and financial support and less accurate in ties with older alters. Conclusions: Most participants reported the identifying characteristics of their alters accurately, and the accuracy was not significantly different in relationships involving illicit behavior compared to those not involving illicit behaviors.

Supported by:	This work was supported by the National Institute on Drug Abuse (Grant R01 DA024598, PI: Havens), the pilot research grant program of the College of Public Health at the University of Kentucky, and the National Center for Advancing Translational Sciences, UL1TR000117. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH.
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Primary Presenter / email:	Su, A.E. / amanda.su@uky.edu Community Science Other
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Mentor / e-mail:	Young, A.M. / april.young@uky.edu
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CCTS Poster Presentation Abstracts

46 Abstract Title: **Peer Mentoring and Substance Abuse Treatment**

Author(s): K. Walling, College of Social Work, U of Kentucky
 S. Biermann, College of Social Work, U of Kentucky
 M. Staton-Tindall, College of Social Work, U of Kentucky
 J. Stamper, Chrysalis House, Inc.
 S. Waters, Chrysalis House, Inc.

Abstract: Substance abuse/misuse continues to be a growing problem nationwide. Peer recovery support services are designed and delivered by those who have experienced both substance abuse and recovery (U.S. Department of Health and Human Services, 2009). These services have been used to help those dealing with substance abuse stay engaged in the recovery process and to decrease relapse rates (U.S. Department of Health and Human Services, 2009). The purpose of this presentation is to describe client and staff perceptions of the peer-mentoring services offered at Chrysalis House, a residential substance abuse treatment center for pregnant and parenting women. Data was collected through process evaluation interviews with administrators, staff and clients. Findings indicated that peer mentoring services play an integral role in the recovery process. The women appreciated having support from someone who had overcome the same challenges they are currently working through. The process evaluation provided information about the peer-mentoring services offered at Chrysalis House and allowed staff and clients to share how peer-mentoring services supported clients in the recovery process. Data from the process evaluation showed that the women felt that they could go to their mentor anytime they needed them. One staff stated that the impact that the mentors had on the women coming into this program had probably been the most significant that she had seen in her 26-year career. These findings have important implications for the field because peer support services can have a positive impact on the recovery process for pregnant and parenting women in recovery.

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Primary Presenter / email: **Walling, K.** / kkwa225@g.uky.edu
Community Science
Other

Mentor / e-mail: Walling, K. / kkwa225@g.uky.edu



CCTS Poster Presentation Abstracts

47 Abstract Title: **Survival in Motor Neuron Disease: an Analysis of Executive Functioning and Behavior**

Author(s): N.E. Garcia, Department of Psychology, U of Kentucky
 A.A. Roach, Frazier Rehabilitation Hospital, Louisville, KY
 E.J. Kasarskis, Department of Neurology, U of Kentucky
 S.C. Segerstrom, Department of Psychology, U of Kentucky

Abstract: Amyotrophic Lateral Sclerosis (ALS) and Primary Lateral Sclerosis are two forms of motor neuron disease (MND). Cognitive and behavioral deficits are frequently comorbid with MND. Executive functions have been identified as a commonly impaired domain. The majority of impairment found in patients is mild, with a small proportion developing dementia. Patients with comorbid ALS and dementia have a shorter survival than patients with either diagnosis exclusively. However, the implications of mild cognitive and behavioral deficits are unclear. The current study examined executive functioning and behavior in patients with MND (N = 37) on survival over a 5-year period. The Wisconsin Card Sorting Task (WCST) is a performance-based executive function index of perseveration and abstract thinking. The Behavior Rating Inventory of Executive Functions (BRIEF-A) is a behavioral index of self-regulation in patients' everyday environment in two subdomains (i.e, Behavioral Regulation and Meta Cognition), reported by patients and caregivers. Cox proportional hazard regressions were conducted controlling for age, disease type, onset site, disease duration, and bi-pap use. Greater patient-reported impairments in Behavioral Regulation and Meta Cognition were associated with a 94% and 100% increased mortality risk respectively (adjusted HR = 1.94, 95% CI 1.84-2.04, p = .03; adjusted HR = 2.03, 95% CI 1.95-2.12, p = .009). Patient WCST perseverative errors were associated with a 40% increased mortality risk, though significance was not reached. Patient-reported behavioral impairment is an important indicator of poor prognosis in patients with MND. The effect of performance-based executive function on survival merits further research.

Supported by: The project described was supported by the CCTS Professional Student Mentored Research Fellowship

Primary Presenter / email: **Garcia, N.E.** / natasha.garcia@uky.edu
Clinical Science
Other

Mentor / e-mail: Segerstrom, S.C. / segerstrom@uky.edu



CCTS Poster Presentation Abstracts

48 Abstract

Title:

Anti-Invasive activity of capsaicin and natural capsaicin-like compounds in human NSCLC

Author(s):

N.A. Nolan, Joan C. Edwards School of Medicine, Marshall U, Huntington, WV
 J.D. Hurley, Pharmacology, Physiology, and Toxicology, Joan C. Edwards School of Medicine, Marshall U
 C. Williams, Pharmacology, Physiology, and Toxicology, Joan C. Edwards School of Medicine, Marshall U
 W.D. Rollyson, Pharmacology, Physiology, and Toxicology, Joan C. Edwards School of Medicine, Marshall U
 K. C Brown, Joan C. Edwards School of Medicine, Marshall U
 A.T. Akers, Joan C. Edwards School of Medicine, Marshall U
 M.N. Eskew, Pharmacology, Physiology, and Toxicology, Joan C. Edwards School of Medicine, Marshall U
 H.E. Perry, Pharmacology, Physiology, and Toxicology, Joan C. Edwards School of Medicine, Marshall U
 R.D. Egleton, Joan C. Edwards School of Medicine, Marshall U
 P. Dasgupta, Joan C. Edwards School of Medicine, Marshall U

Abstract: Non small lung cancer (NSCLC) accounts of 80% of all lung cancer cases. About 30-40% of NSCLC patients present with metastatic disease at the time of their diagnosis. The average survival time of such NSCLC patients is about 7 months. The invasion of neoplastic cells to the surrounding stroma is a vital step of cancer metastasis. Recent studies have shown that nutritional compounds (by themselves or in combination with standard chemotherapy) can suppress metastasis of several human cancers. Capsaicin is the spicy ingredient of chili peppers. Recent studies have shown that capsaicin inhibits the invasion and metastasis of several types of human cancers including melanoma, prostate cancer and cholangiosarcoma. We investigated the anti-invasive properties of capsaicin and two capsaicin-like compounds, capsiate and capsiconiate, found in select variety of chili peppers on NSCLC. We measured the anti-invasive activity of these compounds by the Boyden chamber assay. We found that capsaicin and capsiate displayed equivalent anti-invasive activity in NSCLC cells. In contrast, capsiconiate did not suppress the invasion of NSCLC cells. The anti-invasive activity of capsaicin, capsiate and capsiconiate in human NSCLC was found to be independent of their growth-inhibitory activity. Currently, we are testing the anti-metastatic activity of capsaicin in syngenic mouse models of metastasis. The results of our studies may foster the hope of nutrition-based interventions in NSCLC metastasis.

Supported

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 by: AICR Investigator Grant, and a NASA Undergraduate Fellowship to NAN

Primary Presenter / email:

Nolan, N. / Nolan34@marshall.edu

Basic Science

Cancer

Mentor / e-mail:

Dasgupta, P. / Dasgupta@marshall.edu



CCTS Poster Presentation Abstracts

49 Abstract Title: **Analysis of the acetylcholine-signaling pathway reveals differences between normal and malignant lung tissue**

Author(s): A.T. Akers, Pharmacology, Physiology, & Toxicology, Joan C. Edwards School of Medicine, Marshall U, Huntington, WV
 K.C. Brown, Pharmacology, Physiology, & Toxicology, Joan C. Edwards School of Medicine, Marshall U
 J.K. Lau, Pharmacology, Physiology, & Toxicology, Joan C. Edwards School of Medicine, Marshall U
 B.A. Thornhill, Pharmacology, Physiology, & Toxicology, Joan C. Edwards School of Medicine, Marshall U
 H.E. Perry, Pharmacology, Physiology, & Toxicology, Joan C. Edwards School of Medicine, Marshall U
 D.V. Jones, Dana-Farber Cancer Institute, Boston, MA
 J.F. Pulliam, Markey Cancer Center, U of Kentucky
 J. Martin, Markey Cancer Center, U of Kentucky
 P. Dasgupta, Pharmacology, Physiology, & Toxicology, Joan C. Edwards School of Medicine, Marshall U

Abstract: NSCLC is characterized by aggressive clinical course, rapid doubling time and a dismal survival rate. The development of NSCLC is closely correlated with smoking habits. A small percentage of NSCLC cases also occur in non-smokers. Targeted therapies like EGFR-inhibitors, EML-ALK4 inhibitors, and B-Raf inhibitors show excellent therapeutic response in NSCLC patients who are non-smokers. However, they do not work well in NSCLC patients who are smokers. Therefore, the identification of novel molecular targets in NSCLC patients who are exposed to cigarette smoke is urgently needed. Tobacco components like nicotine and NNK have been known to accelerate the progression of lung cancer. One of the major mechanisms underlying the proliferative actions of nicotine and NNK is that they upregulate the levels of the growth factor acetylcholine (ACh). This ACh binds back to its target receptors (on NSCLC cells) and stimulates the proliferation of NSCLC cells in an autocrine manner. The ACh signaling loop is amplified by exposure to tobacco components and cigarette smoke. With this background in mind, we aim to compare the ACh-signaling machinery between normal lung cells and NSCLC cells. We find that both normal lung epithelial cells and NSCLC cells express all the components of the ACh-signaling pathway, namely choline acetyltransferase (ChAT), vesicular acetylcholine transporter (VACHT), acetylcholinesterase (AChE) and choline transporter (ChT). Some of the ACh-signaling proteins like ChAT, VACHT and AChE show differences in expression and activity between normal lung tissue and NSCLC cells. We believe that such differences may form the basis of targeted therapies in NSCLC patients who are exposed to cigarette smoke.

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Primary Presenter / email: **Akers, A.T.** / akers103@live.marshall.edu
Basic Science
Cancer

Mentor / e-mail: Dasgupta, P. / Dasgupta@marshall.edu



CCTS Poster Presentation Abstracts

50 Abstract Title: **S100A4 drives non-small cell lung cancer invasion, associates with poor prognosis, and is effectively targeted by the FDA-approved anti-helminthic agent niclosamide**

R. L. Stewart, Department of Pathology and Laboratory Medicine, U of Kentucky
 B.L. Carpenter, Department of Molecular and Cellular Biochemistry, U of Kentucky
 D.S. West, Department of Pathology and Laboratory Medicine, U of Kentucky
 T. Knifley, Department of Molecular and Cellular Biochemistry, U of Kentucky
 L. Liu, Province Hospital for Occupational Disease Prevention and Treatment, Guangzhou, Guangdong, China

Author(s): C. Wang, Department of Biostatistics, U of Kentucky
 H.L. Weiss, Department of Biostatistics, U of Kentucky
 T.S. Gal, Division of Biomedical Informatics, U of Kentucky
 E.B. Durbin, Division of Biomedical Informatics, U of Kentucky
 S.M. Arnold, Markey Cancer Center, U of Kentucky
 K.L. O'Connor, Department of Molecular and Cellular Biochemistry, U of Kentucky
 M. Chen, Department of Toxicology and Cancer Biology, U of Kentucky

Abstract: S100A4 (metastasin-1), a metastasis-associated protein and marker of epithelial to mesenchymal transition, contributes to several hallmarks of cancer and has been implicated in the progression of several types of cancer. However, the impacts of S100A4 signaling in lung cancer progression and its potential use as a target for therapy in lung cancer have not been properly explored. Using established lung cancer cell lines, we demonstrate that S100A4 knockdown reduces cell proliferation, invasion and three-dimensional invasive growth, while overexpression of S100A4 increases invasive potential. In patient-derived tissues, S100A4 is preferentially elevated in lung adenocarcinoma. This elevation is associated with lymphovascular invasion and decreased overall survival. In addition, depletion of S100A4 by shRNA inhibits NF- κ B activity and decreases TNF α -induced MMP9 expression. Furthermore, inhibition of the NF- κ B/MMP9 axis decreases lung carcinoma invasive potential. Niclosamide, a reported inhibitor of S100A4, blocks expression and function of S100A4 with a reduction in proliferation, invasion and NF- κ B-mediated MMP9 expression. Collectively, this study highlights the importance of the S100A4/NF- κ B/MMP9 axis in lung cancer invasion and provides a rationale for targeting S100A4 to combat.

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Primary Presenter / email: **Chen, M.** / min.chen@uky.edu

**Basic Science
 Cancer**

Mentor / e-mail: O'Connor, K. / kloconnor@uky.edu



CCTS Poster Presentation Abstracts

51 Abstract
Title:

Acetylcholine-signaling inhibitors for lung cancer therapy

Author(s): P. Dasgupta, Pharmacology, Physiology, & Toxicology, Joan C. Edwards School of Medicine, Marshall U Huntington, WV
 J.K. Lau, Pharmacology, Physiology, & Toxicology, Joan C. Edwards School of Medicine, Marshall U
 K.C. Brown, Pharmacology, Physiology, & Toxicology, Joan C. Edwards School of Medicine, Marshall U
 W.D. Rollyson, Pharmacology, Physiology, & Toxicology, Joan C. Edwards School of Medicine, Marshall U
 C.A. Stover, Pharmacology, Physiology, & Toxicology, Joan C. Edwards School of Medicine, Marshall U
 J.M. Rimoldi, Biomolecular Sciences, U of Mississippi, University, MS
 S.J. Cutler, Biomolecular Sciences, U of Mississippi
 W.E. Hardman, Biochemistry & Microbiology, Joan C. Edwards School of Medicine, Marshall U
 A.B. Carpenter, Pathology, Joan C. Edwards School of Medicine, Marshall U
 Y.C. Chen, Biology, Alderson Broaddus U, Philippi, WV

Abstract: Cigarette smoking is a major risk factor for the development of small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC). Nicotine is the addictive component of cigarette smoke. Nicotine (at concentrations present in the plasma of moderate smokers) accelerates the growth, angiogenesis and metastasis of lung cancers. The biological activity of nicotine is mediated by nicotinic acetylcholine receptors (nAChRs). The endogenous ligand for nAChRs in the lung is the neurotransmitter acetylcholine (ACh). ACh is known to be an autocrine growth factor for both SCLC and NSCLC. One of the ways that nicotine and cigarette smoke promote the growth of lung cancers is by promoting the production of ACh, which binds to its cognate receptor (on lung cancer cells) in an autocrine manner and induces the proliferation of lung cancer cells. The objective of the present study is to investigate the growth-inhibitory activity of acetylcholine-signaling pathway in SCLC and NSCLC. We show that three acetylcholine-signaling inhibitors, BW813U, hemicholinium-3 and vesamicol, cause robust apoptosis in human NSCLCs. The anti-cancer activity of vesamicol was also confirmed in athymic mouse models. Although there are several targeted therapies against NSCLC, they do not provide optimum efficacy in NSCLC patients who are exposed to cigarette smoke. Our studies will facilitate the identification of targeted therapies for the population of lung cancer patients who are smokers.

Supported by: Funding for our study was supported by an NIH R15-AREA Grant (1R15HL113681-01A1), ACTSI Grant from Marshall University, the Flight Attendant Medical Research Institute YCSA Grant (82115), and the West Virginia IDeA Network of Biomedical Research Excellence (P20RR016477 and P20GM103434).

Primary Presenter / email: **Dasgupta, P.** / Dasgupta@marshall.edu
Basic Science
Cancer

Mentor / e-mail: Dasgupta, P. / Dasgupta@marshall.edu



CCTS Poster Presentation Abstracts

52 Abstract Title: **Anti-invasive activity of capsaicin and non-pungent capsaicin analogs in human SCLC**

Author(s): J.R. Friedman, Joan C. Edwards School of Medicine, Marshall U, Huntington, WV
 A.T. Akers, Joan C. Edwards School of Medicine, Marshall U
 J.D. Hurley, Joan C. Edwards School of Medicine, Marshall U
 K.C. Brown, Joan C. Edwards School of Medicine, Marshall U
 N.A. Nolan, Joan C. Edwards School of Medicine, Marshall U
 P. Dasgupta, Joan C. Edwards School of Medicine, Marshall U

Abstract: Small cell lung cancer (SCLC) is the most aggressive lung malignancy. A majority of SCLC patients show extrapulmonary metastasis at the time of their presentation. The common sites of SCLC metastasis are bone and the brain. The invasion of malignant cells to the neighboring blood vessels and lymph nodes is a key step of metastasis. Recent data indicate that dietary compounds (by themselves or in combination with standard chemotherapy) reduce invasion and metastasis of several human cancers. Capsaicin is the pungent ingredient of chili peppers. Recent studies have shown that capsaicin inhibits the invasion and metastasis of several types of human cancers including melanoma, prostate cancer and cholangiosarcoma. We tested the anti-invasive activity of capsaicin, as well as two non-pungent capsaicin analogs, olvanil and arvanil, in human SCLC using the Boyden chamber assay and spherical invasion assay. We found that olvanil and arvanil possess greater anti-invasive activity than capsaicin. The biological activity of capsaicin is mediated by transient receptor potential vanilloid (TRPV) receptors on target cells. However, arvanil and olvanil bind to both TRPV and cannabinoid receptors. Boyden chamber and spherical invasion assay revealed that the anti-invasive effects of capsaicin, olvanil and arvanil were independent of both TRPV and cannabinoid receptors. The capsaicin analogs olvanil and arvanil may prove useful for the management and treatment of SCLC metastasis.

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Primary Presenter / email: **Friedman, J.R.** / Friedman4@marshall.edu

**Basic Science
Cancer**

Mentor / e-mail: Dasgupta, P. / Dasgupta@marshall.edu



CCTS Poster Presentation Abstracts

53 Abstract Title: **Searching for Genetic Links between Natural Missing Teeth and Cancer**

Author(s): E.A. Harvey, College of Medicine, U of Kentucky
 A.N. Vu, Private Practice, Lilburn, Georgia
 S.A. Tackett, Dept. of Oral Health Science, College of Dentistry, U of Kentucky
 J.K. Hartsfield, Jr., Dept. of Oral Health Science, College of Dentistry, U of Kentucky
 L.A. Morford, Dept. of Oral Health Science, College of Dentistry, U of Kentucky

Abstract: Objectives: Literature studies suggest 19-20% of ovarian cancer (OvCA) patients are also diagnosed with naturally missing teeth (NMT), as compared to 3-6% of OvCA-free controls. Our laboratory is interested in identifying potential genetic connections between NMT and OvCA. Using a patient population, where NMT can be accurately diagnosed, we have previously shown that the OvCA-Susceptibility Marker rs10098821 is associated with NMT. This marker is located within a long non-coding RNA gene, LINC01263. The purpose of this study was to compare the DNA sequences of Exon 1 between cases and controls, to identify a causal mutation for the NMT. Methods: This study is being conducted with IRB approval from UK. Following consent/assent, 109 unrelated Caucasian subjects (41-hypodontia, 7-oligodontia, 69-control) supplied dental and medical family histories for 3 generations, along with saliva for genetic testing. A 953-bp region including LINC00824 Exon 1 and the adjacent intronic sequence was PCR-amplified using specific primers. PCR product quality and quantity were evaluated by gel electrophoresis, the products were ExoSAPIT treated and Sanger sequenced. GENEIOUS software was utilized to design PCR primers and to align the sequencing information. Results: Our data analysis is underway. The initial sequence alignments suggest that single nucleotide polymorphisms may be located with the region and their potential association with NMT will be reported. Conclusions: By studying markers previously associated with OvCA in a population where NMT can be well defined (i.e. orthodontic patients), we hope to provide a piece to the puzzle connecting how the two phenotypes may be genetically related.

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Primary Presenter / email: **Harvey, E.A.** / elizabeth.harvey@uky.edu
Basic Science
Cancer

Mentor / e-mail: Morford, L.A. / lorri.morford@uky.edu



CCTS Poster Presentation Abstracts

54 Abstract Title: **Expression of Integrin $\alpha 6\beta 4$ Alters the Response to Chemotherapy in BT-549 Cells.**

Author(s): B.H. MARRS, College of Medicine, U of Kentucky
T. Knifley, Markey Cancer Center, U of Kentucky
M. Chen, Graduate Center for Toxicology, U of Kentucky
K.L. O'Connor, Markey Cancer Center, U of Kentucky

Abstract: Integrin $\alpha 6\beta 4$ is known to increase the aggressiveness of several tumor types by altering transcription via stimulation of DNA repair-mediated DNA demethylation. Since many chemotherapy drugs target DNA, we hypothesize that overexpression of integrin $\alpha 6\beta 4$ will confer drug resistance to those cancer cells. To test this concept, the viability of cells with and without expression of integrin $\alpha 6\beta 4$ was evaluated after treatment with chemotherapy drugs. BT-549 cells, which are derived from triple negative breast cancer, were transfected with either the integrin $\beta 4$ subunit cDNA (which pairs with the endogenous $\alpha 6$ subunit to give integrin $\alpha 6\beta 4$) or an empty vector by retroviral transfection. The cells were treated with cisplatin (a platinum-containing DNA cross-linker), doxorubicin or gemcitabine (a nucleoside analog). After six days of treatment, MTT assays were performed to measure the viability of the cells. The results showed a 2.5 fold reduction in the lethal dose of cisplatin for cells expressing $\alpha 6\beta 4$, whereas, a modest increase in resistance to gemcitabine was seen. No difference was observed with doxorubicin. These results represent progress towards the identification of chemotherapies that can and cannot be used to effectively treat triple negative breast cancers known to express the integrin $\alpha 6\beta 4$. Such cancers are known to be aggressive and are associated with poorer outcomes, further emphasizing the importance of these results. We conclude that the overexpression of integrin $\alpha 6\beta 4$ is directly linked to increased susceptibility to certain classes of chemotherapy and added resistance to others.

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Primary Presenter / email: **MARRS, B.H.** / brock.marrs@uky.edu
Basic Science
Cancer

Mentor / e-mail: O'Connor, K. / kloconnor@uky.edu



CCTS Poster Presentation Abstracts

55 Abstract Title: **Evaluating molecular markers in a colorectal cancer lung metastasis model**

Author(s): J. M. Nagle, College of Medicine, U of Kentucky
P. Rychahou, Department of Surgery, U of Kentucky
B.M. Evers, Department of Surgery, Markey Cancer Center, U of Kentucky

Abstract: Metastasis is a key prognostic indicator for survival in patients with colorectal cancer. However, most cellular models for studying colorectal cancer do not account for the changes that produce a more aggressive metastatic phenotype. Understanding these mechanisms by which tumors become more aggressive will improve patient outcomes by allowing for the earlier detection and treatment of patients at high risk for metastasis. Identifying markers of cells that are likely to become metastatic allows for the development of better therapeutics in the future. In this poster, we show a model for studying metastatic populations of human colon cancer cells. Human colon cancer cells were injected into mice and grew tumors in lung tissue, which were harvested and cultured. The newly derived cells were again injected into mice and the cycle repeated three times to create a distinct metastatic cell population. Here, we present a characterization of key molecular markers in the metastatic population. We have also compared changes from the parental primary tumor cell line and the metastatic line. These changes in protein expression provide insight into the progression of metastatic colon cancer development.

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Primary Presenter / email: **Nagle, J.M.** / jmna226@uky.edu

**Basic Science
Cancer**

Mentor / e-mail: Rychahou, P. / piotr.rychahou@uky.edu



CCTS Poster Presentation Abstracts

56 Abstract Title: **Anti-angiogenic activity of nicotinic receptor antagonists in lung cancer**

Author(s): Z. Robateau, Joan C. Edwards School of Medicine, Marshall U, Huntington, WV
 K.C. Brown, Joan C. Edwards School of Medicine, Marshall U
 R.G. Creel, Joan C. Edwards School of Medicine, Marshall U
 Y.C. Chen, Biology, Alderson Broaddus U, Philippi, WV
 L.M. Grover, Joan C. Edwards School of Medicine, Marshall U
 E.I. Mangiarua, Joan C. Edwards School of Medicine, Marshall U
 R.D. Egleton, Joan C. Edwards School of Medicine, Marshall U
 P. Dasgupta, Joan C. Edwards School of Medicine, Marshall U

Abstract: Small cell lung cancer (SCLC) is a highly angiogenic tumor with a dismal survival rate. Cisplatin-based therapies are initially effective in SCLC. However, the tumor relapses and subsequently becomes resistant to cisplatin-based therapies. Pilot clinical trials have shown that the combination of cisplatin with an anti-angiogenic agent can improve therapeutic response of small cell lung cancer patients. A unique feature of SCLC is that it occurs almost exclusively in smokers. Nicotine, the addictive component of cigarettes, can promote angiogenesis in lung cancer. We show that nicotine stimulates angiogenesis in human retinal microvascular endothelial cells (HRMECs) and human lung microvascular endothelial cells (HMECLs). The proangiogenic effects of nicotine were mediated via the $\alpha 7$ -nAChR subunit. We conjectured that $\alpha 7$ -nAChR antagonists should attenuate nicotine-induced angiogenesis and be useful for the therapy of angiogenesis-related diseases. Our results show that the $\alpha 7$ -nAChR antagonist memantine displays potent anti-angiogenic activity in the Matrigel model and chicken chorioallantoic membrane (CAM) model. Another $\alpha 7$ -nAChR antagonist MG624 also inhibited nicotine-induced angiogenesis in lung endothelial cells. Our studies show that $\alpha 7$ -nAChR antagonists may be useful for novel combination therapies in human SCLC.

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Primary Presenter / email: **Robateau, Z.** / Robateau@marshall.edu

Basic Science
Cancer

Mentor / e-mail: Dasgupta, Piyali / Dasgupta@marshall.edu



CCTS Poster Presentation Abstracts

57 Abstract Title: **2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD)/Aryl Hydrocarbon Receptor (AHR) Regulation of L-Type Neutral Amino Acid Transporter 1 (LAT1) in Breast Cancer Cells**

Author(s): J.K. Tomblin, Department of Pharmacology, Physiology and Toxicology, Marshall U, Huntington, WV
 S. Arthur, Department of Clinical & Translational Science, Marshall U
 D. Primerano, Department of Biochemistry and Microbiology, Marshall U
 A. Chaudhry, Department of Pharmacology, Physiology and Toxicology, Marshall U
 J. Fan, Department of Biochemistry and Microbiology, Marshall U
 J. Denvir, Department of Biochemistry and Microbiology, Marshall U
 T. B. Salisbury, Department of Pharmacology, Physiology and Toxicology, Marshall U

Abstract: The aryl hydrocarbon receptor (AHR) is a ligand-activated transcription factor that is regulated by environmental toxicants that function as AHR agonists such as 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). AHR also plays a role in cancer cell cycle progression. L-Type Amino Acid Transporter 1 (LAT1) is overexpressed in cancer, which has been attributed to its ability to promote leucine uptake by tumor cells. We hypothesized that TCDD regulated the expression of LAT1 in breast cancer cells (BCCs) through an AHR dependent mechanism. RNA sequencing followed by Ingenuity Pathway Analysis (IPA), western blotting, quantitative real time PCR, radioactive leucine uptake experiments and chromatin immunoprecipitation studies were all implemented to study our hypothesis. Our study used MCF-7 and MDA-MB-231 BCCs. TCDD RNA-seq coupled with published TCDD-ChIP-seq identified LAT1 as a potential TCDD/AHR target gene. Pathway analysis of TCDD-RNA-seq data revealed a significant association between TCDD and molecular transport. Short interfering RNA (siRNA)-directed knockdown of AHR confirmed that TCDD-induction of LAT1 mRNA and protein required AHR. Leucine uptake experiments established TCDD-induction of leucine uptake by MCF-7 BCCs. Chromatin immunoprecipitation-quantitative PCR (ChIP-qPCR) assays revealed recruitment of AHR/AHR nuclear translocator (ARNT) heterodimers as well as the histone acetyltransferase p300 to an AHR binding site in the LAT1 gene, which caused increases in histone H3 acetylation. Finally, endogenous AHR regulation of LAT1 was also noted, and knockdown of either AHR or LAT1 with siRNAs compromised MCF-7 and MDA-MB-231 BCC proliferation. This study is the first to fully characterize TCDD/AHR regulation of the LAT1 gene in breast cancer cells.

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Primary Presenter / email: **Tomblin, J.K.** / justintomblinemail@gmail.com
Basic Science
Cancer

Mentor / e-mail: Salisbury, T.B. / salisbury@marshall.edu



CCTS Poster Presentation Abstracts

58 Abstract Title: **Evaluation of small-molecule FASN inhibitors in preclinical models of colorectal cancer**

Author(s): Y.Y. Zaytseva, Department of Toxicology and Cancer Biology, U of Kentucky
P. G. Rychahou, Department of Surgery, U of Kentucky
T. Gao, Markey Cancer Center, U of Kentucky
E. Y. Lee, Markey Cancer Center, U of Kentucky
H. L. Weiss, Markey Cancer Center, U of Kentucky
T. S. Heuer, 3-V Biosciences, Menlo Park, CA
G. Kemble, 3-V Biosciences, Menlo Park, CA
B.M. Evers, Markey Cancer Center, U of Kentucky

Abstract: Fatty Acid Synthase (FASN), a key enzyme of de novo lipid synthesis, is upregulated in colorectal cancer (CRC). Recently, a first-in-class, oral FASN inhibitor (TVB-2640) entered a Phase I clinical trial in solid tumor patients; however, tumor characteristics that would indicate responsiveness to FASN inhibition are not fully understood. The purpose of our study was: (i) to determine the effect of FASN inhibitors on proliferation in vitro, and in CRC patient-derived xenografts (PDXs); and (ii) to identify potential biomarkers associated with CRC responsiveness to FASN inhibition. **METHODS.** The effect of FASN inhibitors on the proliferation and apoptosis was assessed in primary cells and CRC cell lines. Tumor growth was assessed in PDXs established in NSG mice using freshly resected CRC specimens from our patient population. **RESULTS.** TVB compounds showed similar efficacy in primary and established CRC cells with a wide range of sensitivity to FASN inhibition. The 5 cell lines that were most responsive to FASN inhibition demonstrated a low basal level of pAMPK and pAkt as compared to the 5 least responsive cells. Inhibition of proliferation by TVB compounds is associated with a decrease in expression of active β -catenin, c-MYC, pAkt, and survivin and an increase in apoptosis. Consistent with our in vitro studies, a wide range of sensitivity to FASN inhibition was observed in PDXs. TVB-3664 treatment significantly reduced tumor volume in 30% of treated PDXs with no significant weight changes or toxicity observed. **CONCLUSIONS.** Our studies show that the novel FASN inhibitors significantly inhibit CRC growth both in vitro and in vivo. Importantly, our results suggest that basal activation of AMPK and Akt may be predictive of responsiveness to FASN inhibition and may function as potential biomarkers to allow a more personalized treatment approach.

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Primary Presenter / email: **Zaytseva, Y.Y.** / yyzayt2@uky.edu

**Basic Science
Cancer**

Mentor / e-mail: Evers, B.M. / mark.evers@uky.edu



CCTS Poster Presentation Abstracts

59 Abstract Title: Poly-ADP-Ribose-Polymerase as a Therapeutic Target in Pediatric Diffuse Intrinsic Pontine Glioma and Pediatric High Grade Astrocytoma

Author(s):

Y. Chornenkyy, Arthur & Sonia Labatt Brain Tumour Research Centre, Hospital for Sick Children; Dept. of Laboratory Medicine & Pathobiology, Faculty of Medicine, U of Toronto, Toronto, Canada
 S. Agnihotri, Arthur & Sonia Labatt Brain Tumour Research Centre, Hospital for Sick Children
 M. Yu, Arthur & Sonia Labatt Brain Tumour Research Centre, Hospital for Sick Children
 Pawel Buczkowicz, Arthur & Sonia Labatt Brain Tumour Research Centre, Hospital for Sick Children
 P. Rakopoulos, Arthur & Sonia Labatt Brain Tumour Research Centre, Hospital for Sick Children; Dept. of Laboratory Medicine & Pathobiology, Faculty of Medicine, U of Toronto
 B. Golbourn, Arthur & Sonia Labatt Brain Tumour Research Centre, Hospital for Sick Children; Dept. of Laboratory Medicine & Pathobiology, Faculty of Medicine, U of Toronto
 L. Garzia, Arthur & Sonia Labatt Brain Tumour Research Centre, Hospital for Sick Children
 R. Siddaway, Arthur & Sonia Labatt Brain Tumour Research Centre, Hospital for Sick Children
 S. Leung, Arthur & Sonia Labatt Brain Tumour Research Centre, Hospital for Sick Children; Dept. of Laboratory Medicine & Pathobiology, Faculty of Medicine, U of Toronto
 J.T. Rutka, Arthur & Sonia Labatt Brain Tumour Research Centre, Div. of Neurosurgery, Hospital for Sick Children, U of Toronto
 M.D. Taylor, Arthur & Sonia Labatt Brain Tumour Research Centre, Div. of Neurosurgery, Hospital for Sick Children, U of Toronto
 P.B. Dirks, Arthur & Sonia Labatt Brain Tumour Research Centre, Div. of Neurosurgery, Hospital for Sick Children, U of Toronto
 C. Hawkins, Arthur & Sonia Labatt Brain Tumour Research Centre, Hospital for Sick Children; Dept. of Laboratory Medicine & Pathobiology, Div. of Pathology, Faculty of Medicine, U of Toronto

Abstract: Pediatric supratentorial high-grade astrocytomas (pHGA) and diffuse intrinsic pontine gliomas (DIPG) are devastating pediatric malignancies for which no effective therapies exist. Poly-(ADP-Ribose)-Polymerase (PARP) protein expression is found in ~60% of DIPGs suggesting PARP may be a potential therapeutic target. PARP1 levels were characterized by immunohistochemistry in DIPG and pHGA patient samples using tissue microarrays (TMA) and by Western blotting in DIPG tissue samples. PARP1 levels were also characterized by Western blotting in several cell lines: human astrocytes, primary pHGA and DIPG cell lines (SJG2, SF188, KNS42, 462, 626 and DIPG58, DIPGM, DIPG4). Effects on cell viability in response to different doses of PARP inhibitors, Olaparib, Veliparib, or Niraparib were determined using MTT Assay. Western blotting against PAR and immunofluorescent staining against γ H2AX determined PARP activity and DNA damage. The effect of Niraparib on survival was evaluated by treating mice with orthotopic SJG2 xenografts alone or in combination with ionizing radiation (IR) (20 Gy, fractionated). Strong staining for PARP1 was detected in 82% and 76% of pHGA and DIPG samples, respectively and two DIPG tissue samples had increased PARP1 protein levels. PARP-knockdown reduced cell proliferation in SJG2 cells. Across all cell lines tested by Western blotting, PARP1 protein levels were significantly elevated relative to normal human astrocytes. All PARP inhibitors reduced PARP1 activity but Niraparib was most effective at reducing cell viability and clonogenic survival as a single agent. Niraparib (5 μ M) alone induced significant accumulation of γ H2AX foci, reduced ki67 levels, and induced growth arrest in SJG2 and SF188 cells. Pre-treatment with Niraparib (1 μ M) significantly decreased clonogenic survival and reduced the rate of DNA repair after 2 Gy of IR across all cell lines tested. Niraparib (50 mg/kg) inhibited PARP1 activity in vivo, and extended survival of mice with orthotopic pHGA xenografts, when administered before IR (20 Gy, fractionated), relative to control mice (40 days vs. 25 days). Our data provides in vitro and in vivo evidence suggesting that Niraparib may be an effective radiosensitizer for pHGA and DIPG. Furthermore while all PARP inhibitors suppress PARP activity not all PARP inhibitors reduce cell viability as single agents. Thus not all PARP inhibitors can be expected to be equally efficacious in a clinical trial setting.

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Primary Presenter / email:

Chornenkyy, Y. / yevchornenkyy@uky.edu
Clinical Science
Cancer

Mentor / e-mail:

Hawkins, C. / cynthia.hawkins@sickkids.ca



CCTS Poster Presentation Abstracts

60 Abstract Title:	Chloroquine Sensitizes Melanoma Cells to the Action of Ionizing Radiation
Author(s):	M.M. Kudrimoti, College of Arts and Sciences, U of Kentucky N. Shukla, Departments of Toxicology and Cancer Biology, U of Kentucky N. Hebbar, Departments of Toxicology and Cancer Biology, U of Kentucky V.M. Rangnekar, Departments of Radiation Medicine and Markey Cancer Center, U of Kentucky

Abstract: Melanoma is the second most common cancer in men and women ages 15-29 across the world. Melanoma is a highly metastatic cancer that can be potentially fatal, and patient mortality is often associated with tumor resistance to therapy. In an effort to repurpose FDA-approved drugs, we identified Chloroquine (CQ) as an inducer of the proapoptotic tumor suppressor protein Par-4. We next determined whether CQ sensitizes melanoma cells to the action of ionizing radiation. BRAF-inhibitor PLX4032-sensitive melanoma cells or PLX4032-resistant melanoma cells were exposed to ionizing radiation and various doses of CQ. Our findings indicate that the combination of CQ and ionizing radiation exhibits synergistic growth inhibition of both PLX4032-sensitive and PLX4032-resistant melanoma cells. Further studies in pre-clinical mouse models of melanoma will determine the translational relevance of these findings.

Supported by:

Primary Presenter / email: **Kudrimoti, M.M.** / meghanakudrimoti@gmail.com
Clinical Science
Cancer

Mentor / e-mail: Rangnekar, V.M. / vmrang01@uky.edu



CCTS Poster Presentation Abstracts

61 Abstract Title: **Epidemiology of Colon Cancer in Southeastern Kentucky-highest incidence of colorectal cancer in the United States**

Author(s): N. Nataraj, College of Medicine, U of Kentucky
 U. Shankar, Department of Gastroenterology, U of Kentucky
 M. Dignan, Markey Cancer Center, U of Kentucky
 V. Navale, Hamilton H.S. Phoenix, AZ

Abstract: Purpose: Southeastern (SE) Kentucky had the highest age adjusted colorectal cancer (CRC) incidence in the United States between 2007 and 2011. The literature reports that the CRC relative risks were 1.2 for smoking and 1.2 for obesity. Since SE Kentucky has the highest incidence of CRC in the US, we wanted to find the correlation between histology and age over and under 50, gender (M/F), and smoking status respectively. Method: Retrospective data from the Southeastern AHEC tumor registry in Hazard, Kentucky after IRB approval were analyzed. Data from 392 patients from 2002 to 2012 were included. All tumor biopsies were evaluated for mucinous carcinoma (> 50% extracellular mucin) with or without signet ring cells, which are associated with lynch syndrome or high association with microsatellite instability in the tumor. The data were further analyzed with respect to age, gender, and smoking status. Results: Of the data on 392 patients, 57.66% were smokers, 88.01% were > age 50, and 54.6% were male. Among those with mucinous CRC, 57.89% were smokers compared to 57.07% among those with non-mucinous CRC. The odds of mucinous CRC was 1.011 higher among smokers. In the mucinous CRC group, 80.95% were > 50, compared to 88.86% in the non-mucinous CRC group. Overall, the odds of mucinous CRC was 0.47 for those diagnosed > 50. Of those with mucinous CRC, 61.90% female compared to 43.42% of those with non-mucinous CRC. Conclusion: While smokers were more likely to have mucinous CRC than other CRC types, there does not appear to be a significantly greater risk for mucinous over non-mucinous cancer types. Age > 50 is a risk factor all types of CRC, and a higher percentage of patients over 50 had non-mucinous than mucinous CRC. Females had greater odds of having the mucinous variety than other CRCs. Thus it is likely female gender is a risk factor for mucinous CRC. Further study is needed to correlate external factors such as obesity, family history and diet with CRC.

Supported by:

Primary Presenter / email: **Nataraj, N.** / nna229@uky.edu
Clinical Science
Cancer

Mentor / e-mail: Shankar, U. / shankar.gastrohep@gmail.com



CCTS Poster Presentation Abstracts

62 Abstract Title: **Exploring the Mechanism by Which 2,3,7,8,-Tetracholordibenzodioxin (TCDD) Regulates Jagged-1 via the Aryl Hydrocarbon Receptor**

Author(s): S. Piwarski, Dept. of Pharmacology, Toxicology, & Physiology, Marshall U, Huntington, WV
T. Salisbury, Dept. of Pharmacology, Toxicology, & Physiology, Marshall U

Abstract: Approximately 10-20% of breast cancer patients are diagnosed with triple negative breast cancer (TNBC). Jagged1 (JAG1) is a transmembrane receptor protein that has been proven to play a role in cancer biology and is normally over-expressed in TNBC. Studies show that JAG1 plays a key role in metastasis in various cancers. High JAG1 mRNA and protein expression levels are also indicators of poor prognosis and silencing of JAG1 (siRNA) in cancer cells induced anti-metastatic effects. This makes it a potential chemotherapeutic target for hormonal therapy resistant cancers such as TNBC. Decreased expression of JAG1 in the presence of TCDD suggests that the aryl hydrocarbon receptor (AHR) can potentially inhibit JAG1-dependant signaling as a means for inducing anti-metastatic effects in cancer cells. Our lab showed that TCDD decreased the expression of JAG1 in TNBC cells at 12 and 24 hours via western blot compared to control (DMSO). A metastatic regulator down-stream of JAG1, SNAIL, was increased over the course of 24 hours in vehicle (DMSO) treated TNBC cells. However, in TCDD treated TNBC cells we observed similar SNAIL concentrations at 12 and 24 hours, with a slight decrease after 24 hours, indicating that TCDD may suppress SNAIL expression. AHR knockdown studies are currently being conducted to identify any endogenous regulation of JAG1 in TNBC. These findings can identify a novel mechanism that can target JAG1-dependent signaling using non-carcinogenic AHR ligands in combination with other chemotherapy agents as a novel form of treatment for TNBC as well as potentially other types of cancer.

Supported by: Marshall University: School of Medicine, Biomedical Sciences

Primary Presenter / email: **Piwarski, S.** / spiwarsk@gmail.com
Clinical Science
Cancer

Mentor / e-mail: Salisbury, T. / salisburyt@marshall.edu



CCTS Poster Presentation Abstracts**63 Abstract Title: Impact of Perioperative Transfusions and Postoperative Major Complications on Overall Survival after Colon Cancer Resection**

Author(s): M.J. Spitnale, College of Medicine, U of Kentucky
 D. Hnoosh, Department of Surgery, College of Medicine, U of Kentucky
 S.P. Dineen, Department of Surgery, College of Medicine, U of Kentucky
 J.A. Patel, Department of Surgery, College of Medicine, U of Kentucky
 S.J. Beck, Department of Surgery, College of Medicine, U of Kentucky
 J.S. Hourigan, Department of Surgery, College of Medicine, U of Kentucky
 D.L. Davenport, Department of Surgery, College of Medicine, U of Kentucky
 CW.D. Tzeng, Department of Surgery, College of Medicine, U of Kentucky

Abstract: Introduction: Perioperative transfusions and postoperative major complications (PMC) have been suggested to be negatively associated with overall survival (OS) after potentially curative cancer surgery. We sought to evaluate the influence of these perioperative events on OS after colon cancer resection. Methods: An institutional database of consecutive patients (2007-13) who underwent colon cancer resection without neoadjuvant therapy was created and analyzed. Clinicopathologic variables, perioperative events and complications, and outcomes were compared using nonparametric tests. Results: Of 296 patients who met inclusion criteria (stage I-76, II-73, III-80, IV-67), 51 (17.2%) had a transfusion intraoperatively or within 72hrs. With median follow-up of 46.2mo, median OS for transfused patients was 30.3mo (stage II) and 9.1mo (stage III) compared to median OS not reached (MNR) for patients without transfusion ($p<0.001$, $p=0.002$, respectively). Rates of 30-day complications were: Grade 0/none-48.6%, I-7.8%, II-18.9%, III-10.1%, IV-9.8%, V (death)-4.7%. Median OS for patients with/without PMC (Grade \geq III) were 60.4mo vs. MNR for Stage I ($p=0.048$), 23.2mo vs. MNR for stage II ($p<0.001$), and 32.0mo vs. MNR for Stage III ($p=0.001$). On multivariate analysis of stage I-III patients and adjusted for anemia/preoperative hematocrit $<30\%$, independent risk factors for OS were age (hazard ratio, HR-1.05, $p<0.001$), clinical stage (HR-1.51, $p=0.018$), perioperative transfusions (HR-2.43, $p=0.002$), and PMC (HR-3.59, $p<0.001$). Conclusions: Both perioperative transfusions and PMC were independent risk factors for worse OS after colon cancer resection. To improve long-term outcomes in potentially curative colon cancer resections, surgeons should adopt programmatic transfusion avoidance strategies and focus on perioperative risk reduction to limit PMC.

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Primary Presenter / email: **Spitnale, M.J.** / michael.spitnale@uky.edu
Clinical Science
Cancer

Mentor / e-mail: Tzeng, CW.D. / ching-wei.tzeng@uky.edu



CCTS Poster Presentation Abstracts

64 Abstract Title: **Higher Incidence of Early-Onset Colorectal Cancer in Southeastern Appalachian Kentucky due to Genetic and Epigenetic Characteristics**

Author(s): A. Shankar, Sayre School
 U. Shankar, Gastroenterology Associates of Hazard, Hazard, KY
 M. Dignan, Marky Cancer Center, U of Kentucky
 L. Selby, Gastroenterology, U of Kentucky

Abstract: Purpose: The aim of this project is to evaluate the genetic and epigenetic factor (smoking) associated with colorectal cancer (CRC) in Southeastern Appalachian Kentucky. The highest CRC incidence in the United States is in Southeastern Appalachian KY. The age adjusted CRC incidence rate in KY is 61.3% for males and 44% for females. In Appalachian KY the rates are higher, 67.3% for males and 47.8% for females. The CRC relative risk is 1.2 for smokers, 2.2 with one first degree relative and 4 with more than one first degree relative. Method: 41 CRC patients' data were collected retrospectively from 2012-2015 from the Appalachian Regional Hospital in Hazard, KY. We performed germ line genetic testing for Lynch syndrome at Myriad Genetic Lab for 18 of the 41 CRC patients. The other 23 patients had tumor screening for Lynch syndrome using immunohistochemical (IHC) staining of the four mismatch repair proteins at Mayo Medical Laboratories. We further analyzed data according to age, sex, smoking habits, location of tumor (distal/right-sided or proximal/left-sided), family history of CRC and other cancers, age of diagnosis, and type of MMR gene mutation. Results: 51.2% of patients were male. 30.6% were smokers. 10 of the 41 CRC patients were diagnosed under age 50 (22.7%) compared to 10% expected frequency of CRC cases under age 50. 35.63% of smokers with CRC were diagnosed under age 50. 55% of Lynch positive CRC patients were smokers. Of the 9 Lynch patients, 4 were left-sided, 4 were right-sided, and 1 had two synchronous left and right tumors. Of the 10 Lynch CRC negative patients, 7 were right-sided, 3 were left-sided. 55.7% of Lynch positive CRC patients were under 50 years. Of the 9 positive Lynch test patients, 5 had a MSH2 mutation (5 were the MSH2 exon 1-6 deletion), 2 had MLH1 mutations, 1 had a MSH6 mutation, and 1 had a PMS2 mutation. IHC stains were all negative on 23 patients. Of the 29 patients who had detailed family history of CRC, 14.5% had one FDR with CRC, 18% with two FDRs, 16.4% with 3 FDRs, 1.8% with four FDRs, and 1.8% with five FDRs. Conclusion: The incidence of CRC under age 50 is higher in Southeastern Appalachian KY. There seems to be a high correlation between smoking and CRC under age 50 and between Lynch syndrome and CRC under age 50. Our Lynch patients had colon cancer located equally in both proximal and distal colon, indicating increasing incidence of left-sided Lynch syndrome. The MSH2 exon 1-6 deletion, also known as the American Founder Mutation which has been previously linked to families from Southeastern KY, seems to be the predominate mutation seen in Lynch syndrome patients from this region. Genetic factors (MMR mutation), positive family history of CRC and epigenetic external factor (smoking) may be responsible for the higher incidence of CRC in younger patients in our region.

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Primary Presenter / email: **Shankar, A.** / shankar.anjali2@gmail.com
Clinical Science
Other

Mentor / e-mail: Selby, L. / laselb0@uky.edu



CCTS Poster Presentation Abstracts

65 Abstract Title: **Improvement in Quality of Life through the LIVESTRONG Program at the YMCA of Central Kentucky**

Author(s): C. Auberle, College of Medicine, U of Kentucky
 E. Maroudas, College of Medicine, U of Kentucky
 D. Peterson, YMCA Central Kentucky
 C. Donohoo, YMCA Central Kentucky
 E. Dupont-Versteegden, College of Health Sciences, U of Kentucky

Abstract: Many cancer survivors suffer from reduced physical function, but also can experience increased anxiety, depression, and stress. The purpose of this study was to evaluate the effects of a wellness program on physical function as well as quality of life indicators of cancer survivors. The LIVESTRONG program at the YMCA is a community-directed program designed for cancer patients, containing a well-rounded exercise regime, diet counseling, and discussion groups. Measures of physical well-being and quality of life indicators, as measured by the PROMIS-29 instrument, are taken at the onset and at the end of the 12 week program. Physical indicators evaluated included balance (back scratch, arm reach and single leg stance) and grip strength. All but arm reach showed statistically significant improvement ($p < 0.05$). Quality of life indicators as measured on a scale from 1 to 5 showed statistically significant improvement in areas such as anxiety, depression, fatigue, and feelings of physical function ($p < 0.05$). Indicators of sleep disturbance, satisfaction with social role and pain interference showed improvement, but were not determined as statistically significant. Finally, no correlation was found between changes in physical indicators and changes in quality of life indicators. Results from our analyses demonstrate further beneficial effect of the program on strength, cardiovascular fitness, balance, and some indicators of quality of life. Completion of the program is not dependent upon age or biological sex. We conclude that gains in physical indicators are not correlated to gains in quality of life indicators and thus improvements can be made in either area independently.

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Primary Presenter / email: **Auberle, C.** / ceau222@uky.edu
Community Science
Cancer

Mentor / e-mail: Dupont-Versteegden, E. / eedupo2@email.uky.edu



CCTS Poster Presentation Abstracts

66 Abstract Title: **Title: Personalizing Smoking Cessation Pharmacotherapy based on the Nicotine Metabolite Ratio (NMR): A systematic Review**

Author(s): C.T.C. Okoli, College of Nursing, U of Kentucky
V. Anand, Department of Psychiatry, East Carolina U

Abstract: Objectives: The ratio of nicotine metabolites, 3' Hydroxicotinine (3HC)/cotinine (COT), commonly referred to as the nicotine metabolite ratio (NMR) is an important biomarker for CYP2A6 activity, which has high correlation to nicotine dependence. Moreover, the NMR may be a crucial biomarker to predict the efficacy of smoking cessation (SC) pharmacotherapy and guide personalized treatment. As such, we conducted a systematic review of the extant literature to examine the effect of NMR on the efficacy of SC pharmacotherapy. Methods: A literature search of the PubMed database was conducted to examine research in this area prior to January 2016. Keywords for the search included combinations of Smoking cessation and Nicotine Metabolite Ratio and Quitting smoking and NMR. 429 studies were initially retrieved; after removing duplicates and employing a histrionic search of relevant articles, ten studies (7 RCTs, 3 cohort studies) remained applicable for our study. Results: Five RCTs and two Cohort studies found that NMR was significantly associated with the efficacy/effectiveness of SC pharmacotherapy. Specifically, slow metabolizers (lower NMR) were more successful in SC with nicotine replacement therapy, whereas fast metabolizers were more successful with oral SC pharmacotherapy (i.e., bupropion or varenicline). Conclusions: The findings of this study suggest that the NMR is an important biomarker that can be used to personalize and optimize SC treatment. Future studies are needed to examine the outcomes of SC pharmacotherapy that is tailored to smokers based on their NMR. Such studies will be instrumental in reducing the current disease burden associated with tobacco addiction.

Supported by:

Primary Presenter / email: **Okoli, C.T.C** / ctokol1@uky.edu
**Community Science
Cancer**

Mentor / e-mail: Okoli, C.T.C / ctokol1@uky.edu



CCTS Poster Presentation Abstracts

67 Abstract Title: **Identifying community perspectives for a lung cancer screening awareness campaign in Appalachia Kentucky: The Terminate Lung Cancer (TLC) Study**

Author(s): R. Cardarelli, U of Kentucky
 K. Roper, U of Kentucky
 K. Cardarelli, U of Kentucky
 F.J. Feltner, Center of Excellence in Rural Health
 S. Prater, Kentucky Homeplace
 K. Ledford, Kentucky Homeplace
 B. Justice, Kentucky Homeplace
 D. Reese, University of Pikeville
 P. Wagner, TLC Community Board Member
 C. Cantrell, TLC Community Board Member

Abstract: Introduction: Lung cancer screening with low-dose computed tomography (LDCT) scan is now covered by Centers for Medicare & Medicaid Services following an evidence-based recommendation, but a shared decision making process should inform patients of risks and limitations. An awareness campaign promoting LDCT screenings is an opportunity to elicit patient engagement with health providers about the risks and benefits. Focus groups representing three regions of Appalachian Kentucky known for high lung cancer rates discussed development of a lung cancer screening campaign. Recommendations included messaging content, appeals or design, campaign implementation, and trusted information or communication sources. Methods: Community health workers (CHWs) from three Eastern Kentucky regions recruited individuals from their local communities using established client files. CHWs hosted six total focus groups (7-11 participants each) using questions guided by the Communication-Persuasion Matrix framework. All sessions were recorded and transcribed in 2014 for independent content analysis. Results: A total of fifty-four individuals (61.1% female; >55 pack year history) participated. Prior to discussion, most participants had not heard of lung cancer screening. Cited needs for content of a campaign included benefits of early detection and payment information. Messages considered most persuasive were those that include: personal testimony, and messages of hope, prolonged life, and an emphasis on family and the ambition to survive. Having the information come from one's family doctor or specialty provider was considered important to message communication. Conclusions: Messages about survivorship, family, and prolonged life should be considered in lung cancer screening awareness campaigns. Our results provide community input about messages regarding screening options.

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Primary Presenter / email: **Roper, K** / karen.roper@uky.edu
**Community Science
 Cancer**

Mentor / e-mail: Cardarelli, R. / roberto.cardarelli@uky.edu



College of Health Sciences Research Day

Poster Presentation Abstracts

68 Abstract Title: **Patient- Engagement, Literacy, Adherence Study**

Author(s): R. Cardarelli, Family & Community Medicine, U of Kentucky
 C. Studts, College of Public Health, U of Kentucky
 K. Fulda, U. North Texas Health Science Center
 C. Hustedde, Family & Community Medicine, U of Kentucky
 A. Espinoza, U. North Texas Health Science Center
 S. Crocker, Family & Community Medicine, U of Kentucky
 D. Combs, UK Center of Excellence in Rural Health - Hazard
 J. Schilling, Family & Community Medicine, U of Kentucky
 K. Roper, Family & Community Medicine, U of Kentucky
 G. Holmes, UK Center of Excellence in Rural Health - Hazard

Abstract: Clinical use of self-report questionnaires and related forms of assessment of a patient's health, risks and/or other aspects of their health care has grown exponentially to include social, environmental, and psychological dimensions that factor into enhanced patient-centered care. Unfortunately, many assessments have not developed into practical, methodologically sound, clinical tools, primarily due to the impracticality of administering lengthy surveys within the typical time allotted for a primary care office visit. Some assessments also prove less useful or relevant to clinical application. Three constructs that have emerged as especially impactful to health outcomes include health literacy, medication adherence, and the patient's preferences and efforts toward control over their care. The application of brief and accurate measures of these concepts could contribute enormously to improved patient-centered primary care. Using previously validated measures of health literacy, medical adherence, and engagement preferences, we sought to develop and validate an ultra-brief Patient-ELA tool for clinical practice. AIM 1. Select and administer validated full-version instruments measuring health literacy, medication adherence, and engagement preference to 200 individuals in primary care offices. AIM 2. Applying item response theory (IRT) methods to the data obtained in Aim 1, a subset of items will be selected to comprise the Patient-ELA for use as an assessment tool in primary care settings. Our initial pilot study yielded 7 questions (from the original 66 questions) that could be used in a brief survey to assess the constructs of Engagement, Literacy, and Adherence of a patient.

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Primary Presenter / email: **Cardarelli , R.** / roberto.cardarelli@uky.edu

Basic Science

Other

Mentor / e-mail: Cardarelli, R. / roberto.cardarelli@uky.edu

CCTS Poster Presentation Abstracts

69 Abstract Title: **Pathologic Comparison of Angiotensin Induced Superior Mesenteric Artery Aneurysms in Smooth Muscle Low-Density-Lipoprotein-Related-Receptor-1 Deficient Mice between Constitutive and Post-Maturity Deletion Models**

Author(s): Z.Chen, MD/PhD Program, U of Kentucky
 D.L. Rateri, CVRC, U of Kentucky
 J.Post, CVRC, U of Kentucky
 D.Lehnert, CVRC, U of Kentucky
 A.Balakrishnan, CVRC, U of Kentucky
 D.A. Howatt, CVRC, U of Kentucky
 J.J. Moorlegghen, CVRC, U of Kentucky
 A. Daugherty, CVRC, U of Kentucky

Abstract: Recent genome wide association studies have shown a relationship between low-density-lipoprotein-receptor-related-protein-1 (LRP1) and presence of abdominal aortic aneurysms. LRP1 is a large, multifunctional receptor that is involved in a wide range of diverse processes: fetal development, cholesterol homeostasis, and protease clearance. The Daugherty Lab has previously demonstrated that constitutive deletion of smooth muscle cell LRP1 (smLRP1) in mice greatly exacerbates angiotensin (AngII) induced aneurysms. Unexpectedly, AngII infusion promoted a large luminal expansion of the superior mesenteric artery (SMA) and rupture at this location was associated with increased mortality in the sm-LRP1 mice. Due to the ubiquity of LRP1 expression during all stages of life, AngII induced aneurysm pathology in a constitutive smLRP1 deficient mouse may result from disruption of either LRP1 regulated vascular development or LRP1 mediated vascular homeostasis. The purpose of this study was to determine whether AngII-induced SMA aneurysms were different between mice with constitutive LRP1 deletion versus post-maturity induced LRP1 deletion.

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Primary Presenter / email: **Chen, Z.** / zch236@uky.edu
Basic Science
Cardiovascular

Mentor / e-mail: Daugherty, A. / adaugh@uky.edu



CCTS Poster Presentation Abstracts

70 Abstract Title: **Butyrate Modulates Cav-1 and Its Binding Partner AhR, Leading to Differential Cyp1a1 and Cyp1b1 Gene Expression in Vascular Endothelial Cells**

Author(s): J.B. Hoffman, Department of Pharmacology and Nutritional Sciences, U of Kentucky
M.C. Petriello, University of Kentucky Superfund Research Center, U of Kentucky
B. Hennig, University of Kentucky Superfund Research Center, U of Kentucky

Abstract: Dietary fiber and associated metabolites may protect against vascular inflammation and atherosclerosis. The vascular endothelium plays an important role in the inflammatory response and pathology of atherosclerosis. Membrane microdomains called caveolae and their functional proteins, e.g., caveolin-1 (Cav-1), are involved in inflammatory pathways. Past literature has shown that downregulation of Cav-1 can prevent the toxicity of environmental pollutants, such as polychlorinated biphenyls (PCBs), and that Cav-1 interacts with the aryl hydrocarbon receptor (AhR). The AhR regulates the expression of cytochrome P450s, which have been linked to vascular inflammation. We hypothesize that fiber-derived butyrate can protect against pollutant-induced vascular inflammation by modulating caveolae-linked regulatory genes. In experiment one, primary endothelial cells were treated with increasing concentrations of butyrate for 4 hours and examined for mRNA expression of AhR, Cav-1, Cyp1a1, Cyp1b1 and antioxidant enzymes. Our preliminary data show that treatment with physiologically relevant concentrations of butyrate significantly decreased Cav-1 and AhR mRNA levels, but not in a dose-dependent manner. Also, the AhR targets Cyp1b1 and Cyp1a1 were reduced at the lowest concentration tested. To examine the protective role of butyrate against PCB126-induced toxicity, primary vascular endothelial cells were pretreated with 1 μ M of butyrate for 4 hours and then exposed to 0.1 μ M of PCB126 for 16 hours. Our data show that butyrate pretreatment significantly reduced PCB-induced inflammation, evidenced by decreased mRNA levels of monocyte chemoattractant protein-1 (Mcp1) and vascular cell adhesion molecule 1 (Vcam1). At 16 hours post-PCB treatment, no alterations in Cav1, AhR, or target genes were observed. Our data suggest that dietary fiber-derived metabolites have the potential to protect against environmental insults and associated inflammatory events through mechanisms that still need to be elucidated.

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Primary Presenter / email: **Hoffman, J.B.** / jeba237@g.uky.edu
Basic Science
Cardiovascular

Mentor / e-mail: Hennig, B. / bhennig@uky.edu



CCTS Poster Presentation Abstracts

71 Abstract Title: **Sphingosine kinase-1 and sphingosine-1 phosphate receptor-1 regulate bone marrow stem cell mobilization and cardiac remodeling following myocardial infarction**

Author(s): A. Idris, Internal Medicine, Cardiovascular Research Center, U of Kentucky
 S. Ye, Internal Medicine, Cardiovascular Research Center, U of Kentucky
 P.R. Nagareddy, Internal Medicine, Cardiovascular Research Center, U of Kentucky
 M. Mathbout, Internal Medicine, Cardiovascular Research Center, U of Kentucky
 M. Sunkara, Internal Medicine, Cardiovascular Research Center, U of Kentucky
 S.S. Smyth, Internal Medicine, Cardiovascular Research Center, U of Kentucky
 A. Morris, Internal Medicine, Cardiovascular Research Center, U of Kentucky
 A. Abdel-Latif, Internal Medicine, Cardiovascular Research Center, U of Kentucky

Abstract: Introduction and Hypothesis: The sphingosine-1 phosphate (S1P)/ S1P receptor 1 (S1PR1) axis has been linked to the mobilization of bone marrow stem/progenitor cells in the setting of myocardial infarction (MI). Plasma S1P level is tightly regulated by sphingosine kinase (SphK) 1 and 2 for de novo synthesis and S1P lyase and phosphatases for degradation. We sought to examine the role of SphKs and S1PR1 in regulating stem cell mobilization following MI. Methods and Results: SphK1 (SphK1 KO), but not SphK2, dramatically reduced plasma S1P level and concomitantly blunted stem cell mobilization response in a permanent coronary artery ligation mouse model in comparison to wild type (WT) mice. In mice with conditional knockout for S1PR1 (S1PR1 KO) in BM cells, we observed significant reduction in stem cell mobilization following MI. The scar size in SphK1 KO and S1PR1 KO mice was larger than that in the control arms as determined by trichrome staining analysis. Consistently, echocardiography analyses showed significant reduction in cardiac function, infarct wall thickness, and worse adverse remodeling following MI in SphK1 and S1PR1 KO mice in comparison to controls. Intriguingly, the defect in plasma S1P level, stem cell mobilization and cardiac functional recovery following MI in SphK1 KO mice was rescued by the oral administration of the potent S1P lyase inhibitor tetrahydroxybutylimidazole (THI) which was administered day 3-10 post-MI. The beneficial effects of THI further suggests that S1P/S1PR1 axis is critical in regulating stem cell mobilization and cardiac remodeling and function in the setting of myocardial ischemic injury. Conclusion: Our findings demonstrate a novel mechanism of stem cell mobilization and cardiac recovery following MI, and highlight potential therapeutic targets for myocardial regenerative therapies.

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Primary Presenter / email: **Abdel-Latif, A.** / abdel-latif@uky.edu
Basic Science
Cardiovascular

Mentor / e-mail: Abdel-Latif, A. / abdel-latif@uky.edu



CCTS Poster Presentation Abstracts**72** Abstract
Title:**Dioxin-like pollutants increase hepatic flavin containing monooxygenase (FMO3) expression to promote synthesis of the pro-atherogenic nutrient biomarker Trimethylamine N-oxide from dietary precursors**

Author(s):

M.C. Petriello, Superfund Research Program & Lexington Veterans Affairs Medical Center, U of Kentucky
 J.B. Hoffman, Superfund Research Program & Graduate Center for Pharmacology & Nutritional Sciences, U of Kentucky
 M. Sunkara, Div. of Cardiovascular Medicine, U of Kentucky
 B. Wahlang, Superfund Research Program, U of Kentucky
 J.T. Perkins, Superfund Research Program & College of Public Health, U of Kentucky
 A.J. Morris, Superfund Research Program & Div. of Cardiovascular Medicine, U of Kentucky
 B. Hennig, Superfund Research Program & Dept. of Animal and Food Sciences, U of Kentucky

Abstract: The etiology of cardiovascular disease (CVD) is impacted by multiple modifiable and non-modifiable risk factors including dietary choices, genetic predisposition, and environmental exposures. However, mechanisms linking diet, exposure to pollutants, and CVD risk are largely unclear. Recent studies identified a strong link between plasma levels of nutrient-derived Trimethylamine N-oxide (TMAO) and coronary artery disease. Dietary precursors of TMAO include carnitine and phosphatidylcholine, which are abundant in animal-derived foods. Dioxin-like pollutants can upregulate a critical enzyme responsible for TMAO formation, hepatic flavin containing monooxygenase 3 (FMO3), but a link between dioxin-like PCBs, upregulation of FMO3, and increased TMAO has not been reported. Here, we show that mice exposed acutely to dioxin-like PCBs exhibit increased hepatic FMO3 mRNA, protein, as well as an increase in circulating levels of TMAO following oral administration of its metabolic precursors. C57BL/6 mice were exposed to 5 µmol PCB 126/kg mouse weight (1.63 mg/kg). At 48 h post-PCB exposure, mice were subsequently given a single gavage of phosphatidylcholine dissolved in corn oil. Exposure to 5 µmole/kg PCB 126 resulted in greater than 100-fold increase in FMO3 mRNA expression, robust induction of FMO3 protein, and a 5-fold increase in TMAO levels compared with vehicle treated mice. We made similar observations in mice exposed to PCB 77 (49.6 mg/kg twice); stable isotope tracer studies revealed increased formation of plasma TMAO from an orally administered precursor trimethylamine (TMA). Taken together, these observations suggest a novel diet-toxicant interaction that results in increased production of a circulating biomarker of cardiovascular disease risk.

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Primary Presenter / email: **Petriello, M.C.** / michaelcpetriello@uky.edu

Basic Science
Cardiovascular

Mentor / e-mail: Hennig, B. / bhennig@uky.edu



CCTS Poster Presentation Abstracts

73 Abstract Title: **Pro 224-Ala Mutation of the Rat Na/K-ATPase α 1 Subunit Prevents Na/K-ATPase Signaling without Affecting Ouabain-Sensitive Ion-Exchange Function**

Author(s): Y. Yan, Depts. of Clinical and Translational Sciences, Physiology, JCE School of Medicine, Marshall U
 Z-J Xie, MIIR, Marshall U
 J.I. Shapiro, JCE School of Medicine, Marshall U
 J. Liu, Dept. of Physiology JCE School of Medicine and MIIR, Marshall U

Abstract: Background: Renal proximal tubule Na/K-ATPase signaling regulates sodium homeostasis and blood pressure. α 1 Na/K-ATPase acts as a receptor for reactive oxygen species (ROS) and amplifies ROS signaling. To probe the molecular mechanism by which ROS affect cellular function through Na/K-ATPase signaling, we will test the hypothesis that carbonylation modification of Pro224 of rat α 1 Na/K-ATPase is essential for regulating Na/K-ATPase signaling and subsequent transepithelial sodium transport in renal proximal tubules. Methods: Mutation of Pro224 of rat α 1 subunit. Assays for ouabain-sensitive enzymatic and ion-exchange activities of the Na/K-ATPase, as well as ouabain-stimulated Na/K-ATPase signaling function. Results: Direct carbonylation modification of pig Pro222 in the Na/K-ATPase α 1 subunit was required to initiate ouabain-stimulated Na/K-ATPase/c-Src signaling and subsequent regulation of active transepithelial 22Na^+ transport. A single mutation of rat Pro224 (corresponding to pig Pro222) to Ala has no significant effect on the ouabain-sensitive enzymatic activity and ion-exchange activity of the Na/K-ATPase as an ion pump, but abolishes ouabain-stimulated Na/K-ATPase signaling and inhibition of active transepithelial 22Na^+ transport. Computerized docking analysis suggests a change of the binding of the Pro222 to pig c-Src SH2 and Kinase domain, before and after carbonylation. Taking our previous findings, the data indicates that carbonylation modification of Pro224 in rat α 1 subunit of the Na/K-ATPase α 1 subunit dictates ouabain-mediated Na/K-ATPase signal transduction and subsequent sodium transport. Conclusions: Direct carbonylation of Pro224 prevents ouabain-mediated Na/K-ATPase signaling and related sodium handling in renal proximal tubules.

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Primary Presenter / email: **Yan, Y.** / yan@marshall.edu
Basic Science
Cardiovascular

Mentor / e-mail: Liu, J. / liu@marshall.edu



CCTS Poster Presentation Abstracts

74 Abstract Title: **Deficiency of (Pro)renin Receptor in Adipocyte induces Liver Steatosis and increases Blood Pressure in Lean and Obese Male Mice**

Author(s): C.H. Wu, Department of Pharmacology and Nutritional Sciences, U of Kentucky
S.M. Moradi, Department of Pharmacology and Nutritional Sciences, U of Kentucky
M. Gong, Department of Physiology, U of Kentucky
G. Nguyen, College de France, France, USA
F. Yiannikouris, Department of Pharmacology and Nutritional Sciences, U of Kentucky

Abstract: Adipose tissue is an important source of the (pro)renin receptor (PRR). During the development of obesity, the expression of PRR gene is increased in adipose tissue. The purpose of this study was to define the metabolic consequences of the deletion of PRR during the development of obesity-associated hypertension. Male PRR^{fl/Y} mice expressing Adiponectin-driven Cre recombinase were bred to female mice PRR^{fl/fl} to generate littermate controls and adipocyte-PRR deficient mice (PRR^{Adi/Y}). PRR^{Adi/Y} and control mice were fed a low fat diet (LF, 10% kcal as fat) or a high fat diet (HF, 60% kcal as fat) for 16 weeks (n=5-8/groups). Body weight of LF fed-PRR^{Adi/Y} mice were decreased significantly compared to control mice. Adipocyte PRR deficient mice were resistant to diet induced obesity (body weights: PRR^{fl/Y}, 48 ± 1 g; PRR^{Adi/Y}, 34 ± 1 g; P<0.05). Fat mass were drastically decreased in PRR^{Adi/Y} mice fed a LF-or HF-diet compared to control mice. Liver weights were significantly increased in PRR^{Adi/Y} male mice fed a LF- or a HF-diet compared to control mice. The examination of livers revealed an increase of hepatic fat accumulation in male PRR^{Adi/Y} fed a LF-or HF-diet. Interestingly, LF and HF-fed PRR^{Adi/Y} mice had an improved glucose tolerance compared to control mice. When challenged with HF-feedings, adipocyte-specific deficiency of PRR exaggerated diet induced increased-blood pressure (HF: PRR^{fl/Y}, 132, ± 2 mmHg ; HF: PRR^{Adi/Y}, 138 ± 1 mmHg, P< 0.05). PRR^{Adi/Y} mouse model provides evidence for an important link between adipocyte PRR, fat distribution and regulation of blood pressure.

Supported by:

Primary Presenter / email: **Yiannikouris, F.** / fbyian2@uky.edu

Basic Science
Cardiovascular

Mentor / e-mail: Yiannikouris, F. / fbyian2@uky.edu



CCTS Poster Presentation Abstracts

75 Abstract Title: **Bubble Gulp: an Interactive Videogame Designed to Optimize Navigator Efficiency in Children Undergoing Cardiac Magnetic Resonance Imaging**

Author(s): K.N. Andres, College of Medicine, U of Kentucky
 S.M. Hamlet, Department of Electrical Engineering, U of Kentucky
 J.D. Suever, Department of Pediatric, U of Kentucky and Institute for Advanced Application Geisinger Health System
 J.D. Grabau, College of Medicine, U of Kentucky
 G.J. Wehner, Departments of Pediatrics and Biomedical Engineering, U of Kentucky
 M.H. Vandsburger, Department of Physiology, U of Kentucky
 D.K. Powell, Department of Biomedical Engineering, U of Kentucky
 V.L. Sorrell, Department of Internal Medicine, U of Kentucky
 B.K. Fornwalt, Departments of Pediatrics, Biomedical Engineering, Physiology and Medicine, U of Kentucky and Institute for Advanced Application, Geisinger Health System

Abstract: Purpose- Due to movement of the diaphragm during the respiratory cycle all cardiac magnetic resonance (CMR) images are acquired during end expiratory breath-holds. Advanced CMR imaging techniques often require long scan durations which necessitate the use of respiratory navigator gating. This is particularly necessary in children who have limited ability to hold their breath. We hypothesized that visual feedback of respiratory motion using an interactive videogame during CMR acquisition would increase navigator efficiency and improve image quality in children. Methods- We developed a feedback videogame, "Bubble Gulp," which guides children to optimize their breathing pattern during real-time image acquisition by incentivizing positioning their diaphragm within the respiratory navigator "acceptance window." Bubble Gulp is not integrated into any CMR pulse sequence, but rather is externally interfaced with the scanner via a laptop, making it compatible with any respiratory navigator gated scanning protocol. Using a 3T Siemens Tim Trio, 20 healthy children (Age: 13 ± 3, 35% female) underwent 2D spiral cine displacement encoding with stimulated echoes (DENSE) acquisition of navigator-gated mid-ventricular, basal, apical, and 4-chamber images. These four images were acquired while the children were free-breathing and again while they were playing Bubble Gulp. The Bubble Gulp interface was displayed in real time to the children during image acquisition using an angled mirror and MRI-compatible projector. Navigator efficiency and an image quality measurement, signal-to-noise ratio (SNR), were determined for each child and compared between the children's free-breathing and Bubble Gulp acquisitions using a paired student's t-test. Results- The Bubble Gulp feedback videogame improved navigator efficiency by 50% ($p < 0.0001$) and also improved SNR compared to free-breathing ($p = 0.006$). Conclusions- Use of Bubble Gulp, a feedback videogame, during navigator-gated DENSE CMR can improve navigator efficiency by 50% in children compared to traditional free-breathing acquisition methods. The videogame feedback system, also has a slight positive effect on image quality with a 7% increase in SNR, which is likely due to reduced heart rate variability during shorter scan durations. These findings should be generalizable to all CMR acquisition sequences which utilize a respiratory navigator.

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Primary Presenter / email: **Andres, K.** / kristin.andres@uky.edu
Clinical Science
Cardiovascular

Mentor / e-mail: Vandsburger, M. / m.v@uky.edu



CCTS Poster Presentation Abstracts

76 Abstract Title: **Vascular Permeability Effects on Tissue Perfusion: an MRI Phantom Study**

Author(s): A. Anwar, Paul Laurence Dunbar High School
P. Hardy, Department of Radiology, U of Kentucky
S. Leung, Department of Cardiology, U of Kentucky

Abstract: Non-invasive methods of measuring the architecture and behavior of a tissues' microvasculature system are valuable since morphological changes can be observed in the microvasculature before functional changes in the organs they make up. Quantifying tissue perfusion and blood vessel permeability is useful in the early diagnosis and prognosis of diseases, as well as the evaluation of therapeutics. Numerous diseases such as stroke, myocardial infarction, cancer and liver fibrosis are characterized by altered blood perfusion or blood vessel permeability. We sought to develop a simple model of tissue perfusion which would enable testing different MR imaging and image analysis techniques to improve the estimates of perfusion and vessel permeability. In the experiment, a hemodialyzer, consisting of approximately 10,000 polysulfone fibers in a small cylinder, was adapted to represent a two-compartment tissue model. We analyzed dynamic MR images following the injection of a bolus of Gadolinium-based MR contrast agent using the modified Tofts model. In the modified Tofts, model Ktrans refers to the transfer of plasma into the extravascular extracellular space. Ktrans was estimated for two conditions where the fiber permeability was altered by injecting agarose gels of different stiffness into space outside the fibers. The results were reproducible and varied proportional to fluid flow rate. Analysis of the images confirmed Ktrans was reduced with the introduction of the stiffer gel. In conclusion, the model is a useful and effective way to quantify variations in perfusion and vessel permeability which will have application in characterizing some human diseases.

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Primary Presenter / email: **Anwar, A** / amina.anwar@stu.fayette.kyschools.us
Clinical Science
CardiovascularMentor / e-mail: Hardy, P. / Peter.Hardy@uky.edu



CCTS Poster Presentation Abstracts

77 Abstract Title: **Interplay of Latent Tuberculosis Infection and Acute Myocardial Infarction**

Author(s): D. Henson, College of Medicine, U of Kentucky
 E. Ticona, Hospital Nacional Dos De Mayo
 G. Miranda, Hospital Nacional Edgardo Rebagliati Martins
 C. Ticona, Hospital Nacional Dos De Mayo
 E. Aranda, Hospital Nacional Edgardo Rebagliati
 T. Sterling, College of Medicine, Vanderbilt U
 B. Garvy, College of Medicine, U of Kentucky
 M. Huaman, College of Medicine, U of Kentucky

Abstract: Tuberculosis is a very common disease around the world, approximately 1/3 of the population currently is infected, and 90-95% of those people have an asymptomatic form called Latent Tuberculosis Infection (LTBI). In many countries, this latent form is not tested for, and is not treated once discovered because the consensus is that the infection poses no risk. However, new evidence suggest that there are complications from the LTBI centering around a state of chronic inflammation. We hypothesize that the chronic inflammation from an LTBI state increases the likelihood of Acute Myocardial Infarctions (AMI). Patients with a history of AMI are tested for LTBI, as well as matching controls. Patients and controls are enrolled at hospitals in Lima, Peru by nurses and have blood drawn for Quantiferon Testing. The Quantiferon assay is used because it does not require a follow up visit, and because the PPD test often is positive in patients who received the BCG vaccination, which is common in Peru. The data collection is on-going and but preliminary data is presented here: Of the control groups- 19 patients are negative for LTBI, 14 patients are positive for LTBI. This matches the current data that indicates that approx. 40% of Lima's population is positive for LTBI. Of the AMI group 17 patients are LTBI negative and 23 patients are LTBI positive. By the time of the presentation I should have additional data as well as early matching. This data is preliminary and has yet to be properly matched but initial indications support our hypothesis.

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Primary Presenter / email: **Henson, D.M.** / david.henson0@uky.edu
Clinical Science
Cardiovascular

Mentor / e-mail: Huaman, M.A. / moises.huaman@uky.edu



CCTS Poster Presentation Abstracts**78 Abstract Title: A Novel Insight into Stem Cell Mobilization by Using Cell-based and Hydrogel-based Therapies Employing Cathelicidin Related Antimicrobial Peptide (CRAMP) as a Potential Therapeutic Target in Ischemic Heart Disease**

Author(s): A. Idris, Gill Heart Institute & Div. of Cardiovascular Medicine, U of Kentucky, & VA Medical Center
 Y. M. Klyachkin, Gill Heart Institute & Div. of Cardiovascular Medicine, U of Kentucky, & VA Medical Center
 S. Ye, Gill Heart Institute & Div. of Cardiovascular Medicine, U of Kentucky, & VA Medical Center
 P. Nagareddy, Gill Heart Institute & Div. of Cardiovascular Medicine, U of Kentucky, & VA Medical Center
 A. Asfour, Gill Heart Institute & Div. of Cardiovascular Medicine, U of Kentucky, & VA Medical Center
 E. Gao, Temple School of Medicine, Center of Translational Medicine, Temple U, Philadelphia, PA
 A. Morris, Gill Heart Institute & Div. of Cardiovascular Medicine, U of Kentucky, & VA Medical Center
 S. Smyth, Gill Heart Institute & Div. of Cardiovascular Medicine, U of Kentucky, & VA Medical Center
 A. Abdel-Latif, Gill Heart Institute & Div. of Cardiovascular Medicine, U of Kentucky, & VA Medical Center,
 & Dept. of Immunology, Microbiology and Molecular Genetics, U of Kentucky

Abstract: Introduction: Acute myocardial infarction (AMI) triggers mobilization of bone marrow (BM)-derived stem/progenitor cells (BMSPCs) through poorly understood processes. BMSPCs can be used for myocardial repair following myocardial infarction (MI). Limited stem cell retention following intracoronary administration has reduced the clinical efficacy of this novel therapy. Cathelicidins related antimicrobial proteins (CRAMPs) have been shown to enhance chemotactic responsiveness of bone marrow Derived mononuclear Cells (BMMNC) migration towards low gradients of SDF-1 suggesting a potential role in BMMNC retention. Here, we assessed the therapeutic efficacy of CRAMP in the context of BMMNC recruitment and retention via intracardiac delivery of CRAMP-treated BMMNCs or CRAMP-packed hydrogels (HG) post-MI. Methods and Results: During the in vivo cell studies, mice were randomized into 3 groups: MI followed by injection of PBS, BMMNCs alone, and BMMNCs incubated with CRAMP. During the in vivo HG studies, BM GFP chimera mice were randomized into 4 groups: MI followed by injection of HG alone, HG + SDF-1, HG + CRAMP, HG + SDF-1 + CRAMP. Changes in infarct size and cardiac function between 5 days and 5 weeks after MI were assessed using cardiac MRI (CMR) and echocardiography. Treatment of BMMNCs with CRAMP enhanced their migration towards low, yet physiological, levels of SDF-1 in vitro. In vivo, BMMNC+CRAMP or HG + SDF-1 + CRAMP therapy was associated with significant increase in capillary density as compared to the control groups. Moreover, BMMNC+CRAMP or, HG + SDF-1 + CRAMP administration post-MI led to improvement in cardiac function as compared to other groups. In addition, BMMNC+CRAMP or HG + SDF-1 + CRAMP administration led to improvement in scar size using cardiac MRI and Trichrome staining as compared to other groups. Conclusion: Cathelicidins enhance BMMNC retention and recruitment after intramyocardial administration post-MI resulting in improvements in heart physiology and recovery. Therapies employing these strategies may represent an attractive method for improving outcomes of regenerative therapies in human studies.

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Primary Presenter / email: **Idris, A.** / amr.idris@uky.edu

**Clinical Science
 Cardiovascular**

Mentor / e-mail: Abdel-Latif, A. / abdel-latif@uky.edu



CCTS Poster Presentation Abstracts

79 Abstract Title: **Troponin elevation is more predictive than clinical risk scores alone in predicting mortality in septic patients with Type II NSTEMI**

Author(s): M.E. Jesinger, Department of Internal Medicine, U of Kentucky
 V.A. Gupta, Gill Heart Institute, U of Kentucky
 N. Kraitman, Department of Internal Medicine, U of Kentucky
 M.J. Sousa, Department of Internal Medicine, U of Kentucky
 K.E. Wingerter, Department of Internal Medicine, U of Kentucky
 B.C. Takagi, no affiliation
 R. Charnigo, Department of Biostatistics, U of Kentucky
 S.W. Leung, Gill Heart Institute, U of Kentucky
 V.L. Sorrell, Gill Heart Institute, U of Kentucky

Abstract: Background Cardiac Troponin I (TnI) is a marker of myocardial injury developed for diagnosis of acute coronary syndromes (ACS); however, it has prognostic value in non-ACS conditions, such as sepsis. The mechanism of elevation is not well established, but may be related to severity of illness. The purpose of this study was to investigate the additive value of TnI to the Acute Physiology and Chronic Health Evaluation II (APACHE) prediction score in septic patients. Methods In this single-center, non-concurrent cohort study, 272 patients with sepsis and detectable TnI were included from Jan 2013-Jan 2014. TnI ≥ 0.04 mg/L (>99 th percentile of ULN) was considered elevated. APACHE score was calculated. Primary endpoint of all-cause mortality was obtained from the social security death database. Logistic regression analysis was used to calculate effect size. Results 272 patients (age 58 +/- 15 years, 44% female) had data to calculate an APACHE score. When controlled for gender and APACHE score (mean 18 +/- 6), an elevated TnI aided in predicting 30-day mortality (OR=5.14; 95% CI, 1.17-22.56; p=0.03) and 1-year mortality (OR=4.74; 95% CI, 1.57-14.37; p=0.006). TnI stratified those at risk for mortality at 30 days above expected prognosis by APACHE alone (24%) compared to APACHE and positive TnI (33%) with p<0.01 compared to APACHE +negative TnI (7%). Conclusion Elevated TnI in septic patients is a strong predictor of mortality at 30 days and 1 year beyond well-established clinical measures of illness severity, suggesting an important role of TnI in developing future prognostic scoring systems.

Supported by:

Primary Presenter / email: **Jesinger, M.** / mejesi2@uky.edu
Clinical Science
Cardiovascular

Mentor / e-mail: Sorrell, V.L. / v.sorrell@uky.edu



CCTS Poster Presentation Abstracts

80 Abstract Title: **Differences in Incidence of Left Ventricular Thrombus in the setting of an Acute Myocardial Infarction based on P2Y12 inhibitor use**

Author(s): U. Kim, College of Medicine, U of Kentucky
R. Cavalcanti, Internal Medicine - Cardiology, U of Kentucky
A. Abdel-Latif, Internal Medicine - Cardiology, U of Kentucky

Abstract: Objectives The current state of P2Y12 inhibitor use in the setting of an Acute Myocardial Infarction (AMI) is largely dictated by large randomized control trials showing the effectiveness of prasugrel, ticagrelor and clopidogrel on a mortality benefit. The focus has always been to start dual anti-platelet therapy (DAPT) as soon as possible once an AMI is confirmed but little research has been done on the influence of the P2Y12 inhibitor choice on incidence of Left Ventricular Thrombus (LV thrombus). We aimed at determining the incidence of LV thrombus of patients admitted to university of Kentucky between 2010 and 2014 with an AMI based on the choice of P2Y12 inhibitor. Methods This study is a retrospective analysis of patients taken to the cardiac catheterization lab at the University of Kentucky between 2010 and 2014 with a diagnosis of AMI. A total of 927 patients underwent coronary arteriography for a diagnosis of AMI, with 43 patients found to have an LV thrombus during that period. Adults over the age of 18 years old with a diagnosis of NSTEMI or STEMI who underwent an echocardiogram within the same hospitalization were included in the trial. We applied the exclusion criteria of prior full anticoagulation or known LV thrombus. The primary outcome of LV thrombus was determined by transthoracic echocardiogram or cardiac MRI. Results There were a total of 941 patients with a diagnosis of NSTEMI or STEMI who underwent coronary arteriography between 2010 to 2014 who had a transthoracic echocardiogram or a cardiac MRI performed during their hospitalization. LV thrombus were detected among 43 patients, of which 39 (4.76%) patients were started on clopidogrel (819 patients) and 4 (3.27%) of patients were started on ticagrelor (87 patients) or prasugrel (35 patients). The proportion of patients started on clopidogrel ($p\text{-hat}1 = .0476$, $n1 = 819$) was compared to the proportion of patients started on either ticagrelor or prasugrel ($p\text{-hat}2 = .0327$, $n2 = 122$) using a two-tailed z-test for the difference between two proportions. The results are not significant $\alpha = .05$ ($p = .4593$). Conclusion In patients with a diagnosis of acute myocardial infarction we have noted no difference in the incidence of LV thrombus based on which P2Y12 inhibitor was started.

Supported by:

Primary Presenter / email: **Kim, U.** / urian.kim@uky.edu
Clinical Science
Cardiovascular

Mentor / e-mail: Abdel-Latif, A. / abdel-latif@uky.edu



CCTS Poster Presentation Abstracts

81 Abstract Title: **Post-Operative Changes in Platelet Function as Clinical Indicators for Complications After Left Ventricular Assist Device Implantation**

Author(s): T. ShROUT, College of Medicine, U of Kentucky
 T. Sexton, Saha Cardiovascular Research Center, U of Kentucky
 S. Smyth, Division of Cardiovascular Medicine, U of Kentucky
 M. Guglin, Division of Cardiovascular Medicine, U of Kentucky
 C. Hoopes, Cardiothoracic Surgery, U of Kentucky & U of Alabama

Abstract: Post-operative complications commonly arise with implantation of left ventricular assist devices (LVADs). A recent study reported that within one year after implantation, post-operative bleeding occurred in 67% of patients who received a Heartmate II. Another study reported that 30% of all patients who received an LVAD required additional surgery due to related bleeding complications. Bleeding risks are increased in part by the required anticoagulation therapies, but also by LVAD mechanics. In fact, studies have shown that patients with LVADs have increased bleeding events compared to patients without LVADs but with corresponding anticoagulation therapies. Several molecular mechanisms of bleeding in these cases have been investigated. This study aims to analyze platelet function via platelet count and platelet activation assays, which could serve as clinical indicators of bleeding risks after implantation of the Heartmate II and Heartware LVADs. Biomechanical analysis suggest that these devices cause distinct hemolytic and coagulation profiles. The Heartmate II is a continuous axial-flow pump implanted into the left ventricle, while the Heartware is a continuous centrifugal-flow pump implanted in the pericardial space. Recent studies suggest axial flow pumps decrease platelet counts, while centrifugal flow pumps are more likely to induce a pump thrombosis. Both types of devices have been linked with decreased platelet activation function due to sheer effects. This results in a higher risk of bleeding and is considered acquired von Willebrand syndrome. This study is unique, as only one known study has correlated such changes in platelet activation with post-operative LVAD implantation complications between the devices.

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Primary Presenter / email: **ShROUT, T.A.** / tara.shrout@uky.edu
Clinical Science
Cardiovascular

Mentor / e-mail: Smyth, S. / susan.smyth@uky.edu



CCTS Poster Presentation Abstracts

82 Abstract Title: **The pattern of troponin release in sepsis-related type II myocardial infarction predicts mortality**

Author(s): M.J. Sousa, Department of Internal Medicine, U of Kentucky
 V.A. Gupta, Department of Cardiovascular Medicine, U of Kentucky
 M.E. Jesinger, Department of Internal Medicine, U of Kentucky
 N. Kraitman, Department of Internal Medicine, U of Kentucky
 K.E. Wingerter, Department of Internal Medicine, U of Kentucky
 R.J. Charnigo, Department of Cardiovascular Medicine, U of Kentucky
 S.W. Leung, Department of Cardiovascular Medicine, U of Kentucky
 V.L. Sorrell, Department of Cardiovascular Medicine, U of Kentucky

Abstract: Background: Myocardial stress is common with sepsis leading to detectable cardiac troponin (type II myocardial infarction); however, the pattern of troponin release has not been well studied. Our goal was to analyze the impact of the pattern of cardiac troponin I (TnI) release on short and long term mortality. Methods: This is a single center, non-concurrent cohort study including patients who were admitted for sepsis and had a detectable TnI level from January 2013-January 2014. Patients were excluded if they had an obvious source of troponin elevation (ACS, coronary intervention). Mortality at 30 days and 1 year were obtained from the social security death database. Adjusted odds ratios were calculated using logistic regression analysis. Results: 899 patients (age 60+/-15, 47% female) were included in the analysis. When controlled for age and gender, the peak TnI and the absolute change in serial TnI (Delta trop) were both associated with 30-day and 1-year mortality (Table). This association was maintained, even when controlled for common high-risk coexisting medical conditions and cardiovascular medications. Traditional coronary risk factors were not associated with early or late mortality, and not included in the adjustment. Conclusions: The peak value and serial change of cardiac troponin has incremental prognostic value in patients with acute sepsis. If confirmed in larger prospective trials, mapping this simple biomarker may be an important guide to patient management and counselling.

Supported by:

Primary Presenter / email: **Sousa, M.J.** / matthew.sousa@uky.edu

Clinical Science

Cardiovascular

Mentor / e-mail: Gupta, V.A. / vedant.gupta@uky.edu



CCTS Poster Presentation Abstracts

83 Abstract Title: **Comparing the impact of through-plane motion during the cardiac cycle on steady state signal evolution in cine 2D and 3D balanced steady state free precession imaging**

Author(s): T. Spear, SAHA Cardiovascular Research Center, U of Kentucky
T. Stromp, SAHA Cardiovascular Research Center, U of Kentucky
S. Leung, Gill Heart Imaging Center, U of Kentucky
M. Vandsburger, SAHA Cardiovascular Research Center, U of Kentucky

Abstract: Purpose - Due to the excellent contrast between blood and tissue, bSSFP is the current clinical standard for cardiac imaging (CMR). Recently, several studies have noted that changes in tissue structure such as edema and fibrosis can change myocardial signal intensity in quantifiable amounts, though this has only been examined using 2D acquisitions. However, cardiac motion during a scan can influence signal consistency. In this study, we examined the impact of through-plane motion on preservation of steady state magnetization in standard 2D balanced steady state free precession (bSSFP) compared to 3D volume (slab) cine bSSFP. Methods - In this study, nine healthy adult males between 20-30 years of age completed CMR on a 1.5T Seimens Aera. A MATLAB (Mathworks, Nattick, MA) script was used to analyze the myocardial signal intensity and calculate changes throughout the cardiac cycle. Results - The averaged peak systolic ΔS was significantly higher in 2D bSSFP compared to the corresponding peak value in an identical slice acquired at the center of a 3D bSSFP slab. Data analyzed at mid-ventricular locations (center slices of the center slab) show the maximum change in signal from S0 in 2D is $40 \pm 21\%$ and $16 \pm 7\%$ for 3D. The percent of phases in which the signal was within 10% of the S0 value is $48 \pm 11\%$ for 2D and $83 \pm 16\%$ for 3D images at the same location. Discussion - Previously, studies had compared 2D and 3D imaging, but only to demonstrate agreement in calculated cardiac function and diagnostic capabilities. However, with an emerging understanding of how changes in tissue structure alter steady state magnetization in bSSFP acquisitions, it is important to understand the mechanisms behind such change. Our results indicate that while steady state magnetization is only transiently maintained in 2D cine bSSFP, the final 30% of the cardiac cycle shows a return to initial magnetization values, and becomes similar to more stable 3D acquisitions. Further analysis of 3D bSSFP revealed a position dependent steady state behavior, with steady state maintained only at the center of the 3D slab. Conclusion - A more consistent signal can be measured in bSSFP by looking at the center images of a volumetric excitation as opposed to the standard 2D bSSFP. For studies that extract data via quantification of signal throughout the cardiac cycle, it is necessary to understand how the signal changes due to through-plane motion to achieve the most accurate and telling results.

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Primary Presenter / email: **Spear, T.J.** / tyler.spear@uky.edu
Clinical Science
Cardiovascular

Mentor / e-mail: Vandsburger, M. / moriel.vandsburger@gmail.com



CCTS Poster Presentation Abstracts

84 Abstract Title:	Non-Contrast MRI for Safe Assessment of Cardiac Fibrosis in End Stage Renal Disease Patients
Author(s):	T.A. Stromp, Department of Physiology, Saha Cardiovascular Research Center, U of Kentucky J.C. Kaine, College of Medicine, U of Kentucky T.J. Spear, Saha Cardiovascular Research Center, U of Kentucky K.N. Andres, College of Medicine, U of Kentucky R.M. Kidney, Saha Cardiovascular Research Center, U of Kentucky S.W. Leung, Gill Heart Institute, U of Kentucky V.L. Sorrell, Gill Heart Institute, U of Kentucky M.H. Vandsburger, Depts. of Physiology & Biomedical Engineering, Saha Cardiovascular Research Center, U of Kentucky

Abstract: OBJECTIVES End stage renal disease (ESRD) patients on hemodialysis have high cardiac risk attributed to fibrosis and arrhythmias but are contraindicated to standard late gadolinium enhancement (LGE) MRI. We developed non-contrast 2-point bSSFP cardiac MRI in a mouse model, tested against LGE in a first-in-human study and now examine it for safe fibrosis assessment in ESRD patients on hemodialysis. METHODS Cine bSSFP images were acquired at 5° and 45° flip angles, spanning the left ventricle in 18 ESRD patients on hemodialysis and 9 healthy controls. We generated maps of $\Delta S/So = (S_{45} - S_5) / S_5 * 100$ (%) where S_i represents signal intensity at flip angle i . Control $\Delta S/So$ distributions were used to define a reference standard cumulative distribution function, which was dynamically resized to match individual heart size. One-sided Kolmogorov-Smirnov tests compared observed $\Delta S/So$ against appropriately-sized standards, producing divergence values indicating elevated signal. RESULTS ESRD patients had hypertrophy and elevated ejection fraction, $\Delta S/So$, and divergence from standard ($13.4 \pm 10.8\%$) compared to controls ($5.4 \pm 4.6\%$, $p < 0.05$). While strains and relaxation rates were similar, time to peak contraction was delayed in ESRD patients in circumferential and longitudinal directions. DISCUSSION ESRD patients demonstrate heightened $\Delta S/So$ values and divergence, consistent with increased fibrosis, even without changes in contractile function. An association between divergence and time to peak contraction suggests that combined measurement could help evaluate cardiac risk in ESRD patients or investigate future anti-fibrotic therapies. 2-pt bSSFP MRI is a safe evaluation tool for this high-risk population.

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Primary Presenter / email:	Stromp, T.A. / tori.stromp@uky.edu Clinical Science Cardiovascular
Mentor / e-mail:	Vandsburger, M.H. / m.v@uky.edu



CCTS Poster Presentation Abstracts

85 Abstract Title: **Understanding Acute Physiological Responses to Altitude Exposure in Young Adults' Class Lab Project while Studying Abroad**

Author(s): K. M. Wiles, Department of Kinesiology and Health Promotion, U of Kentucky
R. LaCoe, Department of Kinesiology and Health Promotion, U of Kentucky

Abstract: INTRODUCTION: Key physiological variables are altered by exposure to lower partial pressures of oxygen (PO₂) at elevation. Students from Universities in Kentucky participated in an education abroad program to learn about environmental exercise physiology. In a class lab project, we tested the hypothesis that heart rate (HR), ventilation rate, and arterial oxygen saturation (%SpO₂) would differ at moderate altitude when compared to sea level. METHODS: Fourteen females (20.7±1.0 yrs, 63.8±6.9 kg) and three males (23.7±2.9 yrs, 89.1±17.3 kg) participated. Subjects lived in Valencia, Spain (62 m) where baseline characteristics, HR, %SpO₂, and ventilation rate were measured in a lab at the Catholic University of Valencia. Two weeks later, subjects were exposed to elevation for 1 day before visiting CAR Sierra Nevada (2,320 m), a high altitude training center, where HR, %SpO₂, and ventilation rate were again measured. Data were analyzed by paired t-tests and the mean±SD are reported. RESULTS: HR was higher (p<0.01) at altitude, 85.3±11.8 bpm, when compared to sea level conditions, 74.6±12.8 bpm. The %SpO₂ levels were lower at altitude (p<0.01), 94.7±2.3, when compared to sea level, 97.6±2.2. There were no changes in ventilation rate. CONCLUSION: Similar to findings in previous studies, HR and %SpO₂ levels at altitude varied from sea level conditions, while ventilation rate was not changed. These alterations most likely occurred due to a decrease in PO₂ associated with an elevation of 2.3 km. By forming cooperative partnerships while abroad we hope to promote future faculty and student involvement in original global research and collaborations.

Supported by:

Primary Presenter / email: **Wiles, K.M.** / kathleen.wiles@uky.edu
Clinical Science
Cardiovascular

Mentor / e-mail: LaCoe, R. / rosie.lacoe@uky.edu



CCTS Poster Presentation Abstracts

86 Abstract Title: **Sociocultural Influences of Dietary Behavior Change in Appalachian Food Deserts: A Thematic Analysis**

Author(s): F. Hardin-Fanning, College of Nursing, U of Kentucky
E. Adams, College of Communication and Information, U of Kentucky
M. Olson, College of Communication and Information, U of Kentucky

Abstract: Appalachian residents confront a number of environmental, socioeconomic, and cultural barriers to maintaining a healthy diet and reducing the burden of cardiovascular disease (CVD). Geographic isolation from nutritious food sources, pervasive poverty and food insecurity, and dietary traditions are factors contributing to poor cardiovascular health (Ver Ploeg, et al., 2009). Recognizing the numerous factors underlying the burden of CVD in Appalachia, the current qualitative study illuminates the sociocultural factors that influence a person's resistance to or acceptance of dietary behavior change through the narratives of Appalachian residents enrolled in a culturally centered dietary intervention. Through an iterative process of construing meaning and significance from 21 in-depth interviews (Corbin & Strauss, 2008), our formative study identified 5 culturally rooted factors, or coded themes, influencing attitudes about dietary behavior change, including 1. a sense of pragmatism and control in food choices; 2. the primacy of the family unit in dietary decision-making; 3. aversion to specific types of food; 4. financial constraints inhibiting food choices; and 5. pre-existing health conditions complicating positive dietary decisions. These themes lend insight into the social influences, constraints, and barriers to dietary change in the food deserts of Appalachia, providing a contextual framework from which to develop and implement interventional programs and design culturally sensitive messages targeting a population stricken with diet-related illness.

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Primary Presenter / email: **Adams, E.T.** / elizabethadams@uky.edu
Community Science
Cardiovascular

Mentor / e-mail: Hardin-Fanning, F. / fdbowe2@uky.edu



CCTS Poster Presentation Abstracts

87 Abstract Title: **The Antimicrobial Properties of Vertically Aligned Multiwalled Carbon Nanotubes**

Author(s): J. Bilbily, Department of Medicine, U of Kentucky
 V. De Leon, Department of Medicine, U of Kentucky
 J. Kaine, Department of Medicine, U of Kentucky
 M.C. Weisenberger, Dept. of Chemical & Materials Engineering & Center for Applied Energy Research, U of Kentucky

Abstract: Recent studies of nanostructured materials (such as black silicon/cicada wing) have demonstrated that a surface nanoarchitecture composed of nanopillars have the ability to lyse bacterial cells through mechanical tearing of the cell membrane. We have identified a material which shares a similar nanopillar surface, the material is vertically aligned multiwalled carbon nanotubes (MWCNT). MWCNTs are composed of non-uniform carbon pillar-like arrays that differ in height, spacing, diameter of pillars, uniformity of dispersion, and even the shape of the pillars themselves. We hypothesized that due to its nanopillar surface, the MWCNT's nanostructure will also portray antimicrobial properties. The MWCNT material and a control (quartz slides) were attained and positioned into cell culture wells in triplicates. Samples of cultured Escherichia coli were placed into the wells, incubated and sampled at the 3 hour and 18 hour time points, serially diluted to 10⁻⁴ and 10⁻⁵ and plated on blood agar. The plates were incubated overnight and colony forming units (CFU) were counted. A 2-tail t-test was used to compare the results. At the 3 hour time point there was no significant difference between control and MWCNT in the number of CFUs. At the 18 hour time point there was a significant difference between the MWCNT and the control with a mean of 61.6 (±10.9) CFUs for the control and a mean of 27.6(±4.6) CFUs for the MWCNTs 10⁻⁴ dilution (p<0.001). However the 10⁻⁵ dilution at the 18 hour mark demonstrated no significant differences. Although this study reveals that the MWCNT may be antimicrobial with greater contact time, the mismatch between the 10⁻⁴ dilution and the 10⁻⁵ dilution indicates that the study will need to be repeated with more replications.

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Primary Presenter / email: **Bilbily, J** / john.bilbily@uky.edu
Basic Science
Other

Mentor / e-mail: Weisenberger, M.C / matt.weisenberger@uky.edu



CCTS Poster Presentation Abstracts

88 Abstract Title: **Peer Mentors are Non-Inferior to Attendings in Teaching Basic Ultrasound Guided IV Access**

Author(s): J. Kaine, College of Medicine, U of Kentucky
 N. Chien, College of Medicine, U of Kentucky
 K. Kraft, College of Medicine, U of Kentucky
 J. Avila, Department of Emergency Medicine, U of Kentucky
 M. Dawson, Department of Emergency Medicine, U of Kentucky

Abstract: Introduction: Medical students in the United States often utilize student-led peer-mentor systems, such as interest groups, to supplement classroom education and develop procedural skills. Due to its interactive nature, ultrasound lends itself well to a peer-mentor approach to education. Objectives: To demonstrate the noninferiority of peer-mentors versus attending physicians in teaching ultrasound (US) guided peripheral IV (PIV) insertion to second year pre-clinical physician assistant students (PAS). Methods: Forty-two second year PAS with no prior experience with ultrasound were randomized into two groups: Attending-Led Education (ALE) and Student-Led Education (SLE). Prior to training, study participants were evaluated using a 15 question PIV/US knowledge-based exam and asked to rate their comfort interpreting and obtaining US images using a scale of 1 (no comfort) to 10 (expert-level comfort). Both SLE and ALE groups received an identical 15 minute powerpoint presentation and 1 hour of hands-on didactics under the instruction of either students or attendings. Participants then completed a video recorded hands-on skills assessment and were scored using a 6-point scale. Students were given the same 15 question PIV/US knowledge-based exam after training and video assessment. Results: Both attending and medical student taught groups showed improvement in comfort interpreting US images, comfort acquiring US images, and content knowledge assessments using a paired t-test ($p < 0.001$). When compared against each other, there is no significant difference seen in any of the above categories using an unpaired t-test ($p < 0.05$). The video skills assessment, reveals no significant differences in total score: ALE 4.5 ± 1.2 vs. SLE 4.2 ± 1.1 ($p = 0.46$). Conclusions: Interprofessional peer-mentor student teachers are non-inferior to attendings in communicating basic knowledge of ultrasound and demonstrating image acquisition and procedural skills to novice health professions students. Both groups showed marked improvement in comfort interpreting US images, comfort acquiring US images, and content knowledge while no discernable difference was found in overall technical ability as recorded during the video assessment.

Supported by:

Primary Presenter / email: **Kaine, J.** / josh.kaine@uky.edu
Clinical Science
Other

Mentor / e-mail: Dawson, M. / msdaws2@uky.edu



CCTS Poster Presentation Abstracts

89 Abstract	Na-K-ATPase inhibition regulates Na-bile acid absorption in intestinal epithelial cells in obesity
Title:	
Author(s):	S. Arthur, Dept. of Clinical & Translational Sciences, Joan C. Edwards School of Medicine, Marshall U U. Sundaram, Dept. of Clinical & Translational Sciences, Joan C. Edwards School of Medicine, Marshall U

Abstract: Apical sodium bile acid transporter (ASBT) in the brush border membrane of villus cells is the sole bile acid absorptive mechanism in the terminal ileum and plays a vital role in regulation of bile acid absorption. ASBT requires a favorable trans-cellular Na gradient for its optimal activity that is provided by Na-K-ATPase present on the basolateral membrane. Intestinal bile acid levels are known to be elevated in obesity, but how ASBT mediated intestinal bile acid absorption is altered in obesity is not known. Preliminary studies in well-established in-vivo models of obesity, specifically in Obese Zucker rats and TALLYHO mice, and in human intestinal samples from obese, suggest that Na-bile acid co-transport is increased. While it was expected that Na-K-ATPase might be enhanced at the cellular level to support this increase, it was found to be in fact, reduced. To further investigate this novel mechanism of bile acid co-transport increase with reduced Na-K-ATPase activity, we specifically and selectively inhibited Na-K-ATPase in-vitro in rat intestinal epithelial cells (IEC-18). Selective inhibition of Na-K-ATPase for its $\alpha 1$ subunit showed a two-fold increase in Na-bile acid co-transport and a three-fold increase in ASBT expression. Intracellular Na concentration was also increased by two-fold. Expression of Na-dependent serine/threonine kinase, salt-inducible kinase-1 (SIK1), was also found to be significantly elevated. Therefore, direct inhibition of Na-K-ATPase uniquely regulates ASBT, similar to that seen in in-vivo models of obesity. The mechanism of stimulation of ASBT is secondary to an increase in co-transporter numbers, mediated by SIK1 in intestinal epithelial cells.

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Primary Presenter / email: **Arthur, S.** / arthursu@marshall.edu

Basic Science

Other

Mentor / e-mail: Sundaram, U. / sundaramu@marshall.edu



CCTS Poster Presentation Abstracts

90 Abstract	Glucocorticoid-mediated suppression of Wnt/β-catenin signaling impairs intestinal stem cell activation in inflammatory bowel disease
Title:	
Author(s):	E. B. Lynch, Department of Microbiology, Immunology and Molecular Genetics, U of Kentucky T. Goretsky, Department of Internal Medicine, Division of Digestive Diseases and Nutrition, U of Kentucky E. Bradford, Department of Internal Medicine, Division of Digestive Diseases and Nutrition, U of Kentucky T. A. Barrett, Department of Internal Medicine, Division of Digestive Diseases and Nutrition, U of Kentucky

Abstract: Intestinal stem cells (ISC) require Wnt/ β -catenin signaling for maintenance of the crypt proliferative compartment. Exogenous glucocorticoids (GC) are commonly used to treat inflammatory bowel disease (IBD). Despite the clinical benefits, endoscopic data show that GCs delay ulcer healing through mechanisms that are poorly understood. The objective of our study was to determine whether GCs impair ISC activation in ulcer re-epithelialization. Specifically, we hypothesized that that steroids impair canonical Wnt/ β -catenin signaling required for ISC activation needed for mucosal repair. Methods: We examined the effects of dexamethasone, a GC steroid, on cell signaling pathways involved in Wnt/ β -catenin, PI3 Kinase, and NF κ B signaling. We utilized NCM460 cells, which are normal human colonic intestinal epithelial cells (IECs), and epithelial isolations from patient biopsies obtained from University of Kentucky and VA Lexington Hospitals. IEC from untreated and steroid-treated (7 days) UC patients with equivalent levels of colitis were compared to control for the level of inflammation. Results: We recently found that Axin2, a Wnt target gene, marks a population of activated ISCs involved in ulcer healing. In patient biopsies, GC inhibited colitis-induced Axin2, p-LRP6 (marker of Wnt signaling) and nuclear β -catenin accumulation. Together with steroid inhibition of TNF-induced TCF/LEF luciferase response in NCM460 cells, these data indicate GCs impair Wnt signaling. We also found that GCs abrogate colitis-induced IEC NF κ B signaling (nuclear p65 levels). Discussion: Our results indicate that GCs impair Wnt/ β -catenin signaling during ulcer healing. Given new data implicating NF κ B in Wnt signaling, our studies suggest a potential explanation for GC-induced impairment of stem cell activation needed for mucosal repair in IBD.

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Primary Presenter / email: **Lynch, E. B.** / evan.lynch@uky.edu

Basic Science

Other

Mentor / e-mail: Barrett, T. A. / t.barrett@uky.edu



CCTS Poster Presentation Abstracts

91
Abstract Title: Anti-Viral Medication Tenofovir Causes Oxidative Stress and Apoptosis in HK-2 Cells

Title:

R.A. Murphy, Dept. of Pharmacology, Physiology, & Toxicology, Joan C. Edwards School of Medicine, Marshall U, Huntington, WV

Author(s):

R.M. Stafford, Dept. of Pharmacology, Physiology, & Toxicology, Joan C. Edwards School of Medicine, Marshall U

B.A. Petrosovits, Dept. of Pharmacology, Physiology, & Toxicology, Joan C. Edwards School of Medicine, Marshall U

M. Boone, West Virginia Wesleyan College, Buckhannon, WV

Abstract: Tenofovir disoproxil fumarate (Viread) is a highly effective antiviral drug approved for treating Human Immunodeficiency Virus (HIV) and Hepatitis B. It is a first line drug for HIV treatment and is efficacious in both novel and treatment-experienced HIV patients. Tenofovir is administered orally as the prodrug tenofovir disoproxil fumarate (TDF), which is deesterified to the active drug tenofovir. Renal damage is a major adverse effect associated with its use. Tenofovir can induce decreased glomerular filtration rate (GFR), renal failure, and Fanconi Syndrome, but exact mechanism remains unknown, largely due to limited experimental models. Our laboratory has established that clinically relevant concentrations of tenofovir are toxic within 24h. The purpose of this study was to investigate the cellular mechanism of cytotoxicity in a human renal proximal tubular epithelial cell line (HK-2). Tenofovir (TFV) is the active form of Viread and was used for all studies. HK-2 cells were seeded and grown to confluency for 48h followed by a 72h exposure to 0-30uM tenofovir dissolved in phosphate buffered saline (PBS). Cell viability was assessed using the MTT assay. Mitochondrial dysfunction was assessed by measuring ATP and ADP levels. Oxidative stress was assessed using OxyBlot. Tenofovir induced a loss of cell viability when compared to vehicle within 24h. 72h exposure to tenofovir drastically reduces ATP levels compared to control. Increases in protein carbonylation are seen after 48-72h exposure. New studies indicate that tenofovir increases 4-HNE modifications on proteins. Caspase 3 and 9 cleavage was induced by tenofovir as measured by Western blot compared to vehicle. These studies suggest that mitochondrial stress and apoptosis occur in tenofovir treated HK-2 cells.

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Primary Presenter / email:

Murphy, R.A. / murphyrachel63@gmail.com

Basic Science
Other

Mentor / e-mail:

Valentovic, M.A. / valentov@marshall.edu



CCTS Poster Presentation Abstracts

92 Abstract Title: **Influence of Beta-lactam Infusion Strategy on Acute Kidney Injury**

Author(s): S.E. Cotner, Department of Pharmacy Services, U of Kentucky
 W.C. Rutter, Department of Pharmacy Services, College of Pharmacy, U of Kentucky
 D.R. Burgess, Department of Pharmacy Services, College of Pharmacy, U of Kentucky
 C.A. Martin, Department of Pharmacy Services, College of Pharmacy, U of Kentucky
 A. Schadler, College of Pharmacy, U of Kentucky
 D.S. Burgess, College of Pharmacy, U of Kentucky

Abstract: BACKGROUND: Beta-lactam bactericidal activity is time dependent ($t > MIC$). Recently, extended beta-lactam infusions have been promoted as a strategy to optimize the percent of the dosing interval that the concentration of free drug remains above the MIC, thereby potentially improving efficacy. Nephrotoxicity is a known adverse effect of beta-lactam antibiotics; however, there is limited literature available evaluating nephrotoxicity in prolonged beta-lactam infusions. OBJECTIVE: To assess the incidence of acute kidney injury based on beta-lactam infusion strategy. METHODS: Adult patients admitted from July 2006 through September 2015 who received piperacillin-tazobactam, cefepime, or meropenem for greater than 48 hours were included in this retrospective cohort comparison study. Patients were excluded for pre-existing renal dysfunction, pregnancy or breastfeeding, or receipt of a beta-lactam for less than 48 hours. All data analyzed were extracted from our institution's Center for Clinical and Translation Science Enterprise Data Trust. AKI was evaluated using RIFLE criteria. Patients in the bolus infusion group were matched to patients in the prolonged infusion group based on eight parameters: beta-lactam received, age, gender, Charlson score, baseline CrCl, hypotension, receipt of vancomycin, and treatment in ICU. RESULTS: A total of 3843 patients were evaluated in our matched analysis with 2747 receiving bolus beta-lactam infusions and 1096 receiving prolonged infusions. The incidence of any AKI was significantly higher in patients receiving prolonged infusions compared to patients receiving bolus infusions (21.4% vs 17.6%, $p < 0.006$).

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Primary Presenter / email: **Cotner, S.E.** / sarah.cotner@uky.edu
Clinical Science
Other

Mentor / e-mail: Burgess, D.S. / david.burgess@uky.edu



CCTS Poster Presentation Abstracts

93 Abstract Title:	Incidence of Nephrotoxicity in Patients Treated with Polymyxin Antimicrobials
Author(s):	R.L. Crass, Department of Pharmacy Services, U of Kentucky W.C. Rutter, Department of Pharmacy Services and College of Pharmacy, U of Kentucky D.R. Burgess, Department of Pharmacy Services and College of Pharmacy, U of Kentucky K.L. Wallace, Department of Pharmacy Services and College of Pharmacy, U of Kentucky C.A. Martin, Department of Pharmacy Services and College of Pharmacy, U of Kentucky D.S. Burgess, Department of Pharmacy Services and College of Pharmacy, U of Kentucky

Abstract: BACKGROUND: Polymyxin antimicrobials have reentered clinical practice as salvage therapy for multidrug-resistant gram-negative bacterial infections. Additional data on the relative rates of toxicity with these agents are necessary to inform antimicrobial selection. OBJECTIVES: The objective was to determine the incidence of nephrotoxicity in patients with and without cystic fibrosis (CF) treated with intravenous polymyxins. METHODS: This retrospective evaluation included adults treated with intravenous polymyxin B (PB) or colistimethate sodium (CMS) for at least 48 hours between July 1, 2006 and September 30, 2015. Patients receiving renal replacement therapy were excluded. Data were obtained from the University of Kentucky Center for Clinical and Translational Science Enterprise Data Trust and analyzed using R statistical software (version 2.12). Data collected included demographics, admission/discharge dates, comorbidities, Charlson Comorbidity Index, laboratory values, concomitant anti-infectives, and nephrotoxins. RESULTS: In non-CF patients (n = 74 PB; n = 231 CMS) the incidence of nephrotoxicity, defined using RIFLE criteria, was 55.9% with PB and 58.5% with CMS (P = 0.85). Risk factors on multivariate logistic regression were dose (OR 2.9, 95% CI 1.46 – 5.97), duration of therapy (OR 2.95, 95% CI 1.59 – 5.8), and concurrent loop diuretics (OR 2.43, 95% CI 1.31 – 4.57). Admission to a progressive care unit was protective (OR 0.3, 95% CI 0.09 – 0.92). In CF patients (n=30 PB; n = 199 CMS), the incidence of nephrotoxicity was 34.5% with PB and 30.9% with CMS (P=0.86). Admission to a progressive care unit (OR 6.74, 95% CI 1.02 – 60.65) and concurrent loop diuretic use (OR 3.55, 95% CI 1.28 – 10.3) were risk factors on multivariate regression. CONCLUSIONS: Polymyxin B and CMS have substantial and similar rates of nephrotoxicity which were lower in CF patients. In non-CF patients, nephrotoxicity was associated with increasing polymyxin dose and duration of therapy.

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Primary Presenter / email:	Crass, R.L. / ryan.crass@uky.edu Clinical Science Other
Mentor / e-mail:	Burgess, D.S. / david.burgess@uky.edu



CCTS Poster Presentation Abstracts

94 Abstract	Effect of US Drug Enforcement Administration's Rescheduling of Hydrocodone Combinations on Opioid Analgesic Prescribing in Kentucky
Title:	
Author(s):	C.K. Herren, Institute for Pharmaceutical Outcomes and Policy, College of Pharmacy, U of Kentucky J. Talbert, Institute for Pharmaceutical Outcomes and Policy, College of Pharmacy, U of Kentucky P.R. Freeman, Institute for Pharmaceutical Outcomes and Policy, College of Pharmacy, U of Kentucky

Abstract: BACKGROUND In October 2014, the US Drug Enforcement Administration moved hydrocodone combination products to restrictive Schedule II. In January 2016, an article published in the Journal of the American Medical Association suggested that hydrocodone prescribing has decreased in response to rescheduling, with a modest increase in non-hydrocodone combination product prescribing. This study did not consider a potential increase in the prescribing of tramadol, an alternative Schedule IV opioid with a significantly different adverse effect profile. OBJECTIVES To examine prescribing of opioid analgesics in Kentucky before and after hydrocodone combination rescheduling, and to determine if an increase in adverse outcomes associated with utilization of tramadol exists. METHODS This is a retrospective study using administrative data claims from the Kentucky All Schedule Prescription Electronic Reporting (KASPER) dataset, and the Kentucky Medicaid dataset, spanning 2011 to 2015. The quarterly number of (1) dispensed prescriptions and (2) dispensed tablets will be determined for: hydrocodone combination products, non-hydrocodone opioid products, and tramadol. The change in the incidence of adverse effects associated with increased tramadol use will then be determined. RESULTS Preliminary results from the KASPER dataset suggest that hydrocodone combination products decreased by 26% in Kentucky in the year after rescheduling, with 235,000 fewer prescriptions, and 12,000,000 fewer tablets. Non-hydrocodone products, including tramadol, increased by 8.4% with 45,000 additional prescriptions, and 3,000,000 additional tablets. Tramadol alone increased by 23%, with 28,000 additional prescriptions, and 2,400,000 additional tablets. CONCLUSIONS Tramadol containing products make up a large proportion of the offsetting increase in opioid prescriptions and tablets in Kentucky, which could lead to an increase in adverse outcomes associated with tramadol use.

Supported by:	This project was supported by the Institute for Pharmaceutical Outcomes and Policy, University of Kentucky College of Pharmacy
Primary Presenter / email:	Herren, C.K. / katie.herren@uky.edu Clinical Science Other
Mentor / e-mail:	Freeman, P.R. / trish.freeman@uky.edu



CCTS Poster Presentation Abstracts

95 Abstract Title: **Can Chest Width Be Used as a Surrogate for Weight for Selection of Contrast Injection Rate for Computed Tomographic Angiography?**

Author(s): A. Kingsbury, College of Medicine, U of Kentucky
F. Appiah, College of Arts and Sciences, U of Kentucky
C. Woodward, College of Medicine, U of Kentucky
K. Landwehr, College of Engineering, U of Kentucky
A. Chakraborty, College of Medicine, U of Kentucky
C. Lowry, Department of Thoracic and Cardiovascular Radiology, U of Kentucky
M. Winkler, Department of Thoracic and Cardiovascular Radiology, U of Kentucky

Abstract: Introduction For computed tomographic angiography (CTA) both patient weight and chest width (CW) have been shown to have a positive relationship to study noise. Although CW is easy to measure during scanning and weight data is often unavailable, it is weight rather than CW that is used to determine contrast injection rate (CIR) to maintain a contrast to noise ratio (CNR) that suffices for diagnosis. The purpose of this study is to determine if CW can be substituted for weight as the determinant of optimal CIR rate for CTA. Methods CTA examinations performed over a 32-month period were reviewed. Those associated with complete data on weight, CIR, CW, CTDI, noise, and aortic attenuation were identified (2822 exams). Attenuation and CNR data derived from these exams were analyzed using Pearson correlation coefficients and multiple linear regressions. Multiple confounders and the model assumptions of constant variance and normality were examined. Results The correlation between CW and CNR ($r=0.167$, $p\text{-value}<0.001$) and between weight and CNR ($r=0.098$, $p\text{-value}<0.001$) were significantly different from zero. A stronger correlation existed between weight and CW ($r=0.999$, $p\text{-value}<0.01$). Chest width (0.417 , $p\text{-value}<0.001$) had a stronger main effect than weight (0.005 , $p\text{-value}<0.001$) on CNR. In the adjusted models, the effect of CW on CNR increased (0.431 , $p\text{-value}<0.001$) and that of weight attenuated (. Conclusion CW is highly correlated with weight. CW is a stronger predictor of CNR than weight and thus CW may be a better determinant than weight for CIR for CTA.

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Primary Presenter / email: **Kingsbury, A.** / a.kings@uky.edu
Clinical Science
Other

Mentor / e-mail: Winkler, M. / michael.winkler@uky.edu



CCTS Poster Presentation Abstracts

96 Abstract Title: **Evaluating the Role of Early Tracheotomy and Percutaneous Endoscopic Gastrostomy in Critically Ill Hemorrhagic Stroke Patients**

Author(s): M.R. McCann, College of Medicine, U of Kentucky
J.F. Fraser, Department of Neurosurgery, U of Kentucky

Abstract: OBJECTIVE: Tracheotomy and percutaneous endoscopic gastrostomy (PEG) are sometimes performed in critically ill hemorrhagic stroke patients in order to avoid complications associated with prolonged intubation and nasogastric feeding. However, there is a paucity of information regarding the optimal timing of these procedures. In this study, we aimed to evaluate the role of early tracheotomy and PEG in hemorrhagic stroke patients. METHODS: A series of patients treated at University of Kentucky for hemorrhagic stroke between June 1, 2011 and June 1, 2015 was retrospectively reviewed. Data regarding diagnosis, demographics, comorbidities, treatment, hospital course, and performance of tracheotomy and/or PEG were collected and then analyzed using logistic regression and multiple linear regression. RESULTS: Of 366 hemorrhagic stroke patients, 75 underwent tracheotomy and 86 received PEG. Factors significantly associated with tracheotomy and PEG included patient age ($p < 0.01$), pneumonia present on admission ($p < 0.005$), and subtype of hemorrhagic stroke ($p < 0.05$). Tracheotomy and PEG were not significantly associated with patient survival or development of complications. Earlier PEG placement was correlated significantly with shorter overall hospital stay in survivors ($p < 0.001$), but neither tracheotomy nor PEG was correlated with ICU length of stay. CONCLUSIONS: Hemorrhagic stroke is a devastating neurovascular event that requires prompt intervention and vigilant management. Our study identified patient risk factors that may suggest candidacy for tracheotomy and PEG. Additionally, we found that timing of PEG may shape a patient's hospital course. Complication rates related to tracheostomy and PEG in this population were minimal. In conclusion, this retrospective data set supports some benefit to early PEG placement in this population, and justifies the need for further prospective study.

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Primary Presenter / email: **McCann, M.R.** / matthew.mccann@uky.edu
Clinical Science
Other

Mentor / e-mail: Fraser, J.F. / jfr235@uky.edu



CCTS Poster Presentation Abstracts

97 Abstract Title:	Risk Factors for Pseudomonas aeruginosa to Guide Empiric Therapy for Gram-negative Infections
Author(s):	K.N. Mediwala, Department of Pharmacy Services, U of Kentucky W.C. Rutter, Department of Pharmacy Services and College of Pharmacy, U of Kentucky D.R. Burgess, Department of Pharmacy Services and College of Pharmacy, U of Kentucky C.A. Martin, Department of Pharmacy Services and College of Pharmacy, U of Kentucky P.M.D. Zephyr, College of Pharmacy, U of Kentucky K.L. Wallace, Department of Pharmacy Services, U of Kentucky D.S. Burgess, College of Pharmacy, U of Kentucky

Abstract: BACKGROUND Pseudomonas aeruginosa (PSA) is a leading nosocomial pathogen with predisposing risk factors including previous antibiotic exposure, prior hospitalization, and severity of illness. Understanding these is paramount and can lead to appropriate empiric therapy, better patient outcomes and less antibiotic resistance. To our knowledge, there is no risk factor analysis score specific for PSA infections that can guide empiric therapy. OBJECTIVES The primary endpoint of this study was to identify risk factors for PSA infections among our hospital system and utilize these to create a risk-factor analysis score to guide empiric therapy. METHODS This was an IRB-approved, retrospective, case-control study including patients from a single institution from January 1, 2010 through December 31, 2014. Cases were defined as adult patients with PSA-positive cultures, while controls were adults with Enterobacteriaceae (ENT)-positive cultures. Exclusion criteria included cystic fibrosis patients and polymicrobial infections. Demographics, prior hospitalizations, admitting diagnosis by ICD9 codes, discharge disposition, comorbidities, severity of illness based on the Charlson Comorbidity Index, pertinent vital signs, lab values, and microbiological data, were collected from our institution's Center for Clinical and Translational Science Enterprise Data Trust. All analyses were performed using R statistical software (3.12). RESULTS In all, 2770 patients were evaluated (2399 in the ENT group vs. 371 in the PSA group). Male gender was more common in the PSA group (60% vs.40%, $p < 0.0001$). E. coli (50%) and K. pneumoniae (19%) were the most common ENT isolated. Comorbidities including CKD, ESRD, COPD, and liquid tumors were significantly more prevalent in the PSA group. PSA infections were significantly greater in patients with central-lines and mechanical ventilation (12% vs 7%, $p = 0.003$ and 22% vs 15%, $p = 0.002$, respectively). Mean Charlson Comorbidity Index score and the frequency of hospital-acquired infections were higher in PSA group (5.47 vs. 4.83, $p = 0.002$ and 67% vs 58%, $p = 0.0005$, respectively). CONCLUSIONS Past medical history, clinical timeline and comorbidities including COPD, renal dysfunction, liquid tumors, mechanical ventilation and invasive device are significant risk factors for PSA infections and may warrant appropriate antimicrobial coverage.

Supported by:	The project described was supported by the National Center for Advancing Translational Sciences, UL1TR000117. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH.
Primary Presenter / email:	Mediwala, K.N. / krutika.mediwala@uky.edu Clinical Science Other
Mentor / e-mail:	Burgess, D.S. / david.burgess@uky.edu



CCTS Poster Presentation Abstracts

98 Abstract **Acute kidney injury in patients treated with vancomycin and piperacillin-tazobactam: a retrospective cohort analysis**

Title: **Acute kidney injury in patients treated with vancomycin and piperacillin-tazobactam: a retrospective cohort analysis**

Author(s): W.C. Rutter, College of Pharmacy, U of Kentucky
 D.R. Burgess, UK HealthCare
 J.C. Talbert, College of Pharmacy, & Center for Clinical & Translational Science, U of Kentucky
 D.S. Burgess, College of Pharmacy, U of Kentucky

Abstract: Background: Empiric antimicrobial therapy often consists of the combination of Gram-positive coverage with vancomycin (VAN) and Gram-negative coverage, specifically an antipseudomonal beta-lactam, such as piperacillin-tazobactam (PTZ). Nephrotoxicity is commonly associated with VAN therapy; however, recent reports demonstrate increasing nephrotoxicity rates among patients treated with the combination of VAN and PTZ. Objective: This study evaluated the effect of the VAN/PTZ combination on acute kidney injury (AKI) compared to VAN and PTZ monotherapies. Methods: A retrospective cohort analysis of patients receiving VAN, PTZ, or the combination from September 1, 2010 through August 31, 2014, who did not have previous renal injury and who received at least 48 hours of therapy. Patients were followed for the duration of hospitalization. The primary outcome was AKI incidence as defined by the RIFLE criteria. Results: Overall, 11,650 patients were analyzed for AKI incidence, with 1,647 (14.1%) developing AKI during their hospital stay. AKI was significantly more frequent in the VAN/PTZ group (21%) compared to either monotherapy group (VAN 8.3%, PTZ 7.8%, $p < 0.001$ for both). Combination therapy was independently associated with higher AKI odds compared to monotherapy with either agent (aOR=2.03; 95% CI 1.74-2.39; aOR=2.31; 95% CI 1.97-2.71, for VAN and PTZ, respectively). Receipt of concomitant nephrotoxic drugs were independently associated with increased AKI rates, as were increased duration of therapy, length of hospital stay, increasing severity of illness, and increasing baseline renal function. Conclusions: In this study of over 10,000 patients, VAN combined with PTZ was associated with twice the odds of AKI development compared to either agent as monotherapy. This demonstrates the need for judicious use of combination empiric therapy and further antimicrobial stewardship activities.

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Primary Presenter / email: **Rutter, W.C.** / cliff.rutter@uky.edu
Clinical Science
Other

Mentor / e-mail: Burgess, D.S. / david.burgess@uky.edu



CCTS Poster Presentation Abstracts

99 Abstract Title: **Patient Navigation in the Medically Underserved: A Systematic Review**

Author(s): T. L. Shackelford, College of Medicine, U of Kentucky
 R. Shearer, Dept. of Otolaryngology - Head and Neck Surgery, U of Kentucky
 M.L. Bush, Dept. of Otolaryngology - Head and Neck Surgery, U of Kentucky

Abstract: Purpose: Patient navigation is an evidence-based intervention involving trained healthcare workers who assist patients in assessing and mitigating personal and environmental factors to promote healthy behaviors. The purpose of this research is to systematically assess the efficacy of patient navigation and similar programs to improve diagnosis and treatment of diseases affecting medically underserved populations. Methods: A systematic review was performed by searching PubMed, MEDLINE, PsychINFO, CINALH, and Web of Science to identify potential studies. Eligible studies were those containing original peer-reviewed research reports in English on patient navigation, community health workers, vulnerable and underserved populations, and healthcare disparity. Data/Results: The search produced 1,428 articles and 19 were included for review. The majority of papers focused on the role of patient navigation in cancer outcomes in underserved populations. Timing of initial contact with a patient navigator after diagnostic or screening testing is correlated to the effectiveness of the navigator intervention. Studies that took extended periods of time to enroll patients saw fewer significant results overall. However, patient navigation tends to work better on outcomes that span longer periods of time. Studies that analyzed outcomes further from the abnormal screening saw more significant results overall than those that analyzed outcomes closer to the abnormal screening. Conclusions: Patient navigation provides benefit in the diagnosis and treatment of patients in underserved populations. Patient navigation works best when patients are contacted soon after a negative test. Additionally, settings that require longer spans of time between abnormal test and definitive diagnosis or between definitive diagnosis and treatment may see more benefit from patient navigation or similar programs than those requiring shorter time intervals. Expansion of navigation into other areas of healthcare could benefit vulnerable populations.

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Primary Presenter / email: **Shackelford, T.L.** / taylor.shackelford@uky.edu
Clinical Science
Other

Mentor / e-mail: Bush, M. L. / matthew.bush@uky.edu



CCTS Poster Presentation Abstracts

100 Abstract Title: **Navigating High-Risk In-Patient Clients using a Lay-Health Worker Model in Eastern Kentucky (Bridges to Home at St. Claire Regional Medical Center)**

Author(s): R. Cardarelli, Family and Community Medicine, U of Kentucky
 J. Schilling, Family and Community Medicine, U of Kentucky
 K. Gilliam, Kentucky Homeplace
 F. Feltner, Center of Excellence in Rural Health
 M. Horsley, St. Claire Regional Medical Center and CCTS, U of Kentucky
 N. Maggard, St. Claire Regional Medical Center
 L. Ray, St. Claire Regional Medical Center

Abstract: Roughly 20% of all Medicare fee-for-service clients are readmitted within 30 days of hospital discharge, resulting in \$17 billion annually. It is estimated that 75% of these readmissions are avoidable. Research has demonstrated that a broad range of socioeconomic and personal factors impact readmission rates. This study seeks to address such factors through a hospital-based Lay Health Worker (LHW) model for transition of care. This study utilizes a pre/post design that assess the impact of implementing a LHW model on 30-day hospital readmission by assisting high-risk clients with their post-discharge social needs. To determine the effectiveness of this LHW model, outcome measures for the 4-6 months prior to study's program implementation and for 6-months after the study intervention are compared. Both traditional statistical methods and quality improvement evaluation methods, including Statistical Process Control, will be performed.

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Primary Presenter / email: **Schilling, J.** / jennifer.schilling@uky.edu
Community Science
Other

Mentor / e-mail: Cardarelli, R. / roberto.cardarelli@uky.edu



CCTS Poster Presentation Abstracts

101 Abstract Title: **Myopathy-Dependent Long-Term Muscle Weakness in Murine Sepsis Survivors**

Author(s): A.M. Steele, Department of Physiology, U of Kentucky
M.E. Starr, Department of Surgery, U of Kentucky
J. Smith, Department of Molecular and Cellular Biology, U of Kentucky
C.A. Peterson, Department of Rehabilitation Sciences, U of Kentucky
H. Saito, Department of Physiology, U of Kentucky

Abstract: Sepsis is a life-threatening condition accompanied by profound systemic inflammation. Due to an increase in both the incidence rate and survival rate, the number of sepsis survivors has doubled within the past decade. Among survivors, over 70% report chronic muscle weakness which interferes with their ability to resume a normal lifestyle, particularly in aging populations. The objective of this study was to quantify muscle weakness and determine its primary overarching mechanism (i.e. atrophy or myopathy) in murine sepsis survivors at late time-points. Experimental abdominal sepsis was induced in 16-month-old male mice (~50 years old human) by intraperitoneal injection of cecal slurry prepared from stool of donor mice. Changes in body weight and composition were monitored during and after sepsis, and skeletal muscles and plasma were collected. During sepsis mice lost an average of 6.3% lean mass by day four ($p < 0.01$) which recovered to 96.1% by Day 10. Plasma IL-6 levels were comparable to that of non-sepsis controls, indicating that systemic inflammation was resolved by day 14. At this time, a significant reduction in force generation capacity (maximum specific force) of the extensor digitorum longus was observed ($p = 0.01$). Mean specific cross-sectional area of Type I, IIa, and IIb fibers in the gastrocnemius were similar among groups ($p = 0.2, 0.9, \text{ and } 0.1$ respectively), indicating that atrophy was resolved by day 14. Histological examination of the gastrocnemius revealed mononuclear infiltration, rounded myofibers, and centralized nuclei. Loss of Type IIa and IIb, but not Type I, myosin filaments were observed by immunofluorescent labeling. Altogether these data are indicative of long-term myopathy which may underlie the persistent muscle weakness observed in sepsis survivors. Further elucidation of the mechanisms mediating such myopathy will lead to therapeutic targets for prevention.

Supported by: NIH R01 AG039732

Primary Presenter / email: **Steele, A.M.** / a.steele@uky.edu
Basic Science
MuscleMentor / e-mail: Saito, H / hiroshi.saito@uky.edu



CCTS Poster Presentation Abstracts

102 Abstract Title: **Alterations in Quadriceps Morphology Following an Anterior Cruciate Ligament Reconstruction: An MRI Based Assessment**

Author(s): A. Hickey, Exercise Science, U of Kentucky
 P. Hardy, Radiology, U of Kentucky
 A. Andersen, Center for Magnetic Resonance Imaging, U of Kentucky
 B. Damon, Radiology, Vanderbilt University
 D. Johnson, Department of Orthopedics, U of Kentucky
 M. L. Ireland, Department of Orthopedics, U of Kentucky
 B. Noehren, Department of Physical Therapy, U of Kentucky

Abstract: Quadriceps weakness following an ACL reconstruction limits an athlete's ability to return to sport. Little work has been done to assess if the underlying morphology of the muscle is altered. Recent advances in diffusion tensor magnetic resonance imaging (DTI-MRI) allow for the assessment of critical features related to force production such as pennation angle, fiber length, volume and physiological cross-sectional area (PCSA).
HYPOTHESIS: We hypothesized that the vastus lateralis' PCSA, volume, fiber length, and pennation angle would be less in the operative limb compared to the non operative limb after six months of physical therapy. **SUBJECTS:** Six subjects who completed physical therapy post ACL reconstruction (5F, 1M, ages 26.6 ± 8.64 yrs). **METHODS:** DTI-MRI of both the involved and uninvolved legs was performed. Slicer 3D and a custom code were used to calculate volume, fiber length, PCSA, and pennation angle in each leg. Between leg comparisons were made with a pair t-test. **RESULTS:** We found significant differences in pennation angle (15.1 ± 2.9 degrees involved, 17.9 ± 2.6 degrees uninvolved, $p=0.004$), muscle volume (241.2 ± 75.0 cm³ involved, 341.5 ± 83.2 cm³ uninvolved, $p=0.032$), and PCSA (47.2 ± 14.8 cm² involved, 68.6 ± 9.1 cm² uninvolved, $p=0.007$). We found no significant difference in muscle fiber length (5.0 ± 1.3 cm involved, 4.7 ± 0.8 cm uninvolved, $p=0.640$). **CONCLUSION:** The PCSA was significantly lower for the involved leg, which was largely driven by muscle atrophy and pennation angle but not fiber length. This shows that despite intensive therapy, the underlying morphology of the quadriceps does not normalize following surgery.

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Primary Presenter / email: **Hickey, A.** / ajhi225@g.uky.edu
Clinical Science
Muscle

Mentor / e-mail: Noehren, B. / b.noehren@uky.edu



CCTS Poster Presentation Abstracts

103 Abstract Title: **Effects Of Simulated Weight Gain On Muscle Activation During Sit-To-Stand Task**

Author(s): M.C. Walaszek, Department of Kinesiology & Health Promotion, U of Kentucky
 A.L. Ransom, Department of Kinesiology & Health Promotion, U of Kentucky
 S. Capehart, Department of Kinesiology & Health Promotion, U of Kentucky
 R. Shapiro, Department of Kinesiology & Health Promotion, U of Kentucky
 M.B. Pohl, Department of Kinesiology & Health Promotion, U of Kentucky
 L.M. Bollinger, Department of Kinesiology & Health Promotion, Center for Muscle Biology,
 U of Kentucky

Abstract: Obesity increases the risk of lower extremity joint injury and physical disability. Although kinematic alterations in the obese population have been shown to exist, the role of excess mass and mass distribution in biomechanical alterations is unclear. Purpose: To determine the effects of external loads mimicking central and peripheral weight gain on lower-extremity muscle activity during the sit-to-stand (SiTSt) task. Methods: Five (4 male; 1 female) healthy, normal weight subjects have volunteered for the current study. During the SiTSt task, lower extremity muscle activity of the medial gastrocnemius, semitendinosus, vastus lateralis, and vastus medialis were analyzed using surface EMG. Subjects completed the SiTSt task under three load conditions including normal body weight (UN), centrally loaded (CN), and peripherally loaded (PN). The loaded conditions increased the subject's body mass index (BMI) by 5 kg/m² (20.5 ± 0.7% body weight). Results: Peak EMG activity was not altered by either central or peripheral loading (pMG = 0.194; pST = 0.383; pVL = 0.669; pVM = 0.486). Total muscle activity (EMG area under the curve) and timing of peak EMG activity are of interest during this study, but have yet to be analyzed. Conclusions: Increasing body load mimicking central or peripheral weight gain may not affect muscle activity during SiTSt. It is possible that kinematic compensatory mechanisms of the trunk and hips prevent increases in peak EMG activity during this task.

Supported by:

Primary Presenter / email: **Walaszek, M.C.** / michelle.walaszek@uky.edu
Clinical Science
Muscle

Mentor / e-mail: Bollinger, L.M. / lance.bollinger@uky.edu



CCTS Poster Presentation Abstracts

104**Abstract Title: Modulation of Hypothalamic Activity Alters Appetite in a Novel Antioxidant Mouse**

Author(s): D.L. Amos, Dept. of Pharmacology, Physiology & Toxicology, Joan C. Edwards School of Medicine, Marshall U, Huntington, WV
 L. Efav, Dept. of Pharmacology, Physiology & Toxicology, Joan C. Edwards School of Medicine, Marshall U
 C. Cook, Dept. of Pharmacology, Physiology & Toxicology, Joan C. Edwards School of Medicine, Marshall U
 M.B. Massie, Dept. of Pharmacology, Physiology & Toxicology, Joan C. Edwards School of Medicine, Marshall U
 N.S. Mitchell, College of Arts and Sciences, Bluefield State College, Bluefield, WV
 A.M. Gudivada, Dept. of Pharmacology, Physiology & Toxicology, Joan C. Edwards School of Medicine, Marshall U
 N. Santanam, Dept. of Pharmacology, Physiology & Toxicology, Joan C. Edwards School of Medicine, Marshall U

Abstract: Oxidative stress (OS) plays a key role in the metabolic syndrome which includes obesity. Appetite is tightly regulated by orexigenic and anorexigenic pathways within the hypothalamus. Oxygen-derived free radicals regulate the function of metabolic tissues leading to altered glucose and lipid homeostasis. Catalase is an antioxidant that counters reactive oxygen species thus reducing OS. We hypothesized excess catalase expression would deter OS-mediated appetite dysregulation by modifying hypothalamic signaling. Therefore, we assessed appetite regulation and obesogenic changes in Catalase transgenic (Cat-tg) mice that expressed 3-4 fold excess catalase and “Bob-Cat” mice (n=4/group), which are a hybrid of Cat-tg and leptin-resistant Ob-Ob mice. Body fat (ECHO-MRI), and metabolic changes using CLAMS (Comprehensive Laboratory Animal Monitoring System) were measured. Ob-Ob and C57Bl6 mice were controls. Changes in appetite regulating genes (POMC- Proopiomelanocortin and Npy- Neuropeptide Y) in the hypothalamus and adipokines, catalase, and OS in adipose tissue were measured. Graphpad Prism was used for statistical analysis. Although leptin expression was increased in Bob-Cat vs. Cat-tg (>100 fold), there was a lowering of fat/lean ratio in both genotypes compared to Ob-Ob mice. CLAMS showed heat production was higher in Cat-tg and Bob-cat vs C57Bl6. Cat-tg showed an induction in anorexigenic POMC (>2.5 fold), and decrease in orexigenic Npy (<0.5 fold). In contrast, Bob-Cat mice showed reduced levels of appetite genes vs C57Bl6. Our data indicates catalase overexpression modulated appetite regulation and the fat to lean mass ratio, suggesting excess antioxidant, may be regulating metabolic pathways that lower obesity and improve the overall nutritive state.

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Primary Presenter / email: **Amos, D.L.** / amos23@marshall.edu

Basic Science

Other

Mentor / e-mail: Santanam, N. / santanam@marshall.edu



CCTS Poster Presentation Abstracts

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

Author(s): K.K. Hampton, Department of Pharmacology and Nutritional Sciences, U of Kentucky
 P.A. Kern, Department of Medicine, U of Kentucky
 R.J. Craven, Department of Pharmacology and Nutritional Sciences, U of Kentucky

Abstract: Background: As of 2014, 29.1 million Americans suffer from diabetes, creating a severe socioeconomic and medical burden on society. Impaired insulin signaling is central in the development of type 2 diabetes, presenting a unique therapeutic challenge. Insulin resistance is associated with a reduction in Insulin Receptor (IR) kinase activity and activation of the PI3K (phosphatidylinositol 3-kinase) pathway. Additionally, obese individuals show decreased insulin binding due to a reduction in IR levels without an alteration in ligand-receptor binding affinity. The progesterone receptor membrane component 1 (PGRMC1), also known as sigma-2 receptor (S2R), is an endosomal protein that promotes cellular signaling via receptor trafficking. A recent translational study determined that PGRMC1 was decreased in patients with insulin-resistant disease, suggesting a role in insulin signaling. Methods: Human subcutaneous adipose tissue was obtained from human patients with BMI ranging from 28-35 courtesy of Dr. Philip Kern. Tissue samples were maintained at -80C until digestion with RIPA buffer and immunological analysis. Fully differentiated human subcutaneous adipocytes were purchased from Zenbio, Inc., and maintained according to the manufacturer's protocol. Differentiated subcutaneous adipocytes were treated with the PGRMC1/S2R ligands, AG205 (10 μ M) and PB28 (1 μ M), and analyzed via western blot. Visceral adipose tissue explants were isolated from male Sprague Dawley rats and maintained in serum free media (DMEM + 1x penicillin/streptomycin). Explants were treated with 10uM AG205 and insulin stimulated (100 nM) for 10 minutes. Proteome profile arrays (rat cytokine antibody array and human phospho-MAPK array) were purchased from R&D Systems, Inc., and followed the manufacturer's protocol. Results: Both Insulin Receptor β (IR β) and PGRMC1 protein levels decreased with increasing BMI in human subcutaneous adipose tissue. Treatment with AG205 and PB28 significantly increased IR β levels in fully differentiated human subcutaneous adipocytes from pooled donors (p=0.004 and p=0.027 respectively). Additionally, AG205 treatment increased IR β significantly (p=0.013) in differentiated adipocytes derived from a single female donor with a BMI of 38. To increase the scope of the experiments, we used a rat model system. In rat adipose explants, treatment with AG205 significantly increased the adipokines Leptin (3.2-fold, p=0.002) and IGFBP5 (2.7-fold, p=0.002). Treatment with AG205 and insulin stimulation significantly stimulated the AKT and GSK pathway (p=0.001 and 0.019 respectively), but had an inhibitory effect on the ERK pathway, including the RSK and MSK2 kinases (p=0.028, p=0.002 and 0.029 respectively). Conclusion: Treatment with PGRMC1/S2R ligands increases IR β protein levels significantly in human adipocytes and plays a critical role in IR signaling after insulin stimulation.

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Primary Presenter / email: **Hampton, K.K.** / kaia.hampton@uky.edu
Basic Science
Other

Mentor / e-mail: Crave, R.J. / rolf.craven@uky.edu



CCTS Poster Presentation Abstracts

106 Abstract Title: **Role of Na-K-ATPase alpha-1 isoform in tight junction.**

Author(s): I. Larre, Marshall Institute of Interdisciplinary Research, Marshall U, Huntington, WV
Z. Jue, Marshall Institute of Interdisciplinary Research, Marshall U
Z. Xie, Marshall Institute of Interdisciplinary Research, Marshall U

Abstract: Tight junctions (TJ), located at the uppermost portion of the lateral membrane of epithelial cells, are responsible for barrier formation and the regulation of paracellular transport of ions and nutrients. Thus, TJ have a central role in our body's handling of salts and nutrients. The molecular composition of TJ determines the permeability and ion selectivity of different nephron segments along renal tubules. For example, TJ in the proximal segment are permeable to Na⁺ and much leakier than TJ in the distal segment of renal tubules. These changes in permeability are consequences of specific expression of TJ proteins such as claudin isoforms. While proximal tubules express claudin-2, distal nephrons have claudin-4 as a major isoform. Little is known about what controls the composition of TJ along the nephron. This work shows that the signaling function of Na⁺/K⁺-ATPase (NKA) plays an important role in the regulation of the composition of TJ and thus paracellular selectivity and permeability in renal epithelial cells. In the present study, using TER measurement and Western blot, we found that cells expressing NKA alpha-1 mutated at 420 and 425 amino acids (A420P and A425P) had increased grade of sealing of TJ and its molecular composition change in comparison to control and hence are vital for TJ formation. This has fundamental and therapeutic implications for renal function in health and diseases such as obesity, but the precise molecular pathway that links NKA to claudin expression and subsequent modulation of TJ structure and function has to be dissected out.

Supported by:

Primary Presenter / email: **Larre I.** / perezm@marshall.edu**Basic Science****Other**Mentor / e-mail: Xie, Z. / perezm@marshall.edu



CCTS Poster Presentation Abstracts

107 Abstract Title: **Congenic Mice Confirmed QTL Linked to Obesity and Hyperlipidemia on Chromosome 1 in the TALLYHO Mouse**

Author(s): J.K. Parkman, Department of Pharmacology, Physiology, and Toxicology, Marshall U, Huntington, WV
 X. Mao, Department of Pharmacology, Physiology, and Toxicology, Marshall U
 K. Dillon, Department of Pharmacology, Physiology, and Toxicology, Marshall U
 J.H. Kim, Department of Pharmacology, Physiology, and Toxicology, Marshall U

Abstract: The TALLYHO (TH) mouse presents a syndrome of obesity, insulin resistance, type 2 diabetes, and hyperlipidemia. In a genome-wide scan of a [THxC57BL/6 (B6)]F2 population, we identified quantitative trait loci (QTL) linked to obesity and hyperlipidemia on mouse chromosome (Chr) 1. To confirm the QTL and develop a strategy for positional cloning of the responsible gene(s), we generated a congenic mouse strain that carries the Chr 1 QTL, 128 Mb in size, derived from TH on a B6 background (B6.TH-Chr1-128Mb) and a second congenic strain carrying only the proximal segment, (B6.TH-Chr1-92Mb). The purpose of this study was to characterize these congenic mice on chow and high fat diets (HFD) and evaluate gene expression levels of interferon activated gene 202B (Ifi202b) as a positional candidate gene. Body composition, indirect calorimetry, plasma cholesterol, and triglyceride levels were determined. Ifi202b mRNA levels were measured in adipose tissue by qRT-PCR. On chow, B6.TH-Chr1-128Mb mice exhibited significantly larger body fat mass compared with B6.TH-Chr1-92Mb and B6 mice. Similar trends were seen for plasma total cholesterol and true triglyceride levels, suggesting the Chr1 QTL candidate region is likely within the distal segment of the TH congenic interval where the Ifi202b gene, associated with obesity and down-regulated in B6 mice due to a microdeletion, maps. B6.TH-Chr1-128Mb mice showed lower energy expenditure (kcal/kg/hr) than B6.TH-Chr1-92Mb and B6 mice on chow and HFD, without food intake differences. The Ifi202b mRNA levels were 5-fold higher in adipose tissue of B6.TH-Chr1-128Mb mice than B6 mice on chow, and even higher on HFD. In summary, TH mice carry QTL conferring obesity and hyperlipidemia on the distal part of Chr 1.

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 Primary Presenter / email: **Parkman, J.K.** / parkman@marshall.edu
Basic Science
Other
 Mentor / e-mail: Kim, J.H. / kimj@marshall.edu



CCTS Poster Presentation Abstracts

108 Abstract

Title:

Dietary Fat, Lipoprotein, and Lipopolysaccharide: Role in Insulin Resistance

Author(s):

T. Boyechko, College of Medicine, CCTS, U of Kentucky

D.E.R. Ross, CCTS, U of Kentucky

P.A. Kern, CCTS, Department of Internal Medicine, Division of Endocrinology, U of Kentucky

Abstract: According to the CDC, more than 1/3 of US adults have prediabetes, of which 15-30% will develop type 2 diabetes in the next 5 years. For this reason, we are trying to better understand insulin resistance. Studies done in mice have shown that manipulating gut microbiota affects insulin sensitivity and tissue inflammation. Other studies have shown that reduced insulin sensitivity and high LPS levels are associated, and that altering gut microbiota will affect both. Little has been done in humans, and for this reason, we made this the focus of our study. We hypothesize that LPS causes inflammation in adipose tissue, and therefore, contributes to insulin resistance. Using the gut antibiotic rifaximin, which has been shown to reduce LPS levels, gut microbiota will be altered. We hypothesize that LPS will decrease, and therefore, reduce tissue inflammation and improve insulin sensitivity in obese subjects. Nondiabetic subjects with metabolic syndrome were recruited and randomized to receive placebo or rifaximin. Both groups had baseline studies before treatment began, which measured insulin sensitivity, tissue inflammation, and body habitus. These studies were repeated at the end of an 8-week course of the study drug, and results were compared. To date, 6 subjects have completed the study. Preliminary data from the euglycemic clamp procedures show that altering gut microbiota resulted in a 31.8% reduction in glucose infusion rate. Additionally, data obtained from the OGTT show a 4% increase in fasting blood glucose and a 14% increase in 2-hour glucose. These data suggest that altering gut microbiota makes a person more insulin resistant. In conclusion, altering gut microbiota with an antibiotic may have detrimental effects on insulin sensitivity, suggesting that gut microbiota are important to maintaining insulin sensitivity.

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Primary Presenter / email:

Boyechko, T. / tania.boyechko@uky.edu

Clinical Science

Other

Mentor / e-mail:

Kern, P.A. / pake222@uky.edu



CCTS Poster Presentation Abstracts

109 Abstract Title: **Squeeze Me if You Can: Variability in Force Requirements to Extract a Drop from Common Glaucoma Bottles**

Author(s): D.B. Moore, Department of Ophthalmology, U of Kentucky
 J.D. Hammer, College of Medicine, U of Kentucky
 R. Akhtari, College of Medicine, Drexel U
 J. Beck, Department of Ophthalmology, U of Kentucky
 S. Sanders, Department of Ophthalmology, U of Kentucky
 R.J. Kryscio, Departments of Statistics and Biostatistics, U of Kentucky

Abstract: Purpose: To determine the force requirements to dispense a single drop from commonly prescribed brand and generic topical glaucoma medications and correlate these findings with pinch strength in a representative patient population. Patients and Methods: Four bottles of each medication were tested: two in the vertical and two in the horizontal orientation. Bottles were housed in a customized force gauge apparatus designed to mimic ballpoint fingertip contact with a bottle tip. For all bottles, each of the first 10 dispensed drops was tested and then tests were performed in increments of 10 until the bottle was empty. For each tested drop, the maximum force and displacement were electronically measured. Concurrently, maximum pinch strength was measured on consecutive glaucoma patients. Results: A total of 84 bottles from 21 bottle designs were tested. There was significant variability across the designs, with roughly a 7-fold (0.67-4.49 kilograms of force, kgf) and 4-fold (0.81-3.00 kgf) difference in force requirements in the vertical and horizontal positions, respectively. Of 53 enrolled patients in the glaucoma clinic, the mean pinch strength was 5.05 (range 1.23-10.4) and 4.82 (range 1.47-10.67) kgf for the right and left hands, respectively. Conclusions: There is significant variability in the force required to squeeze a drop from common glaucoma medications, and a representative sampling of clinic patients suggests that many likely struggle with the force requirements of several bottle designs. These data further support standardization of topical glaucoma drug delivery and design.

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Primary Presenter / email: **Hammer, J.D.** / jon.hammer@uky.edu
Clinical Science
Ophthalmology

Mentor / e-mail: Moore, D. B. / daniel.b.moore@uky.edu



CCTS Poster Presentation Abstracts

110 Abstract Title: **Patient Reported Outcomes 5-20 years following an ACL reconstruction**

Author(s): J. Bell, College of Medicine, U of Kentucky
 M. Lex, College of Health Sciences, U of Kentucky
 T. Bayers, College of Arts and Science, U of Kentucky
 M.L. Ireland, Department of Orthopaedic Surgery and Sports Medicine, U of Kentucky
 D. Johnson, Department of Orthopaedic Surgery and Sports Medicine, U of Kentucky
 B. Noerhen, Department of Rehabilitation Sciences, Division of Physical Therapy, U of Kentucky

Abstract: Background: There is a paucity of literature for long-term follow-up of anterior cruciate ligament (ACL) reconstruction. Qualitative analysis of patient outcomes, is an important aspect of these surgeries that may yield insight into furthering patient care post-operatively. Methods: Thirty-one subjects, aged 18-55, 5-20 years out from ACL reconstruction were assessed utilizing the Knee Injury and Osteoarthritis Outcome Score, International Knee Documentation Committee Form, The Lower extremity Functional Scale, and Lysholm Knee Questionnaire. Individual questions responses were assessed for the proportion of subjects reporting at least mild difficulties. Results: Monthly knee pain was reported in 71% of the subjects and mild swelling/stiffness was indicated in 68%. Quality of Life self-reported assessments showed 65% of subjects had to modify, their life style to avoid potentially damaging their knee. A lack of confidence in their involved knee was reported in 71%. Minimal difficulty in jumping and landing was reported in 52% of subjects, while 55% of subjects reported they had difficulty with hopping. Difficulty with sharp turns while running was seen in 58% of subjects. Mild pain associated with pivoting was reported in 52% of subjects. Conclusions: Long-term assessment of ACL patients shows that half of the patients experienced deficits in performing high impact activities and associated recurrent pain with these activities. Minimal deficits were seen in daily activities. Post-operative planning and patient advice should reflect both a delayed return to baseline ability and potential long-term deficits in high impact activities. Pain and swelling/stiffness associated with these activities may also exceed patient expectations.

Supported by:

Primary Presenter / email: **Bell, J.** / jebe223@uky.edu

Clinical Science

Orthopedics

Mentor / e-mail: Noerhen, B. / b.noerhen@uky.edu



CCTS Poster Presentation Abstracts

111 Abstract Title: **Bone Microdamage in Patients Treated with Forteo**

Author(s): C. Brooks, Department of Biomedical Engineering, U of Kentucky
S. Pagano, College of Medicine, U of Kentucky
C. Wood, College of Arts and Sciences, Statistics, U of Kentucky
D. Pienkowski, Departments of Biomedical Engineering and Orthopaedic Surgery, U of Kentucky
H. Malluche, University of Kentucky Health Care, U of Kentucky

Abstract: Forteo is a recently introduced drug used to treat osteoporosis. It is a genetically engineered fragment of parathyroid hormone known to stimulate osteoblasts, thus increasing bone formation. The purpose of this study is to determine if the levels of naturally occurring bone microdamage in non-osteoporotic patients with who sustain low-energy fractures, despite normal bone mass, are related to treatment with Forteo. Bone microdamage analyses will be performed on iliac crest biopsies from ten pre-menopausal women treated with Forteo and who had low energy, atypical fractures, but normal bone mineral density. Bone samples will be taken pre- and post-Forteo treatment, stained with basic fuchsin, embedded in MMA and sliced into 100 micron samples using a diamond wire saw. The stained 100 micron samples will then be examined with light and fluorescence microscopy to assess the degree of bone microdamage. Microdamage parameters to be measured include number of cracks per area of examined bone and microcrack length. Analyses of variance, including covariates such as age, weight, and bone mineral density, will be performed to evaluate the relationship between Forteo use and the level of bone microdamage.

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Primary Presenter / email: **Brooks, C.** / csbr233@g.uky.edu
Clinical Science
Orthopedics

Mentor / e-mail: Pienkowski, D. / pienkow@uky.edu



CCTS Poster Presentation Abstracts

112 Abstract Title: **Multicenter Orthopaedic Outcome Network Early Anti-Inflammatory Treatment in Patients with Acute ACL Tear (MOON-AAA Clinical Trial)**

Author(s): C. Lattermann, Department of Orthopaedic Surgery and Sports Medicine, U of Kentucky
 M. Proffitt, Division of Physical Therapy, U of Kentucky
 L.J. Huston, Vanderbilt Orthopaedic Institute
 L.G. Gammon, College of Medicine, U of Kentucky
 D.L. Johnson, Department of Orthopaedic Surgery and Sports Medicine, U of Kentucky
 V.B. Kraus, Duke Molecular Physiology Institute, Department of Medicine, Duke U
 C.A. Jacobs, Department of Orthopaedic Surgery and Sports Medicine, U of Kentucky
 K.P. Spindler, Sports Health Center, Cleveland Clinic

Abstract: Background: Social network analysis (SNA) seeks to understand how people are connected in a population and can be a powerful tool that can yield insights into disease transmission. To map risk networks, researchers collect information (name, age, gender, etc) and behavioral data about participants and their partners (i.e., 'alters'). To construct valid and reliable networks, accuracy in reported data is critical. Objective: This study evaluates the accuracy with which participants report alters' identifying demographic data. Methods: Data were collected from 2008 to 2010 from 503 rural drug users. Network ties (n=897) involved recent (past 6 months) sex, drug co-usage, and/or social support. Study staff cross-reference the data provided about alters with the data that participants provide about themselves to construct a risk network that represents all direct and indirect connections among participants (i.e., a sociometric network). Analyses were conducted to determine the accuracy of reported ages (years) and names (binary). Results: Participants gave alters' exact names and ages within two years in 75% and 79% of relationships, respectively. Name reporting was more accurate in reciprocally reported ties and those involving social support and a male alter. Age was more accurate in reciprocal ties and those characterized by kinship, sexual partnership, frequent communication, recruitment referral, and financial support and less accurate in ties with older alters. Conclusions: Most participants reported the identifying characteristics of their alters accurately, and the accuracy was not significantly different in relationships involving illicit behavior compared to those not involving illicit behaviors.

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Primary Presenter / email: **Gammon, L.G.** / lee.gammon@uky.edu
Clinical Science
Orthopedics

Mentor / e-mail: Lattermann, C. / Christian.Lattermann@uky.edu



CCTS Poster Presentation Abstracts

113 Abstract Title: **Moderating Effects of Immunosuppressive Medications and Risk Factors for Post-Operative Joint Infection Following Total Joint Arthroplasty in Patients with Rheumatoid Arthritis or Osteoarthritis**

Author(s): E.G. Salt, College of Nursing, U of Kentucky
 A.T. Wiggins, College of Nursing, U of Kentucky
 M.K. Rayens, College of Nursing, U of Kentucky
 B.J. Morris, Lexington Clinic, Lexington, KY
 D. Mannino, College of Public Health, Dept. of Internal Medicine, U of Kentucky
 A. Hoellein, College of Medicine, Dept. of Internal Medicine, U of Kentucky
 R.P. Donegan, Bluegrass Orthopedics and Hand Care, Lexington, KY
 L.J. Crofford, Dept. of Rheumatology and Immunology, Vanderbilt U, Nashville, TN

Abstract: Introduction: Inconclusive findings about infection risks, importantly the use of immunosuppressive medications, in patients who have undergone large-joint total joint arthroplasty (TJA) challenge efforts to provide evidenced-based perioperative TJA recommendations. The aim of this study was to describe risk factors for developing a postoperative infection in patients undergoing TJA of a large joint [total hip arthroplasty (THA), total knee arthroplasty (TKA), or total shoulder arthroplasty (TSA)] by identifying clinical and demographic factors, including the use of high risk medications (i.e., prednisone and immunosuppressive medications) and diagnoses (i.e., rheumatoid arthritis [RA], osteoarthritis, gout, obesity, diabetes mellitus), that are linked to infection status, controlling for length of follow-up. Methods: A case-control study (N=2,234) using de-identified patient health claims information from a commercially-insured, U.S. dataset representing 15 million patients annually was conducted. Descriptive statistics, t-test, chi-square test, Fisher's exact test, and multivariate logistic regression were used. Results: Male gender (OR =1.43; p<.001), diagnosis of RA (OR =1.57; p=.014), cancer (OR =2.38; p=.009), diabetes mellitus (OR =1.69, p<.001), obesity (OR =1.55, p<.001) and gout (OR =1.76; p<.001), and a prescription for prednisone (OR=1.81; p<.001) predicted a post-operative infection following TJA. Persons with post-operative joint infections were significantly more likely to be prescribed allopurinol (p=.004), colchicine (p=.021), and mesalamine (p<.001); no significant difference was found for the use of specific disease modifying anti-rheumatic drugs and TNF- α inhibitors. Conclusion: High-risk, post-operative joint infection groups were identified allowing for precautionary clinical measures to be taken.

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Primary Presenter / email: **Salt, E.G.** / egsalt0@uky.edu
Clinical Science
Orthopedics

Mentor / e-mail: Crofford, L.J. / leslie.j.crofford@vanderbilt.edu



CCTS Poster Presentation Abstracts

114 Abstract Title: **Accuracy and efficiency of sequence variation detection methods using high-confidence variation call sets**

Author(s): X. Zhang, Department of Computer Science, U of Kentucky
S. R. Ellingson, Biomedical Informatics, U of Kentucky

Abstract: Objectives As genetic sequence data is now being used to make health care decisions, analysis tools needed for personalized medicine must be well tested and verified while establishing and maintaining competency in the state-of-the-art in both the technology and analysis. This study demonstrates the usefulness of high-confident call sets (validated genomic variations) in testing and optimizing bioinformatics pipelines. Methods The GATK (Genome Analysis Tool Kit) best practices pipeline for genomic variation detection was used on Illumina Hi-Seq genomic data obtained from a sample originating from NA12878, a participant in the HapMap project. Results In this study, several workflow variations were evaluated. 1) Experimental conditions: one sequencing run with a higher depth of coverage has about 1% lower true positive rate and .1% higher positive predictive power than four runs with lower coverage each. 2) Computational architecture: threading to efficiently use a 16 CPU node gives a speed-up of almost 4.5 times that of using only one CPU; however, utilizing a 32 CPU node only gives a speed-up of 1.1 over that of a 16 CPU node. 3) Analysis tools: UnifiedGenotyper is about 7 times faster than HaplotypeCaller which only has about a 1-2% increase in true positive rates. 4) Comparison tools: GATK VariantEval, Useq vcfc comparator, and RTG vcfeval all produce similar comparison results. Discussion A workflow that easily and reproducibly tests the accuracy and efficiency of a given method on a given computational platform is critical in order to confidently and cost-effectively utilize genomic sequencing in a clinical setting.

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Primary Presenter / email: **Ellingson, S.R.** / sally@kcr.uky.edu
Basic Science
Other

Mentor / e-mail: Weiss, H.L. / heidi.weiss@uky.edu



CCTS Poster Presentation Abstracts

115 Abstract Title: **Distinct Synuclein Seeds in Parkinson Disease and Multiple System Atrophy**

Author(s): T.R. Yamasaki, Department of Neurology, U of Kentucky
 B.B. Holmes, Washington U School of Medicine St Louis
 J.L. Furman, Department of Neurology and Neurotherapeutics, U of Texas Southwestern
 D.D. Dhavale, Department of Neurology, Washington U School of Medicine St. Louis
 N.J. Cairns, Department of Neurology, Washington U School of Medicine St. Louis
 P.T. Kotzbauer, Department of Neurology, Washington U School of Medicine St. Louis
 M.I. Diamond, Department of Neurology and Neurotherapeutics, U of Texas Southwestern

Abstract: Objective: Both in vitro and in vivo studies suggest that in many neurodegenerative diseases, including synucleinopathies, cell-to-cell transmission of a pathological protein occurs and may mediate spreading of pathology throughout the brain. This misfolded protein (“seed”), further templates misfolding of native protein within the cell. The objective of this study is to determine whether seeding activity of alpha-synuclein is detectable and differs between two distinct synucleinopathies, Parkinson disease (PD) and Multiple system atrophy (MSA). Methods: We developed a system which combines the sensitivity of fluorescence with the quantitative power of flow cytometry. Monoclonal cell lines stably expressing synuclein fused to cyan or yellow fluorescent protein were generated. Upon aggregation, spectroscopic changes are readily detected as a FRET (Fluorescence Resonance Energy Transfer) signal and quantified by flow cytometry. We used this assay to test seeding activity in detergent soluble and insoluble fractions of brain from PD and MSA. Results: The FRET assay detects seeding from recombinant synuclein fibrils in the picomolar range ($p < 0.007$) while not detecting seeding of other amyloid types. Moreover, it is the first assay to robustly detect synuclein seeding activity in both synucleinopathies. While insoluble fractions showed seeding activity in both diseases ($p < 0.0005$), only MSA showed robust seeding in the soluble fraction ($p < 0.0006$). Control samples of brains from non-synucleinopathy patients did not show significant seeding activity. Morphology of the seeded aggregates was also distinct between the two diseases; PD aggregates were more circumscribed; MSA aggregates were more wispy and filamentous. Significance: Using a novel quantitative cell-based assay, we have found clear differences in synuclein seeding activity and aggregate morphology in MSA and PD, supporting the idea of a conformational difference between the pathologic synuclein found in these diseases.

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Primary Presenter / email: **Yamasaki, T.Y.** / tyamasaki@uky.edu
Basic Science
Other

Mentor / e-mail: Diamond, M.I. / Marc.Diamond@UTSouthwestern.edu



CCTS Poster Presentation Abstracts

116 Abstract	Protease-Activated Receptor 4 Induces Bladder Pain through Disulfide High Mobility Group Box-1 Acting on Receptors for Advanced Glycation End Products
Title:	
Author(s):	D.E. Kouzoukas, Research and Development, Lexington Veteran Affairs Medical Center F. Ma, Research and Development, Lexington Veteran Affairs Medical Center K.L. Meyer-Siegler, Department of Natural Sciences, St. Petersburg College, St. Petersburg, FL K.N. Westlund, Department of Physiology, U of Kentucky D.E. Hunt, Research and Development, Lexington Veteran Affairs Medical Center P. L. Vera, Research and Development, Lexington Veteran Affairs Medical Center

Abstract: Pain without obvious inflammation is a hallmark of Interstitial Cystitis / Painful Bladder Syndrome (IC/PBS). Urothelial protease activated receptor 4 (PAR4) stimulation causes bladder pain without inflammation through macrophage migration inhibitory factor (MIF) release. High mobility group box-1 (HMGB1) mediates bladder pain, but not inflammation. HMGB1 redox forms act through receptors for advanced glycation endproducts (RAGE) and toll-like receptor 4 (TLR4). We investigated whether: 1) bladder PAR4 causes urothelial HMGB1 release; 2) blocking MIF prevents HMGB1 release; 3) blocking HMGB1 prevents PAR4-induced hypersensitivity; 4) HMGB1 redox form causes bladder pain, inflammation and micturition changes; 5) antagonizing HMGB1 receptors affect HMGB1-induced hypersensitivity. Female C57BL/6 mice received intravesical PAR4 peptides (100 μ M; 1 hr). Intraluminal HMGB1 was measured. Abdominal hypersensitivity, micturition and histology were determined 24 hrs after pretreatment with HMGB1 inhibitor (glycyrrhizin: 50 mg/kg; ip), MIF blocker (ISO-1: 20 mg/kg; ip), HMGB1 redox forms (all-thiol; disulfide HMGB1; 1, 2, 5, 10, 20, μ g/150 μ l; 1 hr), RAGE antagonist (FPS-ZM1; 10 mg/kg, i.p.), TLR4 antagonist (TAK-242; 3 mg/kg, i.p.), or vehicle. PAR4 peptide triggered urothelial HMGB1 release which was blocked by MIF inhibition. Blocking HMGB1 prevented abdominal hypersensitivity. Only disulfide HMGB1 (\geq 10 μ g) induced abdominal hypersensitivity and micturition changes. Systemic FPS-ZM1 fully and TAK-242 partially prevented disulfide HMGB1 (10 μ g)-induced hypersensitivity. All doses of HMGB1 produced minimal inflammation. Bladder PAR4 induced urothelial HMGB1 release, mediated by MIF. Disulfide HMGB1 (not all-thiol) mediates bladder pain acting mainly through RAGE receptors. Urothelial MIF and HMGB1 receptors represent novel therapeutic targets for bladder pain.

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Primary Presenter / email: **Ma, F.** / fei.ma@uky.edu
Basic Science
Other

Mentor / e-mail: Vera P.L. / Pedro.Vera@va.gov



CCTS Poster Presentation Abstracts

117 Abstract	Urine Levels of Macrophage Migration Inhibitory Factor are Increased in Patients with Bladder Inflammation
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Title:	
Author(s):	F. Ma, Research and Development, Lexington Veteran Affairs Medical Center D.E. Kouzoukas, Research and Development, Lexington Veteran Affairs Medical Center M. Fall, Department of Urology, University of Gothenburg, Gothenburg, Sweden R.M. Moldwin, The Arthur Smith Institute for Urology, North Shore-LIJ Health System, Long Island, NY D.M. Preston, Research and Development, Lexington Veteran Affairs Medical Center D.R. Erickson, Department of Urology, U of Kentucky B. Kahn, Department of Urology, U of Kentucky K. L. Meyer-Siegler, Department of Natural Sciences, St. Petersburg College, St. Petersburg, FL P.L. Vera, Research and Development, Lexington Veteran Affairs Medical Center

Abstract: Macrophage migration inhibitory factor (MIF), a pro-inflammatory cytokine, mediates bladder inflammation and pain. We examined urine MIF levels from patients with conditions including: interstitial cystitis (IC) with and without Hunner lesions, urinary tract infection (UTI) and radiation cystitis compared to a control population. Specimens from males included those from patients with culture confirmed UTI, radiation cystitis (after undergoing radiation therapy) and a control population. Specimens from females include those from IC patients with and without Hunner lesions, and control subjects. Patients with Interstitial Cystitis met NIDDK diagnostic criteria. All IC patients were symptomatic at the time of urine collection. Urinary MIF and Creatinine levels were assayed using commercially available kits. MIF levels were significantly increased in the urine of UTI patients (>4-fold; N=51) or radiation cystitis patients (10-fold; N=18) when compared to controls (N=117). Similarly, MIF levels were significantly increased (5-fold) in the urine of IC patients with Hunner lesions (N=47) when compared to female controls (N=102). Urine MIF levels in IC patients without Hunner lesions (N=63) were not different from controls. Urinary MIF is increased in a variety of bladder inflammatory conditions including interstitial cystitis with Hunner lesions, UTI and radiation cystitis. Conversely, urine MIF levels from IC patients without Hunner lesions were similar to controls. MIF may be useful for diagnosis or prognosis of IC patients with Hunner lesions and may represent a novel therapeutic target for reducing bladder pain in IC and other bladder inflammatory disorders.

Supported by: NIH: DK0093496 (PLV)

Primary Presenter / email: **Vera, P.L.** / Pedro.Vera@va.gov
Clinical Science
Other

Mentor / e-mail: Vera, P.L. / Pedro.Vera@va.gov



CCTS Poster Presentation Abstracts

118 Abstract Title: **Buprenorphine Modulates Angiogenesis**

Author(s): W. O'Toole, Department of Physiology, Marshall U
R. Egleton, Department of Physiology, Marshall U

Abstract: In 2012 the NIH National Institute on drug abuse reported a fivefold increase of babies born with neonatal abstinence syndrome as compared to 2000. This NAS was induced by maternal opiate abuse during pregnancy. Buprenorphine, a semisynthetic thebaine derivative with mixed agonist/antagonist activity at the opioid receptor, has been shown to reduce the incidence of NAS. Of interest to us is the effect buprenorphine may have on the developing vasculature of the fetus. Several studies have shown that opioids modulate angiogenesis, though whether they positively or negatively modulate angiogenesis depends on cell type, receptor type, specific ligand used, and dose involved. It is known that opioids can regulate VEGF receptors and their signaling cascades indicating that there is the potential for altering fetal development. Recent publications suggest that mu-opioid agonists induce src mediated phosphorylation of the VEGF receptor Flk-1 (promoting angiogenesis), while kappa-opioid agonists inhibit the expression levels of Flk-1. This mixed action of mu and kappa agonists is very important for the treatment of neonates, as buprenorphine is a Mu agonist and a Kappa antagonist. Based on the previous studies outlined above, It is our hypothesis that buprenorphine will promote angiogenesis in part by inhibiting the kappa-mediated reduction of VEGF signaling and promoting mu opioid induced Src mediated activation of VEGF signaling. In this study we investigated the effects of acute and chronic buprenorphine (at clinically relevant doses) on Rat Brain Microvascular Endothelial Cell (RBMVEC) on angiogenesis and identified some signaling pathways that may regulate this response. We show changes in expression and activation of src family tyrosine kinases and phospho erk 1/2 with chronic treatment of buprenorphine and an associated increased angiogenesis of RBMVEC in a wound healing assay. These preliminary studies indicate that buprenorphine may indeed promote angiogenesis at clinically relevant doses.

Supported by: pilot funding from University of Marshall

Primary Presenter / email: **O'Toole, W.** / otoole4@marshall.eduMentor / e-mail: Egleton, R. / egleton@marshall.edu



CCTS Poster Presentation Abstracts

119**Abstract Title: Parity Influences Neonatal Gene Expression**

Author(s): N.R. Chavan, Div. of Maternal Fetal Medicine, Dept. of Obstetrics & Gynecology, U of Kentucky
 L.J. Reynolds, Dept of Pharmacology & Nutritional Sciences, U of Kentucky
 R. Pollack, Div. of Maternal Fetal Medicine, Dept. of Obstetrics & Gynecology, Carolinas Medical Center, Charlotte, NC
 J.M. O'Brien, Div. of Maternal Fetal Medicine, Dept. of Obstetrics & Gynecology, U of Kentucky
 K.J. Pearson, Dept. of Pharmacology & Nutritional Sciences, U of Kentucky

Abstract: Introduction: Increasing parity has been shown to be associated with offspring adiposity, inflammation, and impaired glucose metabolism in an animal model. However, similar studies examining the impact of parity and higher birth order in humans are lacking. The goal of this pilot study was to evaluate the effects of parity on the fetal programming of gene expression in neonates. Methods: Foreskin samples were collected from 55 non-anomalous neonates. Parity was abstracted from review of medical records. Samples were flash frozen, and RNA was isolated from the epidermal/dermal layer. Nine epidermal/dermal samples were excluded (n=4 from twins; 2 from preterm infants; 3 due to RNA degradation). RNA expression levels were analyzed using the NanoString Technologies nCounter system. Expression of genes involved in glucose/lipid metabolism and inflammatory response was quantified and normalized to housekeeping genes. The average gene expression levels among neonates born to mothers with a lower parity (1 or 2) (n = 35) vs. higher parity (3 or more) (n = 11) were compared, using Student's t test. Results: The mean parity was 1.54 ± 0.51 vs. 3.64 ± 0.92 , in the low vs. high parity group respectively. Demographic characteristics were similar in both groups. Expression levels of oxidative and inflammatory stress response genes - cytochrome P450 1b1 ($p < 0.01$) and hypoxia inducible factor 1 alpha ($p < 0.01$), as well as apoptotic regulatory genes, B-cell lymphoma 2 ($p < 0.05$) were significantly increased in babies born to women with a higher parity. Likewise, tissue from these infants was also noted to have significantly increased expression of adipocyte differentiation markers chemerin ($p < 0.01$), cAMP responsive element binding protein 1 ($p < 0.01$), forkhead box protein O1 ($p < 0.01$), very low density lipoprotein receptor ($p < 0.01$), suggestive of an increased adipogenic milieu. Interestingly, both adiponectin receptor 2 ($p < 0.05$) and fatty acid transport protein 4 ($p < 0.01$) were significantly down-regulated. Conclusion: Genes involved in the inflammatory response as well as metabolism were differentially expressed in infants born to mothers with a lower vs. higher parity. Further studies are warranted to evaluate if these changes will be sustained through epigenetic interactions.

Supported by: Funding provided through the Graduate Center for Nutritional Sciences at the University of Kentucky College of Medicine.

Primary Presenter / email: **Chavan, N.R.** / niraj.chavan@uky.edu

Basic Science

Other

Mentor / e-mail: Pearson, K.J. / kevin.pearson@uky.edu



CCTS Poster Presentation Abstracts

120 Abstract Title: **Extubation failure in preterm infants: A role for monitoring intermittent hypoxemia**

Author(s): A. Gabrani, Division of Neonatology, Department of Pediatrics, U of Kentucky
 D. Wasemiller, Department of Biomedical Engineering, U of Kentucky
 D. Mamilla, Division of Neonatology, Department of Pediatrics, U of Kentucky
 B. Schanbacher, Division of Neonatology, Department of Pediatrics, U of Kentucky
 A. Patwardhan, Department of Biomedical Engineering, U of Kentucky
 P.J. Giannone, Division of Neonatology, Department of Pediatrics, U of Kentucky
 M.D. Cunningham, Division of Neonatology, Department of Pediatrics, U of Kentucky
 E.G. Abu Jawdeh, Division of Neonatology, Department of Pediatrics, U of Kentucky

Abstract: Background: The use of mechanical ventilation for respiratory failure in extremely preterm infants is commonly associated with significant morbidities. In order to minimize days on mechanical ventilation, there is practice shift towards early extubation to non-invasive ventilator strategies. However, the lack of clear clinical indications to predict successful extubation places infants at increased risk for ventilation related complications. Objective: Identify the role of intermittent hypoxemia (IH) in predicting respiratory failure following extubation from mechanical ventilation in preterm infants less than 29 weeks gestation. Methods: We prospectively enrolled infants with GA \leq 29wks from level-IV neonatal ICU. Oxygen saturation was monitored using high resolution pulse-oximetry (2s averaging time, 1s sampling rate). Novel software was developed to filter/analyze oxygenation data. Respiratory failure data was collected from medical records. Failure was defined as reintubation within 72-hours. Extubation events were grouped as A-(failed) and B-(successful). We compared IH measures 72-hours pre and post extubation: (1.)IH<80: number of events/hour with SpO₂ drop<80%; (2.)%time<80: percent time spent SpO₂<80%. Results: A total of 38 extubation events were identified (11-failed, 27-successful). There was no difference in IH measures between groups during the 72-hours prior to extubation (mean IH<80: failed 8.3 vs successful 8.2, p=NS; %time<80: 5.2% vs 4.7% respectively, p=NS). Patients with successful extubation had improvement in IH measures post-extubation (IH<80, pre 8.2 vs post 4.6, p=0.053; %time<80: 4.7% vs 2.1% respectively, p=0.048). There was no improvement in IH parameters after extubation in cases of failure with a trend towards increased IH (IH<80, pre 8.3 vs. post 10.1; p=NS; %time<80: 5.2% vs. 5.8% respectively; p=NS). Conclusion: A lack of improvement in IH events may predict respiratory failure following extubation in preterm infants. Continuous IH monitoring with subsequent adjustment of non-invasive ventilator support strategies in post-extubation infants is imperative.

Supported by: Grant support from The Gerber Foundation and Children's Miracle Network

Primary Presenter / email: **Abu Jawdeh, E.G.** / eab224@uky.edu
Clinical Science
Other

Mentor / e-mail: Abu Jawdeh, E.G. / eab224@uky.edu



CCTS Poster Presentation Abstracts

121 Abstract Title: **The Effect of Single Nucleotide Polymorphisms in Opioid and Adrenergic Receptor Genes on Response to Treatment of Neonatal Abstinence Syndrome**

Author(s): S.E. Czack, College of Medicine, U of Kentucky
H.S. Bada, Department of Neonatology, U of Kentucky

Abstract: Neonatal Abstinence Syndrome (NAS) is a collection of symptoms that manifest in neonates who are undergoing withdrawal from substances used during the pregnancy. It is a growing social and medical problem, especially in Kentucky: our incidence is almost five times the national average. Current treatment involves pharmacotherapy in the neonatal intensive care unit (NICU) to mitigate withdrawal symptoms; however, response to treatment varies from neonate to neonate. It has been found that there is significant variability in the length of stay as a result of treatment. We hypothesized that this variability may be explained by differences in single nucleotide polymorphisms (SNPs) of different genes related to drug response. This study looks at the effects 10 different SNPs in 3 genes - μ -opioid receptor (OPRM1), catechol-O-methyltransferase (COMT), and G-protein β 3 (GNB3) subunit gene of the α 2-adrenergic receptor. All of these have been preliminarily shown to affect treatment outcomes in neonates with NAS, specifically affecting the length of treatment, maximum dose, and the ability to achieve control of NAS symptoms. This study analyzed the DNA at these 3 distinct genes (10 SNPs total) of 30 infants diagnosed with NAS at birth. We collected the DNA via buccal swabs and performed DNA purification. The DNA is now undergoing sequencing, and we expect to find that specific genotypes of each SNP affect the length of stay and characteristics of necessary treatment. The ultimate goal of this study is to discover whether or not these associations exist in the NAS population seen at the University of Kentucky, and if this preliminary study does indicate that, to expand this study even further to include more infants. Further, this study could lead to advances in tailored pharmacotherapy for neonates with specific genotypes.

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Primary Presenter / email: **Czack, S.E.** / sarah.czack@uky.edu
Clinical Science
Other

Mentor / e-mail: Bada, H.S. / hbada2@uky.edu



CCTS Poster Presentation Abstracts

122 Abstract Title: **Effect of Prenatal Maternal Tobacco Use on Intermittent Hypoxemia and Length of Stay in Preterm Infants: Pilot Study**

Author(s): D. Mamilla, Division of Neonatology, Department of Pediatrics, U of Kentucky
 P. Westgate, Department of Biostatistics, U of Kentucky
 A. Gabrani, Division of Neonatology, Department of Pediatrics, U of Kentucky
 A. Pant, Division of Neonatology, Department of Pediatrics, U of Kentucky
 D. Wasemiller, Department of Biomedical Engineering, U of Kentucky
 A. Patwardhan, Department of Biomedical Engineering, U of Kentucky
 M. Joshi, Division of Neonatology, Department of Pediatrics, U of Kentucky
 H. Bada, Division of Neonatology, Department of Pediatrics, U of Kentucky
 J. Bauer, Division of Neonatology, Department of Pediatrics, U of Kentucky
 P.J. Giannone, Division of Neonatology, Department of Pediatrics, U of Kentucky
 E.G. Abu Jawdeh, Division of Neonatology, Department of Pediatrics, U of Kentucky

Abstract: Background: Tobacco exposure during pregnancy causes central respiratory control abnormalities in neonates such as delayed arousal leading to prolonged apnea and subsequent intermittent hypoxemia (IH). During Neonatal Intensive Care Unit (NICU) stay, preterm infants have rising incidence of IH peaking around 4 weeks postnatal age where it plateaus and subsequently decreases at 6-8 weeks. Often, persistent apnea and oxygen desaturations prolong NICU length of stay in preterm infants. Objective: Test the hypothesis that preterm infants with prenatal tobacco exposure have higher incidence of intermittent hypoxemia and longer NICU length of stay. Methods: Oxygen saturation was continuously monitored using high resolution pulse-oximetry during the first 2 months of life. Infants with gestational age ≤ 29 wks admitted to the Kentucky Children's Hospital level IV neonatal intensive care unit were included. Novel software was developed to filter and analyze oxygenation data. Prenatal tobacco exposure data was collected from infants medical records. A model correcting for repeated measures and 2 sample t-test were used to compare differences in outcome measures in tobacco exposed versus unexposed. Outcome measures (1.) IH<80: number of events/week with SpO₂ drop <80%; (2.) %time<80: percent time spent below SpO₂ of 80%; (3.) length of stay. Results: A total of 60 preterm infants less than 29 weeks gestation were enrolled. Analyzable data was present on 57 patients (19 tobacco exposed, 38 unexposed). In the tobacco exposed group there was trend towards higher IH<80 (50-200 more events/week) and %time<80 (1-2% more) beyond the 4th week of life peak that persisted for the study period (8 weeks), p=NS. Length of stay was 23 days longer in tobacco exposed infants (mean tobacco exposed = 101 days versus unexposed 78 days, p=0.06). Conclusion: This pilot project suggests that the prenatal tobacco exposure may be an additional factor leading to the rise in intermittent hypoxemia frequency and prolonged length of stay. We are proposing a prospective cohort study aimed at better understanding these relationships as it may have a direct impact on daily and discharge management of preterm infants.

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Primary Presenter / email: **Pant, A.** / amsu3@hotmail.com
Clinical Science
Other

Mentor / e-mail: Abu Jawdeh, E.G. / eab224@uky.edu



CCTS Poster Presentation Abstracts

123 Abstract Title: **Effect of Limiting Intercourse on Perinatal Outcomes**

Author(s): L. Meints, Obstetrics & Gynecology, U of Kentucky
 J. Redfield, College of Medicine, U of Kentucky
 D. Akers, Statistics, U of Kentucky

Abstract: Purpose: Providers regularly counsel patients about sexual intercourse during pregnancy, yet little is known about the effects of limiting intercourse on perinatal outcomes. Our aim is to determine whether limiting intercourse during pregnancy is associated with differences in perinatal outcomes including preterm birth (PTB). Methods: This is a secondary analysis of a multicenter, prospective cohort designed to predict spontaneous PTB among singleton gestations. The exposure was limitation of intercourse: (1) Intercourse limited, (2) No intercourse, (3) Intercourse without limitation advised by provider. The primary outcome was PTB < 37 weeks gestation. Secondary outcomes were PTB < 34 weeks; PTB < 28 weeks; cervical length (CL) at 24 weeks; fetal fibronectin (FFN) values at 24 weeks; serum inflammatory cytokine levels; validated maternal stress, anxiety, and depression scores; and neonatal morbidity. We performed univariate and multiple logistic regression to determine the potential association between primary outcome and exposure. These associations are reported as adjusted odds ratios (aORs) and 95% confidence intervals (CIs). Results: There were 3073 women included in the analysis: 243 with intercourse limited, 1029 who had intercourse that was not limited, and 1801 who did not have intercourse during pregnancy. There were statistically significant differences among groups in race, tobacco use, previous PTB, infection present during pregnancy, CL, FFN, and vaginal bleeding (VB) during the first or second trimester. There was a statistical difference in PTB < 37 weeks by exposure in univariate ($p < .001$) and multivariate analyses ($p = .001$); aOR 0.48 for intercourse vs advised to limit (CI 0.33, 0.70), 0.58 for no intercourse vs advised to limit (CI 0.41, 0.81). There was also a statistically significant difference in PTB < 34 weeks in both univariate ($p < .001$) and multivariate models ($p = .001$): aOR 1.89 for intercourse vs advised to limit (CI 1.11, 3.22), aOR 1.32 for no intercourse versus advised to limit (CI 0.82, 2.12). No significant differences were seen in maternal stress, anxiety, or depression scores; CL; serum inflammatory cytokine levels; or neonatal morbidity. Conclusions: This study showed significant differences in PTB < 37 and < 34 weeks by whether the patient had been advised to limit sexual intercourse. Further work is needed to examine pathophysiologic mechanisms.

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Primary Presenter / email: **Redfield, J.** / jordanredfield@uky.edu
Clinical Science
Other

Mentor / e-mail: Meints, L. / laura.meints@uky.edu



CCTS Poster Presentation Abstracts

124 Abstract Title: **Longitudinal 3-Dimensional Evaluation of Placental Development**

Author(s): M. E. Riley, College of Medicine, U of Kentucky
 B. St. Martin, College of Medicine, U of Kentucky
 L. Meints, Obstetrics and Gynecology, U of Kentucky

Abstract: Introduction: Abnormal placental development is associated with miscarriage, fetal demise, growth restriction, and other short- and long-term problems for the child. To date, serum analyses and fetal-growth assessment are the best predictors of abnormal placental development, though they are neither sensitive nor specific. Recent innovations in ultrasound technology has allowed for 3-dimensional (3D) quantification of placental size and vascularity. Our goal is to see whether longitudinal 3-dimensional ultrasound quantification of the placenta coupled with demographic information and serum analyses may facilitate identification of abnormal placental development and related adverse pregnancy outcomes. Methods: This study is an observational, longitudinal, prospective cohort study of singleton gestations who presented for first-trimester (10 0/7 – 13 6/7 estimated gestational age [EGA]) ultrasound assessment of their pregnancy. It was approved by the Institutional Review Board at the University of Kentucky. At the first ultrasound, patients were enrolled into this study and asked to give a urine sample for cotinine analysis. 3D placental measurements were then taken. When patients returned during the second trimester (17 0/7 – 22 6/7 EGA), patients again provided urine sample for cotinine analysis and underwent 3D placental measurements. Medical records were then reviewed for pregnancy and birth outcomes. Descriptive statistics were performed. Scatterplots were generated to evaluate placental size and vascularity across time. Collection of birth data is ongoing, so regression models predicting birth weight, pre-eclampsia, gestational diabetes, and EGA at delivery will be presented at a future time. Results: Fifty-two women were enrolled in our study. To date, all women remain in the study without loss to follow up. 73% of the women were white, 10% black, and 12% Hispanic. Mean pre-pregnancy BMI was 27, with 25% of our population obese. 12% had experienced a prior preterm delivery. 10% smoked tobacco, and 12% used marijuana. Scatterplots depicting first-trimester and second-trimester placental size and flow will be presented during the poster session. Conclusion: TBD

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 Professional Student Mentored Research Fellowship (PSMRF)

Primary Presenter / email: **Riley, M.E.** / megan.riley@uky.edu
Clinical Science
Other

Mentor / e-mail: Meints, L. / laura.meints@uky.edu



CCTS Poster Presentation Abstracts

125 Abstract Title: **Demographic Disparities in Children with Behavioral or Conduct Disorders**

Author(s): C.E. Dunworth, Departments of Psychology and Epidemiology, U of Kentucky
 C.R. Studts, Department of Health Behavior, U of Kentucky
 C.M. Williams, Department of Health Behavior, U of Kentucky
 K.S. Eddens, Department of Health Behavior, U of Kentucky

Abstract: This study examines the demographic disparities in children with externalizing behavior disorders, such as oppositional defiant disorder and conduct disorder, utilizing secondary data from the 2011/2012 National Survey of Children's Health (NSCH). Current literature suggests that children with externalizing behavior disorders are more likely to be male, live in a low-income family, receive lower grades in school, and to develop later conditions such as depression. Chi square tests and logistic regression were used to examine the associations of presence of a current behavioral or conduct problem with age group, race/ethnicity, sex, household income level, and insurance type. Additionally, associations were assessed between mild versus moderate/severe behavioral or conduct problems with the same set of demographic variables. Approximately one in twenty children has a behavioral or conduct problem, and significant independent associations were observed with age, race/ethnicity, sex, poverty, and insurance type. This study's findings confirm the importance of early detection of behavioral or conduct problems, consistent insurance coverage that provides access to mental health care, and the need for refined tools to measure behavioral or conduct problem severity in large samples.

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Primary Presenter / email: **Dunworth, C.E.** / cdunworth@uky.edu
Community Science
Other

Mentor / e-mail: Studts, C.R. / tina.studts@uky.edu



CCTS Poster Presentation Abstracts

126 Abstract Title: **Disruption of human metapneumovirus interaction with heparan sulfate inhibits infection in human lungs cells and airway tissues**

Author(s): E. M. Klimyte, Department of Molecular & Cellular Biochemistry, U of Kentucky
R. E. Dutch, Department of Molecular & Cellular Biochemistry, U of Kentucky

Abstract: Human metapneumovirus (HMPV) is a recently discovered paramyxovirus that infects nearly 100% of the world population. This enveloped RNA virus causes severe respiratory disease in infants, the elderly, and immunocompromised patients. Our group previously showed that HMPV binds heparan sulfate (HS), a repeating sulfated disaccharide found on the cell surface. Unlike other paramyxoviruses that utilize the coordinated activity of an attachment glycoprotein and fusion glycoprotein, F, for entry, HMPV binding is dependent on F alone, which supports that F mediates the attachment to HS. In order to exploit this viral requirement for infection as a therapeutic target, we evaluated two strategies to inhibit HMPV infection: HS mimetics and occlusion. Iota-carrageenan, a sulfated polysaccharide derived from red seaweed, had potent anti-HMPV activity by inhibiting binding to lung cells mediated by the F protein. Furthermore, analysis of a minilibrary of variably sulfated derivatives of Escherichia coli K5 polysaccharide revealed the highly sulfated K5 polysaccharides, specifically those O-sulfated at position C6', inhibited HMPV infection, identifying a potential feature of HS critical for HMPV binding. To occlude HS, we employed peptide dendrimer SB105-A10 and observed anti-HMPV effects by inhibition of particle binding via F. HMPV infection was also inhibited by these modulating compounds in polarized airway tissues, suggesting these interactions take place in a physiologically relevant model of the human airway. Therefore, compounds that interrupt the critical interaction between the F protein and the binding target on host cells serve as a platform for potential antiviral development.

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Primary Presenter / email: **Klimyte, E. M.** / edita.klimyte@uky.edu

Mentor / e-mail: Dutch, R.E. / rdutc2@uky.edu



CCTS Poster Presentation Abstracts

127 Abstract Title: **Pulmonary Embolism in Youth, Clinical and Epidemiological Characteristics**

Author(s): M. Freeman, U of Kentucky
 N. Wallis, Internal Medicine and Pediatrics, U of Kentucky
 K. McQuerry, Statistics, U of Kentucky
 Q. Meng, Statistics, U of Kentucky
 M. Christy, Radiology, U of Kentucky
 V. Radulescu, Pediatric Hematology and Oncology, U of Kentucky

Abstract: A pulmonary embolism is a potentially fatal health condition where one or more arteries in the lungs are blocked by clots, usually coming from a deep venous thrombosis. The incidence of pulmonary embolisms in both the adult and pediatric populations seem to have increased over the decade. This could be a true change in incidence due a change in the risk factors or an increased recognition of PE due to better diagnostic methods and an increased awareness. There is limited data on the risk factors and clinical course in the pediatric population. What is known is that pulmonary embolisms in children are rare, most often linked to central venous catheter use, and have a better outcome than in adults. This is a retrospective chart review of patients, ages 0-21, from 1999-2014, comparing patients diagnoses with a PE to patients admitted to the PICU/ICU with similar diseases but no PE. The purpose of this study is to 1) Determine the trends in the incidence of PE in infants, children and young adults in Kentucky. 2) Identify risk factors associated with the development of PE in infants, children and young adults. 3) Describe the clinical presentation of PE in this age group. 3) Assess short-term outcomes in infants, children and young adults diagnosed with PE at the University of Kentucky. We are expecting the risk factors to be obesity, more central line use, more smoking, and OCP use in the PE population.

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Primary Presenter / email: **Freeman, M.** / megan.freeman@uky.edu
Clinical Science
Pulmonary

Mentor / e-mail: Radulescu, V. / vcradu2@email.uky.edu



CCTS Poster Presentation Abstracts

128 Abstract Title: **Clinical and Quality of Life Assessment of Patients Undergoing Laparoscopic Hiatal Hernia Repair**

Author(s): D.A. Borman, College of Medicine, U of Kentucky
 K.E. Sunshein, College of Medicine, U of Kentucky
 K.S. Stigall, College of Medicine, U of Kentucky
 D.L. Davenport, Department of Surgery, U of Kentucky
 M.A. Plymale, Department of Surgery, U of Kentucky
 J.S. Roth, Department of Surgery, U of Kentucky

Abstract: Introduction: The use of synthetic mesh in laparoscopic hiatal hernia repair (LHHR) has been demonstrated to reduce recurrences. Polyglycolic acid/Trimethylene carbonate (PGA/TMC), an absorbable synthetic mesh, may be utilized to reinforce the hiatal closure during repair. This study evaluates the clinical signs and symptoms (CSS) and clinical outcomes of patients undergoing LHHR with PGA/TMC mesh. Methods: A retrospective review of a single surgeon's cases of LHHR utilizing PGA/TMC mesh between August 2012 and April 2014 was performed. Preoperative, intraoperative and postoperative data was recorded. GERD CSS questionnaire responses were recorded and evaluated according to 4 time periods: 1) pre-operative (< 90 days); 2) post-operative within 6 weeks; 3) post-operative 6 weeks and 6 months; and 4) long-term post-operative (15 to 40 months) via telephone questionnaire. Operative data and questionnaire responses were evaluated to determine symptomatic changes and clinical outcomes. Results: The study contained 97 patients. Hernia defect size was classified as large (> 5cm, n= 49) or small-to-medium (< 5cm, n= 44). 274 GERD CSS questionnaires were recorded and analyzed. Post-operatively, regurgitation symptoms, swallowing difficulties, laryngeal symptoms and antacid use decreased ($p < .05$). Comparatively, small-to-medium hiatal defects had increased CSS ($p = .027$) and post-operative readmissions ($p = .043$). Conclusions: Patients undergoing HHR with PGA/TMC mesh experience improved regurgitation and laryngeal symptoms, and decreased use of antacid medication. Also, patients with small-to-moderate hiatal defects experience worsened post-operative reflux symptoms and clinical outcomes.

Supported by: PSMRF grant

Primary Presenter / email: **Borman, D.A.** / daniel.borman@uky.edu
Clinical Science
Surgery

Mentor / e-mail: Roth, J.S. / s.roth@uky.edu



CCTS Poster Presentation Abstracts

129 Abstract Title: **Hearing Loss in Rural Adults: A Geographic Comparison of Access to Care in Hearing Aid Recipients**

Author(s): S.A. Chan, College of Medicine, U of Kentucky
 B. Hixon, Department of Otolaryngology-Head and Neck Surgery, U of Kentucky
 M. Adkins, Department of Otolaryngology-Head and Neck Surgery, U of Kentucky
 J.B. Shinn, Department of Otolaryngology-Head and Neck Surgery, U of Kentucky
 M.L. Bush, Department of Otolaryngology-Head and Neck Surgery, U of Kentucky

Abstract: Objective: Rural access to care and the impact of hearing loss are poorly understood. This study aims to determine socioeconomic status, timing of hearing aid (HA) acquisition, and impact of hearing loss in rural and urban adult HA recipients. Study Design: Cross-sectional questionnaire survey. Methods: Questionnaires were mailed to adult HA recipients assessing demographics, timing of HA fitting from onset of hearing loss, and effects of hearing impairment on employment/education. Amplification benefit was assessed using the International Outcome Inventory for Hearing Aids (IOI). Results: Of 336 participants, 225 reside in urban areas and 111 in rural areas (48 rural and 63 very rural). Very rural participants experienced longer commutes to hearing specialists (68 versus 26 minutes, $p < 0.001$), were less likely to achieve a degree beyond high school ($p < 0.001$) and more likely to possess Medicaid coverage ($p = 0.01$) compared to urban participants. There was a trend toward greater time delay for acquisition of HA for very rural participants compared to urban participants (10.9 versus 7.9 years, $p = 0.226$). Hearing impairment caused job performance difficulty in 60% of all participants. Rural participants reported more hearing-related difficulty in job promotion compared to urban participants (14% versus 3%, $p = 0.033$). All participants reported amplification benefit with a trend toward greater benefit in very rural participants. Conclusions: Rural adults with HA differ in socioeconomic factors than urban adults. Distance from specialized care may impact timely access of hearing healthcare. Further research is indicated to assess factors affecting timely hearing healthcare and expand access to care.

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Primary Presenter / email: **Chan, S. A.** / stephen.chan@uky.edu
Clinical Science
Surgery

Mentor / e-mail: Bush, M.L. / matthew.bush@uky.edu



CCTS Poster Presentation Abstracts

130 Abstract Title: **Hiatal Hernia Cruroplasty with a Running Barbed Suture Compared to Interrupted Sutured Repair**

Author(s): A. Wade, College of Medicine, U of Kentucky
A. Dugan, Department of General Surgery, U of Kentucky
M. Plymale, Department of General Surgery, U of Kentucky
J. Hoskins, Center for Advanced Training and Simulation, U of Kentucky
A. Zachem, Department of General Surgery, U of Kentucky
J.S. Roth, Department of General Surgery, U of Kentucky

Abstract: BACKGROUND Interrupted sutures are commonly utilized to approximate the diaphragmatic crura during hiatal hernia repair. Barbed sutures allow for approximation of tissues with multiple points of fixation utilizing a running sutured technique. Prior studies utilizing barbed sutures in crural closure during laparoscopic hiatal hernia repair have not been reported. METHODS An IRB approved retrospective review of hiatal hernia repairs was performed. Operative video recordings of crural closure during laparoscopic hiatal hernia repairs were reviewed to determine: type of suture, number of throws, total time elapsed, and crural closure complications. RESULTS 60 video recordings were reviewed: 38 cases with standard silk suturing and 22 with running barbed sutures. Pre-operative characteristics were similar. Overall time for cruroplasty was similar with increased number of suture passes with running sutures rather than interrupted (mean 7.59 vs. mean 3.42, $p < 0.001$) while each had similar overall times (mean 3.3 min, 95% CI (2.89, 3.71) vs. mean 1.3 min, 95% CI (1.05, 1.59), $p < 0.001$). There was no difference in early recurrence rate. CONCLUSION Laparoscopic hiatal hernia repair with a running barbed suture is an efficient method of crural closure. Short-term outcomes following running barbed cruroplasty are similar to interrupted sutured closures. Future studies evaluating the impact on clinical outcomes are required.

Supported by:

Primary Presenter / email: **Wade, A.** / alex.wade31@gmail.com
Clinical Science
Surgery

Mentor / e-mail: Roth, J.S. / s.roth@uky.edu



CCTS Poster Presentation Abstracts

131 Abstract **Peripheral Nerve Autografts to the Substantia Nigra in Combination with Deep Brain Stimulation Surgery for the Treatment of Parkinson's Disease**

Title: A.S. Welleford, Brain Restoration Center, Dept. of Anatomy and Neurobiology, U of Kentucky
 J.E. Quintero, Brain Restoration Center, Dept. of Anatomy and Neurobiology, U of Kentucky
 J.T. Slevin, Brain Restoration Center, Dept. of Neurology, U of Kentucky; Neurology Service, Veterans Affairs Medical Center, Lexington, KY

Author(s): J.A. Gurwell, Brain Restoration Center, Dept. of Neurology, U of Kentucky
 G.A. Gerhardt, Brain Restoration Center, Depts. of Anatomy & Neurobiology & Neurosurgery, U of Kentucky
 C.G. van Horne, Brain Restoration Center, Depts. of Anatomy & Neurobiology & Neurosurgery, U of Kentucky

Abstract: Purpose Examine the safety and feasibility of combining deep brain stimulation (DBS) surgery with the implantation of peripheral nerve tissue into the substantia nigra for the treatment of Parkinson's disease (PD). Methods Two clinical trials with an 8 patient (NCT01833364) and 16 patient (NCT02369003) cohort have been created. Trials differ in the DBS brain region targeted (subthalamic nucleus for NCT01833364, internal globus pallidus for NCT02369003). Patients were selected based on the following criteria: Progressive idiopathic Parkinson's disease for >5 years; Medication responsive to motor fluctuations; Cognitively intact; Met criteria for DBS surgery. Sural nerve tissue was harvested initially at Stage I of DBS surgery for later study. Graft tissue as well as sample tissue from the remaining sural nerve was then collected during Stage II of DBS surgery 3-5 days later. Graft tissue was implanted using a custom cannula. Graft target was the substantia nigra, located 1-6 mm below the base of the subthalamic nucleus. Trajectory for graft implantation was set 3 mm posterolateral to DBS based on visual targeting in pre-op MRI. 12 months post-surgery MRI, neuropsychological exam, full unified Parkinson's disease rating scale (UPDRS) testing off/on medication and stimulation, and Parkinson's Disease Questionnaire (PDQ-8) testing are performed. Adverse events are monitored for this period. Data/Results 12 month post-surgical data is available for clinical trial NCT01833364. UPDRS off stimulation/medication motor scores improved by an average of 7 points. On stimulation medication scores improved 2.5 points. 7 minor adverse events occurred, 3 of which were unrelated to surgery. All adverse events have been resolved. Conclusions The surgical procedure proved to be a feasible method of delivering biologic therapy in combination with DBS surgery. Adverse event profile was comparable to standard DBS surgery.

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Primary Presenter / email: **Welleford, A.S.** / andrew.welleford@uky.edu
**Clinical Science
 Surgery**

Mentor / e-mail: Gerhardt, G.A. / gregg@uky.edu



CCTS Poster Presentation Abstracts

132 Abstract **Home Safety in the Elderly: Patient-Centered Outcomes Research Focused on Assessment of Knowledge, Needs, and Barriers.**

Title: R.R. Murphy, Department of Neurology and Sanders Brown Center on Aging, U of Kentucky
 Author(s): A. Caban Holt, Sanders Brown Center on Aging, U of Kentucky
 S. Bardach, Sanders Brown Center on Aging, U of Kentucky
 S. Tarrant, Sanders Brown Center on Aging, U of Kentucky
 G.A. Jicha, Department of Neurology and Sanders Brown Center on Aging, U of Kentucky

Abstract: Safety issues, especially: falls, medication problems, and hazards in the home, are major causes of morbidity and mortality for elderly persons living in the community. They pose an even greater risk for those with cognitive impairment due to dementing disease. We surveyed 600 current research subjects and caregivers that are part of the UK Alzheimer Disease Center (ADC) Research Cohort, on their perception of home safety problems and needs in these domains. Home safety concerns were greater for those with cognitive disease (present in about 33%), but were also present in 20% of normal older individuals. When both a participant with mild cognitive impairment or mild dementia, and a caregiver, returned a response, nearly a third of the impaired participants reported no safety concerns despite their caregiver reporting a concern. Impaired participants who were unaware of a safety concern, were also more unaware of their memory problem, compared to those who recognized the safety concern (50% vs 29%), although this was not statistically significant. Home safety concerns are well recognized in elderly with established cognitive impairment, however in our study, safety needs increased even with relatively mild cognitive problems, a level of impairment where driving is still generally considered safe. Mildly impaired individuals, especially those unaware of their deficit, may represent an under-recognized high-risk group with regard to home safety. Further study is needed to validate and confirm safety needs and barriers to communication such as Anosognosia (lack of awareness) in this group.

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Primary Presenter / email: **Murphy, R.A.** / ronan.murphy@uky.edu

Mentor / e-mail: Murphy, R. / ronan.murphy@me.com



CCTS Poster Presentation Abstracts

133 Abstract Title: **Early life exposure to glucocorticoids exaggerates diet-induced obesity in female rats**

Author(s): M.O. Murphy, Pharmacology and Nutritional Sciences, U of Kentucky
 B. Herald, Pharmacology and Nutritional Sciences, U of Kentucky
 C. Wills, Pharmacology and Nutritional Sciences, U of Kentucky
 L. Gilbert, Pharmacology and Nutritional Sciences, U of Kentucky
 D. Cohn, Pharmacology and Nutritional Sciences, U of Kentucky
 A.S. Loria, Pharmacology and Nutritional Sciences, U of Kentucky

Abstract: Studies in humans and animal models have shown a positive correlation between early life stress (ELS) and the development of cardiometabolic disease. Previously, we have shown that adult MatSep, a model of ELS, does not change body weight and glucose tolerance in male rats fed a high fat diet (HFD) for 17 weeks. The aim of this study was to determine whether female rats exposed to MatSep display increased susceptibility to develop cardiometabolic disease in response to a HFD feeding. MatSep was performed in WKY rats by separation (3 hr/day) from the dam during the first two weeks of life and placed on a HFD (60% kcal fat) for 12 weeks at weaning. Non-disturbed littermates were used as controls. MatSep exaggerated body weight gain and fat pad weights ($p < 0.05$). MatSep increased plasma leptin (2113 ± 446 vs. 1548 ± 371 pg/ml) and aldosterone (491 ± 99 vs. 231 ± 30 pg/ml) levels compared to control. OGTT was impaired in MatSep rats showing a greater AUC compared to control rats ($p < 0.05$). In a parallel study, we performed a treatment prior to the daily MatSep with metyrapone to reduce the stress-induced glucocorticoid synthesis (MTP, 50g/kg, postnatal day 2-14 s.c.). As adults, we found that MTP-treated female rats show attenuated diet-induced obesity and glucose intolerance ($p < 0.05$), indicating that stress-induced CORT early in life prevents the exaggerated obesity-related metabolic derangements in adulthood. Taken together, these data indicate that MatSep enhances diet-induced obesity via early exposure to glucocorticoids. Thus, glucocorticoid receptors could be potential therapeutic targets in early life stress-induced cardiometabolic disease.

Supported by: R00 HL111354

Primary Presenter / email: **Herald, B.** / blakeherald95@uky.edu

Basic Science
Cardiovascular

Mentor / e-mail: Loria, A.S. / analia.loria@uky.edu



CCTS Poster Presentation Abstracts

134 Abstract Title: **High school educational health module with in class and distance learning: Guided inquiry in modeling cardiovascular health risks**

Author(s): R.L. Cooper, Dept. of Biology, U of Kentucky
 S. Poepelman, Lewis County High School, Vanceburg, KY
 S. Behrendt, Lewis County High School, Vanceburg, KY
 R. McNall Krall, Dept. of STEM Education, U of Kentucky
 A. Spence, Dept. of Biology, U of Kentucky
 G.J. Capilouto, College of Health Sciences, U of Kentucky
 S.R. Martha, College of Nursing, U of Kentucky
 D. Johnson, PIMSER, U of Kentucky
 K. Zeidler-Watters, PIMSER, U of Kentucky

Abstract: The targeted educational community for this project ranks high in obesity, inactivity, cardiovascular diseases, and overall poor quality of health. Most of these issues relate to the life style choices people are making and the lack of understanding of the disease process as a consequence. Bringing middle and high school science teachers into the fold to promote healthy behaviors by elucidating the science behind physiological processes, screening techniques, advancements in health care, and mechanisms of diseases and technologies associated with health care can be engaging and life improving for students. We approached this by providing robust teaching modules aligned with Next Generation Science Standards. A unique aspect of our educational approach was that the students investigated their own health status as well as the health status of their community. Then, within their classroom, they related the health issues to STEM based curricular activities. In addition, the students had a dialogue about their research and their STEM based project to university undergraduate and graduate students as well as faculty in a mentoring based course via on line video recording in conjunction with blogging. Acclaim accounts allowed all participants to annotate posted audio and video clips generated via mini- classes which promoted easy and effective feedback, discussion, and collaboration. University students using multimedia to make presentations on their students' activities and progress to expand science content knowledge & foster collaboration. We hope to grow this program across our campus and implement this outreach educational approach to other university credited courses around the nation and worldwide.

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Primary Presenter / email: **Cooper, R.L.** / RLCOOP1@uky.edu
Community Science
Cardiovascular

Mentor / e-mail: Cooper, R.L. / RLCOOP1@uky.edu



CCTS Poster Presentation Abstracts

135 Abstract Title: **Walking for Wellness: An Elementary School Based Intervention to Promote Exercise and Health Education in Rural Kentucky**

Author(s): K.J. Jayne, College of Medicine, U of Kentucky
 C.T. Jayne, College of Medicine, U of Kentucky
 S. Sharber, Department of Pediatrics, U of Louisville, Louisville, KY
 P.K. Arnett, Rural Physician Leadership Program, U of Kentucky

Abstract: Based on the 2014 Community Health Needs Assessment completed for Rowan and surrounding counties, pediatric obesity was listed as one of the 5 main target areas for improvement. In an effort to prevent and reduce the prevalence of childhood obesity in Rowan County, the Walking for Wellness Program was created in 2013. The goal of this program was to assess the effectiveness of classroom based interventions including set exercise, cardiovascular health, and nutrition curriculum along with in school pedometer use. 10 Rowan county 4th and 5th grade classrooms participated in the program (Nov. 2015-Jan. 2016). Initially pedometers were distributed to classrooms to be worn by 5-6 different students daily. Each students step counts were recorded at the end of the school day for 5 days. A medical student from the University of Kentucky presented a standardized exercise, cardiovascular health, and nutrition workshop to the classrooms. Step counting resumed for 4 weeks after the workshop/educational intervention. Students were also competing for t-shirts for the most improved class average step counts and greatest average step counts overall. Average step counts from 8 classes were compared from before and after the educational intervention/workshop. Paired t-test was performed for which T statistic was 2.09 and p value < 0.05 (n=8). This shows that there is statistical significance in step count improvement from before to after the educational intervention even sustained over a 4-week period. Future goals will be to study the impact of a longer curriculum spanning multiple years. The competition element of the program may also be a confounding variable to the data. Overall the data suggests a significant improvement in step counts after providing exercise and cardiovascular health education to the 4th and 5th grade students.

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Primary Presenter / email: **Jayne, K.J.** / kpesco33@yahoo.com
Community Science
Cardiovascular

Mentor / e-mail: Arnett, P.K. / paula.arnett@uky.edu



CCTS Poster Presentation Abstracts

136 Abstract Title: **Clay County Summer Fitness & Nutrition Program**Author(s): H. Ghayyur, Marketing & Outreach, Manchester Memorial Hospital

Abstract: Background: Clay County is the 9th poorest county in the US and is located in an area with many labels such as the 'Coronary Valley' due to high incidence of heart disease, 'Diabetes Belt' and 'Stroke Belt'. Manchester Memorial Hospital and Promise Neighborhood partnered to host an 8-week, 24-session Summer Fitness & Nutrition Program to provide adults with an opportunity to become more physically active, and educate them on how to make healthier nutrition and lifestyle choices. Objective: Primarily, we wanted to reduce obesity risk and promote activity. The secondary goal was to increase their knowledge of nutrition. Methods: The Summer Fitness and Nutrition Program provided 1.5 hour classes dedicated to exercise, nutrition and adopting a healthy lifestyle. We hired 5 instructors who led various fitness activities (running, Zumba, Pilates etc.) and conducted nutrition seminars. The program objectives were measured with pre and post weigh-ins and BMI/body fat percentage screenings. To conclude the program, participants with an attendance rate of 80% or higher were given an Amazon Fire 6, pre-loaded with workout and diet apps that they can benefit from after the program ended. Conclusions: We had 15 participants complete the entire course with them seeing a 1.01% decrease in body weight, a 0.54 decrease in BMI and a 1.12% decrease in body fat percentage. We also saw 35%, 65% and 47% participants increase their knowledge of cruciferous vegetables, proteins and carbohydrates respectively.

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Center for Clinical and Translational SciencePrimary Presenter / email: **Ghayyur, H.** / hurriyat.ghayyur@ahss.org
Community Science
OtherMentor / e-mail: Ghayyur, H. / hurriyat.ghayyur@ahss.org



CCTS Poster Presentation Abstracts

137 Abstract Title: **Community Coordinated Screening and Outreach in The Big Sandy Area Development District**

Author(s): B.M. Martin, Big Sandy Health Care, Inc., Prestonsburg, KY

Abstract: Background: Pike County ranks 108 out of 120 Kentucky counties in overall health outcomes. 16% of Pike County residents have diabetes, compared to 10.6% of Kentuckians, though an additional 138,000 Kentuckians are estimated to be living undiagnosed. While diabetes rates are high throughout eastern Kentucky, diabetes is significantly more prevalent among low-income individuals and those aged 65 and older. We aimed to improve detection, prevention and treatment of diabetes through screening paired with awareness of local diabetes resources to lower A1c's. Methods: The Big Sandy Diabetes Coalition, through a Community Screening and Outreach Project, conducted "Health Fairs" that offered free diabetes screenings and other preventative health activities. Data were collected among participating residents of Myers Towers, a low-income senior housing facility located in Pikeville, KY at baseline and six months. Results: At the initial screening of 28 individuals the following results were drawn: 38.46% were diabetic and 26.9% were classified as being prediabetic. In the post screening event over half of the original participants returned yielding a 53.3% success rate of lowered A1c's as a result of follow-ups with local community resources and primary care checkups. Conclusions: According to the CDC 2014 National Diabetes Report 9.3% of the US population have diabetes and in the Myers Towers sample the percentage was over double that number indicating that diabetes is at an epidemic rate in Appalachia. This project showed that high rates of diabetes can be addressed by offering community members information about local resources to improve their diabetes outcomes.

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Primary Presenter / email: **Martin, B.M.** / b.martin@bshc.org
Community Science
Other

Mentor / e-mail: Schoenberg, N.E. / nesch@uky.edu

