84 **Abstract Title:** **An Internet Behavioral Weight Loss Intervention With or Without Commercially Available Portion-controlled Foods: A Pilot Study.**

Author(s): K.H. Webber, Department of Nutiriton and Food Science, U of KY
S.A. Rose, Department of Internal Medicine, U of KY

Abstract:
Background: Internet behavioral weight loss programs have produced clinically significant weight loss; however weight loss in these programs is generally not as high as in face-to-face behavioral weight loss programs. Improving the effectiveness of these widely accessible and cost-effective Internet-based treatments is desirable. The provision of commercially available portion controlled foods has been shown to improve weight loss in face-to-face behavioral weight loss treatments. It is hypothesized that adding portion controlled foods to an Internet program will also improve weight loss outcomes. Methods: This study evaluated the short-term impact of portion controlled food provision in combination with a standard Internet behavioral weight loss program on weight, blood cholesterol, and blood glucose levels. Fifty participants, mean age 46 + 10.7 years and mean body mass index 35.1 + 3.8 kg/m2, were randomized to one of two study groups, a standard Internet behavioral weight loss program (Internet-alone) or a standard Internet behavioral weight loss program plus a commercially available portion-controlled diet (Internet+PCD) for 12 weeks. Results: Completers in both groups (Internet-alone: n=25; Internet+PCD: n=22) achieved significant weight loss at 12 weeks with a non-significant trend (p=0.10) favoring Internet+PCD (6.5 + 5.5 kg) over Internet-alone (4.1 + 4.0 kg). Total cholesterol, LDL-C, and fasting blood glucose levels decreased significantly in the Internet+PCD group, but not the Internet-alone group. Conclusions: These data suggest that there may be short-term benefit in using a PCD in conjunction with a standard behavioral Internet-based weight loss program to enhance weight loss and improve health indicators.

Supported by: The Obesity Society and Nutrisystem, Inc.
Primary Presenter / e-mail: Webber, K. H. / kelly.webber@uky.edu
Mentor or Senior Author / e-mail: Webber, K. H. / kelly.webber@uky.edu

85 **Abstract Title:** **Application of the PRECEDE-PROCEED Model in an Eastern Kentucky Food Desert**

Author(s): F. D. Hardin-Fanning, College of Nursing, U of Kentucky

Abstract:
The PRECEDE-PROCEED model was used to 1) determine dietary patterns and 2) evaluate predisposing, reinforcing and enabling factors that impact diet in an Eastern Kentucky food desert. Breathitt is one of seven southeastern Appalachian Kentucky counties considered a food desert with 54% of residents having difficulty accessing healthy foods (USDA, 2011). A cross-sectional study was completed from September 2009 to August 2010 to explore the dietary patterns of community-living adults (N=102). A majority of participants consumed at least two vegetable and two fruit servings daily, but none consumed the recommended 5-8 servings daily. Fish intake was below the recommended 2 servings weekly in 98% of participants and 80% of participants consumed red meat consumption daily. Focus groups were recruited in the fall of 2011 (N=48) to determine predisposing, enabling and reinforcing factors that impact dietary habits. Younger participants {F (2, 40) = 3.53, p=.04} and those of lower (<$25,000) income status {F (7, 35) = 2.75, p=.02} were more likely to identify food cost as a barrier to adherence. Participants with lower educational levels were more likely to report family members would be hesitant to try a Mediterranean diet {F (4, 38) = 4.08, p = .008}. Gender was associated with lack of knowledge about healthy food choices, with women being more likely to view food as a means of health promotion {t (41) = -7.18, p = >.000}. Targeting predisposing, reinforcing and enabling factors in the PRECEDE-PROCEED model will provide synergism to the interventions' benefits.

Supported by: U of Kentucky College of Nursing Research Funds
Primary Presenter / e-mail: Hardin-Fanning, F. D. / fdbowe2@uky.edu
Mentor or Senior Author / e-mail: Hardin-Fanning, F. D. / fdbowe2@uky.edu

86	**Abstract Title:**	**Changes in Leptin concentration in gestational diabetes vs. non-diabetic controls: A longitudinal assessment antepartum and postpartum.**

Author(s):
R. I. Epstein, Department of Obstetrics and Gynecology, U of Kentucky
C. F. Pearce, Department of Obstetrics and Gynecology, U of Kentucky
S. Mast, Department of Obstetrics and Gynecology, U of Kentucky
K. S. Playforth, Department of Obstetrics and Gynecology, U of Kentucky
J. M. O'Brien, Department of Obstetrics and Gynecology, U of Kentucky
K. Pearson, Department of Nutritional Sciences, U of Kentucky

Abstract:
Background: Leptin is produced by adipocytes, is elevated in obesity, and further elevated in normal pregnancy. Longitudinal data of leptin concentrations is limited, particularly in women with gestational diabetes mellitus (GDM). Objective: To evaluate leptin levels in GDM vs. non-diabetic controls in pregnancy and postpartum and correlate them with BMI and weight change. Study Design: Pregnant women (17 GDM, 15 controls) were enrolled between 24 and 34 weeks gestation. Serum leptin levels were obtained at enrollment and 6 -12 weeks postpartum (13 GDM, 12 controls). Changes in leptin were correlated with BMI and changes in weight using t-test, ANOVA, and linear regression analysis. Results: Twenty-five of the 32 patients were defined as obese with BMI >30. Women diagnosed with GDM had higher BMI than controls (p=.05). Higher leptin levels were seen with increasing BMI during pregnancy and postpartum. However, there was no correlation between GDM and leptin levels ante or postpartum. Weight loss was not different in GDM vs. controls. There was a trend towards a larger decrease in leptin with larger postpartum weight loss. Women with elevated fasting glucose postpartum (n=5) had higher initial leptin levels (p=.0542). Conclusion: Elevated leptin levels were correlated with increasing BMI during and after pregnancy. We did not identify a correlation between GDM and leptin levels. Leptin is increased in obese patients and may signify risk for persistent or long-term metabolic abnormalities. Further study is needed to assess this hormone's role and whether it can prognosticate the need for any alteration in clinical management.

Supported by:
Primary Presenter / e-mail: Epstein, R. E. / riep222@uky.edu
Mentor or Senior Author / e-mail: Pearson, K. / kjpe222@uky.edu

87	**Abstract Title:**	**Differential mRNA Expression in Myometrial Tissue of Obese Gravidas.**

Author(s):
M. Strong, Department of Obstetrics and Gynecology, U of Kentucky
R. Epstein, Department of Obstetrics and Gynecology, U of Kentucky
J. M. O'Brien, Department of Obstetrics and Gynecology, U of Kentucky
T. Curry, Department of Obstetrics and Gynecology, U of Kentucky
M. Garabedian, Department of Obstetrics and Gynecology, Samta Clara Valley Medical Center

Abstract:
Introduction: Obese women have an increased risk of dysfunctional labor, higher rates of induction, failed induction, and cesarean section. We investigate gene expression in the myometrial tissue of obese women undergoing cesarean section. This study was approved by the Institutional Review Board of the University of Kentucky. Methods: Study Population: Women presenting for primary term cesarean delivery at UK. Patients were grouped by BMI; 1, BMI 25 – 35 (n=2); 2, BMI 35 – 45 (n=3); 3, BMI ≥ 45 (n=3). Data Collection: A full thickness myometrial biopsy was obtained from the upper edge of the hysterotomy. For each group, the pooled mRNA was analyzed with an Affymetrix GeneChip. Statistical Analysis: Target gene products were identified by magnitude of fold-change across groups as well as analysis for trend on the following scales: linear, logarithmic, squared, square root. Gene products of interest were identified by a P-value < 0.05 being deemed statistically significant. Gene pathways were identified and explored using the Ingenuity pathway analysis program. Results: These genes are involved in a variety of functions including muscle fiber structure and contractility, hormone cleavage, cell cycle control, transcription/translation, immunity, intracellular maintenance, and extracellular communication. Conclusions: These results suggest obesity is associated with differential gene expression patterns in myometrial tissue. With increasing BMI, molecular-level changes were identified relating to a wide variety of cellular functions. The full physiologic consequences of these changes are still unknown. Further research is needed to better understand the effects of obesity on gene expression and resulting tissue function.

Supported by:
Primary Presenter / e-mail: Strong, M. / mollycstrong@gmail.com
Mentor or Senior Author / e-mail: Curry, T. / tecurry@uky.edu

88 **Abstract Title:** **Effects of Atherosclerosis Development and Blood Cholesterol Levels in Mice treated with SPX-106T**

Author(s):
B.M. Metts, Chemistry Dept, U of Kentucky
S.E. Thatcher, Graduate Center of Nutritional Sciences, U of Kentucky
L.A. Cassis, Graduate Center of Nutritional Sciences, U of Kentucky
R.A. Lodder, Chemistry Dept and College of Pharmacy, U of Kentucky and Biospherics Inc, Bethesda, MD

Abstract:
Dyslipidemia is a common precursor to atherosclerosis as well as many other diseases. Dyslipidemia can be manifested in high triglycerides, increased apolipoprotein (apo) B, high levels of LDL, and low levels of HDL. SPX-106T is a combination drug composed of a carbohydrate, D-tagatose, and SPX-106, which promotes lipid catabolism. In apoE -/- mice this combination has been found to significantly lower the amount of atherosclerosis as well as lower blood cholesterol levels. D-tagatose has been studied for the treatment of diabetes for several years and went into phase 2 trials several years ago because of its ability to lower blood insulin levels and decrease glycogen formation. SPX-106 is a natural substance that may sometimes act as a PPAR agonist. PPAR agonists are known to inhibit dyslipidemia. This experiment used 26 male apoE -/- mice- (n=13 in each group, control and treated). The control group received the normal "Western" diet (Harlan TD88137) and the treatment group received a modified version in which the sucrose was replaced with D-tagatose and 1g of SPX-106 was added for every kilogram of chow. Mice were fed the diet for 8 weeks and then sacrificed via cardiac puncture. Blood serum was analyzed for cholesterol concentration. Aortas were also taken and preserved in formalin to be quantified for atherosclerosis. Aortic sinuses were frozen in OCT and sectioned using a cryostat and then quantified for atherosclerosis. Treated mice showed statistically significant reduction in atherosclerosis in the aortic arch ($p<0.01$), the thoracic aorta ($p<0.05$), and the aortic sinus ($p<0.05$) as well as a reduction of cholesterol ($p<0.05$).

Supported by: Biospherics Inc., Bethesda, MD
Primary Presenter / e-mail: Metts, B. M. / bmme222@uky.edu
Mentor or Senior Author / e-mail: Lodder, R. A. / lodder@uky.edu

89 **Abstract Title:** **Expression of miR-17-92 Cluster in Adipose Tissue: Potential Role in the Regulation of Fibrosis and Angiogenesis**

Author(s):
L. Muniappan, Department of Internal Medicine, Division of Endocrinology & Molecular Medicine, U of Kentucky
R. Unal, Department of Internal Medicine, Division of Endocrinology & Molecular Medicine, U of Kentucky
B.S. FInlin, Department of Internal Medicine, Division of Endocrinology & Molecular Medicine, U of Kentucky
C.A.Peterson, College of Health Sciences, U of Kentucky
P.A.Kern, Department of Internal Medicine, Division of Endocrinology & Molecular Medicine, U of Kentucky

Abstract:
A prominent feature of adipose tissue with obesity is an increase in fibrosis and a decrease in capillaries. Thrombospondin (TSP1) is pro-fibrotic and anti-angiogenic, and TSP1 expression in adipose is increased with obesity and insulin resistance. Because the mechanism for TSP1 up-regulation is unknown, we examined the functional significance of the microRNA (miR) 17-92 cluster, which is composed of 7 miRs (miR 17-3p, 17-5p, 18a, 19a, 19b, 20a and 92) in tandem. In this cluster, miR-19a and 19b are known to decrease TSP1 and CTGF expression in cancer and other cell types, but no studies have examined adipose tissue. We hypothesized that miR-17-92 plays an important role in the development of obesity associated insulin resistance through regulation of TSP1 and other targets. Adipose tissue biopsies from 14 obese (BMI: 33.5 ±1.2, SI: 1.87 ±0.2) and 14 lean human subjects (BMI: 24.2 ±1.2, SI: 4.57 ±1.2) were examined for miR-17-92 cluster expression using a cluster plate assay and were confirmed by qRT-PCR experiments. Expression of all miR-17-92 cluster members was significantly lower in obese subjects, compared to lean, by 30-80% (all $p<0.05$). Overexpression of miR-17-92 cluster members miR-19a/b and 18a in cultured 3T3L1 adipocytes decreased TSP1 and CTGF expression by 80% and 75%, respectively ($p<0.05$). In addition, the knockdown of miR-19a/19b with siRNA increased the abundance of TSP1 and CTGF mRNA by 65% and 59%, respectively ($p<0.05$). TSP1 is expressed by both macrophages and adipocytes, and the coculture of macrophages with adipocytes induces TSP1 expression by both cells, but especially M2c polarized macrophages. Adipocyte conditioned medium (ACM) increased TSP1 expression, and the knockdown of miR-19a and 19b in M2c macrophages in the presence of ACM further increased TSP1 mRNA. These results suggest that down-regulation of miR-17-92 in obese subjects may provide a mechanism for the increase in TSP1, and hence the increased fibrosis and decreased angiogenesis.

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Primary Presenter / e-mail: Muniappan, L. / latha.muniappan@uky.edu
Mentor or Senior Author / e-mail: Kern, P. A. / philipkern@uky.edu

90 **Abstract Title:** **Long Term Surgical Complications of Bariatric Surgery and Associated Costs**

Author(s): T. G. Duncan, College of Medicine, U of Kentucky
L. D. Procter, Section on Acute Care Surgery, Department of Surgery, U of Kentucky
A. C. Bernard, Section on Acute Care Surgery, Department of Surgery, U of Kentucky

Abstract:
Introduction: Bariatric surgery is cost effective for the treatment and prevention of obesity related disease in select patients. However, the breadth, incidence and cost of long-term complications of bariatric surgery have not been well described. We hypothesize that long-term complications of bariatric surgery requiring surgical intervention are relatively common, sometimes severe, and costly. Methods: We retrospectively reviewed discharge data from 4/5/2007 to 4/5/2011 to identify patients who underwent a surgery, with ICD-9 code indicating a prior bariatric procedure. For patients requiring surgery, charts were abstracted to determine whether their procedure was related to prior bariatric surgery. Demographics, type of bariatric procedure, subsequent surgical intervention, and hospital charges were analyzed. Perioperative complications following the initial bariatric procedure were excluded. Results: 284 patients had prior bariatric surgery. 49/284 (17.3%) had 60 late surgical complications. Complications included incisional hernia (24), cholecystitis (7), adhesive bowel obstruction (7), mandatory modification of future surgical approach (7), biliary obstruction (4), anastomotic/pouch ulcer or perforation (3), anastomotic hemorrhage (2), internal hernia (3), roux limb perforation (1), gastric necrosis (1), gastropleural fistula (1). Mean number of admissions for surgical complications was 1.43 (range 1-5). Mean length of stay was 18.73 days (range 2-291). Mean charge per admission was $98,200 (range 10,000-1,235,700). Conclusions: Long term surgical complications of bariatric surgery were relatively common at this referral center during the 4 year study period. Type of complication varied, but incisional hernia was most common. Surgical complications are costly, may require an extended stay, and could be morbid.

Supported by:

Primary Presenter / e-mail: Duncan, T. G. / taylor.duncan@uky.edu
Mentor or Senior Author / e-mail: Bernard, A. C. / andrew.bernard@uky.edu

91 **Abstract Title:** **Obesity as a Risk Factor for Predicting Deep Venous Thrombosis in Children**

Author(s): S. Stokes, College of Medicine, U of Kentucky
V. Radulescu, Department of Pediatrics - Hematology and Oncology, U of Kentucky

Abstract:
Background: Obesity is a recognized risk factor for deep venous thrombosis (DVT) in adults, but there is less data regarding this association in the pediatric population. The aim of this study is to compare the body mass index (BMI) of children diagnosed with deep venous thrombosis versus that of children with other conditions. Methods: We conducted a retrospective chart review of children discharged from the University of Kentucky Children Hospital with a diagnosis of DVT over a 5 year period (2007-2011). We assessed the age, sex, BMI, DVT location, and DVT risk factors for each patient. The control group consisted of children discharged from the same hospital without the diagnosis of DVT. The age, sex and BMI were recorded in this population. Age adjusted odds ratios were calculated, with a 95% confidence interval. Results: We identified 52 patients with DVT; 6 were overweight and 22 were obese. Most of the patients had at least one generally accepted risk factor for thrombosis. The control group consisted of 260 patients; 39 were overweight and 45 were obese. The age adjusted odds ratios for having a DVT were 0.8 (0.2-2.1) for the overweight population and 2.5 (1.2-5.2) for the obese population. Conclusion: Our study suggests that obesity may represent a risk factor for deep venous thrombosis in the pediatric population.

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Primary Presenter / e-mail: Stokes, S. / sean.stokes@uky.edu
Mentor or Senior Author / e-mail: Radulescu, V. / vcradu2@uky.edu

92 **Abstract Title:** **Omentin as a Marker of Abnormal Glucose Metabolism in Pregnancy**

Author(s):
S. Mast, Department of Obstetrics and Gynecology, U of Kentucky
C. Pearce, Department of Obstetrics and Gynecology, U of Kentucky
R. Epstein, Department of Obstetrics and Gynecology, U of Kentucky
K. Playforth, Department of Obstetrics and Gynecology, U of Kentucky
K. Lain, Department of Obstetrics and Gynecology, Norton Healthcare, Louisville, KY
K. Pearson, Department of Nutritional Sciences, U of Kentucky

Abstract:
Objective: Omentin is a novel adipokine that is preferentially produced by visceral adipose, but is also strongly expressed by the ovary and placenta. Omentin enhances glucose uptake and decreases insulin resistance. Little is known about the role of omentin in pregnancy. The purpose of this study is to examine the role of omentin in gestational diabetes (GDM) versus non-diabetic controls. Study design: Pregnant women (17 GDM, 15 controls) were enrolled between 24 and 34 weeks gestation after diagnosis by glucose challenge testing. Serum omentin levels were compared between gestational diabetics and non-diabetics. Statistical analyses included t-test, ANOVA, and linear regression analysis. Results: The mean values of omentin were similar between gestational diabetics versus controls (1.3 versus 1.2). With linear regression analysis, although not statistically significant, trends indicate that for patients with known serum glucose levels less than 300 (14 GDM, 10 controls), serum omentin levels are positively correlated with serum glucose levels in gestational diabetics ($p = 0.07$) but not correlated for non-diabetics ($p = 0.76$). Conclusion: Elevated omentin levels were associated with higher screening glucose levels in gestational diabetics. The up-regulation of omentin expression in GDM may implicate a novel mechanism of placental glucose homeostasis in pregnancy. Further study is needed to elucidate the purpose of placental expression of omentin and its role in pregnancy.

Supported by:
Primary Presenter / e-mail: Mast, S. / samantha.mast@uky.edu
Mentor or Senior Author / e-mail: Playforth, K. / karen.playforth@uky.edu

93 **Abstract Title:** **Prevalence and Risk Factors for Undiagnosed Diabetes in the Emergency Department**

Author(s):
M. Mart, Department of Emergency Medicine, U of Kentucky
B. Kolstelnik, Department of Pediatrics, U of Kentucky
R. Rowe, Department of Emergency Medicine, U of Kentucky
M.N. Graber, Department of Emergency Medicine, U of Kentucky

Abstract:
Background: Diabetes mellitus (DM) represents a substantial health burden with an estimated 7 million undiagnosed. The emergency department (ED), though untraditional, represents a promising setting for screening. There has been little research into the viability of ED screening for DM, the frequency of undiagnosed pre-diabetes or diabetes, or the characteristics of patients that present to the ED without a diagnosis. Objectives: To derive the rate of undiagnosed diabetes or prediabetes in the ED as well as determine if there are any risk factors or demographics that correlate with disease prevalence in this population. Methods: This study is an ongoing, IRB-approved cross-sectional, observational study being conducted at the University of Kentucky with the goal of enrolling 500-600 patients. Patients presenting to the ED who are age 40 or older are randomly screened for inclusion. Those eligible for enrollment are asked a series of demographic questions and then have their height, weight, and a single, point-of-care (POC) glucose measurement taken. Preliminary Results: 112 patients have been screened with 57 enrolled in the study (mean age: 54.2 +/- 11.8 years). 5 patients (8.77%) have had positive results for pre-diabetes or diabetes as determined by POC glucose measurement. The median age for those with positive results was 50 years of age and included 4 males and one female. Mean age for patients not enrolled was 53.8 +/- 11.3 years. Tentative Conclusions: The preliminary results indicate that it is possible to identify ED patients with aberrant glucose measurements without a prior diagnosis. Further data collection and analysis will allow the derivation of the rate of undiagnosed DM and its risk factors for an ED presentation in an urban Kentucky emergency department.

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Primary Presenter / e-mail: Mart, M. / matthew.mart@uky.edu
Mentor or Senior Author / e-mail: Graber, M. N. / mngraber@gmail.com

94 **Abstract Title:** **Regulation of Thrombospondin (TSP-1) in Adipocytes and Macrophages by Coculture and Docosahexaenoic acid (DHA)**

Author(s):
B. S. Finlin, Department of Internal Medicine, U of Kentucky
B. Zhu, Department of Internal Medicine, U of Kentucky
C. P. Starnes, College of Public Health, U of Kentucky
C. A. Peterson, College of Health Sciences, U of Kentucky
P. A. Kern, Department of Internal Medicine, U of Kentucky

Abstract:
Adipose tissue dysfunction with obesity includes both inflammation and fibrosis. In recent work from our lab, obese adipose tissue was associated with an increase in both inflammatory (M1) and anti-inflammatory (M2) macrophages, which contribute to fibrosis. Our objective was to understand whether fatty acids, including the ω-3 fatty acid DHA, affect fibrosis pathways during coculture of macrophages and adipocytes. Human adipocytes were prepared from stem cells, along with human THP-1 macrophages that were differentiated to either M1or M2 phenotypes. The coculture of adipocytes with M1 or M2c macrophages induced the expression of TSP-1, a key regulator of fibrosis and angiogenesis. Coculture induced TSP-1 gene expression in both adipocytes (5.5-fold, P<.05) and M1 or M2c macrophages (> 30-fold, P<.05) and induced TSP-1 protein secretion into the media (>10 fold, P<.05). DHA treatment during the coculture potently inhibited both the macrophage TSP-1 mRNA level (85% inhibition, P<.05) and the level of TSP-1 protein secreted into the media (>70% inhibition, P<.05). TSP-1 activates TGF-β, and CTGF, a target of TGF-β, displayed a similar expression pattern to TSP-1. We explored the mechanism of inhibition of TSP1 in M2c macrophages and found that DHA did not affect the differentiation state. However, IL-10 expression in M2c macrophages displayed a similar pattern to TSP-1: induced by coculture and inhibited by DHA. Since IL-10 has been shown to regulate TSP-1 in other cell types, we reduced IL-10 expression with siRNA in the M2c cells and found that this caused TSP-1 to be reduced in response to adipocyte coculture by 60% (P<.05). Thus, these data show that DHA reduced TSP1 in adipocytes and macrophages, likely through a decrease in IL-10, resulting in decreased TGF-β signaling. These results suggest that supplementation with dietary ω-3 fatty acids could have an unappreciated benefit of reducing fibrosis in human adipose tissue.

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Primary Presenter / e-mail: Finlin, B. S. / bfinlin@uky.edu
Mentor or Senior Author / e-mail: Kern, P. A. / philipkern@uky.edu

95 **Abstract Title:** **Utility of Estimated Total Body Composition (as Assessed by DXA Scanning) in the Diagnosis of Obesity in Post Menopausal Women in Comparison to the Conventional BMI Method**

Author(s):
A. H. Maghrabi, Department of Internal Medicine, Marshall U
A. Yaqub, Department of Endocrinology, Marshall U

Abstract:
Objectives: 1. To study the utility of estimated total body composition in diagnosis of obesity in post-menopausal women in comparison to the conventional BMI method. 2. To assess the correlation of Fat Mass Index (FMI), Body Mass Index (BMI) and Android to Gynoid (A/G) ratio with various components of metabolic syndrome. Methods: We studied charts and DXA scans of 99 post menopausal women being followed at the department of medicine clinics. We calculated FMI, BMI, A/G ratio and percentage body fat (PBF) and studied the correlation between FMI, BMI and PBF as well as the correlation between FMI and BMI with various components of metabolic syndrome. Results: Misclassification of the weight categories between BMI and FMI was found in 30% of the studied population. 27% of the patients were upgraded to a higher weight class by FMI. 8%, 14%, 4% and 2% of patients, classified as Normal, Overweight, Obese class 1 and Obese class 2 by BMI criteria, respectively, were classified as Excess Fat, Obese class 1, Obese class 2, and Obese class 3, respectively, by the FMI criteria. 80% of women with normal BMI were found to have PBF > 34%. BMI and FMI both correlated significantly with Diabetes Mellitus, hyperlipidemia, and sleep apnea. BMI, FMI and PBF were all significantly correlated with each other. Conclusion: Our study highlights the limitations of conventional BMI criteria in diagnosing and classifying obesity in post-menopausal women compared to FMI as assessed by DXA scans. Further studies are needed with wider population samples and larger numbers to further confirm our findings.

Supported by:
Primary Presenter / e-mail: Maghrabi, A. H. / adammaghrabi@gmail.com
Mentor or Senior Author / e-mail: Yaqub, A. / yaqub1@marshall.edu

96 **Abstract Title:** **Acute Management of Hypertensive Crises in the Emergency Department**

Author(s): S. Wilkie, Pharmacy Services, UK HealthCare, Lexington, KY
S. Baker, Pharmacy Services, UK HealthCare, Lexington, KY
K. Weant, North Carolina Public Health Preparedness and Response, NC Dpt of HHS, Raleigh, NC

Abstract:
Practitioners in the Emergency Department (ED), routinely encounter patients who are hospitalized for hypertensive crises and neurologic sequelae secondary to hypertension Thus, it is important that appropriate management of hypertension be initiated appropriately as it is critical for positive outcomes in these patients. Treatment should be initiated in the ED to decrease cardiovascular events and mortality. It is our belief that a medication; nicardipine, sodium nitroprusside, labetalol or hydralazine; will best control hypertensive crises in the ED by minimizing the time blood pressure is outside the goal target range. Secondarily, the management of hypertensive crises with the appropriate medication and the presence of pharmacy personnel in the ED will decrease Intensive Care Unit (ICU) and hospital lengths of stay, improve time to transition to oral therapy as well as the time a patient is on a particular antihypertensive agent. The intent of this project is to determine which antihypertensive medication (labetalol vs. hydralazine and nicardipine vs. sodium nitroprusside) best manages hypertensive crises in the ED. This was a retrospective chart review of patients who presented to the ED between January 1, 2007 and December 31, 2010. Four study groups will be assessed, analysis of patients receiving antihypertensive therapy labetalol, hydralazine, nicardipine, nitroprusside or any combination of the aforementioned. Inclusion criteria include adults greater than 18 years of age; patients admitted through the ED and who received one of the aforementioned antihypertensive therapies Exclusion criteria include pregnancy. The variables measured will include ICU length of stay, hospital length of stay, worsening of clinical indication, time to transition to oral antihypertensive, and time on antihypertensive medication.

Supported by:
Primary Presenter / e-mail: Wilkie, S. / scott.wilkie@uky.edu
Mentor or Senior Author / e-mail: Baker, S. / snba222@uky.edu

97 **Abstract Title:** **Cyp-epoxygenases mediate adenosine A2A receptor induced vascular relaxation via KATP channels**

Author(s): D.S. Ponnoth, Dept. of Physiology & Pharmacology, Center for Cardiovascular and Respiratory Sciences, West Virginia U
M.A. Nayeem, Dept. of Physiology & Pharmacology, Center for Cardiovascular and Respiratory Sciences, West Virginia U
S.S.Kunduri, Dept. of Physiology & Pharmacology, Center for Cardiovascular and Respiratory Sciences, West Virginia U
S.L.Tilley, Dept. of Medicine, UNC Chapel Hill, NC
C.Ledent, Université Libre de Bruxelles, Brussels, Belgium
S. J. Mustafa, Dept. of Physiology & Pharmacology, Center for Cardiovascular and Respiratory Sciences, West Virginia U

Abstract:
A2A adenosine receptor (AR) causes aortic relaxation through generation of epoxyeicosatrienoic acids (EETs) formed via Cyp-epoxygenases (Nayeem et al, AJP 2008). We hypothesize that A2AAR-mediated aortic relaxation occurs via EETs through opening of KATP channels in smooth muscle cells. Organ bath experiments were done with isolated aortas from A2AKO and wild type (WT) mice. Pinacidil (KATP opener; 10-6M) caused higher relaxation in WT aorta compared to A2AKO (48.09±5.23% vs. 25.41±2.37%; $p<0.05$). Cyp-epoxygenase inhibitor MSPPOH (10-5M) caused significant decrease ($p<0.05$) in pinacidil response in WT (48.09±5.23% vs. 24.93±5.34%) and A2AKO (25.41±2.37% vs. 14.66±3.88%) aorta. Adenosine analog NECA (10-5M) caused significant relaxation in WT aorta (19.65±3.25%) compared to contraction (13.94±6.57%) in A2AKO, that was lowered by KATP blocker glibenclamide in WT (0.17±6.43%) while higher contraction was observed in KO (28.47±5.1%). Relaxation to A2A agonist CGS 21680 (10-6M) in WT (19.02±2.75%) changed to contraction (23.66±6.31%; $p<0.05$) with glibenclamide. Mitochondrial KATP opener diazoxide had no effect on precontracted tissues, while 5-HD (mitochondrial KATP blocker, 100uM) had no effect on CGS 21680 response in WT and A2AKO aorta. These data suggest adenosine mediated aortic relaxation occurs via generation of EETs through sarcolemmal KATP channels.

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Primary Presenter / e-mail: Ponnoth, D. S. / dponnoth@hsc.wvu.edu
Mentor or Senior Author / e-mail: Mustafa, S. J. / sjmustafa@hsc.wvu.edu

98 **Abstract Title:** **Depression is Associated with Cardiovascular Disease Risk in Prison Inmates**

Author(s): M. L. Chung , College of Nursing, Univeristy of Kentucky
T. A. Lennie, College of Nursing, University of Kentucky
A. Connell, College of Nursing, University of Kentucky
A. Bailey, College of Medicine, University of Kentucky
D.K. Moser, College of Nursing, University of Kentucky

Abstract:
Background: Cardiovascular disease is the leading cause of death in prison inmates. Depression is a known predictor of cardiovascular disease in the general population. Inmates who are incarcerated and live in stressful conditions may have higher levels of depression than seen in the general population. Higher levels of depression in inmates may be one reason for the high prevalence of cardiovascular disease in this population but this association has not been examined. The purpose of this study was to compare cardiovascular risk factors between depressed and non-depressed male inmates. Method: Male inmates in 4 Kentucky medium security state prisons without major psychiatric comorbidity completed a physical exam including blood pressure, body mass index (BMI), waist circumference, and lipid panel (high density lipoprotein, low density lipoprotein, total cholesterol, triglyceride). Depression was assessed using the Patient Health Questionnaire (PHQ-9). Patients were grouped by depressed (PHQ-9 score > 9) and non-depressed groups using the standard cut point of 9 on the PHQ-9 score. Results: Of the 300 male inmates (mean age 36 ± 9.3 years; 63% white), 70 (23%) were depressed (PHQ-9 score > 9). Depressed inmates were older (38.7 ± 11 vs. 36.0 ± 9 years, $p < .05$) and had higher BMI (29.9 ± 5.9 vs. 27.9 ± 4.2 kg/m2, $p < .01$), higher waist circumference (38.9 vs. 36.4 inches, $p< .01$), lower levels of high density lipoprotein (34 ±12 vs. 38 ±12 mg/dL, $p < .05$) and higher levels of triglyceride (190 ± 130 vs.150 ± 102 mg/dL, $p < .05$) than non-depressed inmates. There were no significant differences in total cholesterol, low density lipoprotein, and systolic and diastolic blood pressure between depressed and non-depressed groups. Conclusion: The prevalence of depression in this sample of inmates was high. BMI, waist circumference, and levels of high density lipoprotein and triglycerides of depressed patients were indicative of increased cardiovascular disease risk. This study provides evidence that depression may play a role in increasing risk of cardiovascular disease in inmates. It would be beneficial to include management of depression in an intervention aimed at improving cardiovascular health in inmates.

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Primary Presenter / e-mail: Chung, M. L. / misook.chung@uky.edu
Mentor or Senior Author / e-mail: Moser, D. K. / dmoser@uky.edu

99 **Abstract Title:** **Evidence For the Involvement of NADPH Oxidase in Adenosine Receptors-mediated Control of Coronary Flow Using Knockout Mice**

Author(s): M. S. El-Awady, Department of Physiology and Pharmacology, West Virginia University
S. L. Tilley, Department of Medicine, University of North Carolina
S. J. Mustafa, Department of Physiology and Pharmacology, West Virginia University

Abstract:
The NADPH oxidase (Nox) is the major source for reactive oxygen species (ROS) in cardiovascular system. In conditions such as ischemia-reperfusion injury and hypoxia, both ROS and adenosine are released suggesting a possible interaction. A2A and A2B adenosine receptors (ARs) are involved in coronary vasodilation, while A1AR and A3AR have been shown to decrease coronary flow (CF). Our aim in this study is to examine the role of A1AR and A3AR in control of CF and their relationship with Nox using isolated hearts from wild type (WT; C57/BL6) and A1 and A3 AR double knockout (A1/A3DKO) mice. The basal CF was significantly ($p<0.05$, n=12) higher in A1/A3DKO (20.9±1.6 ml/min/g tissue) compared to WT (16.7±1.6 ml/min/g tissue), suggesting negative roles for A1AR and A3AR in the control of CF. Moreover, adenosine concentration-response curve (10-8-10-5.5 M) produced increasing CF with Emax in A1/A3DKO (42.75±0.53 ml/min/g tissue) significantly ($p<0.05$, n=8) higher compared to WT (38.28±0.38 ml/min/g tissue). Inhibition of Nox by apocynin (10-5 M) significantly ($p<0.001$, n=6) decreased the enhanced CF to adenosine in both WT (Emax= 33.97±0.51 ml/min/g tissue) and A1/A3DKO (Emax= 31.86±1.07 ml/min/g tissue). The CF in A1/A3DKO was more sensitive (25.47 % decrease) to apocynin inhibition compared to WT (11.26% decrease), suggesting that Nox is involved mainly in adenosine-induced coronary vasodilation more than constriction. In conclusion, both A1AR and A3AR play a negative role in the control of CF, with Nox being involved as a major signaling pathway in adenosine-induced coronary vasodilation. ROS measurement and the specific involvement of either A1AR or A3AR and the role of different Nox isoforms are being investigated.

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Primary Presenter / e-mail: El-Awady, M. S. / melawady@hsc.wvu.edu
Mentor or Senior Author / e-mail: Mustafa, S. J. / sjmustafa@hsc.wvu.edu

100 **Abstract Title:** **Mice with endothelial-targeted inactivation of Ppap2b (lipid phosphate phosphatase 3) display enhanced vascular inflammation and permeability.**

Author(s):
M. Panchatcharam, Department of Cardiovascular Medicine, U of Kentucky
S. Miriyala, Department of Cardiovascular Medicine, U of Kentucky
P. Patil, Department of Cardiovascular Medicine, U of Kentucky
A. Nguyen, Department of Cardiovascular Medicine, U of Kentucky
M. Sunkara,Department of Cardiovascular Medicine, U of Kentucky
A.J. Morris, Department of Cardiovascular Medicine, U of Kentucky
D.E. Alcalde, Departamento de Neurociencias, U Nacional Autonoma de Mexico
S.S. Smyth Department of Cardiovascular Medicine, U of Kentucky

Abstract:
Meta-analysis of data from a series of genome-wide association studies (GWAS) revealed a striking association between the PPAP2B loci and coronary artery disease. The PPAP2B gene encodes for the lipid phosphate phosphatase 3 (LPP3) integral membrane enzyme, that dephosphorylates lysophosphatidic acid (LPA), sphingosine 1-phosphate (S1P) and related bioactive lipids. We report that constitutive inactivation of LPP3 in vascular endothelial cells accomplished by breeding mice with floxed Ppap2b to mice expressing Cre recombinase under control of the Tie1 promoter results in embryonic lethality, indicating that dysregulation of LPP3-dependent vascular endothelial cell function likely underlies the developmental phenotype observed in Ppap2b-null embryos. Using an estrogen inducible Cre transgene under control of the Tie1 promoter, we have inactivated Ppap2b expression in endothelial cells in adult mice. The absence of vascular endothelial LPP3 results in a 200 fold increase in basal vascular permeability, as assessed by Evans blue dye extravasation in lung tissue. The permeability difference is exaggerated following an inflammatory challenge (LPS; 2 mg/kg), and LPS-induced expression of plasma inflammatory markers IL6 and KC were 3.3±0.5 and 1.9±0.6 fold higher in mice lacking endothelial LPP3. LPS-enhanced permeability in the absence of LPP3 was attenuated by administration of an LPA receptor antagonist. Mice lacking LPA receptors 1 and 2 (LPA1, LPA2) or LPA receptor 4 (LPA4) were protected from LPS-mediated permeability. These results demonstrate a fundamental role for LPP3, possibility via modulation of local LPA levels and signaling through LPA1, LPA2, and LPA4 receptors, in maintaining the integrity of the vascular endothelium.

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Primary Presenter / e-mail: Panchatcharam, M. / manikandan@uky.edu

Mentor or Senior Author / e-mail: Smyth, S. S. / susansmyth@uky.edu

101 **Abstract Title:** **Potential Role of Sphingosine-1-Phosphate and S1P Receptors on Cardiac and Endothelial Differentiation Pathways in Mobilized Bone Marrow Stem/Progenitor Cells**

Author(s):
A. K. Karapetyan, Department of Internal Medicine U of Kentucky
Y. M. Klyachkin, Department of Internal Medicine U of Kentucky
S. S. Smyth, Department of Internal Medicine U of Kentucky
A. J. Morris, A. K. Karapetyan, Department of Internal Medicine U of Kentucky
A. Abdel-Latif, Department of Internal Medicine U of Kentucky

Abstract:
Background: Bone marrow (BM) stem/progenitor cells (SPCs) are mobilized from the bone marrow into peripheral blood during tissue injury, particularly after the ischemic events of a myocardial infarction. Recent studies suggest that Sphingosine-1-Phosphate (S1P) signaling plays an important role in BMSPC mobilization, egress, and homing to ischemic tissue. While evidence exists that S1P promotes the differentiation of human umbilical cord mesenchymal stem cells into cardiomyocytes, its role in differentiation of BMSPCs is less understood. Methods: G-CSF mobilized human peripheral blood (mPB) (N = 10) was plated and treated with 250nM S1P alone, 5μM VPC 23019 (S1PR antagonist) alone, S1P + VPC, or vehicle control. Cultures were examined for cardiac (Nkx and GATA4) and endothelial (VWF and VE-cadherin) gene expression at 48 and 72 hours using QPCR; and protein expression (GATA4, Nkx, myosin heavy chain, troponin; and VWF, VE-cadherin, PDGFRα, and PDGFRβ) at 4 weeks using confocal microscopy. Results: At 48, and more at 72 hours, mPB cells expressed cardiac and endothelial markers at higher rate compared to controls (4-6 fold change). Higher percentage of cells expressing cardiac and endothelial proteins and adopting the cardiac and endothelial morphology was observed on cultures treated with S1P (~10 fold). In parallel with this differentiation, mPB cells demonstrated phosphorylation of MAPK42/44 and ERK when incubated with S1P. Conclusion: This data suggests that exposure to S1P intitiates the phosphorylation of multiple kinases which stimulate downstream pathways culminating in the differentiation of BMSPCS. This data can be of clinical significance in refining bone marrow stem cell therapy in ischemic heart disease.

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Primary Presenter / e-mail: Karapetyan, A. K. / anush.karapetyan@uky.edu

Mentor or Senior Author / e-mail: Abdel-Latif, A. / akabde2@uky.edu

102	Abstract Title:	**Project R.E.A.C.H. West Virginia: The Triumphs and Obstacles of Developing a Student-ran Rural Outreach Program**

Author(s): H. Miller, Medical Student, West Virginia University School of Medicine
K. Pennington, Medical Student, West Virginia University School of Medicine

Abstract:
This poster describes the obstacles and successes in developing a rural health outreach program in West Virginia. The purpose of this program is to have community members in medically underserved areas examine their current health behaviors and provide a positive alternative for potentially negative actions/in-actions as well as expose medical students to the needs of rural West Virginia. To achieve this purpose, medical students from West Virginia University in collaboration with medical students from Marshall University initiate, organize, and work monthly health fairs in rotating locations throughout rural West Virginia. These medical students have forged non-traditional partnerships with food pantry directors, elementary school teachers, missionary workers, and librarians in order to establish a presence and find venues in these rural communities. Several stations are set-up including blood pressure screening, body mass index calculation, breast cancer awareness, smoking cessation, and exercise and nutrition education. Moreover as an increased number of patients in rural areas rely on emergency departments for primary care, patients are given a list and contact information of primary care providers and low-cost/free clinics in the area and are encouraged to establish care. In four months, 18 medical students and 277 community members have participated in the outreach program, and blood pressures as high as 198 systolic and 108 diastolic have been recorded.

Supported by:

Primary Presenter / e-mail: Miller, H.
Pennington, K. / hmiller4@mix.wvu.edu

Mentor or Senior Author / e-mail: Cather, G. A. / acather@hsc.wvu.edu

103	Abstract Title:	**Relationship between high salt and adenosine-induced vasular response in A2A AR+/+ and A2A AR-/- mice**

Author(s):
I. Pradhan, Department of Pharmaceutical and Pharmacological Science, West Virginia U
S. J. Mustafa, Department Physiology and Pharmacological sciences, West Virginia U
D. C. Zeldin, Pulmonary Division, NIH/NIEHS, Research Triangle Park, NC
C. Ledent, IRIBHN, Universite Libre de Bruxelles
J. R. Falck, Biochemistry, University of Texas, Dallas
M. A Nayeem, Department of Physiology and Pharmacological sciences, West Virginia U

Abstract:
Recent studies have shown that salt loading enhances adenosine-induced vascular relaxation (Nayeem et al., 2010). The main goal of this study is to investigate the mechanistic role of A2A adenosine receptor (A2AAR) in high salt (HS) fed mice using A2AAR-/- and A2AAR+/+ mice. Therefore, we hypothesized that in the presence of A2AAR, HS enhances adenosine-induced relaxation through cyp epoxygenase, whereas in the absence of A2AAR, HS exaggerates contraction through ω-hyxroxylase. Organ bath and western blot experiments were conducted in 4% NaCl (HS) and 0.18% NaCl (NS) fed A2AAR-/- and A2AAR+/+ mice. Adenosine analog (NECA; 10–6 M) showed relaxation (+17.34 ±2.5 %, $p<0.05$) in HS-A2A AR+/+ vs. contraction in NS-A2A AR+/+ (-27.6.3 ± 3.3%), NS-A2AAR-/- (-51.10 ± 3.01%) and HS-A2AAR-/- (-56.77 ± 3.49%). CGS-21680 (A2A AR agonist); 10–6 M enhanced relaxation in HS-A2A AR+/+ (+21.4 ± 1.34%, $P < 0.05$) vs. less relaxation in NS-A2AAR+/+ (+8.07 ± 2.36%), and relaxation in HS-A2A AR+/+ was blocked by an EET antagonist (14,15-EEZE ; 10–6 M, -1.08 ± 2.95%) but not by L-NAME (NO inhibitor) and Indomethacin (Cyclooxygenase inhibitor). Compared to NS-A2AAR+/+, HS-A2AAR+/+ demonstrated up-regulation of A2AAR, cyp2c29 (60%, 64%, respectively) and down-regulation of A1 AR, cyp4a (18%, 46%, respectively). Up-regulation of A1AR (38%) and cyp4a (49%) and down-regulation of cyp2c29 (104%) in HS-A2AAR-/- vs. HS-A2AAR+/+ were observed. In conclusion, HS enhances relaxation through cyp2c29 in A2A AR+/+, whereas HS exaggerates contraction via A1AR and cyp4a in A2AAR-/- mice.

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Primary Presenter / e-mail: Pradhan, I. / ipradhan@hsc.wvu.edu

Mentor or Senior Author / e-mail: Nayeem, M. A. / mnayeem@hsc.wvu.edu

104 **Abstract Title:** **Role of L-type calcium and large conductance potassium channels in A1AR -Cyp4a mediated vasoconstriction**

Author(s):
S.S. Kunduri,Department of Physiology and Pharmacology, West Virginia U, Morgantown, WV
M.A. Nayeem, Department of Physiology and Pharmacology, West Virginia U, Morgantown, WV
D.S. Ponnoth, Department of Physiology and Pharmacology, West Virginia U, Morgantown, WV
B.Teng, Department of Physiology and Pharmacology, West Virginia U, Morgantown, WV
S.S. Tilley, Dept. of Medicine, Div. of Pulmonary and Critical Care Medicine, U of North Carolina, Chapel Hill, NC
S.J. Mustafa, Department of Physiology and Pharmacology, West Virginia U, Morgantown, WV

Abstract:
Adenosine A1 receptor (A1AR) induces vasoconstriction possibly via generation of arachidonic acid-derived metabolite (20-HETE) by Cyp4a. 20-HETE plays important role in regulation of vascular tone. We hypothesize A1AR-mediated vasoconstriction depends on Cyp4a through activation of L-type voltage dependent calcium channels (L-VDCC) and inhibition of large conductance potassium (BK) channels. Using WT and A1KO mouse aortae, vascular responses for adenosine agonists were obtained with Cyp4a inhibitor (HET0016, 10-5M), L-VDCC inhibitor (Nifedipine, 10-6M) and BK activator (NS1619, 10-5M). In addition, vascular responses in the WT and A1KO mesenteric arteries were obtained with 20-HETE. Immunoblot results suggest higher Cyp4a levels in WT than A1KO ($p<0.05$). CCPA (A1AR agonist)-elicited contraction was significantly blunted with HET0016 (-7.9 ± 1.9% vs. -32.5 ± 1.7% at 10-7M, $p<0.05$) and Nifedipine (-11.5 ± 5.9% vs. -32.5 ± 1.7% at 10-7M, $p<0.05$) in WT with no effect in A1KO. NECA(adenosine analog) induced relaxation was unaltered in control and NS1619 treated WT. NS1619 magnified NECA elicited relaxation (32.4 ± 4.2% vs. -1.7 ± 4.2%) in A1KO. 20-HETE (10-7M) induced contraction was higher in WT than A1KO both in aorta (33.4 ± 2.9% vs. 23.9 ± 2.4%) and mesenteric arteries (10.5 ± 1.52% vs.0.3±1.6%). %). Nifedipine and NS1619 significantly abated this contraction in WT and A1KO.This NECA and 20-HETE mediated response was restored to control levels by BK channel inhibitor Penitrem A in A1KO. These data suggest A1AR mediates vasoconstriction through 20-HETE by activating L-type calcium and inhibiting BK channels, having important implications in cardiovascular disorders (HL027339, HL094447, HL071802).

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Primary Presenter / e-mail: Kunduri, S. S. / skunduri@hsc.wvu.edu
Mentor or Senior Author / e-mail: Mustafa, S. J. / sjmustafa@hsc.wvu.edu

105 **Abstract Title:** **Self-rated Health Perception Predicts Coronary Heart Disease Risk Factors in Prison Inmates**

Author(s):
Z. T. Saleh, College of Nursing, U of Kentucky
T. A. Lennie, College of Nursing, U of Kentucky
M. L. Chung, College of Nursing, U of Kentucky
A. Connell, College of Nursing, U of Kentucky
D. K. Moser, College of Nursing, U of Kentucky

Abstract:
Introduction: Coronary heart disease (CHD) is the primary cause of death in prison inmates. Screening for CHD risk factors is not routinely done in prisons. There is evidence that self-rated health perception is a predictor of health status in the general population and may serve as an inexpensive screening tool for identifying prisoners at risk for CHD. The purpose of this study was to determine the potential of self-rated health perception as a screening tool for identifying prisoners with CHD risk factors. Method(s): The study included 256 male inmates (aged 19 to 77 years; mean age = 36.8 ± 9.8 years) from 4 Kentucky State prisons. All participants underwent a physical assessment for CHD risk factors, including blood pressure (BP), waist circumference, body mass index (BMI), and lipid profile (cholesterol, triglyceride, low density lipoprotein [LDL], high density lipoprotein [HDL]). Health perception was assessed using a single item from the Medical Outcomes Survey Short-Form 36, asking participants to rate their overall health as excellent, very good, good, fair, or poor. Due to low frequencies, inmates with excellent health perceptions were combined with very good and inmates with fair health perceptions were combined with poor. Results: A total of 78 (30.5%) of inmates perceived their health as excellent or very good, 115 (44.9%) perceived their health as good, and 63 (24.6%) perceived their health as fair or poor. After adjusting for age in logistic regressions, inmates who reported fair or poor health had a significantly greater likelihood of triglycerides ≥ 150 mg/dl (odds ratio [OR] = 2.9; confidence interval [CI] = 1.4 - 5.9), HDL < 40 mg/dl (OR = 4.8; CI = 2.2 - 10.5), waist circumference > 40 in. (OR = 3.6; CI = 1.5 - 8.3), and BMI ≥ 30 kg/m2 (OR = 2.5; CI = 1.1 - 5.3) compared with those reporting excellent or very good health. Health perception did not predict elevated systolic BP, cholesterol, or LDL. Discussion & Conclusions: Inmates with fair or poor health perceptions had greater likelihood of having several major CHD risk factors after controlling for age. These data suggest that simple self-rated health perception may identify inmates most likely to need screening for CHD risk factors.

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Primary Presenter / e-mail: Saleh, Z. T. / zyad.saleh@uky.edu
Mentor or Senior Author / e-mail: Lennie, T. A. / talenn2@email.uky.edu

106 **Abstract Title:** **Shock Index Predicts Mortality But Not Ventilator Days in Critically Ill Patients Requiring Mechanical Ventilation**

Author(s):
K. M. Moore, College of Nursing, U of Kentucky
S.K. Frazier, College of Nursing, U of Kentucky
M.H. Pierce, College of Nursing, U of Kentucky

Abstract:
Background: Hemodynamic instability is a frequent complication of critical illness and injury. Heart rate and blood pressure are insensitive indicators of instability because of compensatory mechanisms. Shock index is a marker of hemodynamic instability that is not influenced by compensation. Purpose: The aims of this study were: 1) to compare demographic and clinical variables between those with high and low shock index, and 2) to determine the independent predictive power of shock index for ventilator days and mortality after controlling for age, gender and APACHE III score. Methods: We performed a retrospective medical records review in a random sample of adults (n = 77) who required mechanical ventilation for more than 12 hours. Shock index was calculated as heart rate divided by systolic blood pressure. High and low shock index groups were formed and variables were compared by Chi square and independent t tests based on the level of measurement. Linear and logistic regression evaluated the predictive power of shock index for ventilator days and mortality. Results: There were no differences in demographic or clinical variables between the high and low shock index groups. Shock index was not an independent predictor of ventilator days. However, shock index was a significant independent predictor of mortality in this group of critically ill adults (OR 0.005, CI 0.000 to 0.320, p = 0.01). For every 0.1 increase in shock index, the likelihood of mortality is increased by 5%. Conclusions: Shock index is an independent predictor of mortality in critically ill adults receiving mechanical ventilation and may be a useful marker of hemodynamic instability in a variety of patient populations, which merits further investigation. Shock index may provide a key opportunity for early recognition and intervention to improve outcomes.

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Primary Presenter / e-mail: Moore, K. M. / kathryn.moore@uky.edu

Mentor or Senior Author / e-mail: Frazier, S. K. / skfraz2@email.uky.edu

107 **Abstract Title:** **Significant Levels of Hypertension Across Appalachian Regions**

Author(s):
D. Y. Han, Department of Neurology, U of Kentucky
A. L. Shandera-Ochsner, Department of Neurology, U of Kentucky
D. R. Rose, Department of Neurology, U of Kentucky
E. Addo, Department of Neurology, U of Kentucky
C. Sawyers, Department of Neurology, U of Kentucky
B. Young, Department of Neurology, U of Kentucky
L. Bellamy, Department of Neurology, U of Kentucky
M. R. Dobbs, Department of Neurology, U of Kentucky

Abstract:
Hypertension is a well-established risk factor for cardiovascular disease and stroke. It is important to establish and understand base rates and trends in hypertension at the local, regional, and state level in order to design effective interventions. The most recent (2009) statistic available from the survey conducted by the Center for Disease Control and Prevention (CDC) indicates that 36.4% of adult Kentucky residents reported they have been told by a health care provider that they have high blood pressure. The same survey shows that the average rate of hypertension in the United States was 26%, indicating that Kentucky's rate of hypertension is 40% higher than the national average. The Appalachian region of Kentucky is commonly believed to have poorer health than other regions in the state. The current study looked at an objective estimate of hypertension via blood pressure readings obtained by Kentuckians attending community screening events held in 2011 in counties throughout the commonwealth. 8 counties were located in Appalachia (n = 1049) and 8 were located in the Bluegrass region (n=1309). We found 41.30% of screening participants in Appalachia and 41.89% of screening participants in the Bluegrass had blood pressure readings greater than 140/90. The results of this study show that CDC estimated hypertension rates (while high) may undershoot the magnitude of the current problem in Kentucky. In addition, the results clearly indicate that increased risk for high blood pressure in Kentucky is not limited to Appalachian counties and must be addressed at the state level.

Supported by:

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

Mentor or Senior Author / e-mail: Dobbs, M. R. / mrdobb0@uky.edu

108 **Abstract Title:** **Transmural heterogeneity and depressed function in the mechanical properties of ventricular tissue from patients with end-stage heart failure**

Author(s):
P. Shekar, Department of Physiology and Center for Muscle Biology, U of Kentucky
M. I. Mitov, Department of Chemistry, U of Kentucky
L.F. Ferreira, Department of Applied Physiology and Kinesiology, U of Florida
S.G. Campbell, Department of Physiology and Center for Muscle Biology, U of Kentucky
S. A. Stasko, Department of Physiology and Center for Muscle Biology, U of Kentucky
A. M. Jarrells, Department of Physiology and Center for Muscle Biology, U of Kentucky
B. A. Lawson, Department of Physiology and Center for Muscle Biology, U of Kentucky
M.B. Reid, Department of Physiology and Center for Muscle Biology, U of Kentucky
C. W. Hoopes, Division of Cardiothoracic Surgery and Center for Muscle Biology, U of Kentucky
M.R. Bonnell, University of Toledo Medical Center, Toledo
K. S. Campbell, Department of Physiology and Center for Muscle Biology, U of Kentucky

Abstract:
Heart failure is a progressive condition in which the ventricles can no longer pump enough blood to meet the body's basal demands. Our lab is investigating whether the transmural variation in cellular contractile properties that occurs in normal hearts (and which is thought to be important for ventricular function) is altered in heart failure. We procured through wall samples of failing left ventricles from patients receiving transplants at the University of Kentucky and non failing samples from brain dead organ donors. The tissue was divided into epicardial, midmyocardial and endocardial regions and snap frozen in liquid nitrogen within 30 minutes. Multicellular chemically permeabilized preparations were subsequently obtained from these samples by mechanical homogenization and triton treatment. The samples were attached between a force transducer and a motor and subjected to mechanical protocols. Parameters including and maximum power output, isometric force, short range stiffness, short range force were measured. The results suggested a 30% decrease in maximum power output (p-value = 0.01) and isometric force (p-value=0.03) in heart failure samples (n=8, total of 72 preparations) as compared to non failing patients samples (n=4, total of 36 preparations). Short range stiffness (p-value=0.008) and short range force (p-value=0.002) also significantly decreased in heart failure vs. non failing. Transmurally there was a significant difference in maximum power output between the regions (p-value=0.02). The data suggests that mechanically the midmyocardium maybe affected the most in heart failure. Further studies need to be done to understand the protein modifications that may be responsible for these variations.

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Primary Presenter / e-mail: Shekar, P. / premi.shekar@uky.edu
Mentor or Senior Author / e-mail: Campbell, K. S. / k.s.campbell@uky.edu

109 **Abstract Title:** **Bringing Stroke Systems of Care to Appalachia: The UK Stroke Affiliate Network**

Author(s):
M. R. Dobbs, Department of Neurology, U of Kentucky
R. L. Edwards, EVPHA Office, U of Kentucky
J. O. Claypool, EVPHA Office, U of Kentucky
L. M. Bellamy, Department of Neurology, U of Kentucky
D. R. Rose, Department of Neurology, U of Kentucky

Abstract:
Despite advances in treatment, stroke remains a significant disease burden, both in the United States and Kentucky specifically. The Appalachian region of the state in particular shoulders a significant part of this burden, with stroke hospitalization and death rates significantly above the national average. Unfortunately, many of the citizens of Appalachia face economic, geographic and social obstacles that impede their ability to receive optimal medical care. Medical providers and healthcare facilities in the region combat similar difficulties in treating an underserved population with limited resources. Given this situation, both Appalachian healthcare facilities and patients stand to benefit greatly from the establishment of systems of care and integration into a statewide stroke network. In 2008, the UK Stroke Affiliate Network was created with the goal of improving stroke care and outcomes for the state of Kentucky by recruiting and integrating facilities into a network based on the guidelines for the establishment of evidence-based stroke systems of care as outlined by the American Heart Association/American Stroke Association and other bodies. In early 2012, the Appalachian Regional Healthcare (ARH) hospital system became the network's first system affiliate, bringing on eight facilities across Eastern Kentucky. This sudden expansion of the network heralds a period of network stability and potential synergy in improving patient care. This report will provide a brief history of the UK Stroke Affiliate network and its progress in improving stroke care in the state. The network's future expansion in Appalachia will also be discussed, including a discussion of future challenges as the network strives to improve the vascular health of Appalachia.

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Primary Presenter / e-mail: Rose, D. R. / drrose2@uky.edu
Mentor or Senior Author / e-mail: Dobbs, M. R. / mrdobb0@uky.edu

110 **Abstract Title:** **Health-Related Quality of Life and Loneliness for Ischemic and Hemorrhagic Stroke Survivors Living in Appalachia**

Author(s):
L.A. Theeke, Department of Health Restoration, West Virginia U
P. Horstman, West Virginia U Healthcare
T. Barr, Department of Health Restoration, West Virginia U
S. Culp, Department of Health Restoration, West Virginia U
A. Lucke-Wold, School of Nursing, West Virginia U
J. Domico, West Virginia U Healthcare
L. Guttman, West Virginia U Healthcare

Abstract:
Background and Purpose – Negative psychological outcomes of stroke have been associated with lower health related quality of life (HRQoL) and may impact stroke recovery yet these relationships are understudied in stroke survivors. The purpose of this study was to describe the HRQoL domains, loneliness, and the relationships among these domains and loneliness in a sample of rural Appalachian stroke survivors within one year of stroke. Methods - Using survey methodology, 121 ischemic and hemorrhagic stroke survivors living in West Virginia reported sociodemographics, HRQoL measured by the Neuro-QOL and loneliness measured by the 3-item UCLA Loneliness Scale. Data analysis was accomplished using SPSS for descriptive, comparative, and finally regression analyses to assess significant variables for explanatory value for each HRQoL domain. Results - Ischemic stroke patients reported higher HRQoL compared to hemorrhagic stroke survivors. There were no significant differences in HRQoL based on living arrangement for those who were discharged to home but participants who were discharged to a nursing home reported lower HRQoL. A history of co-morbid emotional, nervous or psychiatric problem negatively correlated with all HRQoL domains and loneliness scores. Stroke survivors who continued to smoke were less satisfied with social roles and activities and reported higher mean depression scores. Conclusion –Providers should be screening stroke victims for pre-existing psychiatric co-morbidity, loneliness which is a major predictor of depression, and depression. Aggressively pursuing smoking cessation could positively impact HRQoL and depression.

Supported by: West Virginia University School of Nursing Research Fund
Primary Presenter / e-mail: Theeke, L. A. / ltheeke@hsc.wvu.edu
Mentor or Senior Author / e-mail: Theeke, L.A. / ltheeke@hsc.wvu.edu

111 **Abstract Title:** **Identification of a genomic profile following ischemic stroke that may mediate stroke recovery**

Author(s):
R.L. VanGilder, Deps of Health Restoration and Emergency Medicine, West Virginia U, Morgantown, WV
T.L. Barr, Deps of Health Restoration and Emergency Medicine, West Virginia U, Morgantown, WV
S.L. Rellick, Deps of Health Restoration and Emergency Medicine, West Virginia U, Morgantown, WV
Y. Conley, Dept of Health Promotion and Development, U of Pittsburgh, Pittsburgh, PA
J. Ding, National Institute on Aging, Bethesda, MD
J. Denvir, Dept of Biochemistry and Microbiology, Marshall U Huntington, WV
D. Chen, Division of Preventive Medicine, University of Alabama
A. Dillman, National Institute on Aging, Bethesda, MD
S.Warach, National Institute of Neurological Disorders and Stroke, Bethesda, MD
A. Singleton, National Institute on Aging, Bethesda, MD
M. Matarin, Molecular Neuroscience and Clinical and Experimental Epilepsy, U College London Institute of Neurology, London, England

Abstract:
Objective: The objective of this study was to provide insight into the molecular mechanisms changing as a result of acute ischemic cerebrovascular syndrome (AICS) through gene expression profiling and pathway analysis. Methods: Peripheral whole blood samples were collected from n=34 MRI diagnosed AICS patients' ≥18 years of age at two time points: within 24 hours from last known normal and 24-48 hours later. Modified rankin scale (MRS) was used to determine 30 day stroke outcome. Total RNA was extracted from whole blood stabilized in Paxgene RNA tubes, amplified, and hybridized to Illumina HumanRef-8v2 bead chips. Gene expression was compared in a univariate manner between stroke patients at both time points and good versus bad outcome using t-test in GeneSpring. Inflation of type one error was corrected by Bonferroni and Ingenuity Systems Pathway analysis (IPA) was performed. Results: Three genes were significantly downregulated over time (LY96, IL8, and SDPR). Pathway analysis revealed cytotoxic t-lymphocyte antigen 4 (CTLA4) and dopamine signaling as highly significant canonical pathways present in the peripheral whole blood of AICS patients 24-48 post onset of symptoms. Seven genes were associated with 30 day MRS, with Arginase 1 (ARG1) as the most significant. Conclusions: Markers of immune dysfunction in the early post-stroke phase, such as arginase and T-cell activity may prove useful for identifying patients with increased risk of post-stroke immune suppression and novel therapeutic stroke treatments.

Supported by: Funding Pending
Primary Presenter / e-mail: VanGilder, R. L. / rvangilder@hsc.wvu.edu
Mentor or Senior Author / e-mail: Barr, T. L. / tlbarr@hsc.wvu.edu

112 **Abstract Title:** **Long-term cortical reorganization following stroke in a single subject with severe motor impairment**

Author(s):
K.C. Chelette, Dept. of Physical Medicine and Rehabilitation, U of Kentucky
C. Carrico, Dept. of Physical Medicine and Rehabilitation, U of Kentucky
L. Nichols, Dept. of Physical Medicine and Rehabilitation, U of Kentucky, Cardinal Hill Rehabilitation Hospital
L. Sawaki, Dept. of Physical Medicine and Rehabilitation, U of Kentucky

Abstract:
Introduction: This case study presents the trajectory of neuroplastic and upper extremity (UE) motor performance change during early (ie, <12 months post-stroke) and late (ie, >12 months post-stroke) phases of recovery after an extensive middle cerebral artery (MCA) stroke. Methods: We used transcranial magnetic stimulation (TMS) to assess motor map volume. Change in map volume is a measure of cortical reorganization related to excitability of motoneurons. We used the Fugl-Meyer Assessment (FMA) and Wolf Motor Function Test (WMFT) to evaluate UE motor performance. Evaluations were performed at 7, 9, 10, 13, 20, and 21 months poststroke. Results: Motor performance scores trended towards improvement throughout the evaluation period. Dramatic improvement in motor performance occurred twice (ie, between 7 and 10 months post-stroke and between 20 and 21 months post-stroke). Decreases in contralesional map volume accompanied both incidences of dramatic improvement in motor performance. Additionally, contralesional volume decrease always accompanied ipsilesional volume increase and followed periods of intense motor training. Discussion: Our findings suggest that some areas of contralesional cortex that were formerly dedicated to control of the unaffected UE shifted function following stroke, perhaps enhancing control of the affected UE, but ceded control of the unaffected UE as the ipsilesional hemisphere was able to regain function. This case demonstrates that neuroplastic change and associated motor recovery can occur well past the early poststroke phase.

Supported by: This work was supported in part by NIH grant # 5R01HD056002 and the Cardinal Hill Rehabilitation Hospital Stroke and Spinal Cord Injury Endowment, # 0705129700.

Primary Presenter / e-mail: Chelette, K. C. / kenneth.chelette@uky.edu
Mentor or Senior Author / e-mail: Sawaki, L. / lumy.sawaki@uky.edu

113 **Abstract Title:** **Multidisciplinary Stroke Care and Quality Improvement**

Author(s):
A. J. Anderson, Department of Neurology, U of Kentucky
D. Y. Han, Department of Neurology, U of Kentucky

Abstract:
Introduction: Neuropsychological assessments can enhance both acute and chronic post-stroke management by identifying pertinent cognitive sequelae: 64% of stroke patients exhibit cognitive impairment and a third develop dementia (Hachinski et al., 2006). However, due to scheduling incompatibilities between traditional neuropsychology and stroke services in most settings, neuropsychological assessments often remain underutilized in stroke care. To address this, we developed a novel model of care that incorporated neuropsychological screening into comprehensive stroke care by utilizing the Vascular Cognitive Impairment (VCI) half-hour assessment protocol, proposed by the National Institute of Neurological Disorders and Stroke–Canadian Stroke Network (NINDS-CSN) VCI harmonization standards (Hachinski et al., 2006) and by analyzing subsequent patient/provider satisfaction. Methods: A Multidisciplinary Stroke Clinic (MSC) model was implemented by administering the NINDS-CSN VCI screening protocol before and after patient discharge from the stroke service. After a pilot year, modified Press Ganey scales (an industry standard) were used to assess patient and provider satisfaction. Results: Results from the 10-item provider surveys revealed high provider satisfaction with improved clinic efficacy, improved data turnaround time, and with the neuropsychology service's added value to the Comprehensive Stroke Service. Results from the 18-item surveys derived from Press Ganey showed all scores above 4.4/5.0 for patient satisfaction. Discussion: The MSC model was successfully associated with high provider and patient satisfaction after the pilot year. The NINDS-CSN VCI assessment protocol demonstrated high clinical utility, proving to be an efficient method of providing focused neuropsychological services in a clinical setting that is prohibitive for full, traditional cognitive assessments.

Supported by: Ambulatory Care Innovation Grant Physicians Plus and University of Wisconsin Medical Foundation

Primary Presenter / e-mail: Anderson, A. J. / aanderson@uwhealth.org
Mentor or Senior Author / e-mail: Han, D. Y. / d.han@uky.edu

114 **Abstract Title:** **Needs Assessment of People with Stroke in Appalachian Kentucky: A Theoretical Model**

Author(s):
S. Campbell, Department of Rehabilitation Sciences, U of Kentucky
M. Danzl, Department of Rehabilitation Sciences, U of Kentucky
K. Maddy, Department of Rehabilitation Sciences, U of Kentucky
V. Sylvia, Appalachian Regional Healthcare
B. Hunter, Director of Research, Cardinal Hill Rehabilitation Hospital
J. Kuperstein, Department of Rehabilitation Sciences, U of Kentucky
A.L. Harrison, Department of Rehabilitation Sciences, U of Kentucky

Abstract:
Kentucky Appalachian Rural Rehabilitation Network researchers are completing an assessment of the barriers to and facilitators of community re-integration for people with stroke and their caregivers in Appalachian Kentucky. A multi-modal approach of qualitative methodology with interpretative phenomenological analysis and a quantitative instrument, the Stroke Impact Scale, were used to study the lived experience of participants, their transition through the healthcare system, return to the community and life post stroke. The purpose of this presentation is to describe the team's theoretical approach to data collection, analysis and how the integration of existing theories can enrich the findings. Elements of the Social-Ecological Model were used to analyze data at the microsystem (individual, caregiver) and exosystem levels (health care, community)to determine if there were linkages between the two (mesosystem). Components of self-determination theory (autonomy, competence, relatedness) provide an additional framework for analysis. Finally, elements of social support theories were used to identify assets and needs to facilitate community re-integration. The collaboration of theory with participants' experiences supports the need for a competent mesosystem to link the microsystem and exosystem, facilitating self-determination across the continuum of care. Preliminary analysis demonstrates a sharp decline in mesosystem support once individuals are discharged home, a time when the need and readiness for learning appear to be at high levels. Future research will focus on how the development of the mesosystem may reduce medical costs by reducing the impact of secondary complications while improving quality of life for people affected by stroke in rural regions.

Supported by:
Primary Presenter / e-mail: Campbell, S. / scamp3@uky.edu
Mentor or Senior Author / e-mail: Harrison, A. / anne.harrison@uky.edu

115 **Abstract Title:** **The Neutrophil-Lymphocyte Count Ratio as a Predictor of Ischemic Stroke Prognosis**

Author(s):
C. C. Spears, School of Medicine, West Virginia University, Morgantown, WV
C. Cummings, Department of Neurology, West Virginia University, Morgantown, WV
La. Gutmann, Department of Neurology, West Virginia University, Morgantown, WV
J. Domico, Department of Interventional Neuroradiology, West Virginia University, Morgantown, WV
S. Culp, School of Nursing, West Virginia University, Morgantown, WV
J. Carpenter, Department of Interventional Neuroradiology, West Virginia University, Morgantown, WV
A. Rai, Department of Interventional Neuroradiology, West Virginia University, Morgantown, WV
T. Barr, School of Nursing, West Virginia University, Morgantown, WV

Abstract:
Biomarkers of stroke have been sought in order to improve clinical diagnosis, identify those at risk, and guide treatment. Literature supports a stroke-associated inflammatory process and studies have identified the neutrophil and lymphocyte counts as plausible parameters for the intensity of inflammation. The objective of this project was to identify the relationship between the neutrophil-lymphocyte count ratio (NLCR) and ischemic stroke prognosis. This was a retrospective analysis of patients who underwent endovascular therapy for acute ischemic stroke (AIS). WBC differentials were performed and recorded from the patient medical record then analyzed as a ratio (NLCR). Stroke severity was measured by the NIHSS and recovery by the mRS at 90 days. Univariate relationships between the NLCR, Infarct volume, and NIHSS were performed by correlation coefficients and for the NLCR and mRS t-test. Logistic regression was used to identify the ability of the NLCR to predict 90 day stroke outcome when controlling for age and infarct volume. 122 patients were reviewed and included in this analysis with a mean age of 66 years and 53% being female. Baseline NIHSS was 16 and mean 90-day mRS was 4. There was a significant relationship between the NLCR and 90 day mRS (t=-2.38; p=0.019) that remained when controlling for infarct volume and age (p=0.048). A higher PMN and lower lymphocyte count predicted death and worse stroke outcome. This study showed that the NLCR, a readily available and inexpensive test, may be utilized by clinicians as a tool for risk stratification in patients undergoing endovascular therapy.

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Primary Presenter / e-mail: Spears, C. C. / cspears@mix.wvu.edu
Mentor or Senior Author / e-mail: Barr, T. / TLBarr@hsc.wvu.edu

116 **Abstract Title:** **Validation of a Gene Expression Profile of Ischemic Stroke**

Author(s):
S. L. Rellick, School of Nursing and The Center for Neuroscience, WVU
R. VanGilder, School of Nursing, Dept Emergency Medicine and The Center for Neuroscience, WVU
M. Power, Dept of Neurology, WVU
P. Altemus, Dept of Neurology, WVU
L. Gutmann, Dept of Neurology, WVU
T. Crocco, Dept of Emergency Medicine, WVU
S. Davis, Dept of Emergency Medicine, WVU
T. L. Barr, School of Nursing and Depts of Emergency Medicine and the Prevention Research Center, WVU

Abstract:
In the Emergency Department, ischemic stroke poses diagnostic challenges and gene expression profiling may help to identify biomarkers and signaling pathways associated with ischemic stroke. Recently, we identified that 9 genes were differentially expressed in the whole blood of ischemic stroke patients that may be valuable for diagnosing ischemic stroke. In this current study, we are evaluating these 9 genes in different patient populations (ischemic stroke (IS) vs. transient ischemic attack (TIA) and stroke mimic) to determine if a unique gene panel can be identified for each group. Additionally, we are also evaluating serum and plasma expression of these proteins in the above patient populations. Gene expression profiling and protein analysis of these specific patient populations may potentially lead to novel therapeutic targets to diagnose and treat ischemic stroke as well as augment ischemic stroke recovery.

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Primary Presenter / e-mail: Rellick, S. L. / srellick@hsc.wvu.edu

Mentor or Senior Author / e-mail: Barr, T. L. / tlbarr@hsc.wvu.edu

117 **Abstract Title:** **Level of Nicotine Exposure Does Not Correlate with Human Serum Cathepsin-D Activity in Mid-Gestation**

Author(s):
C. F. Pearce, Departement of OB/GYN U of Kentucky
K. Y. Lain, Division MFM Norton Healthcare
L. Al-Alem, Department of OB/GYN U of Kentucky
R. I. Epstein, Department of OB/GYN U of Kentucky
S. H. Mast, Department of OB/GYN U of Kentucky
J. M. O'Brien, Department of OB/GYN U of Kentucky
K. S. Playforth, Department of OB/GYN U of Kentucky
W. F. Hansen, Department of OB/GYN U of Kentucky
T. E. Curry, Departmetn of OB/GYN U of Kentucky

Abstract:
Background: Activated cathepsin D is an enzyme important for the formation of anti-angiogenic prolactin fragments in human serum. Anti-angiogenic prolactin has been implicated in the pathogenesis of severe preeclampsia. Literature suggests that cathepsin D activity may be inhibited by nicotine. Preeclampsia risk has been reported to be decreased in a dose-dependent fashion in those pregnant women who smoke. We chose to examine the relationship of nicotine exposure (via cotinine levels) and cathepsin D activity in pregnancy at mid-gestation. Methods: Women between 16-22 weeks gestation were recruited who self-reported to be smokers (n=29) and non-smokers (n=31). Serum was obtained for measurement of cotinine and cathepsin D activity. Cotinine was reported in ng/ml after measurement with Immulite 2000. Cathepsin-D activity was reported as percentage of control well after fluorescence measurement with SensoLyte 520 Cathepsin D Assay Kit. Statistical analysis included Student's t-test, ANOVA, and linear regression. Results: There was no difference in the mean cathepsin D activity level between those women with cotinine exposure (495.89% ±1.44) and those without (475.33% ±1.07), p=0.53. Linear regression of cotinine and cathepsin D activity as continuous variables showed no trend, r-squared =0.0059. Discussion: In this sample at mid-gestation, smoking exposure is not associated with a decrease in serum cathepsin D activity. Though cathepsin D may still be implicated in the pathophysiology and even pathogenesis of preeclampsia, the attenuated risk of preeclampsia seen in smokers does not appear to be mediated in mid-gestation by a pathway of nicotine induced cathepsin D inhibition.

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Primary Presenter / e-mail: Pearce, C. F. / Christy.pearce@uky.edu

Mentor or Senior Author / e-mail: Curry, T. E. / tecurry@uky.edu

118 **Abstract Title:** **Pain Associated MicroRNAs in Women with Endometriosis**

Author(s):
C. Kocher, Dept of Pharmacology, Physiology, & Toxicology, Marshall University School of Medicine
C. Cook, Dept of Pharmacology, Physiology, & Toxicology, Marshall University School of Medicine
B. Dawley, Dept of Obstetrics & Gynecology, Marshall University School of Medicine
N. Santanam, Dept of Pharmacology, Physiology, & Toxicology, Marshall University School of Medicine

Abstract:
Endometriosis is the growth of endometrial tissue outside the uterus and is estimated in over 70-90% of women suffering from chronic pelvic pain. Though medical and surgical therapies are currently used to alleviate pain, high recurrence rates of the disease prevent adequate treatment. The exact causal link between endometriosis and pain is unclear. MicroRNAs are recently identified master regulators of gene expression making them ideal candidates for investigation in various diseases. The objective of this study was to investigate the causative factors that regulate pain in women with endometriosis; we therefore conducted a preliminary investigation on miRNAs that are altered depending on the pain status of the women with endometriosis. Identification of these miRNAs will help in understanding the etiology of endometriosis-associated pain. An IRB approved study was conducted to obtain eutopic or ectopic endometriotic tissue from: (i) women with endometriosis but no pain (ii) women with endometriosis and pain (iii) women with no endometriosis but with pain and (iv) women with no endometriosis and pain; attending MU Ob-Gyn clinic. An International pain questionnaire was administered to calculate the pain scores. Human whole genome miRNA microarray was performed on all tissues collected, followed by pathway analyses to identify miRNAs relevant to endometriosis and pain. Preliminary results identified miRNAs that were uniquely altered due to the pain symptom. Future plans include validation of the pain associated miRNAs identified through microarray analyses. In conclusion, we anticipate that identification of these miRNAs can be used as therapeutic targets for pain associated with endometriosis.

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Primary Presenter / e-mail: Santanam, N. / santanam@marshall.edu
Mentor or Senior Author / e-mail: Santanam, N. / santanam@marshall.edu

119 **Abstract Title:** **What Clinical Variables Predict the Onset of Cardiac Dysfunction in Preeclampsia?**

Author(s):
C. F. Pearce, Department of Obstetrics and Gynecology, U of Kentucky
D. S. McGehee, Department of Obstetrics and Gynecology, U of Kentucky
R. I. Epstein, Department of Obstetrics and Gynecology, U of Kentucky
S. H. Mast, Department of Obstetrics and Gynecology, U of Kentucky
K. S. Playforth, Department of Obstetrics and Gynecology, U of Kentucky
W.F. Hansen, Department of Obstetrics and Gynecology, U of Kentucky
J. M. O'Brien, Department of Obstetrics and Gynecology, U of Kentucky

Abstract:
Background: Preeclampsia affects 5% of pregnancies and can be associated with transient cardiac dysfunction in the peripartum period. Current diagnostic criteria do not predict severity or incidence of adverse maternal outcomes including cardiac dysfunction. We sought to determine what clinical variables seen on admission may predict cardiac dysfunction associated with preeclampsia. Methods: A retrospective case-control study of preeclamptic women admitted to our institution over a 2 year period. ICD-9 codes cross referenced with the echocardiography records identified charts for review. Patients diagnosed with preeclampsia who did not experience cardiac dysfunction were included as controls, and those with cardiac dysfunction diagnosed after preeclampsia were included as cases. Clinical variables recorded on the day of admission were compared. Statistical analysis included Student's t-test and Fisher's exact. A Bonferroni correction was used. Results: 112 controls and 8 cases were identified. Clinical variables found to be strong predictors of cardiac dysfunction in the setting of preeclampsia included systolic blood pressure (SBP)> 160 mmHg [OR 10.4], diastolic blood pressure (DBP)> 110 mmHg [OR 35.7], mean arterial pressure (MAP)> 126 mmHg [OR 7.7], the use of IV anti-hypertensives [12.3], chronic hypertension [9.2], uric acid>7.2 mg/dl [3.8], lactate dehydrogenase (LDH)> 234 U/L [8.3], and creatinine (CR)> 1 mg/dl [35.7]. Conclusions: Cardiac dysfunction in the setting of preeclampsia may be predicted by clinical variables that are indicative of cardiac strain, severity of disease, preexisting cardiac stress, or even evidence of pre-renal underperfusion.

Supported by: Department of Obstetrics and Gynecology U of Kentucky
Primary Presenter / e-mail: McGehee, D. S. / suzanne.mcgehee@uky.edu
Mentor or Senior Author / e-mail: O'Brien, J. M. / john.obrien2@uky.edu

120	Abstract Title:	**Attenuation of Methamphetamine-Induced Neurotoxicity and Genetic Alterations in the Striatum by Targeting Sigma Receptors**

Author(s): M. J. Robson, Department of Pharmaceutical and Pharmacological Sciences, West Virginia University
N. Kaushal, Department of Pharmaceutical and Pharmacological Sciences, West Virginia University
R. R. Matsumoto, Department of Pharmaceutical and Pharmacological Sciences, West Virginia University

Abstract:
Methamphetamine (METH) is an illicit drug whose chronic use is associated with striatal neurotoxicity and an increased risk of Parkinson's disease. Currently, there are no FDA approved medications for the treatment of METH-induced neurotoxicity. METH, in addition to interacting with classical monaminergic targets, binds to sigma receptors at physiologically relevant concentrations. The purpose of the current study was to determine if two selective sigma receptor ligands, AC927 and SN79, attenuate the neurotoxic effects of METH in the striatum of male, Swiss Webster mice. Repeated dosing with METH resulted in significant decreases in dopamine (DA) and dopamine transporters (DAT) in the striatum of these animals as measured by ultrasensitive DA ELISA kits and DAT immunohistochemistry. Pretreatment with AC927 or SN79 significantly attenuated METH-induced decreases in DA and DAT. To determine potential mechanisms by which sigma ligands attenuate METH-induced dopaminergic neurotoxicity, an exploratory study aimed at delineating the underlying genetic alterations associated with these effects was measured using Affymetrix microarrays and quantitative real-time PCR. Pretreatment with AC927 and SN79 resulted in the attenuation of METH-induced increases in glial fibrillary acidic protein (gfap), oncostatin m receptor (osmr) and leukocyte immunoglobulin-like receptor, subfamily B, member 4 (lilrb4) mRNA expression prior to the manifestation of striatal neurotoxicity. Results from the current study suggest that METH-induced genetic alterations related to reactive gliosis and immunological responses contribute to neurotoxicity in the striatum. Moreover, selective sigma receptor ligands attenuate dopaminergic neurotoxicity and transcriptional changes associated with METH.

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Primary Presenter / e-mail: Robson, M.J. / mjrobson@hsc.wvu.edu
Mentor or Senior Author / e-mail: Matsumoto, R. R. / rmatsumoto@hsc.wvu.edu

121	Abstract Title:	**Balancing Disease Management and Prevention Counseling with Complex Patients: Challenges and Opportunities**

Author(s): S. H. Bardach, Graduate Center for Gerontology, U of Kentucky
N. E. Schoenberg, Department of Behavioral Science, U of Kentucky

Abstract:
The prevalence of multiple health conditions or multiple morbidity (MM) is increasing. Providing medical care for adults with MM presents challenges, including balancing disease management with prevention. We conducted in-depth semi-structured interviews with 12 primary care physicians to explore their perspectives on prevention counseling among patients with MM. Participants described the complex relationship between disease management and prevention, highlighted the importance of patient motivation, and discussed various strategies to promote receptivity to prevention recommendations. The perceived potential benefits of prevention recommendations encouraged physicians to persist with such counseling, despite challenges presented by visit time constraints and reimbursement procedures and concerns over futility. Physicians recommended the development of alternate care delivery and reimbursement models to overcome challenges of the existing health care system and meet the prevention needs of patients with MM. We explore implications of these findings for maximizing the health and quality of life of adults with MM.

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Primary Presenter / e-mail: Bardach, S. H. / shbardach@uky.edu
Mentor or Senior Author / e-mail: Schoenberg, N. E. / nesch@uky.edu

122 **Abstract Title:** **Characterizing Vocal Development in Pre-pubertal Children**

Author(s): H. Unnikrishnana, Center for Visualization and Virrual Environments, College of Engineering, U of Kentucky
K. D. Donohue, Center for Visualization and Virrual Environments, College of Engineering, U of Kentucky
R. R. Patel, Department of Rehabilitation Sciences, U of Kentucky

Abstract:
Nationwide over 6-9% of children suffer from dysphonia that can be detrimental both psychologically and academically, hence early identification and restoration of optimal vocal health is critical. Objective assessments of pediatric vocal physiology are non-existent, leading to delayed diagnosis and deferred treatments. The goal of this prospective study is to identify the impact of growth and development of the layered structure of the vocal folds on vocal physiology. Vocal fold oscillations recorded at 4000 frames per second from high speed imaging of 33 children (Girls = 13, Boys = 20) and 32 adults (Male = 14, Female = 18) were analyzed. Custom developed vocal fold edge displacement waveforms extracted features related to related to normal phonation (greater than 25 cycles). Reduction of quantization errors for extracting features was achieved by using a novel denoising and hybrid interpolation / extrapolation scheme. Features included those previously reported, such as open quotient, speed quotient, phase asymmetry, and pitch frequency, in addition to novel features related to closure displacement, velocity and acceleration ratios at fold opening, closing, and maximum extension. Statistical analysis revealed significant differences for features related to impact stress such as the fold velocity and acceleration, as well as the closure displacement, which may help explain the higher occurrence of vocal fold nodules in children. This work is first to examine physiological biomarkers of unique vibratory features of vocal development which will lay the foundation for development of biomechanical modeling and assessment tools to identify children at risk of developing voice disorders.

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Primary Presenter / e-mail: Patel, R. / rita.patel@uky.edu

Mentor or Senior Author / e-mail: Donohue, K. / donohue@engr.uky.edu

123 **Abstract Title:** **Concurrent Conditioned Place Preference for Amphetamine vs. Social Interaction in Adolescent Rats**

Author(s): J. R. Yates, Department of Psychology and Center for Drug Abuse Research Translation, U of Kentucky
J. S. Beckmann, Department of Psychology and Center for Drug Abuse Research Translation, U of Kentucky
A. C. Meyer, Department of Psychology and Center for Drug Abuse Research Translation, U of Kentucky
M. T. Bardo, Department of Psychology and Center for Drug Abuse Research Translation, U of Kentucky

Abstract:
Although social influences contribute to drug use, social interactions are important in the treatment of substance-use disorders. In a preclinical model of abuse, social interaction reverses cocaine reward. However, it is unclear whether this reversal was the result of social interaction or the novelty of the social partner. The current experiment examined concurrent conditioned place preference (CPP) for amphetamine vs. social interaction in adolescent rats that were either individually or pair-housed. Twenty-four male, Sprague Dawley rats were allowed to explore a three-compartment CPP apparatus during a 15-min session at postnatal day 28. Individually (n=6) or pair-housed (n=6) rats received four conditioning sessions in which social interaction was paired with one side of the CPP chamber and four sessions in which injections of amphetamine (1 mg/kg) were paired with the other side of the CPP chamber. Subsets of pair-housed rats (n=6 per group) received conditioning sessions with (a) amphetamine or (b) social interaction paired with one side of the CPP chamber and conditioning sessions with saline paired with the other side of the CPP chamber. Following conditioning, rats were allowed to explore both ends of the CPP chamber. Individually housed rats spent more time in the compartment previously paired with social interaction, whereas pair-housed rats spent more time in the compartment paired with amphetamine. These results indicate that the therapeutic effects of social interaction observed in previous preclinical reports may be explained by novelty of the social partner, rather than to social interaction per se.

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Primary Presenter / e-mail: Yates, J. R. / yates0615@gmail.com

Mentor or Senior Author / e-mail: Bardo, M. T. / mbardo@email.uky.edu

124 **Abstract Title:** **Development and Initial Testing of a Brief Patient Health Literacy Screening Tool: The BHLS**

Author(s): K. Sand-Jecklin, School of Nursing, West Virginia University
S. Coyle, School of Nursing, West Virginia university

Abstract:
Introduction: Patient health literacy limitations are associated with many negative health outcomes. Older adults and individuals with lower education/income levels (including many Appalachian residents) are at high risk for having low health literacy levels. Studies indicate that healthcare providers correctly identify only about ½ of their patients who have health literacy limitations. Most health literacy assessment tools are unwieldy for use in busy hospital or clinic settings, or address only ability to understand written health information. A simple, yet effective tool is needed to help providers identify patients with limited health literacy. This study explored the feasibility of using a newly developed Brief Health Literacy Scale (BHLS) to identify health literacy limitations among rural West Virginia clinic patients. Methods: 100 adults attending four rural WV health clinics completed the BHLS and the Test of Functional Health Literacy in Adults Short Version (S-TOFHLA), and answered questions about both tools. Results: Participant mean age was 44 years, and median education level was high school graduate. The majority of participants were native West Virginians, Caucasian, and unemployed or retired. Response consistency to the BHLS was strong (Cronbach's alpha = .79). There were significant correlations between BHLS and S-TOFHLA scores, with higher correlations between BHLS items addressing written health literacy and the S-TOFHLA. Comparative discrimination findings were significant at BHLS cut-point of 18 and STOFHLA cut-point of <23. Patients rated the BHLS significantly less difficult to complete than the S-TOFHLA. Discussion/Conclusion: Initial testing indicates that the BHLS is an efficient, effective, and patient-friendly screening tool for health literacy.

Supported by:
Primary Presenter / e-mail: Sand-Jecklin, K. / ksandjecklin@hsc.wvu.edu
Mentor or Senior Author / e-mail: Sand-Jecklin, K. / ksandjecklin@hsc.wvu.edu

125 **Abstract Title:** **Development of Disulfiram Metabolites for the Treatment of Alcohol Abuse, Prevention of Noise-Induced Hearing Loss, and Treatment of Malaria**

Author(s): J. V. Schloss, Department of Pharmaceutical Science and Research, School of Pharmacy, Marshall U

Abstract:
Since 1950 disulfiram has been used to assist recovering alcoholics maintain sobriety. The therapeutic effectiveness of disulfiram is thought to be mediated by inhibition of aldehyde dehydrogenase, which induces alcohol intolerance. Disulfiram also prevents noise-induced hearing loss, which is achieved by partial down-regulation of glutamate receptors of the NMDA subtype. Disulfiram has been reported to kill Plasmodium falciparum in infected human red blood cells. None of these effects are achieved directly by disulfiram in vivo. N,NDiethylthiocarbamate S-methyl sulfoxide (DETC-MeSO) is responsible for inhibition of aldehyde dehydrogenase and the alcohol aversive effect of disulfiram. DETC-MeSO is also responsible for the anti-malarial activity of disulfiram. S-(N,N-Diethylthiocarbamoyl)glutathione (carbamathione) is responsible for down-regulation of NMDA receptors. The stability, bioavailability, and other issues affecting the future development of DETC-MeSO, carbamathione, other disulfiram metabolites, and their analogs will be presented.

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Primary Presenter / e-mail: Schloss, J. V. / schloss@marshall.edu
Mentor or Senior Author / e-mail: Schloss, J. V. / schloss@marshall.edu

126 **Abstract Title:** **Do Sound Conditions of Operating Rooms (ORs) Negatively Impact Performance in OR Personnel?**

Author(s): A.A. Long, Department of Otolaryngology, U of Kentucky
J. Way, Department of Otolaryngology, U of Kentucky
J. Shinn, Department of Otolaryngology, U of Kentucky

Abstract:
It has been demonstrated that the typical operating room averages approximately 65 dBA of ambient noise with peak levels reaching as high as 120 dBA (Love, 2003). This has been seen as problematic because patients and personnel may be exposed to dangerous levels of noise over an extended period of time. What is of equal concern is the negative impact of OR noise related to hearing and overall communication. The purpose of this study is to determine if the sound conditions of the OR negatively impact performance in OR personnel (nurses and surgeons). We hypothesize that as the hearing environment and related tasks become more complex, performance will significantly decline. This study will have significant impact on determining auditory performance in a setting with less than ideal acoustics and critical demands on communication. This will lead to recommendations regarding modifications to the environment and personnel in order to maximize hearing and communication, and improve patient safety. This study seeks to determine if conditions of the OR, including ambient OR noise and music, present as a negative variable in the OR suite to personnel involved in patient care. Additionally, this study seeks to quantify the different degrees of contribution by each of the associated variable on auditory function.

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Primary Presenter / e-mail: Long, A. A. / aalong2@uky.edu
Mentor or Senior Author / e-mail: Shinn, J. / jennifer.shinn@uky.edu

127 **Abstract Title:** **Geriatric Depression in a Rural Clinic Population**

Author(s): A. Mani, East Kentucky Family Medicine Residency Program, Hazard, KY
T. Knox, U of Kentucky, Hazard, KY

Abstract:
Background: Depression affects 15-20 % of Americans aged 65 and older. Depression is often reversible with appropriate treatment. Depression results in cognitive and social impairment, increased health care utilization, disability and suicide. Objectives:1)To obtain a baseline demographic and socioeconomic profile of the elderly aged 65-89 receiving primary care at a Community Health Center. 2) To determine the proportion of elderly with depression as measured by Geriatric Depression Scale-15 (GDS-15). 3) To enumerate the factors associated with elderly depression. Methods: A total of 142 patients aged 65-89 were analyzed for depression using the GDS-15 and a socio-demographic questionnaire. Results: The majority of participants were females (58% vs. 42%) and in the 65-69 age range. Of this sample, 53.7% reported chronic disease and 55.4% acknowledged disability. Mean GDS -15 score was 3.92, with 34.5% of participants falling within the depressive range. Of those who scored positive for depression, 48% were not on anti-depressants. Low educational status, living alone, disability, stress and use of antidepressants were significantly associated with depression (Multiple Logistic Regression analysis). Discussion: This population of elderly rural patients with depression far exceeds prevalence rates found with other samples. In addition, this sample was under-diagnosed and inadequately treated. Conclusion: Rural family physicians should screen the elderly for depression, inquire about social risk factors for depression and adjust medications as needed. Rural physicians should also involve family members in the treatment of the elderly and encourage elderly participation in spiritual, community and social organizations.

Supported by:
Primary Presenter / e-mail: Mani, A. / anju.mani@uky.edu
Mentor or Senior Author / e-mail: Knox, T. / tamara.knox@uky.edu

128	**Abstract Title:**	**Glial cell line-derived neurotrophic factor (GDNF) Replacement Improves Parkinsonism in Middle-aged Mice with a Partial GDNF Depletion (Gdnf+/-)**

Author(s):
O.M. Littrell, Department of Anatomy and Neurobiology, U of Kentucky
H.A. Boger, Department of Neurosciences, Medical U of South Carolina
F. Pomerleau, Department of Anatomy and Neurobiology, U of Kentucky
P. Huettl, Department of Anatomy and Neurobiology, U of Kentucky
A-Ch Granholm, Department of Neurosciences, Medical U of South Carolina
G.A. Gerhardt, Department of Anatomy and Neurobiology, U of Kentucky

Abstract:
A functional loss of midbrain dopamine (DA) neurons in the substantia nigra (SN) is a hallmark feature of Parkinson's disease (PD), a neurodegenerative movement disorder. In addition, a loss of DA-neuron function and motor impairment are seen in animal models of aging and human aging – termed age-associated parkinsonism. Because glial cell line-derived neurotrophic factor (GDNF) treatment appears to enhance measures of DA-neuron function, DA-neuron function has been investigated in mice with a genetic reduction of GDNF (GDNF heterozygous/Gdnf+/-). Middle-aged Gdnf+/- mice display age-related locomotor deficits and fewer DA neurons in the SN than age-matched WT mice. GDNF replacement in Gdnf+/- mice was investigated to test the hypothesis that age-related decreases in DA-neuron function and motor function are improved by GDNF treatment. Gdnf+/- mice (n=13) and age-matched WT littermate mice (n=9) were treated with GDNF. Spontaneous locomotor activity was determined weekly (1-4 weeks after treatment) for GDNF- and vehicle-treated mice of both genotypes. Locomotor behavior was higher after GDNF treatment in Gdnf+/- and WT mice. However, the effect of GDNF was prolonged in Gdnf+/- mice [2(genotype) x 2(treatment) x 4(intervals) mixed-factor ANOVA with repeated measures on the interval factor, genotype x treatment ($F_{1,79}$= 5.114, *p = 0.0265), treatment x time ($F_{3,79}$ = 9.255, ***p < 0.0001)]. GDNF treatment also increased markers of DA-neuron function in the SN of Gdnf+/- mice (***p < 0.001 versus vehicle, one-way ANOVA). These studies support that GDNF treatment is a potential therapy for functional deficits associated with a chronic and partial GDNF depletion in middle-aged Gdnf+/- mice i.e. DA-neuron- and motor-dysfunction.

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Primary Presenter / e-mail: Littrell, O. M. / omlitt2@uky.edu
Mentor or Senior Author / e-mail: Gerhardt, G. A. / gregg@email.uky.edu

129	**Abstract Title:**	**Health-related Quality of Life and Risky Sexual Behaviors in Adolescent and Young Adult Female Childhood Cancer Survivors**

Author(s):
J.A. Rodocker, Department of Psychiatry, U of Kentucky
K.M. Lommel, Department of Psychiatry, U of Kentucky
E. Van Meter, Kentucky Pediatric Research Institute, Markey Cancer Center Biostatistics Shared Resource Facility, U of Kentucky
A. Wiggins, Kentucky Pediatric Research Institute, Markey Cancer Center Biostatistics Shared Resource Facility, U of Kentucky
M. Tucker, Kentucky Pediatric Research Institute, Markey Cancer Center Biostatistics Shared Resource Facility, U of Kentucky

Abstract:
Objective: To determine reported risky sexual behaviors and health-related quality of life (HRQOL) in adolescent and young-adult female childhood cancer survivors. Methods: This cross-sectional case-control study enrolled 90 adolescent and young-adult female childhood cancer survivors (Mean current age 24 ± 6.38 and mean age at diagnosis 12 ± 6.41). Demographic and other independent variables were obtained in a survey format. Participants were recruited through the Kentucky Cancer Registry (KCR) housed within the University of Kentucky. The KCR provided date of birth, diagnosis, age at diagnosis, and treatment modality. All participants completed three questionnaires including self-reported demographics, the Health and Well-Being Questionnaire (SF-36v2), and the Adolescent Risk Inventory (ARI). Results: SF-36v2 normalized component scores were dichotomized into good (>40) and poor (≤40) health status. Risk scores were calculated by the sum of risky behavior responses from 25 questions in the ARI and then categorized by risk status. Results from a Chi-Squared test for association indicates a significant association between risk status and SF-36 component status (Poor vs. Good) for Role Physical, Role Emotional, Vitality, Mental Health, Social Functioning, Bodily Pain and overall Mental Component Scores. Higher proportions of high-risk status are found in those with poor component status compared to those with good. Conclusions: Female survivors of childhood cancer with an overall poor health-related Quality of Life (HRQOL) are more likely to exhibit risky sexual behaviors and attitudes. Further investigation is needed to develop an intervention to target the area risky sexual behaviors in this cohort.

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Primary Presenter / e-mail: Rodocker, J. A. / aaron.rodocker@uky.edu
Mentor or Senior Author / e-mail: Lommel, K. M. / karen.lommel@uky.edu

130 **Abstract Title:** **Impulsivity and Risky Sexual Behavior Among Rural Probationers Abusing Prescription Drugs**

Author(s): PK Elliston, Center on Drug and Alcohol Research, U of Kentucky
J. Matthew Webster, Dept of Behavioral Science & Center on Drug and Alcohol Research, U of Kentucky
Carl Leukefeld, Dept of Behavioral Science & Center on Drug and Alcohol Research, U of Kentucky

Abstract:
Impulsivity has been found to be associated with risky sexual behavior (Hayaki et al., 2006) and illicit drug use (Moeller & Dougherty 2002). Previous studies have found associations between impulsivity and risky sexual behavior in cocaine and heroin users (Lejuez et al 2005), as well as methamphetamine users (Semple et al., 2005), but none to our knowledge have examined the association between impulsivity, risky sexual behavior, and the growing problem of illicit prescription drug use. Criminal justice populations have higher levels of HIV risk behaviors, which include unprotected sexual activity and injection drug use (Sabol & Couture 2008). In addition, they may have higher levels of impulsivity, which contribute to these risk behaviors (Moffit 1993). The current study examines the association between impulsivity and risky sexual behavior among rural probationers who misuse prescription drugs (N=416). A hierarchical multiple regression analysis was used to assess how much of the variance in risky sexual behaviors was attributable to impulsivity after controlling for age, gender, and injection drug use. The addition of impulsivity to a model containing only the control variables significantly increased the amount of explained variance ($\Delta R2$ change = .023, $F(4, 408) = 25.96$, $p < .001$). Findings suggest that interventions to reduce risky sex behaviors among drug abusers should incorporate impulsivity. This research was supported by NIDA grant # R01DA11580.

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Primary Presenter / e-mail: Elliston, PK / pk.elliston@uky.edu

Mentor or Senior Author / e-mail: Webster, J. M. / webster@uky.edu

131 **Abstract Title:** **Individual Differences in the Central Control of Vocalization During Stressor Exposure**

Author(s): M. Dietrich, Department of Rehabilitation Sciences, U of Kentucky
R. D. Andreatta, Department of Rehabilitation Sciences, U of Kentucky
Y. Jiang, Department of Behavioral Science, U of Kentucky
A. Joshi, Department of Rehabilitation Sciences, U of Kentucky
J. C. Stemple, Department of Rehabilitation Sciences, U of Kentucky

Abstract:
The objectives of the study were to investigate (1) the relation between limbic system function and the cortical control of voice in a group of vocally healthy speakers under an imposed psychological stress condition and (2) individual differences in the cortical control of voice during stress as a function of psychobiological characteristics. The hypotheses were that stressor-induced limbic activity affected the central control of vocalization and that individual differences in stress responding played a role. Thirteen vocally healthy female adults (18-35 years) participated in a fMRI study using an event-related sparse sampling design to acquire brain activation data during sentence production tasks (whispered, overt). The participants produced short sentences with and without exposure to a social-evaluative stressor and were evaluated on personality characteristics. In response to stressor exposure, decreased blood oxygenation level dependent activity was observed in the dorsolateral prefrontal cortex, orbitofrontal cortex, anterior cingulate cortex, and hippocampus, which was also accompanied by decreases in sensorimotor cortical activity. Introversion scores were significantly correlated with lower activity in the primary motor cortex and higher activity in BA32 and the periaqueductal gray. Neuroticism scores were also significantly correlated with higher activity in the BA32. The data will be complemented by physiological measures collected during the experiment (salivary cortisol, heart rate) and respective data on individual differences in stress responding. The findings are intriguing with respect to functional consequences for voice production considering the structural and reciprocal functional connectivity of the laryngeal motor cortex with the dlPFC and cingulate cortex.

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Primary Presenter / e-mail: Dietrich, M. / maria.dietrich@uky.edu

Mentor or Senior Author / e-mail: Andreatta, R. D. / randr2@email.uky.edu

132 **Abstract Title:** **Intranasal Hydrocodone-Acetaminophen Abuse Induced Necrosis of the Nasal Cavity and Pharynx**

Author(s): D. Alexander, College of Medicine, U of Kentucky
K. Alexander, Otolaryngology, Central Baptist Hospital
J. Valentino, Department of Otolaryngology, U of Kentucky

Abstract:
Objectives: Two million new users will abuse prescription narcotics this year, most commonly hydrocodone. The most commonly prescribed form is hydrocodone-acetaminophen (HA). Many individuals crush the tablets and snort the product to take advantage of the rapid trans mucosal delivery of narcotics. The resultant pathology of intranasal hydrocodone acetaminophen abuse (INHAA) has been described only in a few case studies. Study Design: Retrospective chart review. Methods: Two private and one academic otolaryngology practice in Kentucky searched their patient charts for patients with morbidity from intranasal abuse of hydrocodone acetaminophen tablets. We identified thirty-five patients who presented for treatment between 2004 and 2011 constituted the subjects of this study. Results: The majority of patients will initially deny the behavior frequently delaying diagnosis. Physical exam findings of white powder covering an underlying nasal mucosal necrosis are characteristic of this condition during active INHAA. Follow up was limited as only 26% returned for follow up care. Patients commonly presented with orofacial-nasal pain (43%) and sino-nasal congestion and discharge (43%). Active necrosis or prior tissue loss was noted in 77% of patients. Fifty-one percent of patients presented with septal perforations, and 26% with palatal perforations. Two cases of invasive fungal sinusitis were clearly documented with one resulting in death. Conclusions: The vast majority of cases presented with characteristic acute necrosis of soft tissue that can progress to destroy bony oronasal structures. In the absence of invasive fungal disease, the condition is self-limited after cessation INHAA and local nasal debridement and hygiene.

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Primary Presenter / e-mail: Alexander, D. / dkalex2@uky.edu
Mentor or Senior Author / e-mail: Valentino, J. / jvale00@email.uky.edu

133 **Abstract Title:** **Intranasal oxycodone self-administration in sporadic opioid abusers**

Author(s): L.S. Middleton, Dept of Behavioral Science, Center on Drug & Alcohol Research, U of Kentucky
P.A. Nuzzo, Center on Drug & Alcohol Research, U of Kentucky
M.R. Lofwall Depts of Behavioral Science and Psychiatry, Center on Drug & Alcohol Research, U of Kentucky
A.J. Siegel, Dept of Psychiatry, U of Kentucky
S.L. Walsh, Deps of Behavioral Science and Psychiatry, Center on Drug & Alcohol Research, U of Kentucky

Abstract:
Oxycodone, an opioid with known abuse liability, is misused by the intranasal route. Our objective was to develop a model of intranasal oxycodone self-administration useful for assessing the relative reinforcing effects of opioids and potential pharmacotherapies for opioid use disorders. Healthy, sporadic intranasal opioid abusers (n=8) completed this inpatient 2.5-week, randomized, double blind, placebo-controlled, crossover study. Each intranasal oxycodone dose (0, 14 & 28 mg) was tested in a separate 3-day block of sessions. The first day of each block was a sample session in which the test dose was given. Two randomized progressive ratio sessions were conducted on the next 2 days: 1) subjects could work for the test dose over 7 trials (1/7th of total dose/trial), and 2) subjects could work for either a portion of the dose (1/7th) or money ($3) over 7 trials. Physiological and subjective measures were collected before and after drug administration for all sessions. Subjects never worked to self-administer placebo regardless of whether money was available. In both self-administration sessions, oxycodone self-administration was dose-dependent. Subjects worked less for drug (28 mg oxycodone) when money was available, but only modestly so. Oxycodone dose-dependently increased VAS ratings of positive drug effects (e.g., 'like') during sample sessions ($p<0.05$). These reports were positively correlated with self-administration behavior (e.g., 'like', $r=0.65$). These data suggest that both procedures are sensitive for detecting the reinforcing properties of intranasal oxycodone and may be employed to further explore the characteristics of opioid compounds and potential pharmacotherapies for treatment.

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Primary Presenter / e-mail: Middleton, L. S. / lisa.middleton@uky.edu
Mentor or Senior Author / e-mail: Walsh, S. L. / sharon.walsh@uky.edu

134 **Abstract Title:** **Novel Mixed Mu/Delta Opioid Analgesic Agents Aimed at Reducing Chronic Tolerance Liability**

Author(s):
J. R. Healy, Basic Pharmaceutical Sciences, West Virginia University, Morgantown, WV
P. Bezawada, Department of Pharmaceutical Sciences, University of Maryland, Baltimore, MD
T. A. Smith, Department of Pharmaceutical Sciences, University of Maryland, Baltimore, MD
M. Metcalf, Department of Pharmaceutical Sciences, University of Maryland, Baltimore, MD
C. Cunningham, Department of Pharmaceutical Sciences, University of Maryland, Baltimore, MD
S. Kudrimoti, Department of Pharmaceutical Sciences, University of Maryland, Baltimore, MD
A. Coop, Department of Pharmaceutical Sciences, University of Maryland, Baltimore, MD
R. R. Matsumoto, Basic Pharmaceutical Sciences, West Virginia University, Morgantown, WV

Abstract:
The three opioid receptor subtypes mu, delta and kappa have long been associated with analgesia. Traditional opioid analgesics exert their effects through mu receptors located in the CNS; yet, side effects, including chronic tolerance, are problematic. Therefore, there is a pressing need to identify a pharmacological agent that maintains potent analgesic properties while alleviating these adverse effects. Recent studies suggest that the development of an agent displaying dual properties of mu agonism and delta antagonism could be of benefit to individuals who require chronic administration of opioid analgesics. We hypothesize that our chemical design rationale will produce compounds that elicit said pharmacological profile, thereby inducing analgesia with a reduction in chronic tolerance. A variety of novel compounds have been tested for their affinity at the respective opioid receptor subtypes. Of significance, our data indicates that UMB 425 and 426 display high affinity at the mu receptor and moderate affinity at the delta receptor, with moderate to low affinity at the kappa receptor. In vitro [35S]GTPγS functional assay results indicate that UMB 425 and 426 behave as partial agonists at the mu receptor, whilst having antagonistic properties at the delta receptor. In vivo animal assays were conducted to identify the analgesic properties of UMB 425. Early indications suggest that UMB 425 produces similar analgesic effects to that of morphine itself, while producing a longer analgesic response. In the near future, in vivo assays will be conducted to determine the level of tolerance induced by UMB 425 compared to traditional opioid analgesics.

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Primary Presenter / e-mail: Healy, J. R. / jrhealy@hsc.wvu.edu
Mentor or Senior Author / e-mail: Matsumoto, R. R. / rmatsumoto@hsc.wvu.edu

135 **Abstract Title:** **Observed Affect Provides Caregivers Clinically Valid Information About the Stresses Experienced by Institutionalized Persons with Dementia**

Author(s):
G. Ice, Department of Social Medicine, Ohio U Heritage College of Osteopathic Medicine
A. Farbman, OMS II, Ohio U Heritage College of Osteopathic Medicine
D. Mann, Department of Social Medicine, Ohio U Heritage College of Osteopathic Medicine

Abstract:
Background: Institutionalized persons with dementia experience difficulty communicating their needs to caregivers, which can hinder the identification of environmental stressors and other threats to quality-of-life. Furthermore, quality-of-life interventions can be difficult to evaluate in a naturalistic setting. Several observational instruments allow caregivers and researchers to reliably and reproducibly identify changes in affect and behavior, but the relationship between these evaluations and underlying physiological states is not well understood. We chose sympathetic and corticosteroid activations as markers of a stress response, and attempted to correlate continuous measurements of heart rate, blood pressure, and salivary cortisol with simultaneous affect and behavior observation to determine whether naturalistic observation was a valid proxy tool for investigating environmental stressors and interventions. Methods: 42 nursing-home residents with dementia were followed for four-hour blocks on each of three days by trained observers, who recorded their location and body posture, and rated their affect and behavior according to the Philadelphia Geriatric Center's Observed Affect Rating Scale and the Cohen-Mansfield Behavior Inventory. Subjects wore an ambulatory blood pressure monitor set to record at 15-minute intervals, and salivary cortisol samples were taken at the midpoint and at the end of each period. Results: Fear/Anxiety, as identified by the OARS, was associated with sympathetic and corticosteroid activation, as compared with Neutral Affect. ($p<0.001$) No other affect, posture, location, or behavior other than sleeping was associated with a significant physiologic stress response. Overall frequency of anxiety and average cortisol showed some association with disease progression and supportive interventions. Conclusions: Affect rating by trained observers shows promise as a tool for the assessment of stress markers in institutionalized subjects with dementia.

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Primary Presenter / e-mail: Farbman, A. / af708209@ohio.edu
Mentor or Senior Author / e-mail: Ice, G. / iceg@ohio.edu

136 **Abstract Title:** **Patient- and Family-Centered Rounds on a Geriatric Inpatient Service: Patient Perspectives**

Author(s): A. M. Stecher, U of Cincinnati College of Medicine
J. Schlaudecker, The Christ Hospital/U of Cincinnati Family Medicine Residency Program

Abstract:
Patient- and family-centered rounds (PFCR) is a model for empowering patients and families and improving communication and care in an academic, inpatient setting. In contrast to traditional rounding, PFCR occurs at the bedside and actively includes patients and their families, encouraging genuine collaboration to determine best care. While well studied in the pediatric setting, little is known about the application of PFCR to the geriatric population. In this study, fourteen older adults (mean = 68 years) admitted to the Christ Hospital received either traditional care or PFCR during their stay. Patients and their families were asked to participate in interviews focusing on satisfaction with overall care and communication with their hospital healthcare team. Follow-up interviews were performed approximately three weeks following discharge. Both interviews consisted of open-ended questions followed by the rating of statements using a Likert scale. Patients had a very positive reaction to the PFCR, one commenting, for example, that, "I felt I wasn't alone and someone was in my corner, trying to find out what was happening in my body," and another commenting that, "[with PFCR] you feel like not only do they care about you as a person but… about your opinion." No significant difference was seen in the Likert ratings between those receiving traditional care and PFCR; however, the ratings for PFCR were very positive with, for example, 100% of patients agreeing or strongly agreeing with the statement, "My questions were answered during the bedside rounding process." The positive responses of those receiving PFCR indicate that PFCR can lead to positive outcomes for geriatric patients and more research should be done with a larger sample to determine how these outcomes compare with traditional care.

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Primary Presenter / e-mail: Stecher, A. M. / anna.m.stecher@gmail.com
Mentor or Senior Author / e-mail: Schlaudecker, J. / jeff.schlaudecker@gmail.com

137 **Abstract Title:** **Pharmacological Characterization of Sigma-2 Preferring Compounds: Implications for Cocaine-induced Behaviors**

Author(s): B. Noorbakhsh, Department of Basic Pharmaceutical Sciences, West Virginia U, Morgantown, WV
M. Seminerio, Department of Basic Pharmaceutical Sciences, West Virginia U, Morgantown, WV
Y. XU, Department of Basic Pharmaceutical Sciences, West Virginia U, Morgantown, WV
C. Mesangeau, Department of Medicinal Chemistry, U of Mississippi, University, MS
C.R. McCurdy, Department of Medicinal Chemistry, U of Mississippi, University, MS
R.R. Matsumoto, Department of Basic Pharmaceutical Sciences, West Virginia U, Morgantown, WV

Abstract:
Cocaine is a powerful psychostimulant that is highly abused by 1.9 million people in the United States. It remains one of the most abused illicit drugs, yet no pharmacological treatments currently exist. Many attempts at finding a pharmacotherapy for cocaine abuse and addiction have been made but have proven unsuccessful. Cocaine is known to bind sigma receptors at physiologically relevant concentrations, deeming them potential targets for cocaine pharmacotherapies. Two subtypes of sigma receptors have been described, sigma-1 and sigma-2. Sigma-1 receptor antagonists have shown to attenuate cocaine-induced convulsions and locomotor hyperactivity. Minimal information is known about the function of sigma-2 receptors in relationship to cocaine-induced effects. This is attributed to the inability to clone the subtype and the absence of highly selective ligands. In the present study, four novel compounds (CM699, CM398, CM777 and CM775) were found to possess substantially high affinities for sigma-2 receptors versus sigma-1 and non-sigma receptor sites. Behavioral studies, performed in male, Swiss-Webster mice, showed that pretreatment of the putative antagonists CM398, CM777 and CM775 to a convulsive or stimulatory locomotor dose of cocaine led to significant attenuation of cocaine-induced convulsions and hyperactivity. Additionally, administration of pretreatment doses of the putative agonist, CM699, to non-convulsive doses of cocaine led to the occurrence or exacerbation of cocaine-induced convulsions. The availability of these sigma-2 receptor preferring compounds provide pharmacological tools to elucidate the relationship between sigma-2 receptors and cocaine effects. Furthermore, the putative antagonists represent potential pharmacological treatments for cocaine abuse and addiction.

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Primary Presenter / e-mail: Noorbakhsh, B. / bnoorbakhsh@hsc.wvu.edu
Mentor or Senior Author / e-mail: Matsumoto, R. R. / rmatsumoto@hsc.wvu.edu

138 **Abstract Title:** **Relative Reinforcing Efficacy and Abuse Liability of Oral Tramadol in Humans**

Author(s): S. Babalonis, Dept. of Behavioral Science, Center for Drug and Alcohol Research, U of Kentucky
M. R. Lofwall, Dept. of Psychiatry, Center for Drug and Alcohol Research, U of Kentucky
A. J. Siegel, Dept. of Psychiatry, U of Kentucky
P. A. Nuzzo, Center for Drug and Alcohol Research, U of Kentucky
S.L. Walsh, Dept. of Behavioral Science, Center for Drug and Alcohol Research, Dept. of Psychiatry, U of Kentucky

Abstract:
Aims: Tramadol, a monoaminergic reuptake inhibitor, is metabolized hepatically to an opioid known as M1. This atypical opioid analgesic is generally considered to have limited abuse liability and is not scheduled by the DEA. Recent reports of its abuse have increased, leading to more stringent scheduling in some U.S. states. The purpose of this study was to examine the relative abuse liability and reinforcing efficacy of tramadol to both a high (oxycodone) and low efficacy opioid agonist (codeine). Methods: Healthy, non-dependent prescription opioid abusers (n=9) participated in this within-subject, randomized, double blind, placebo-controlled study. A total of 14 paired sessions (7 sample, 7 self-administration) were conducted. During each sample session, an oral dose of tramadol (200, 400 mg), oxycodone (20, 40 mg), codeine (100, 200 mg) or placebo was given and a full array of abuse liability measures was collected. During self-administration sessions, volunteers were able to work on 7 trials (via progressive ratio) for some, none or all of the sample dose (in 1/7 increments) or money ($21 available in $3 increments). Results: All active doses were self-administered, but placebo engendered no responding. Tramadol and oxycodone functioned as dose-dependent reinforcers, as the higher doses were readily self-administered (70%, 59% of available drug, respectively), while the lower doses and both doses of codeine maintained intermediate levels of drug taking (in the range of 31-44%). All three drugs dose-dependently increased measures typically associated with abuse liability (e.g., drug liking, high), relative to placebo ($p < .05$); however, the magnitude and time course of these and other pharmacodynamic effects varied qualitatively across drugs. Conclusions: This study demonstrates that, like other opioids, higher doses of tramadol function as reinforcers in opioid abusers, providing new empirical data for regulatory evaluation.

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Primary Presenter / e-mail: Babalonis, S. / babalonis@uky.edu
Mentor or Senior Author / e-mail: Walsh, S. L. / sharon.walsh@uky.edu

139 **Abstract Title:** **The Relationship between Social Support and Employment Needs of Drug Court Clients**

Author(s): M.F. Dickson, Department of Sociology and Center on Drug and Alcohol Research, U of Kentucky
J.M. Webster, Department of Behavioral Science and Center on Drug and Alcohol Research, U of Kentucky
M. Staton-Tindall, College of Social Work, U of Kentucky
C. Leukefeld, Department of Behavioral Science and Center on Drug and Alcohol Research, U of Kentucky

Abstract:
Past research has highlighted the role social support plays in the recovery process for drug abusers. However, the literature investigating the relationship between social support and other important areas within a drug abuser's life, such as employment, is limited. The goal of the current study was to explore social support as it relates to employment needs, as well as health, substance use, and criminal behavior. As part of an employment intervention trial, 135 drug court clients were recruited and interviewed. The sample was dichotomized into individuals reporting high (n=68) and low (n=67) levels of social support. Analyses revealed that although the two groups were similar demographically, individuals reporting low social support scored significantly higher on several employment barriers and significantly lower on work ethic. Participants reporting low social support were also more likely to report mental and physical health problems and more extensive criminal histories. Substance use histories, however, were similar between the two groups. These data suggest that social support may be a protective factor for problems other than substance use that can hinder recovery. Results have implications for drug court and other substance use treatment programs, demonstrating the need to work with drug abusers to identify potential sources of social support to aid in the recovery process.

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Primary Presenter / e-mail: Dickson, M. F. / megan.dickson@uky.edu
Mentor or Senior Author / e-mail: Webster, J. M. / matt.webster@uky.edu

140 **Abstract Title:** **The Role of Stress in the Health Behaviors of College Students**

Author(s):
J. Brown, University Health Service, U of Kentucky
B. Reeves, University Health Service, U of Kentucky
M. Saeed, Department of Statistics, U of Kentucky
H. Bush, Department of Biostatistics, U of Kentucky

Abstract:
BACKGROUND: Stress is a common complaint among college students with many students experiencing above average stress. Stress can impact students in several ways, including poor academic performance and inadequate sleep. The hypothesis for this study is that higher levels of stress and inadequate sleep will increase unhealthy behavior choices in college students. METHODS: Participants and Procedure: A random sample of 7,183 students was asked to complete an on-line survey designed to describe health behaviors among college students. Students were sent an e-mail inviting them to participate. The response rate was 16.2% (n=1,161). Stress in the past month was divided into 3 groups (none/some, moderate, and much/very much) and comparisons of health behaviors were made using chi-square tests of independence. Results: Participants were white (85.8%), graduate/professional students (57.5%), and female (58.9%). Additionally, 81.2% reported not belonging to a fraternity/sorority. Most students reported much/very much stress (41.0%) compared to moderate stress (36.6%) and none/some stress (22.4%). Coping with stress in unhealthy ways was greater in those with much/very much stress compared to those with lower stress (40.2% vs. 29.2% vs. 15.5%, $p<0.05$). Stress and sleep were found to be related ($p<0.05$); 13.2% of students with some stress reported insufficient sleep more than 14 days in the last month, compared with 23.4% among students with moderate stress and 46.3% among students with much stress. Conclusion: Students with high stress engage in a greater number of unhealthy behaviors compared with students with lower stress. These unhealthy behaviors also include getting less sleep, which can impact students academically.

Supported by:
Primary Presenter / e-mail: Reeves, B. / brandy.reeves@uky.edu
Mentor or Senior Author / e-mail: Bush, H. / heather.bush@uky.edu

141 **Abstract Title:** **The Use of Research Teams in Qualitative Research**

Author(s):
M. Danzl, Dept of Rehabilitation Sciences, U of Kentucky; Cardinal Hill Rehabilitation Hospital, Lexington KY
A. Harrison, Dept of Physical Therapy and Dept of Rehabilitation Sciences, U of Kentucky
E. Hunter, Cardinal Hill Rehabilitation Hospital, Lexington KY; Dept of Rehabilitation Sciences, U of Kentucky
G. Rowles, Graduate Center for Gerontology, U of Kentucky

Abstract:
The purpose of this poster presentation is to critically assess the use of teams as a methodological tool in qualitative research. Team-based research is a method in which more than one researcher collaborates in study design, data collection and analysis. In the realm of rehabilitation, where multidisciplinary teams are the gold standard in terms of service provision, it is conceivable that multidisciplinary research teams would be beneficial in qualitative investigations. The use of a team, however, requires critical reflection and intentional selection. Based on a review of the literature as well as drawing on our own experience in conducting team qualitative research, benefits, challenges and limitations, and strategies to enhance it's use are reviewed. Benefits include translation of knowledge across disciplines/perspectives, strengthened breadth of study, divergent perspectives that expand the interpretive lens, mentorship for novice researchers, collective labor and energy that enhances motivation and productivity, use of creative data collection methods, and improved research capacities in broad geographic settings. Challenges include resource distribution, team dynamics/relationships, division of labor and responsibilities, potential loss of rapport and intimacy with the data, compromises in interpretation, issues related to shared leadership, agreement on author status, and changing team membership/roles. Strategies to enhance team research include intentional approach to team formation, clarification of leadership roles, consistent and clear communication, identification and negotiation of team member roles, consistent incorporation of reflexivity, and early planning for dissemination. Careful reflection on the benefits, limitations, and challenges may assist researchers in selecting the use of a team as a methodological tool in qualitative research. Strategies to facilitate success that are provided in this report may provide a useful guide to researchers wishing to utilize this methodology.

Supported by:
Primary Presenter / e-mail: Harrison, A. / anne.harrison@uky.edu
Mentor or Senior Author / e-mail: Danzl, M. / megan.danzl@uky.edu

142 **Abstract Title:** **Theoretical Model of Nurse Outcomes: Associations among Nurse Characteristics, Psychological Empowerment, Generation, Quality of Work life, and RN Job Satisfaction**

Author(s): A. M. Sparks, School of Nursing, West Virginia University

Abstract:
Aims: The aims of this study were to investigate the relative influence of nurses' characteristics, psychological empowerment, generation, and quality of work life on RN job satisfaction; and to examine the relationships among the concepts in a newly developed Theoretical Model of Nurse Outcomes. The Theoretical Model of Nurse Outcomes was developed to guide this study using the inductive and deductive theory synthesis process described by Walker and Avant (2005). Methods: This predictive, non-experimental study was conducted using anonymous national web-based survey design. The sample included 223 RNs currently practicing in the United States. Correlations, Chi-square test for independence, t-test, ANOVA, and General linear modeling (GLM) procedures were used in this study. Results: Psychological empowerment was significantly related to nurses' age ($r=0.166$, $p<.05$), experience ($r=0.345$, $p<.01$), quality of work life ($r=-0.369$, $p<.01$), and RN job satisfaction ($r=-0.642$, $p<.01$). Quality of work life ($F=92.007$), psychological empowerment ($F=90.029$) years in current position ($F=3.668$) and generation ($F=3.116$) were significant predictors of RN job satisfaction explaining 63.7% of the variance in RN job satisfaction ($p<.05$). Discussion: The findings of this study support the proposed relationships among the concepts in the Theoretical Model of Nurse Outcomes. In a profession in which nurse's job performance is directly influenced by their perceptions, understanding the factors that predict perceived job satisfaction is necessary to create environments that support nurses.

Supported by:
Primary Presenter / e-mail: Sparks, A. M. / amsparks@hsc.wvu.edu
Mentor or Senior Author / e-mail: Sparks, A. M. / amsparks@hsc.wvu.edu

143 **Abstract Title:** **Validation of Phosphodiesterase-2 as a Pharmacological Target for the Discovery of Novel Anxiolytic and Antidepressant Drugs**

Author(s): J. M. O'Donnell, Department of Behavioral Medicine & Psychiatry, West Virginia University
C.G. Zhan, Department of Pharmaceutical Sciences, U of Kentucky

Abstract:
Phosphodiesterase-2 (PDE2) is a cyclic nucleotide phosphodiesterase that is highly expressed in the brain and catalyzes the hydrolysis of cyclic AMP and cyclic GMP. Inhibitors of PDE2 such as Bay 60-7550 and ND7001, when administered systemically, produce anxiolytic- and antidepressant-like effects on behavior and reverse the behavioral effects of stress. The behavioral effects of these PDE2 inhibitors are antagonized by ODQ, an inhibitor of soluble guanylyl cyclase, suggesting mediation by cyclic GMP. Experiments were carried using RNAi to verify that reduced PDE2 activity accounts for the behavioral effects observed. Male ICR mice were implanted with guide cannula targeting the central nucleus of the amygdala bilaterally. Following recovery from surgery, mice were administered either Bay 60-7550 or lentiviral vector/microRNA targeted to PDE2. The effects of pharmacological inhibition were assessed 30 min post-treatment while those of PDE2 knockdown were assessed beginning one week after treatment with the lentiviral vector/microRNA. Behavioral effects were assessed in the elevated plus-maze and the tail-suspension tests; ODQ was used to assess cyclic GMP involvement. Cannula placement and viral vector localization were determined histologically via its GFP tag. Administration of Bay 60-7550 into the central nucleus of the amygdala resulted in anxiolytic- and antidepressant-like effects on behavior of mice in the elevated plus-maze and tail-suspension test, respectively; these effects were blocked by pretreatment with ODQ. Viral vector/microRNA-induced knockdown of PDE2 resulted in similar effects on behavior in these tests, which also were blocked by ODQ. The treatment reduced PDE2 expression by approximately 80%. While it is difficult to unambiguously infer the mechanism by which PDE2 inhibitors produce anxiolytic- and antidepressant-like effects on behavior, the present study does provide an additional line of support that reduced PDE2 activity, achieved in this case via lentiviral vector/microRNA-induced knockdown, is associated with such behavioral effects. While PDE2 catalyzes the hydrolysis of both cyclic AMP and cyclic GMP, antagonism of the behavioral effects of both pharmacological inhibition and knockdown by ODQ suggests a predominant role for increased cyclic GMP signaling. Computational modeling and in vitro and in vivo pharmacological assessments are being carried out for newly discovered PDE2 inhibitors.

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Primary Presenter / e-mail: O'Donnell, J. M. / jodonnell@hsc.wvu.edu
Mentor or Senior Author / e-mail: O'Donnell, J. M. / jodonnell@hsc.wvu.edu

144 **Abstract Title:** **Alteration in Bone Quality with Bisphosphonate Treatment**

Author(s): D.S. Porter, Center for Biomedical Engineering, U of Kentucky
D. Pienkowski, Center for Biomedical Engineering, U of Kentucky
M.C. Faugere, Division of Nephrology, Bone & Mineral Metabolism, U of Kentucky
H.W. Mawad, Division of Nephrology, Bone & Mineral Metabolism, U of Kentucky
H.H. Malluche, Division of Nephrology, Bone & Mineral Metabolism, U of Kentucky

Abstract:
Osteoporosis is a major health problem affecting over 24 million Americans and is more frequent in Appalachia than in the general population. Bisphosphonates are used to treat osteoporosis by increasing bone mass and thus reducing fracture risk. Long-term bisphosphonate treatment; however, has been associated with atypical fractures, which may be due to altered bone quality. This study evaluates the hypothesis that long-term bisphosphonate treatment is associated with altered bone quality. Methods: 31 iliac crest bone specimens from Caucasian post-menopausal osteoporotic females were selected for this IRB approved study. Bone specimens were matched for age and turnover and then allocated to one of three groups: 1) no treatment (n=10), 2) treatment < 5 years (n=10), or 3) treatment ≥ 5 years (n=11). Fourier Transform Infrared spectroscopy was performed on undecalcified bone sections to assess bone quality (e.g., mineral-to-matrix ratio). Data were analyzed using nonparametric tests. Results: mean mineral-to-matrix ratio was 11% greater in the treatment < 5 years group (3.84±0.12, $p<0.05$) and 19% greater in the treatment ≥ 5 years group (4.20±0.13, $p<0.05$) compared to the no treatment group (3.50±0.11). Conclusions: this novel observation showing an elevation in mineral-to-matrix ratio is clinically relevant because small deviations from normal bone mineralization are associated with reduced fracture toughness. Our results point to a previously unknown negative effect of bisphosphonates on bone quality and call for further studies to identify when the positive benefits of bisphosphonates on bone quantity are outweighed by the negative effects on bone quality. This should lead to a clinical practice paradigm change.

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Primary Presenter / e-mail: Porter, D. S. / daniel.porter@uky.edu

Mentor or Senior Author / e-mail: Malluche, H. H. / hhmall@email.uky.edu

145 **Abstract Title:** **Compliance to a Standardized Exercise Protocol for Patients with Superior Labral Lesions**

Author(s): K.A. Seekins, Dept of Rehabilitation Sciences, U of Kentucky, Lexington, KY
S.D. Moore, Dept of Rehabilitation Sciences, U of Kentucky, Lexington, KY
A.D. Sciascia, Shoulder Center of Kentucky, Lexington, KY
T.L. Uhl, Dept of Rehabilitation Sciences, U of Kentucky, Lexington, KY
W.B. Kibler, Shoulder Center of Kentucky, Lexington, KY

Abstract:
Hypothesis: Responders to physical therapy (PT) will be more compliant with a standardized exercise protocol. Secondly, responders will be enrolled in supervised PT longer. Participants: 40 patients (age=40±12yrs) presenting with shoulder pain who were clinically diagnosed with a superior labral lesion were included. Procedures: Patients were prescribed PT and provided a standardized 4-phase protocol. Patients were instructed to complete exercises to increase motion, neuromuscular control and strength as deemed appropriate by their treating PT based on patient symptoms. PT notes and exercise logs were collected at 6-week follow-up. Exercises performed and weeks enrolled in PT were recorded. Responders were defined as patients who met the clinically meaningful change criteria on at least 2 of three criterion: Global Rating of Change, Quick Disabilities of the Arm, Shoulder, and Hand, and Numeric Pain Rating Scale. Statistical Analysis: Mann-Whitney U tests were used to analyze data. Results: 16/40 (40%) patients were classified as responders with 24/40 (60%) defined as non-responders. 6/24 non-responders did not attend 1 PT visit. Responders (72±28%) were not significantly different compared to non-responders (57±37%) in compliance to protocol ($p=.292$). However, responders were enrolled in PT (6±3 wks) longer than non-responders (3±2 wks) ($p=.004$). Conclusions: The duration of therapy appears to be a more critical factor than the specific exercise protocol to result in a positive outcome of improved function and decrease in shoulder pain. Emphasis on adequate duration, approximately 6 weeks of PT, should be encouraged at outset of treatment plan to optimize outcome.

Supported by:

Primary Presenter / e-mail: Sciascia, A. D. / aaron.sciascia@uky.edu

Mentor or Senior Author / e-mail: Uhl, T. L. / tluhl2@uky.edu

146 **Abstract Title:** **Development of an EEG Brain-Computer Interface to Facilitate Motor Recovery from Incomplete Spinal Cord Injury: a Feasibility Study**

Author(s):
E. Salmon, Center for Biomedical Engineering, U of Kentucky
K. Chelette, Department of Physical Medicine and Rehabilitation, U of Kentucky
L. Sawaki, Department of Physical Medicine and Rehabilitation, U of Kentucky
S. Sunderam, Center for Biomedical Engineering, U of Kentucky

Abstract:
Spinal cord injury and stroke can impair one's ability to perform everyday motor tasks. Brain-computer interfaces (BCIs) have been developed to decode brain signals into control commands for prosthetic devices. We are developing such a BCI to be driven by the sensorimotor or "mu" rhythm (8-12Hz) of the EEG. Mu rhythm suppression can occur with actual or imagined movement. In this protocol, approved by the IRB for healthy volunteers, scalp EEG is monitored with electrodes over sensorimotor cortex and mu band power is estimated to classify the EEG state as rest or motor imagery. The EEG classifier is constructed during a training session, in which the subject is presented with intermittent visual cues to imagine hand movement. A preliminary analysis indicated that detection of motor imagery from the EEG is feasible. Subsequently, the classifier will be used to predict motor imagery from EEG measurements in real time. Beyond their use as assistive devices, we believe that BCIs can facilitate motor recovery. Studies suggest that repetitive exercises can induce beneficial neuroplastic changes in motor cortex, and electrical stimulation of peripheral nerves or muscles can augment this recovery. We hypothesize that stimulus-induced plastic changes could be enhanced further through timing-dependent reinforcement by stimulating only in response to intended movement. To that end, we propose to use the EEG-BCI to detect the intent and then trigger electrical impulses. Following development and testing of the BCI on healthy individuals, we will investigate the effects of closed-loop stimulation on patients with incomplete spinal cord injury.

Supported by: University of Kentucky Startup Funds
Primary Presenter / e-mail: Salmon, E. / elizabeth.salmon@uky.edu
Mentor or Senior Author / e-mail: Sunderam, S. / ssu223@uky.edu

147 **Abstract Title:** **Effects of Proximal Stability on Sport Performance and Proximal Stability Measures**

Author(s):
T. G. Palmer, Department of Rehabilitation Sciences, Department of Kinesiology, U of Kentucky
C.G. Mattacola, Department of Rehabilitation Sciences, U of Kentucky
D. Howell, Department of Rehabilitation Sciences, U of Kentucky
T. L. Uhl, Department of Rehabilitation Sciences, U of Kentucky
T. Hewett, Department of Rehabilitation Sciences, U of Kentucky
K. Veile, Department of Rehabilitation Sciences, U of Kentucky

Abstract:
Recent literature suggests proximal stability or the neuromuscular control of the pelvis, lumbar spine and trunk has been reported to function along a stability-mobility continuum. Neuromuscular control is provided by various degrees of muscular endurance, strength, and power regulated by the stability and mobility demands specific to sport. Training and assessment measures are limited in tracking neurological adaptation at the proximal segments that account for sport performance along the stability-mobility continuum. The purpose of this study was to investigate the effects of a neuromuscular control training program on overhead throwing velocity and measures of proximal stability. A randomized control trial was implemented with forty-six healthy, Division II collegiate players. Volunteers were randomly assigned to one of two training groups; a traditional endurance group (ET) (n=21) or a neuromuscular control proximal stability group (PS) (n=25). The primary dependent variable of interest was the change in peak throwing velocity/Kg of body weight in mph, power outputs from a one-repetition maximum chop-lift test in watts/Kg body weight and muscular endurance hold-times for a prone and side plank in seconds. Student's t-tests were used to demonstrate a significant increase in peak throwing velocity and power outputs in the PS when compared the ET, (ET= .21 ±.55, PS= 3.4 ±1.1, $p < .001$). There was no difference for prone plank and side plank hold-times (seconds). A proximal stability training program that targeted the neuromuscular properties along a stability-mobility continuum provided a compressive investigation regarding functional performance of the proximal stabilizers and sport.

Supported by:
Primary Presenter / e-mail: Palmer, T. G. / Thomas.Palmer@uky.edu
Mentor or Senior Author / e-mail: Mattacola, C. G. / carl.mattacola@uky.edu

148	**Abstract Title:**	**Improvements in Muscular Endurance Following a Baseball Specific Strengthening Program in High School Baseball Players**

Author(s):
S. D. Moore, Department of Rehabilitation Sciences, U of Kentucky
T. L. Uhl, Department of Rehabilitation Sciences, U of Kentucky
L. E. Haegele, Department of Rehabilitation Sciences, U of Kentucky
W. B. Kibler, Shoulder Center of Kentucky, Lexington, KY

Abstract:
Hypothesis: Upper extremity muscular endurance will improve in adolescent baseball players over the course of a 20 week pre-season training program. Secondarily strength will improve, range of motion will be maintained and participants will incur minimal in-season time lost to injury. Methods: 14 baseball players (age=16±2years) with no recent injury attended 3 supervised training sessions/week. Strengthening of the upper extremity and lower extremity (LE) was performed using a progression that emphasized repetition over load. Testing was completed at baseline, 4, 8 and 20 weeks. Internal rotation (IR) motion and external rotation (ER) motion and strength were assessed. The posterior shoulder endurance test (PSET) required the participant to perform repetitions to failure of prone horizontal abduction using 2% of body mass. PSET reliability was performed a priori (ICC=.85, MDC=4 repetitions). Unilateral hop-work was used to evaluate LE strength. Mixed model linear analyses were performed for each variable ($\alpha \leq .05$). Results: Posterior shoulder endurance improved ($p<.001$), increasing 36 repetitions at 4 weeks ($p=.001$) and 22 repetitions from 4 weeks to 20 weeks ($p=.048$). Hop-work improved ($p<.001$), increasing by a mean of 496Nm in both legs at 4 weeks ($p<.001$). IR motion and ER/IR strength ratio remained similar over the course of the program ($p>.05$). For the 13 who played spring baseball, the total player-games equaled 270 exposures. Three participants sustained LE injury for a total of 7 games missed. No shoulder or elbow injuries were reported. Conclusions: A pre-season training program increased muscular endurance while maintaining internal rotation ROM throughout the 20 week program. Shoulder rotation strength remained unchanged, likely due to high baseline strength ratio in this cohort. This evidence suggests that participants in the pre-season program were adequately prepared for the season and incurred minimal time loss due to injury.

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Primary Presenter / e-mail: Moore, S. D. / sdmo222@uky.edu
Mentor or Senior Author / e-mail: Uhl, T. L. / tluhl2@uky.edu

149	**Abstract Title:**	**Nerve Stimulation and Modified Constraint-Induced Therapy to Enhance Post-Stroke Neuroplasticity and Motor Recovery: A Pilot Study**

Author(s):
C.L. Carrico, Dept of Physical Medicine and Rehabilitation, U of Kentucky
K.C. Chelette II, Dept of Physical Medicine and Rehabilitation, U of Kentucky
L. Nichols, Cardinal Hill Rehabilitation Hospital and Dept of Physical Medicine and Rehabilitation, U of Kentucky
L. Sawaki, Dept of Physical Medicine and Rehabilitation, U of Kentucky; and Dept of Neurology, Wake Forest U

Abstract:
Research has shown that peripheral nerve stimulation (PNS) can enhance motor learning. No studies have shown whether PNS combined with motor training will have functional relevance in stroke. Therefore, we conducted a pilot study of PNS to enhance the effects of modified constraint-induced therapy (mCIT) in stroke. mCIT is a form of one of the most current, well-validated approaches to post-stroke motor rehabilitation. We hypothesized that mCIT paired with active PNS would lead to significantly more improved motor function in the affected UE than mCIT paired with sham PNS in subjects with stroke. Outcome measures included Wolf Motor Function Test (WMFT), Fugl-Meyer Assessment Scale (FMA), and Action Research Arm Test (ARAT). Nineteen chronic stroke subjects with mild to moderate UE motor deficit received 2 hours of either active (n=10) or sham (n=9) PNS preceding 4 hours of mCIT for 10 consecutive weekdays. Changes in WMFT, FMA, and ARAT were analyzed using factorial ANOVA. Results show significance ($p<0.05$) in all measures at completion compared to baseline (WMFT ($p=0.030$); FMA ($p=0.005$); ARAT ($p=0.019$)) and 1-month follow-up compared to baseline (WMFT ($p=0.045$); FMA ($p=0.047$); ARAT ($p=0.047$)). Thus, PNS paired with mCIT shows enormous promise to enhance recovery in individuals with mild to moderate post-stroke motor deficit.

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Primary Presenter / e-mail: Carrico, C. L. / clcarr2@uky.edu
Mentor or Senior Author / e-mail: Sawaki, L. / lsawa2@uky.edu

150 **Abstract Title:** **Non-Uniform Phosphorylationod P70S6 Kinase in Skeletal Muscle following Eccentric Exercise**

Author(s): S.M. Abshire, Department of Rehabilitation Sciences, U of Kentucky
T. A. Butterfield, Department of Rehabilitation Sciences, U of Kentucky

Abstract:
INTRODUCTION: Repeated bouts of lengthening muscle contractions, also known as eccentric exercise (EEX), result in sarcomere number addition in rabbit TA [1]. We have shown that there is a disparate regional response in rabbit TA following EEX: the deep fibers of the TA lost sarcomeres and the superficial fibers exhibited the largest gains [1]. p70s6k (p70) governs myofibrillogenesis in muscle. Therefore, we hypothesize that p70 phosphorylation following EEX will be non-uniform through the muscle. METHODS: Dorsiflexors of three female NZW rabbits were subjected to a single bout of EEX. Rabbits were euthanized and muscles were excised and separated into regions. Western blot analyses for p70 and pp70 were performed with samples of the TA muscles. The ratio of phosphorylated p70s6k (p-p70s6k) to total phosphorylated (p-p70s6k/(p-p70s6k + p70s6k)) was used for quantification of protein activation. RESULTS: Differences in protein expression for p-p70s6k/total p70s6k levels were found for distal and proximal regions ($p=0.63$ and $p=0.54$) of the TA. Interestingly, p-p70s6k/total p70s6k following exercise was higher in the superficial TA region compared to both the deep TA region and the EDL ($p<0.001$). CONCLUSIONS: Previously, we have shown that EEX in rabbit TA muscle exhibits disparate regional adaptations in serial sarcomere numbers that serve to provide the muscle with altered function and resistance to damaging effects of future EEX bouts. Non-uniform cell signaling responses of p70s6k are in close agreement with regional of serial sarcomere number adaptations we have shown previously [1]. Further work is underway to isolate pathways governing serial sarcomere number adaptations to exercise.

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Primary Presenter / e-mail: Abshire, S. M. / smwall3@uky.edu
Mentor or Senior Author / e-mail: Butterfield, T. A. / tim.butterfield@uky.edu

151 **Abstract Title:** **Normative Serum Cartilage Oligomeric Matrix Protein (sCOMP) Levels in an Uninjured, Physically Active Population**

Author(s): J.M. Hoch, Department of Rehabilitation Sciences, University of Kentucky
J.L. Mateer, Division of Athletic Training, University of Kentucky
C. G. Mattacola, Department of Rehabilitation Sciences, University of Kentucky
C. Lattermann, Department of Orthopaedics and Sports Medicine

Abstract:
Serum cartilage oligomeric matrix protein (sCOMP) is a biomarker primarily associated with cartilage degradation. Elevations in sCOMP have been exhibited following acute knee injury and bouts of exercise. To further explore and better understand sCOMP elevations following acute knee injury and exercise, baseline values for an uninjured, physically active cohort are necessary. Purpose: To establish normative sCOMP values for physically active patients ages 18-40 with no reported history of lower extremity surgery and to determine if differences exist between males and females. Methods: A total of 70 physically active subjects (28 males age:21.1±4.0years, height:178.2±7.3cms, weight:77.7±12.1kgs and 42 females age:22.1±4.9years, height:168.3±6.4cms, weight:65.4±8.6kgs) with no history of lower extremity surgery participated. ELISA tests were run (IBL Euro-Diagnostica, Malmo, Sweden) for human sCOMP. The average sCOMP value and associated standard deviation (SD) was calculated. In addition, the average sCOMP value and SD were calculated for each sex and an independent samples t-test was employed to determine if a significant difference was present. Serum COMP values are expressed as ng/mL. Results: The average normative sCOMP value for all participants was 1493.3±409.1ng/mL. A statistical difference between sexes was determined, with males having higher baseline levels (1767.5±479ng/mL) when compared to females (1317.1±225.4, $p<0.0001$). Conclusion: The results indicate normative sCOMP values for a physically active cohort ages 18-40 with no history of lower extremity surgery are 1493.3±409.1ng/mL, and that males have higher levels than females. These normative values are important in understanding differences following acute knee injury or bouts of exercise for future research investigations.

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Primary Presenter / e-mail: Hoch, J. M. / johanna.clark@uky.edu
Mentor or Senior Author / e-mail: Mattacola, C. G. / carlmattacola@uky.edu

152	**Abstract Title:**	**Orofacial Somatosensory Perception in Healthy Aging Adults and those with Acquired Dysarthria of Speech**

Author(s): N.M. Etter, Department of Rehabilitation Sciences, U of Kentucky
R.D. Andreatta, Department of Rehabilitation Sciences, U of Kentucky

Abstract:
The lower face is a highly coordinated yet adaptive sensorimotor system. Unfortunately, little is currently known about the adaptive neural mechanisms underlying normal and disordered orofacial activities, particularly in aging populations. As a cohort, the aged are especially vulnerable to degradation of speech and feeding behaviors as a function of normal aging, disease and acquired neurological injury. Recently, orofacial perceptual sensitivity in 15 healthy aging adults was characterized (ages 65+) against previously published data in healthy young adults (aged 18-29). Healthy aging adults demonstrated significantly elevated lip vibrotactile detection thresholds (less sensitivity) compared to younger participants and substantially greater variance in the stability of their detection performance. These data suggest that perceptual detection reliability in the aging orofacial system may undergo aging-related alterations, with such alterations potentially influencing speech intelligibility. The implications for such changes in compromised aged populations are unknown. These data are the foundation of planned investigations to determine the relationship between oromotor skill performance and orosensory perceptual abilities in healthy aging adults and aged patients with non-progressive motor speech disorders. Given our initial finding of decreased orosensory perception in healthy aging, we hypothesize that oromotor skill performance may be affected similarly. Current interventions for speech disorders focus almost exclusively on motor training and performance-based goals. Given the theoretical position that clinical interventions are driven primarily through sensory channels5, the combination of sensory and motor goals in novel interventions for speech dysarthria will be aided by greater understanding of the perception-action changes that occur with aging.

Supported by:
Primary Presenter / e-mail: Etter, N. M. / nicole.etter@uky.edu
Mentor or Senior Author / e-mail: Andreatta, R. D. / richard.andreatta@uky.edu

153	**Abstract Title:**	**The Role of the Innate Immune System in Muscle Regeneration for Patients with Idiopathic Inflammatory Myopathies**

Author(s): K. B. Linscott, College of Medicine, U of Kentucky
L. J. Crofford, Internal Medicine and Rheumatology, Center for the Advancement of Women's Health, U of Kentucky
C. Horbinski, Pathology and Laboratory Medicine, U of Kentucky
C. A. Peterson, College of Health Sciences, U of Kentucky
B. Y. Hanaoka, Internal Medicine and Rheumatology, U of Kentucky

Abstract:
The idiopathic inflammatory myopathies are systemic autoimmune diseases characterized by chronic skeletal muscle inflammation and proximal muscle weakness. While many patients initially respond to high-dose corticosteroid therapy and second line immunosuppressive drugs, most suffer from long-term muscle weakness, disability, and steroid-related morbidity. We hypothesize that these immunosuppressive drugs inhibit specific innate immune responses that are important for muscle regeneration. Several animal models support the relevance of anti-inflammatory M2 macrophages in promoting skeletal muscle regeneration, while M1 macrophages are known for their pro-inflammatory effects. The purpose of this study is to characterize the macrophage phenotype of the skeletal muscle inflammation and determine how this phenotype relates to the patient's therapeutic response. Formalin-fixed paraffin embedded skeletal muscle biopsies were acquired through the University of Kentucky Muscle Tissue Bank and immunohistochemistry was performed to detect and differentiate between these macrophage subtypes. M1 macrophages were detected by double staining tissue sections using antibodies against CD63 and CD11b. Alternatively, CD163 and CD206 were targeted as markers of M2 macrophages, and the ratio of M1 to M2 macrophages was determined by counting monoclonal cells demonstrating overlapping fluorescence from each marker. Preliminary results show M1 macrophages are present in higher numbers and in a more diffuse distribution, while M2 macrophages are less frequent and more focally concentrated. Additional staining for embryonic myosin heavy chain will be used to determine whether these focal regions of M2 macrophages correlate to areas of muscle regeneration. The ratio for each biopsy will then be compared to the patient's documented clinical outcome.

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Primary Presenter / e-mail: Linscott, K. B. / kristin.linscott@uky.edu
Mentor or Senior Author / e-mail: Crofford, L. J. / leslie.crofford@uky.edu

154	**Abstract Title:**	**Upregulation of Autophagy through the Mechanotransductive Properties of Massage in Healthy Skeletal Muscle**

Author(s): C. Waters-Banker, Department of Rehabilitation Sciences, Division of Athletic Training, U of Kentucky
E.E. Dupont-Versteegden, Department of Rehabilitation Sciences, Division of Physical Therapy, U of Kentucky
T.A. Butterfield, Department of Rehabilitation Sciences, Division of Athletic Training, U of Kentucky

Abstract:
Muscle trauma initiates an inflammatory response, often resulting in secondary hypoxic injury. Modulation of the inflammatory response utilizing cyclic compressive loading (CCL) in the initial stages following injury has shown to attenuate tissue necrosis, in eccentrically exercised muscle. Selected removal of damaged organelles, such as mitochondria, through the cell survival pathway autophagy, takes place through the formation of specialized vacuoles referred to as: autophagsomes. Autophagy, considered an alternative pathway to apoptosis, reduces cell death and necrosis following injury. Targeting beneficial cellular signaling pathways utilizing manual therapies, could serve beneficial following muscle injury. CCL mimics massage, a commonly utilized manual modality following muscle injury. However, mechanisms behind massage are poorly understood. This study was designed to assess the effects of CCL on healthy skeletal muscle in 12 male Wistar rats. Rats were randomly assigned to either a treatment (4.5N load, n=6), or control (0N load, n=6 limbs) group. Rats selected for treatment, received a single bout of CCL for 30min over 4 consecutive days. Following the fourth treatment, tissue was harvested and cryogenically preserved for analyses. RNA isolation was performed, and samples underwent microarray analysis to evaluate differences in gene expression between treatment and control. The massage treatment group demonstrated increased expression in various genes clusters including immune response and vacuoles. Western blot investigating BCLN1 (autophagy marker) protein expression showed a significant difference in expression in treatment versus control (p=0.056). Collectively, these findings suggest that a massage-mimetic activates potential cell survival pathways, such as autophagy, utilizing the properties of mechanotransduction.

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Primary Presenter / e-mail: Waters-Banker, C. / chris.waters@uky.edu
Mentor or Senior Author / e-mail: Butterfield, T. A. / tim.butterfield@uky.edu

155	**Abstract Title:**	**Visual Distraction Does Not Alter Static or Dynamic Upright Postural Stability in Healthy Subjects**

Author(s): A.E Cripps, Department of Rehabilitation Science, U of Kentucky, Lexington, KY
S.C. Livingston, Department of Rehabilitation Science, U of Kentucky, Lexington, KY

Abstract:
An individual's ability to maintain upright standing balance involves the integration of the sensory systems which may be altered following a concussion. Research documenting the impact of visual perturbation on static or dynamic standing balance among healthy or concussed subjects is lacking. Hypothesis: Healthy subjects will have unaltered ability to maintain upright standing balance with the presentation of visual perturbations. Subjects: Thirty subjects (13 males, 17 females, 22.57±1.61 years). Procedures: Subjects completed the Sensory Organization Test (SOT), Adaptation Test (ADT), and the Modified Clinical Test of Sensory Interaction on Balance (mCTSIB) on the NeuroCom® Smart Balance System. Each subject's standing balance was tested under two visual testing conditions: with and without visual perturbation. A computer-generated optical flow pattern was used as the visual perturbation. Results The presence of visual distraction had no significant effect on upright postural stability as measured by the SOT composite equilibrium scores (t29=0.552, p=0.585, 95% confidence interval [CI],-1.441-2.510), SOT sensory analysis [somatosensory (t29=-0.193, p=0.848, 95%CI,-.012-0.010), visual (t29=1.747, p=0.091, 95%CI,-0.006-0.078), vestibular (t29=0.375, p=0.710, 95%CI,-0.025-0.036), sensory system preference (t29=-0.914, p=0.368, 95%CI,-0.053-0.020)], ADT magnitude of response (toes up t29=-0.368, p=0.715, , 95%CI,-6.818-4.738; toes down t29=0.278, p=0.783, 95%CI.-2.590-3.403) and mCTSIB mean center of gravity sway velocity (t27=-0.462, p=0.648, 95%CI,-0.058-0.0369). Statistical analyses: Dependent paired samples t-test. Conclusions: Visual perturbation had no significant effect on standing balance and postural stability in the presence of altered optical flow in healthy subjects. The influence of visual perturbation on static and dynamic standing balance among individuals with concussion is unknown and warrants investigation.

Supported by:
Primary Presenter / e-mail: Cripps, A. E. / andreacripps@uky.edu
Mentor or Senior Author / e-mail: Livingston, S. C. / scott.livingston@uky.edu

156	**Abstract Title:**	**Comparison of Beta-Lactam Plus Aminoglycoside vs. Beta-Lactam Plus Fluoroquinolone Empiric Therapy in Nosocomial Gram Negative Infections**

Author(s):
B. Ereshefsky, Department of Pharmacy, University of Kentucky
P.S. Winstead, Department of Pharmacy, University of Kentucky
M. Al-Hasan, Department of Infectious Diseases, University of Kentucky
C. Martin, Department of Pharmacy, University of Kentucky

Abstract:
Purpose: Nosocomial infections with resistant gram negative bacteria are difficult to treat, and inappropriate initial therapy results in worse patient outcomes. With few to no new options in the pharmaceutical pipeline to treat these resistant pathogens, empirical use of two agents that have in vitro activity against gram negative organisms is one option to increase appropriateness of initial therapy. Combination therapy consists of an anti-pseudomonal beta-lactam with either an aminoglycoside or a fluoroquinolone. At our institution, there is high variability in the choice of combination agent. Our incremental antibiogram showed that the addition of an aminoglycoside allows for more appropriate empiric coverage compared to fluoroquinolone containing regimens. To that end, the primary objective of this study is to evaluate achievement of a composite clinical endpoint at day 7 of treatment between patients who received empiric beta-lactam and aminoglycoside vs. beta-lactam and fluoroquinolone regimens. Methods: A retrospective analysis of ICU patients treated for hospital acquired gram negative infections from January 1, 2005 to August 30, 2011 at UK Chandler hospital was conducted. The primary patient population includes patients ≥18 years of age who have positive blood cultures, PAL, or BAL with a gram negative bacillus. The primary outcome will be evaluated by univariate statistical tests and multivariate logistic regression. Continuous variables will be evaluated with the t-test or Wilcoxon Rank Sum test as appropriate and categorical variables will be evaluated with the $\chi 2$ or Fisher's Exact Test as appropriate. Results: Data collection is ongoing.

Supported by:
Primary Presenter / e-mail: Ereshefsky, B. / b.ereshefsky@uky.edu
Mentor or Senior Author / e-mail: Martin, C. / craig.martin@uky.edu

157	**Abstract Title:**	**Development of biodegradable hydrogels for controlled release of antimicrobial and antioxidant agents**

Author(s):
A. L. Vasilakes, Chemical Engineering, U of Kentucky
D. A. Puleo, Biomedical Engineering, U of Kentucky
J. Z. Hilt, Chemical Engineering, U of Kentucky
T. D. Dziubla.Chemical Engineering, U of Kentucky

Abstract:
A major challenge facing the medical community is the decreasing number of useful antibiotics due to the emergence of antibiotic resistant bacterial strains. Mitigation of these resistant bacteria in wounds would be greatly beneficial towards the reduction of infection and prognosis of patients. In this research, a biodegradable hydrogel, co-loaded with vancomycin and catalase, has been developed to interfere with the ability of Staphylococcus aureus to develop resistance against vancomycin. To inhibit bacterial resistance emergence, the antioxidant-enzyme catalase was used to break down H_2O_2, a signaling molecule that can increase risk of DNA break/repair mutagenicity. Co-loaded poly(β-amino ester) hydrogels were formed through free-radical polymerization. Vancomycin release was tested on S.aureus seeded agar plates as well as via sink-condition degradation in PBS solution. Catalase release in PBS was tested through 125I radiolabeling and activity with an ODP/HRP assay. Extended release was shown for both vancomycin and catalase under sink conditions, and vancomycin release on bacteria using a modified Kirby-Bauer assay. Importantly, the presence of catalase did not reduce the inhibitory effects of vancomycin, nor did vancomycin interfere with catalase activity. By acting upon the bacteria with two agents which function through independent mechanisms, it may be possible to suppress the ability of bacteria to propagate via the antibiotic vancomycin, as well as evolve resistance through H_2O_2 induced antibiotic resistance emergence with the antioxidant enzyme catalase.

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Primary Presenter / e-mail: Vasilakes, A. L. / andrew.vasilakes@uky.edu
Mentor or Senior Author / e-mail: Dziubla, T. D. / dziubla@engr.uky.edu

158 **Abstract Title:** **Effect of Age on Tobramycin High-Dose Extended Interval Dosing Pharmacokinetics in Cystic Fibrosis (CF) Patients**

Author(s):
C. A. Hempel, Department of Pharmacy, U of Kentucky
R. J. Kuhn, Department of Pediatric Pharmacy, U of Kentucky
B. M. Gardner, Department of Pediatric Pharmacy, U of Kentucky
M. I. Anstead, Department of Pulmonology, U of Kentucky
G. A. Davis, Department of Pharmacy, U of Kentucky

Abstract:
Purpose: The 2009 Cystic Fibrosis Foundation (CFF) guidelines recommend for adult and pediatric CF patients >5years old with normal renal function a tobramycin dose of 10mg/kg/day. Previous pharmacokinetic literature has established clear differences in aminoglycoside pharmacokinetics between adults (>18years) and pediatric patients, such as increased Vd and CL in the pediatric population, but there is limited PK data in the CF population. The CF population is getting older and current guidelines do not differentiate between these age groups. The purpose of this study is to evaluate the effect of age on tobramycin pharmacokinetics following high-dose extended interval dosing (HDEI) in CF patients. Methods: This is a retrospective chart review looking at all CF patients >5 years old who were admitted to UK Chandler Medical Center between August 2007 and September 2011 and who received HDEI tobramycin. Patients were included if they received tobramycin and had two serum concentrations. Patients who were post-lung transplant were excluded. Pharmacokinetic parameters including CL, AUC, t1/2, ke, and Vd will be compared between three populations: ≤18 years, 19-30 years, and >30 years using one-way ANOVA and Kruskal Wallis tests. Post hoc analyses will be used to evaluate pair wise relationships between groups to determine if there are significant differences. The primary objective is to determine any differences in pharmacokinetic parameters between the three age groups. Secondary outcomes are investigating whether baseline SCr, other nephrotoxic agents, past aminoglycoside exposure, or history of diabetes are contributing. Results/Conclusions: Data collection is in progress and results will be presented.

Supported by:
Primary Presenter / e-mail: Hempel, C. A. / che226@uky.edu
Mentor or Senior Author / e-mail: Davis, G. A. / gadavi00@email.uky.edu

159 **Abstract Title:** **Effect of Azithromycin on MMP-9, TGF-β, and Inflammatory Cytokines in Human Sputum**

Author(s):
S. E. Birket, Department of Pharmacy Practice and Science, U of Kentucky
T. J. Cory, Department of Pharmacy Practice and Science, U of Kentucky
B. S. Murphy, Department of Internal Medicine, U of Kentucky
D. J. Feola, Department of Pharmacy Practice and Science, U of Kentucky

Abstract:
Cystic fibrosis (CF) is characterized by chronic pulmonary inflammation, damage and fibrosis. The alternatively activated macrophage (AAM) is an important cell involved in tissue remodeling, yet its role in CF has not been investigated. Our previous work has associated AAM markers with pulmonary function decline in a CF patient population. We have also demonstrated that azithromycin (AZM), used for immunomodulation in CF, induces AAM markers and results in increased activated TGF-β in vitro and in vivo. Interestingly, the protease matrixmetalloproteinase-9 (MMP-9), which has a role in extracellular matrix (ECM) turnover, was also increased by AZM. Therefore, we hypothesize that AZM would increase TGF-β and MMP-9 in sputum samples from human subjects with CF. Sputum samples were collected from patients with CF who were currently at baseline lung function. Clinical data at the time of the sputum sample was also collected. TGF-β and MMP-9, other fibrotic markers, and inflammatory cytokines were analyzed. In human sputa, MMP-9 concentrations from subjects receiving AZM therapy were increased compared to those subjects not receiving AZM, while TGF-β protein concentrations were decreased in subjects receiving the drug. Interestingly, in subjects receiving AZM, MMP-9 and TGF-β were correlated, a relationship not observed in subjects not receiving AZM. We confirmed our hypothesis that AZM would increase MMP-9 but disproved the hypothesis regarding AZM's effect on TGF-β. We found interesting correlations between fibrotic markers and inflammatory cytokines, specifically IL-1β. AZM affected the correlation of IL-1β to lung function. Overall, the data suggest a complex impact for AZM in regulating ECM turnover, which may include a restoration of homeostasis.

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Primary Presenter / e-mail: Birket, S. E. / sebirk2@uky.edu
Mentor or Senior Author / e-mail: Feola, D. J. / djfeol2@uky.edu

160 **Abstract Title:** **Evaluation of Oral Sulfamethoxazole/Trimethoprim Dosing in the Treatment of Skin and Soft Tissue Infections in Patients Discharged from the Emergency Department**

Author(s):
M. A. Mason, Pharmacy Services, U of Kentucky
S. N. Baker, Pharmacy Services, U of Kentucky
K. E. Vollman, Pharmacy Services, U of Kentucky
B. Adkins, Department of Emergency Medicine, U of Kentucky

Abstract:
Background: Approximately 14 million outpatient visits occur annually for suspected Staphylococcus aureus skin and soft tissue infections (SSTIs). Community acquired methicillin resistant S. aureus (CA-MRSA) is isolated from approximately 59% of overall patients in the emergency department (ED). Recommended medication therapy in the SSTI guidelines includes sulfamethoxazole/trimethoprim at standard doses of 1-2 double strength (DS) tablets (800/160 mg) every 12 hours. Based on the pharmacokinetics of this medication, higher doses of trimethoprim may be needed to achieve adequate drug distributions in adipose tissue. Optimized dosing may significantly improve infection eradication, especially since 34% of the current US population is classified as obese. Purpose/Objectives: The purpose of this study is to determine if the dosing of sulfamethoxazole/trimethoprim changes outcomes and resolution of CA-MRSA SSTIs. The investigators hypothesize high dose sulfamethoxazole/trimethoprim (2 DS tablets twice daily) will result in decreased return ED visits and decreased utilization of intravenous antibiotic therapy. The secondary outcome will assess the incidence of intravenous antibiotic therapy in patients who return to the ED and/or exhibit treatment failure. Methods: The study is a retrospective chart review conducted at UK Medical Center from January 1, 2007 through December 31, 2010. Inclusion criteria include patients > 18 years of age who present to the ED and received sulfamethoxazole/trimethoprim after initiation of therapy for possible or known CA-MRSA SSTIs. Exclusion criteria include pregnant patients and patients who developed a sulfamethoxazole/trimethoprim allergy after initiation of therapy. Results: Preliminary results will be presented at the conference.

Supported by:
Primary Presenter / e-mail: Mason, M. A. / molly.mason@uky.edu
Mentor or Senior Author / e-mail: Baker, S. N. / stephnbaker@uky.edu

161 **Abstract Title:** **Overview of patient profile, diagnosis and treatment of Clostridium difficile in a Teaching Hospital**

Author(s):
J.O. Odetunde, College of Medicine, U of Kentucky
P.B. Shores, Dept of Biostatistics, Applied Statistics Laboratory, College of Public Health, U of Kentucky
C.P. Starnes, Biostatistics, Epidemiology, and Research Design, CCTS, U of Kentucky
R.N. Greenberg, Internal Medicine, Infectious Disease Dept, College of Medicine, U of Kentucky

Abstract:
Clostridium difficile is an infectious bacterium that has become one of the more prevalent hospital-acquired patient infections in healthcare facilities in the United States. The most common clinical manifestation of a C. difficile infection (CDI) is mild to severe watery diarrhea and pseudomonas colitis. The study was a retrospective review of patients admitted to the Intensive Care Units (ICUs) and Bone Marrow Transplant (BMT) unit of Markey Cancer Center at the University of Kentucky Healthcare hospital. Fifty-four patient stool samples tested positive for C. difficile toxin B between the years of 2007 – 2009. Median age of the patient population was 50.5 years. 57.69% of the patient population was male. The average prevalence of C. difficile in all units combined declined progressively with each year between the years of 2007 – 2009. The prevalence in the BMT unit declined in 2008 then increased in 2009 to a similar prevalence as 2007. 19.23% of the patients with CDI had complications of pseudomonas colitis. 7.7% of the patients with CDI experienced recurrence of CDI. The prevalence in the BMT unit declined in 2008 and increased in 2009. The fluctuating trend in the BMT unit suggests that the declining trend observed in the other units may be temporary. There are a variety of factors associated with the prevalence of CDI; including, environmental, hospitalizations, advanced age and exposure to antibiotics. Risk factors for CDI in each unit will be assessed in the near future in comparison to controls from each unit.

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Primary Presenter / e-mail: Odetunde, J. O. / jodetunde@uky.edu
Mentor or Senior Author / e-mail: Greenberg, R. N. / rngree01@email.uky.edu

162 **Abstract Title:** **Procalcitonin as a marker of infection in the adult critically ill patient**

Author(s):
S. E. Parli, Department of Pharmacy, U of Kentucky
E. Bensadoun, Department of Internal Medicine - Pulmonology, U of Kentucky
K. W. Hatton, Department of Anesthesiology - ICU, U of Kentucky
C. A. Martin, Department of Pharmacy, U of Kentucky
P. Branson, Department of Nursing Practice and Support Services, U of Kentucky
J. D. Flynn, Department of Pharmacy, U of Kentucky

Abstract:
Purpose Sepsis is a leading cause of death of intensive care unit (ICU) patients with increased mortality in delayed appropriate antibiotic administration. At the same time, clinicians are faced with the ever increasing prevalence of multidrug resistant organisms causing infection. Serum procalcitonin (PCT), a biomarker of inflammation, has been studied as both an aid in sepsis identification as well as a tool in antibiotic discontinuation. In practice, the use of PCT for these reasons has been difficult to standardize due to varying clinician interpretation and utilization. The intent of this project is to determine the correlation of serum PCT level to infection in the adult critically ill patient at the University of Kentucky. Methods A retrospective analysis of adult patients who had at least one PCT level drawn while admitted to the ICU from January 1, 2009 to December 31, 2011 will be conducted. The presence of infection will be determined based on various data collected including cultures, radiographic images as well as clinical and laboratory findings. The primary outcome will be analyzed using regression statistics with binary outcome.

Supported by:
Primary Presenter / e-mail: Parli, S. E. / sara.parli@uky.edu
Mentor or Senior Author / e-mail: Flynn, J. D. / jeremy.flynn@uky.edu

163 **Abstract Title:** **Pneumocystic induced Polarazation of Mactrophage Phenotype**

Author(s):
L.M. Schutzman, College of Medicine, U of Kentucky
J.M. Breslow-Deckman, Department of Microbiology, Immunology and Molecular Genetics, U of Kentucky
J. McGillis, Department of Microbiology, Immunology and Molecular Genetics, U of Kentucky
D. J. Feola, Department of Pharmacy Practice and Science, U of Kentucky
B.A. Garvy, Department of Microbiology, Immunology and Molecular Genetics, U of Kentucky

Abstract:
It is recognized that macrophages exist along a continuum between two unique phenotypes. On one side of the spectrum lie those cells, typically referred to as the classically activated macrophage (M1). These cells produce pro-inflammatory cytokines and chemokines and initiate phagocytosis and death of pathogens. The second general phenotype, known as the alternatively activated macrophage (M2), initiates a regulatory response that attempts to counteract the inflammatory process and leads to repair of the damaged tissue. This alternatively activated pathway has also been implicated in the production of fibrotic scar tissue in the distressed organ. We are characterizing polarization of the macrophage phenotype in the presence of Pneumocystis, an opportunistic fungus known to cause pneumonia in the critically immunosuppressed population. Preliminary data led us to hypothesize that Pneumocystis induces properties of an alternatively activated macrophage phenotype. Macrophage polarization studies were performed using a hematopoietic stem cell engineered with a fusion protein between an estrogen receptor and the transcription factor PU.1. Activation of the estrogen receptor with Tamoxifen results in macrophage differentiation. Phenotypic characterization of differentiated macrophages was performed via flow cytometry analysis, mRNA expression analysis, and protein activity was assessed by arginase activity assay. Preliminary data suggest that Pneumocystic induces an M2-like phenotype as exemplified by up regulation of M2 associated cell surface markers, mRNA expression and an increased arginase activity expression. Together, these data suggest that the polarization of macrophages induced by Pneumocystis may play a role in the lung pathology demonstrated by this patient population.

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Primary Presenter / e-mail: Schutzman, L. M. / linda.schutzman@uky.edu
Mentor or Senior Author / e-mail: Garvy, B. A. / bgarv0@email.uky.edu

164 **Abstract Title:** **Time to first dose of appropriate antifungal therapy for Invasive Candidiasis**

Author(s): E. C. Markway, Department of Pharmacy Practice, U of Kentucky
P. S. Winstead, Department of Pharmacy Practice, U of Kentucky
C. A. Martin, Department of Pharmacy Practice, U of Kentucky

Abstract:
Background: Invasive candidiasis (IC) is the fourth most common cause of nosocomial infection and most common cause of invasive fungal infection. It causes significant morbidity and mortality of up to 47% of cases. The current diagnostic standard is blood culture despite limitations in sensitivity and delays to final results. There is significant clinical impact of this delay to diagnosis and treatment as time to appropriate antifungal therapy has been shown to be an independent predictor of mortality. To address this concern, a university-affiliated, academic medical center implemented guidelines for the empiric use of antifungal therapy in non-neutropenic, critically ill patients. These guidelines incorporated the Candida score, a bedside risk stratification tool, to identify high risk patients for empiric antifungal therapy. Objective: The purpose of this study is to determine the time to order entry of appropriate antifungal therapy before and after the implementation of guidelines. Methods: A retrospective analysis of non-neutropenic, adult patients with documented positive Candida blood cultures hospitalized at the study institution from June 2007 to August 2011 was conducted. A total of 236 patients were identified with 151 patients meeting inclusion criteria. Patients were excluded from January 2009 to May 2009 to allow for implementation of the guidelines, if they received an appropriate anti-fungal prior to the positive culture or if they never received an appropriate anti-fungal agent, or if they were neutropenic (defined as ANC<1500) at the time of blood culture. The primary outcome analyzed was time from the first positive blood culture to order entry of appropriate antifungal. Secondary outcomes included all-cause mortality, risk factors for IC and length of stay. Results: Data collection and analysis are in progress and will be presented.

Supported by:
Primary Presenter / e-mail: Markway, E. C. / ema236@uky.edu
Mentor or Senior Author / e-mail: Martin, C. A. / craig.martin@uky.edu

165 **Abstract Title:** **Antibody Fragments for the Targeted Treatment and Diagnosis of Prostate Cancer**

Author(s): R.M. Williams, Basic Pharmaceutical Sciences, West Virginia University, Morgantown, WV
S. Nayeem, Morgantown High School, Morgantown, WV
L.J. Sooter, Basic Pharmaceutical Sciences, West Virginia University, Morgantown WV

Abstract:
It is estimated that one in six men in the United States will be diagnosed with prostate cancer. Of these, approximately 14% will die from the disease. Current methods of detection and treatment are not specific for prostate cancer. The standard in detection, prostate specific antigen (PSA) levels in the blood, has a false positive rate of greater than 75% due to abnormal but benign prostatic conditions. Therefore, the US Preventative Services Task Force no longer recommends its use. To address this problem, molecular recognition elements (MREs) that specifically bind to prostate cancer cells and not benign prostate cells have been selected. This was done through the Selective Evolution of Ligands by Exponential Enrichment (SELEX). Using this in vitro selection process, a library of 109 yeast-displayed antibody fragments were exposed to a prostate cancer cell line. Antibody fragments that bound to those cells were then amplified and incubated with benign prostate cells. These cell lines represented Prostatic Intraepithelial Neoplasia (PIN), Benign Prostate Hyperplasia (BPH), normal prostate tissue, and prostate-specific membrane antigen (PSMA) protein. Those antibody fragments that did not bind to these cells were amplified. Seven rounds of positive and negative selection were completed and a small number of antibody fragment MREs have been identified. Their ability to bind to human prostate cancer tissue and not benign prostate tissue, from the WVU Tissue Bank, will be confirmed. This work will identify and characterize antibody fragments to be used in the specific detection and targeted therapy of prostate cancer.

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Primary Presenter / e-mail: Williams, R. M. / rwilliams@hsc.wvu.edu
Mentor or Senior Author / e-mail: Sooter, L. J. / lsooter@hsc.wvu.edu

166	**Abstract Title:**	**Benzyl Isothiocyanate Targets Chemoresistant And Metastatic Head And Neck Squamous Cell Carcinoma Cells**

Author(s): M. A. Wolf, McKown Translational Genomic Research Institute, Joan C. Edwards School of Medicine, Huntington, WV
A. Palumbo, McKown Translational Genomic Research Institute, Joan C. Edwards School of Medicine, Huntington, WV
P. P. Claudio, McKown Translational Genomic Research Institute, Joan C. Edwards School of Medicine, Huntington, WV.

Abstract:
Background: Approximately 500,000 cases of head and neck squamous cell carcinoma (HNSCC) are reported worldwide each year. Despite recent improvements in cancer treatment, the increase in overall survival of advanced HNSCC has not improved in the past 3 decades. Consequently, the need for new therapeutic options to enhance survival of patients with advanced HNSCC is needed. Benzyl isothiocyanate (BITC), a natural compound found in cruciferous vegetables, is showing promising results in targeting chemoresistant and metastatic HNSCC cell lines. Methods: Approximately 500,000 cases of head and neck squamous cell carcinoma (HNSCC) are reported worldwide each year. Despite recent improvements in cancer treatment, the increase in overall survival of advanced HNSCC has not improved in the past 3 decades. Consequently, the need for new therapeutic options to enhance survival of patients with advanced HNSCC is needed. Benzyl isothiocyanate (BITC), a natural compound found in cruciferous vegetables, is showing promising results in targeting chemoresistant and metastatic HNSCC cell lines. Results: Our data suggests BITC enhanced cell death and decreased cell viability of HN30 and HN12 to cisplatin after 24, 48 and 72 hours. A migration assay indicated that the HN12 and HN30 are inhibited by BITC in a dose dependent manner. Additionally, 10μM BITC inhibited migration of the highly metastatic HN12 cell line, and when combined with 10μM cisplatin this effect appeared to be enhanced. Treatment with cisplatin alone resulted in migration rates similar to the vehicle control. Conclusions: The present results suggest that BITC may be able to chemosensitize HNSCC cancer cells to cisplatin. BITC also appears to reduce migration of HNSCC cells. Consequently, our current data suggests that BITC may be a novel adjuvant therapy for patients with aggressive HNSCC.

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Primary Presenter / e-mail: Wolf, A. / teter6@marshall.edu
Mentor or Senior Author / e-mail: Claudio, P. P. / claudiop@marshall.edu

167	**Abstract Title:**	**CAL-120, an Orally Available Isoform Selective PI3K Inhibitor in Combination with Erlotinib for the Potential Treatment of Advanced Non-Small Cell Lung Cancer (NSCLC)**

Author(s): C.L. Westendorf, Pharmacy Services, UK HealthCare, College of Pharmacy, U of Kentucky, Lexington, KY
C. Stamatkin, College of Pharmacy, U of Kentucky, Lexington, KY
B. Lannutti, Gilead Pharmaceuticals, Inc, Seattle, WA
E.P. Black, College of Pharmacy, U of Kentucky, Lexington, KY

Abstract:
Specific Aims: To test oral isoform-selective Phosphatidylinositol 3-kinase (PI3K) inhibitor and Erlotinib, EGFR inhibitor, in lung cancer cell lines. Background: Lung cancer is the leading cause of cancer-related mortality in the US with an estimated 157,300 deaths in 2010. EFGR inhibitors have been used in the clinic; however, most patients experience partial response or stable disease due to an increase in resistance. New therapeutic targets and agents are needed to improve patient outcomes. PI3K pathway is deregulated in lung cancer. We hypothesize that PI3K inhibitors combined with EGFR inhibitors will show synergistic activity in lung cancer. Methods: NSCLC cell lines exposed to single agent of a delta/beta PI3K inhibitor, CAL-120, single agent of an EGFR inhibitor, Erlotinib, and the combination of the two agents. The cell lines were evaluated for cell proliferation, death, apoptosis, cell cycle effect, and signaling inhibition.

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Primary Presenter / e-mail: Westendorf, C. L. / cwe226@uky.edu
Mentor or Senior Author / e-mail: Black, E. P. / Penni.Black@uky.edu

168 **Abstract Title:** **Comparison Of Microbubble Assisted P53, Prb, And P130 Gene Therapy In Combination With Radiation Therapy In Prostate Cancer In Vitro And In Vivo.**

Author(s):
R. Nande, McKown Translational Genomic Research Institute, Joan C. Edwards School of Medicine, Huntington, WV
M. S. Gossman, McKown Translational Genomic Research Institute, Joan C. Edwards School of Medicine, Huntington, WV
J. P. Lopez, McKown Translational Genomic Research Institute, Joan C. Edwards School of Medicine, Huntington, WV
C.M. Howard, McKown Translational Genomic Research Institute, Joan C. Edwards School of Medicine, Huntington, WV
J. Denvir, McKown Translational Genomic Research Institute, Joan C. Edwards School of Medicine, Huntington, WV
P.P. Claudio, McKown Translational Genomic Research Institute, Joan C. Edwards School of Medicine, Huntington, WV

Abstract:
Background: There are limited options for patients with therapy resistant prostate cancer. The ineffectiveness of current treatments is due to loss or mutation in p53 and/or pRB. We used a novel approach using adenoviral (Ad) delivery of cell cycle proteins encapsulated inside microbubbles (MBs), in combination with radiation to target p53 and pRB mutant prostate cancer cells. MBs deliver effective therapeutic Ads, combined with ultrasound-targeted microbubble destruction (UTMD), allowing for a site-specific gene transfer system. Methods: DU145 radio-resistant human prostate cancer cells were exposed to 10 and 20Gy of x-ray radiation in vitro. Immediately after irradiation, cells were transduced with Ads carrying p53, pRb, or p130. Cell death was evaluated by flow cytometry and Annexin-V assay between 24-96-hours. DU145 tumors were grown to a volume of 200 mm^3 in nude mice in their flanks. Mice were treated with intravenous injections of the Ads, each at concentration of 10^4 pfu/µL, ± MB. Intravenous treatments were compared to intratumoral injections of the Ads. Combinational therapy groups were irradiated at 8Gy, and injected intravenously with MB/Ads ± ultrasound, every week for 4 weeks. Gene transfer was confirmed by western blot analysis. Results: In vitro, a higher percentage of cell death was observed in 20Gy vs. 10Gy irradiated cells. Cells transduced with adenoviruses carrying RB, p53, and p130 showed a decreasing order of cell death. Combination of radiation and p53 or RB Ads treatments showed increased cell cycle G1 arrest, while p130 combination treatments demonstrated G0 arrest when compared to control Ad or radiation alone. Statistically significant ($p<0.05$) reduction of the ultrasound-targeted MB/p53 or RB Ad transduced tumors was observed when compared to intratumoral treatments or radiation alone. Ultrasound targeted MB/Ads in combination with x-radiation therapy resulted in the most efficient treatment. Conclusions: Combination treatments of radiation and UTMD gene therapy increased the treatment option for therapy resistant prostate cancer.

Supported by: The present studies were supported in part by the awards number CA131395 and CA140024 from the National Cancer Institute (to PPC). The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Cancer Institute or the National Institute of Health.

Primary Presenter / e-mail: Nande, R. / nande@marshall.edu
Mentor or Senior Author / e-mail: Claudio, P. P. / claudiop@marshall.edu

169 **Abstract Title:** **Defining thiazolidinedione targets in ovarian cancer to identify novel diagnostic markers**

Author(s):
L. F. Al-Alem, Deps of Obstetrics and Gynecology and Molecular and Biomedical Pharmacology, U of Kentucky
R. C. Southard, Dept of Molecular and Biomedical Pharmacology, U of Kentucky
M. W. Kilgore, Dept of Molecular and Biomedical Pharmacology, U of Kentucky
H. Zhu, Dept of Molecular and Cellular Biochemistry, U of Kentucky
T. E. Curry, Jr. Dept of Obstetrics and Gynecology, U of Kentucky

Abstract:
Ovarian cancer is the leading cause of death in women with gynecological malignancies. Peroxisome Proliferator-Activated Receptor gamma (PPARγ) is a nuclear transcription factor that has been implicated in diseases like cancer and diabetes, yet little is known about PPARγ's role in ovarian cancer. Recently, PPARγ agonists, such as the thiazolidinediones (TZDs), have been studied for their potential use as cancer therapeutic agents. We hypothesized that selective activation of PPARγ may be used to diagnose and/or treat ovarian cancer. The current study investigated the effect of two FDA approved TZDs, Rosiglitazone (Rosi) and Pioglitazone (Pio), on cellular pathways in ovarian cancer. Microarray technologies were used to define TZD regulated targets as potential markers in ovarian cancer cells. Ovcar3 cells were treated for 24h with Rosi, Pio or vehicle. RNA was collected and microarrays were performed (n=3). Possible target genes included integrin beta 3 (ITGβ3) and TP53INP, and genes involved in cell movement such as dipeptidyl-peptidase-4. This led us to investigate the effects of Rosi and Pio on cell migration and invasion. Both treatments caused a decrease in cell invasion (30-40%) but not migration. The lack of ovarian cancer diagnostic markers has been a major impediment to improving treatment outcomes; therefore, we have investigated a novel approach where we utilized TZDs to force cancer cells to secrete proteins that will alert us to their presence. Ovcar3 cells were serum starved and then treated with Rosi, Pio or vehicle for 24h. Conditioned media was collected, concentrated and then subjected to SDS-PAGE. Samples were extracted and run through HPLC and MALDI-TOF and potential diagnostic marker proteins were identified: moesin, follistatin-like-protein 1 (FSTL1), and cathepsin L2. In summary, Rosi and Pio stimulates expression of genes associated with cell signaling (ITGβ3), cell survival (TP53INP), and cell motility. Rosi and Pio also stimulated the secretion of proteins associated with cell adhesion (moesin), tumor suppression (FSTL1) and proteolysis (cathepsin L2). These results provide a foundation to understand how specific TZDs can be used to mediate changes in ovarian cancer cell expression and support our approach to drive the secretion of ovarian cancer biomarkers.

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Primary Presenter / e-mail: Al-Alem, L. F. / lfalal2@uky.edu
Mentor or Senior Author / e-mail: Curry, T. E. / tecurry@uky.edu

170 **Abstract Title:** **Disruption of Cell-Cell Interactions During Anoikis Impairs Prostate Cancer Metastasis**

Author(s): P. Hensley, Departments of Surgery/Urology, U of Kentucky
S. Sakamoto, Departments of Surgery/Urology, U of Kentucky
N. Kyprianou, Departments of Surgery/Urology, Toxicology, Pathology, U of Kentucky

Abstract:
OBJECTIVES: The complexity of the tumor microenvironment in progression to metastasis has confounded efforts to establish effective clinical treatment of castration-resistant prostate cancer. Our drug-discovery efforts generated a novel lead quinazoline-based Doxazosin® derivative, DZ-50, which impairs tumor growth and metastasis via induction of anoikis and targeting tumor vascularity. This study pursued identification of the molecular targets of DZ-50 in androgen-independent DU-145 human prostate cancer cells. Considering the ability of the focal adhesion regulator Talin to confer anoikis resistance, the impact of DZ-50-mediated disruption of cell-cell interactions and anoikis induction was investigated relative to Talin expression. METHODS: DU-145 cells were stably transfected to overexpress Talin (Talin+) and knock-down Talin expression via shRNA (shTalin). Cells were treated with DZ-50 (5μM). Microarray analysis was performed to identify lead gene targets of DZ-50. Quantitative Real Time-PCR (qRT-PCR) was used to validate changes in gene expression in response to treatment. Protein expression of key focal adhesion regulators was profiled using Western Blotting. Cell viability and anoikis were determined using MTT and Annexin-V Poly-HEMA assays, respectively. RESULTS: Microarray and qRT-PCR analysis revealed specific genetic targets for DZ-50-mediated anoikis, with treatment resulting in transcriptional downregulation of Thrombospondin-1, IGF-BP3 and Claudin-11. Talin expression levels were significantly correlated with susceptibility to DZ-50: Talin+ cells demonstrated increased cell viability and anoikis resistance, while the opposite was observed in shTalin cells. Focal adhesion complex signaling effectors which temporally precede the anoikis response to DZ-50 were altered, with Talin+ cells exhibiting anoikis resistance. CONCLUSIONS: Our results suggest that DZ-50 targets integrin-mediated extracellular matrix interactions, potentially impairing prostate tumor metastatic behavior. Overexpression of Talin conferred anoikis resistance while attenuation of Talin expression increased susceptibility to anoikis-inducing therapeutics. Ongoing dissection of the antitumor mechanism of DZ-50 will expand our understanding of the protective role of anoikis in prostate cancer metastasis.

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Primary Presenter / e-mail: Hensley, P. / patrick.hensley@uky.edu
Mentor or Senior Author / e-mail: Kyprianou, N. / nkypr2@email.uky.edu

171 **Abstract Title:** **Do Vocal Function Exercises improve voice quality following radiation therapy for early glottic cancers?**

Author(s): V. Angadi, Rehabilitation Sciences, Div. of Communication Sciences and Disorders, U of Kentucky
J.Stemple, Div. of Communication Sciences and Disorders, U of Kentucky

Abstract:
At a rate of 12.6%, Kentucky has one of the highest incidences of head and neck cancers (HNC) in the Unites States. Glottic cancer originates at the level of the vocal folds. Early glottic cancers include lesions (T1/T2) that are limited to the vocal folds without distant or nodal metastasis. These cancers can be treated conservatively by radiotherapy. Though curative in nature, radiotherapy is known to cause significant damage to the vocal fold structures and surrounding tissues leading to hoarseness. A number of studies have documented the adverse effects of radiation on vocal fold structures and subsequently voice quality. However, no studies have focused on voice rehabilitation with these patients. The present study idea proposes to investigate the efficacy of a voice rehabilitation program in patients who have been treated with radiation therapy for early glottic cancers. The study will be conducted using a three prong approach which will: 1) identify and characterize the regional HNC population with a retrospective chart review, 2) document the effects of radiotherapy on voice quality in patients with early glottic cancers (identified during the chart review), and 3) prospectively investigate the therapeutic effect on voice improvement of Vocal Function Exercises (VFEs), an evidence based management approach used for treating voice disorders. Information from these studies may influence future treatment strategies with this population.

Supported by:

Primary Presenter / e-mail: Angadi, V. / vrushali.angadi@uky.edu
Mentor or Senior Author / e-mail: Stemple, J. / jcstem2@uky.edu

172 **Abstract Title:** **Eicosapaentenoic Acid Increases the Sensitivity of Colon Cancer Stem-Like Cells to Chemotherapy**

Author(s):
F. De Carlo, McKown Translational Genomic Research Institute, Joan C. Edwards School of Medicine, Huntington, WV
S. Mathis, McKown Translational Genomic Research Institute, Joan C. Edwards School of Medicine, Huntington, WV
T. R. Witte, McKown Translational Genomic Research Institute, Joan C. Edwards School of Medicine, Huntington, WV
W. E. Hardman, McKown Translational Genomic Research Institute, Joan C. Edwards School of Medicine, Huntington, WV
P. P. Claudio, McKown Translational Genomic Research Institute, Joan C. Edwards School of Medicine, Huntington, WV

Abstract:
Diets high in fat especially from animal sources are emerging as one of the major causes of colon cancer. Recent in vitro and in vivo experiments have linked n-3 polyunsaturated fatty acids (PUFAs) to attenuated cell proliferation of various types of cancers, including colon. Additionally, n-3 PUFAs have been shown to increase the efficacy of various cancer chemotherapy drugs in vitro as well as in vivo. However, all these studies addressed the effects of n-3 PUFA treatments on the bulk of tumor cells, NOT on the colon Cancer Stem-Like Cells (CSLCs). Colon CSLCs are a rare and undifferentiated CD133(+) cellular population, responsible for tumor formation, resistance to chemotherapy, and tumor relapse following failed therapy. The Effects of Eicosapaentenoic Acid (EPA) on Colo320DM cell proliferation and CD133 expression was determined by viable cell count and FACS analysis. EPA incorporation into the FAs of the treated colon cancer cells was evaluated by gas chromatography. CD133 and CK20 expression was studied by Real-Time PCR and western blot analysis CD133(+) colon CSLCs were magnetically sorted, treated with EPA and subsequently with CPT-11 or 5-Fluorouracil to assess their sensitivity to therapy with respect to the total cellular population. We have demonstrated that EPA was incorporated into the fatty acids of the treated Colo320DM cells. Lower physiological concentrations (25-50µM) of EPA decreased the number of the overall tumor cells, while the CD133(+) CSLCs resulted affected only by higher EPA concentrations (100µM). Moreover, colon cancer cells cultured with EPA exhibited lower CD133 protein expression and higher CK20 mRNA expression than without EPA, indicating increased differentiation. We also demonstrated that EPA increased the sensitivity of CD133(+) Colo320DM cells to chemotherapy. EPA affected the proliferation and increased the sensitivity to chemotherapy of colon CSLCs, paving the road to future targeted dietary interventions during chemotherapy regimens for colon cancer patients.

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Primary Presenter / e-mail: De Carlo, F. / decarlof@marshall.edu

Mentor or Senior Author / e-mail: Claudio, P. P. / claudiop@marshall.edu

173 **Abstract Title:** **Finding a Bridge that Connects the p53 and pRb Tumor Suppressor Pathways**

Author(s):
M.B. Carper, McKown Translational Genomic Research Institute, Joan C. Edwards School of Medicine, Huntington, WV
G. Boskovic, McKown Translational Genomic Research Institute, Joan C. Edwards School of Medicine, Huntington, WV
J. Denvir, McKown Translational Genomic Research Institute, Joan C. Edwards School of Medicine, Huntington, WV
D. Primerano, McKown Translational Genomic Research Institute, Joan C. Edwards School of Medicine, Huntington, WV
P.P. Claudio, McKown Translational Genomic Research Institute, Joan C. Edwards School of Medicine, Huntington, WV

Abstract:
The tumor suppressors p53 and pRb both regulate cell cycle, DNA repair, apoptosis, differentiation, and senescence. Both tumor suppressor genes are found inactivated in a variety of malignancies, including osteosarcoma. Patients who have mutations and/or inactivations in both p53 and pRb have increased tumor recurrence and metastasis. Evidence suggests p53 and pRb cooperate to inhibit cancer progression and that communication exists between the p53 and pRb pathways, however, the complete mechanism is unknown. We hypothesize that p53 and pRb cross-regulate downstream effector proteins responsible for initiating anticancer processes. The focus of the present study is to investigate the cross-talk between p53 and pRb and determine a downstream effector protein for further analysis. Microarray analysis was conducted on normal lung fibroblast cells (WI38) following p53, pRb, or both p53 and pRb over-expression. Five genes (RGS16, BTG2, STAT4, IL-6, and BIM) were chosen to verify the microarray results using real-time PCR (qPCR) and Immunoblot analysis in WI38 and Saos-2 cells (which contain non-functional p53 and pRb). IPA (Ingenuity Pathway Analysis) was used to analyze the microarray data and pinpoint target proteins for further analysis. Analysis of the microarray data showed, 294-p53, 650-Rb, and 514-p53/pRb differentially expressed genes compared to the controls. We narrowed our focus to 39 genes commonly regulated by p53 and pRb, and 140 genes differentially expressed only when p53 and pRb are over-expressed. The results of the qPCR analysis support the microarray data. Regulation of RGS16 (downstream effector) by p53 and pRb was further investigated due to its ability to decrease signaling of oncogenic pathways responsible for metastasis, invasion, and chemoresistance. Our results demonstrate that both p53 and pRb regulate RGS16. However, further analysis will have to be conducted to determine the function and therapeutic benefits of RGS16 in the p53 and pRb cross-talk pathway.

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Primary Presenter / e-mail: Carper, M. / carper29@marshall.edu

Mentor or Senior Author / e-mail: Claudio, P. P. / claudiop@marshall.edu

174	**Abstract Title:**	**Inhibition of Membrane Bound and Soluble VEGF Receptor-2 Activity Enhances the Proliferation of the BON Carcinoid Cell Line**

Author(s): S.R. Silva, Department of Surgery, U of Kentucky; J.D. Valentino, Department of Surgery, U of Kentucky; Y.Y. Zaytseva, Markey Cancer Center, U of Kentucky; C.M. Townsend, Jr., Department of Surgery, U of Texas, Galveston, TX; B.M. Evers, Department of Surgery, U of Kentucky

Abstract:

There is a growing interest in using angiogenesis inhibitors to treat neuroendocrine tumors. Previously, we detected the expression of vascular endothelial growth factor receptor-2 (VEGFR-2) and its soluble isoform (sVEGFR-2) in the epithelial component of carcinoid tumors and in the BON carcinoid cell line. Recent studies have demonstrated that VEGF inhibitors transiently inhibit tumor growth, followed by increased tumor invasion and metastasis. Also, we have reported that shRNA reduction of VEGFR-2 increases BON cell proliferation and invasion. Thus, the purpose of our current study was to: i) assess the effect that the VEGF signaling inhibitors bevacizumab, an antibody against VEGF-A, or sunitinib, a small molecule inhibitor of VEGFR-2, have on BON cell proliferation and, ii) evaluate the effect of knockdown and overexpression of sVEGFR-2 on BON cell proliferation. Methods: i) BON cells were cultured in media supplemented with bevacizumab (50 ng/ml), sunitinib (50 ng/ml), or vehicle control for two weeks. Media was replaced every other day, and cell lysates for western blot and RNA analysis were collected after one and two weeks. After two weeks, cell proliferation was measured using a cell counting kit-8 assay. ii) Knockdown or upregulation of sVEGFR-2 was achieved by transfecting BON cells with shRNA to sVEGFR-2 or a cDNA plasmid expressing the sVegfr2 gene, respectively. Proliferation following sVEGFR-2 knockdown or upregulation was determined and compared to cells transfected with the appropriate controls. Results: i) BON cell proliferation was significantly increased in cells treated with bevacizumab or sunitinib compared to vehicle control. Western blot analysis demonstrated an increase in phospho-ERK and phospho-Akt following treatment with bevacizumab. Interestingly, there were no observed changes in activation of ERK or Akt following treatment with sunitinib. However, sunitinib treatment increased protein and mRNA expression of VEGFR-2, as assessed by western blot and qRT-PCR, respectively. ii) BON cells with reduced expression of sVEGFR-2 demonstrated increased proliferation at 24 h, 48 h, 72 h, 96 h, and 120 h following plating. Conversely, BON cells transfected with plasmid cDNA encoding sVEGFR-2 displayed reduced proliferation at the aforementioned time points compared to cells transfected with empty plasmid. Conclusions: We have demonstrated that the VEGF inhibitors bevacizumab and sunitinib can enhance the proliferation of BON cells in vitro and that sVEGFR-2 inhibits BON cell proliferation, possibly by sequestering VEGF ligands. While VEGF inhibitors have been shown to effectively inhibit angiogenesis, they may also enhance the aggressiveness of surviving tumor cells, suggesting that a multimodal treatment plan is warranted in carcinoid patients.

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Primary Presenter / e-mail: Silva, S. R. / scott.silva@uky.edu

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

175	**Abstract Title:**	**Inhibition of Nuclear Factor Kappa B activation in Early Stage Chronic Lymphocytic Leukemia by Omega 3 Fatty Acids**

Author(s): J. F. Farhmann, Biochemistry and Microbiology, Marshall U School of Medicine; O. F. Ballester, Edwards Comprehensive Cancer Center, Marshall U School of Medicine; G. Ballester, Edwards Comprehensive Cancer Center, Marshall U School of Medicine; T. R. Witte, Biochemistry and Microbiology, Marshall U School of Medicine; A.J. Salazar, Marshall U School of Medicine; G. Ion, Biochemistry and Microbiology, Marshall U School of Medicine; D. A. Primerano, Department of Biochemistry and Microbiology, Marshall U School of Medicine; G. Boskovic, Department of Biochemistry and Microbiology, Marshall U School of Medicine; J. Denvir, Department of Biochemistry and Microbiology, Marshall U School of Medicine; W. E. Hardman, Department of Biochemistry and Microbiology, Marshall U School of Medicine

Abstract:

Targeting the NFκB pathway has been proposed for therapy of various malignancies including chronic lymphocytic leukemia (CLL). Omega 3 (n-3) fatty acids consumption reduced NFκB activation in animals. Our pilot study tested the hypothesis that consumption of an n-3 supplement would suppress NFκB activation in lymphocytes of patients with early stage CLL. Following informed consent, participants consumed an n-3 supplement initially containing 2.4 g n-3/day gradually increasing to 7.2 g n-3/day. Blood cell counts and assay for NFκB activation of lymphocytes were performed before n-3 initiation and monthly afterwards. Lymphocytes from 5 healthy individuals established normal NFκB activation. After n-3 consumption: (1) n-3 was increased in both red and white blood cells of all participants; (2) NFκB activation was suppressed in lymphocytes of all patients following consumption of n-3; (3) expression of 32 genes in lymphocytes was significantly decreased by n-3 in patients with higher initial NFκB activation. There was no disease progression. Omega 3 consumption suppressed NFκB activation in patients' lymphocytes and would be expected to slow progression of early stage CLL.

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Primary Presenter / e-mail: Witte, T. R. / witte@marshall.edu

Mentor or Senior Author / e-mail: Hardman, W. E. / hardmanw@marshall.edu

176 **Abstract Title:** **Personalized Chemotherapy For A Case Of Progressing And Recurring Spinal Ependymoma**

Author(s): S. Mathis, McKown Translational Genomic Research Institute, Joan C. Edwards School of Medicine, Huntington, WV
J. Valluri, McKown Translational Genomic Research Institute, Joan C. Edwards School of Medicine, Huntington, WV
G. A. Kimmey, McKown Translational Genomic Research Institute, Joan C. Edwards School of Medicine, Huntington, WV
T. Dougherty, McKown Translational Genomic Research Institute, Joan C. Edwards School of Medicine, Huntington, WV
P.P. Claudio, McKown Translational Genomic Research Institute, Joan C. Edwards School of Medicine, Huntington, WV

Abstract:
Background: Administration of ineffective anticancer therapy is associated with unnecessary toxicity and development of resistant clones. Many attempts have been made over the years to develop an ex-vivo anti-cancer test that would provide clinically relevant treatment information. Each time patients are treated, they have a high chance of relapse and their cancer may become more resistant to therapy. Unlike bulk of tumor cells, cancer stem-like cells (CSLCs) resist chemotherapy and can regenerate the various cell types in the tumor, thereby causing relapse of the disease. Thus, development of a test that identifies the most effective chemotherapy management offers great promise for individualized anticancer treatments. Methods: The test we developed (ChemoIDSM) involves growing primary cell cultures from tumor biopsies. CSLCs are then isolated using a rotating wall bioreactor and immunophenotyped by flow cytometry. Both bulk of tumor cells and CSLCs are exposed to a variety of chemotherapeutic agents in a range of concentrations. A full dose response curve is generated for each drug evaluated, and the data are presented as a cytotoxic index (% kill). Results: A 19-year-old patient affected by a recurring undifferentiated spinal ependymoma was biopsied in July 2009. The primary cell culture obtained was immunophenotyped showing an elevated percentage of CD133(+) cells. Patient had already been treated in the past three years by cyber knife, surgery, and several chemotherapy regimens, but was recurring on average of 3-5 months. Arabinoside-C, busulfan, cisplatin, CPT-11, etoposide, methotrexate, and oxaliplatin were tested in various concentrations flanking the clinically relevant doses. ChemoIDSM determined that the most effective treatments for this ependymoma were CPT-11 or Cisplatin as measured on both bulk of tumor cells and CSLCs. Patient was treated with a regimen of CPT-11, and showed no disease progression for 18 months. Conclusions: More testing is needed for this new assay that could lead to more effective anticancer treatments.

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Primary Presenter / e-mail: Mathis, S. / kelly81@marshall.edu

Mentor or Senior Author / e-mail: Claudio, P. P. / claudiop@marshall.edu

177 **Abstract Title:** **Cell Based Endothelium Activation Potential (EAP) Sensor for the Diagnosis and Monitoring of Sepsis, Severe Sepsis, and Septic Shock**

Author(s): R. E. Eitel, Chemical and Material Engineering, U of Kentucky; J. Luo, Chemical and Material Engineering, U of Kentucky; M. Dickerson, Chemical and Material Engineering, U of Kentucky; W. Mercke, Chemical and Material Engineering, U of Kentucky; K. W. Anderson, Chemical and Material Engineering, U of Kentucky; T. Dziubla, Chemical and Material Engineering, U of Kentucky; A. C. Bernard, General Surgery, U of Kentucky

Abstract:
Sepsis has been declared a “Global Medical Emergency” with an incidence rate of an estimated 18 million cases annually. However, the accurate diagnosis and monitoring of sepsis remains limited to summative measures that are often nonspecific and require verification using slow laboratory practices. The hypothesis of the current CCTS pilot program is that a proposed microfluidic Endothelium Activation Potential (EAP) cell based assay will enable the rapid diagnosis of systemic inflammatory response syndrome (SIRS) in sepsis and stratification of the severity of vascular dysfunction. These objectives will be evaluated by the following specific aims. Specific Aim 1 (10 subjects): The primary focus of aim one is to demonstration and optimization EAP sensing in the microfluidic sensor platform including sensor geometry and size, sample collection, preparation and volume requirements, dose-response profiles and assay sensitivity in blood samples taken from healthy patients which have been spiked with inflammatory agents. Specific Aim 2 (20 subjects): In order to validate the translational relevance of the proposed EAP assay, blood samples will be collected from ICU patients in the UK medical center. Results of the EAP assay will be benchmarked against other proposed diagnostic markers (IL-6, procalcitonin (PCT), C-reactive protein (CRP)) and correlated with patient clinical diagnosis (non-infectious SIRS, sepsis, severe sepsis) and outcome (e.g. days in ICU, and 28 day mortality). Preliminary results have shown both fresh and previously frozen serum samples provide similar diagnostic capabilities and that elevated concentrations of inflammatory markers can be detected spiked sample in less than 2 hours.

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Primary Presenter / e-mail: Eitel, R. E. / reitel@engr.uky.edu

Mentor or Senior Author / e-mail: Bernard, A. C. / acbern00@uky.edu

178	**Abstract Title:**	**Drug Shortages: A Look at Sepsis Management in the Emergency Department Before, During, and After**

Author(s):
T. L. Bockenstedt, Department of Pharmacy, U of Kentucky
K. A. Weant, NC Public Health Prepardeness and Response
S. T. Stearley, Department of Emergency Medicine, U of Kentucky
S. N. Baker, Department of Pharmacy, U of Kentucky

Abstract:
Purpose: Drug shortages have plagued the healthcare system throughout the years, however the number of drug shortages over the last five years has more than doubled. Drug shortages, specifically norepinephrine and succinylcholine, have impacted the initial resuscitation of septic patients presenting to the ED. To our knowledge, there is no data analyzing the impact of drug shortages on patients with sepsis, in particular patient outcomes including hospital length of stay and mortality. We aim to evaluate the impact of drug shortages on the clinical decision patterns of physicians and to identify correlations between drug shortages and clinical outcomes of septic patients who present to the ED. Methods: The research protocol has been approved by the institutional review board. Data will be collected via a retrospective chart review of patients diagnosed with sepsis who received medications for rapid sequence intubation (RSI) and/or vasopressor therapy and presented to the ED prior to, during, and following resolution of the norepinephrine and succinylcholine shortages. Data will be analyzed to determine the effect of drug shortages on the prescribing patterns of alternative agents during and following resolution of the drug shortages and the associated clinical implications of the drug shortages on sepsis management. Clinical implications of the drug shortages will be assessed by reviewing the attainment of goal mean arterial pressure, incidence of tachyarrhythmias, the hospital length of stay, overall mortality, and the time to initiation of pain and sedation management following RSI. Results: Data collection is currently in progress.

Primary Presenter / e-mail: Bockenstedt, T. L. / tricia.bockenstedt@uky.edu
Mentor or Senior Author / e-mail: Baker, S. N. / stephnbaker@uky.edu

179	**Abstract Title:**	**Phenylephrine versus Norepinephrine Infusion in Patients with Severe Sepsis and Septic Shock: A Retrospective Cohort Study**

Author(s):
S.D. Schepcoff, Department of Pharmacy Services, U of Kentucky
S.N. Baker, Department of Pharmacy Services, U of Kentucky
P. Branson, Department of Nursing, U of Kentucky
S.D. Brouse, Department of Pharmacy Services, U of Kentucky
Y. Gokun, Department of Pharmacy Practice and Science, U of Kentucky
K.W. Hatton, Department of Anesthesiology, U of Kentucky
J.D. Flynn, Department of Pharmacy Services, U of Kentucky

Abstract:
Purpose: The 2008 Surviving Sepsis Campaign guidelines for the management of patients with septic shock recommend norepinephrine or dopamine as first-line vasoactive agents and recommend against the use of phenylephrine as the initial vasopressor. In late 2010 to mid-2011, there was a national shortage of norepinephrine that severely impacted its availability in hospitals across the country. Clinicians were forced to use alternative vasoactive agents as initial therapy, such as phenylephrine. However, there are little clinical data regarding the use of phenylephrine in patients with severe sepsis and septic shock. The objective of this study is to compare the efficacy and safety of phenylephrine and norepinephrine infusions in patients with severe sepsis and septic shock. For statistical purposes, we hypothesize that 20% more patients achieve goal mean arterial pressure (MAP) of 65 mm Hg at 6 hours with norepinephrine infusion than phenylephrine infusion. Methods: Adult patients admitted to the intensive care units (ICUs) during the time period of norepinephrine shortage who received treatment for severe sepsis or septic shock with phenylephrine infusion but not norepinephrine infusion will be identified via an institutional database. These patients will be matched by Acute Physiology and Chronic Health Evaluation II (APACHE II) score at time of initiation of vasoactive therapy to a group of adult patients admitted prior to the norepinephrine shortage who received treatment for severe sepsis or septic shock with norepinephrine infusion but not phenylephrine infusion. Data collected at the time of initiation of vasoactive therapy will include demographic information, systemic inflammatory response criteria, utilization of antimicrobials, drotrecogin alfa, corticosteroids, renal replacement therapy, and mechanical ventilation, as well as components of the APACHE II and Sequential Organ Failure Assessment (SOFA) scores. Additionally, the time to goal MAP, CVP at this time point, time to addition of other vasoactive medications and doses of phenylephrine and norepinephrine at these time points, maximum daily phenylephrine and norepinephrine doses during sepsis, and the doses of phenylephrine and norepinephrine, APACHE II, and SOFA at the time of discontinuation of these agents will be collected. To assess for the study outcomes, the time to goal MAP, need for reinitiation of the first agent stopped, any and all adverse events, expected and observed ICU and hospital length of stay, expected and observed costs and status at discharge will be collected.

Primary Presenter / e-mail: Schepcoff, S. D. / sara.schepcoff@uky.edu
Mentor or Senior Author / e-mail: Flynn, J. D. / jeremy.flynn@uky.edu

180 **Abstract Title:** **Acute Liver Failure Associated with Acetaminophen Prescribing in Combination Opioid Products**

Author(s):
A. J. Sowell, Department of Pharmacy, University of Kentucky HeathCare
G. A. Davis, Department of Pharmacy, University of Kentucky HealthCare
J. C. Talbert, College of Pharmacy, University of Kentucky
X. Zhang, Applied Statistics Laboratory, University of Kentucky
C. J. Brancato, Applied Statistics Laboratory, University of Kentucky
D. A. Lewis, Department of Pharmacy, University of Kentucky HealthCare

Abstract:
Purpose: Acute liver failure (ALF) cases attributed to acetaminophen increased by 23% from 1998 to 2003. During a similar period, prescribing of common opioid products increased by 70%. The maximum recommended dose of acetaminophen is 4 grams/day. By 2014, the FDA is mandating that the amount of acetaminophen must be limited to 325 mg per dosage unit in all prescription acetaminophen products. To date, it is not known to what extent reducing the acetaminophen strength of combination opioid products will have on the overall incidence of liver injury. The primary objective of this study is to determine the incidence of ALF in patients prescribed opioid-acetaminophen combination products versus opioids alone. The secondary objective is to determine the incidence of ALF in patient prescribed combination opioid products with varying levels of acetaminophen. Methods: This is a retrospective study conducted using a nationwide healthcare claims database of approximately 15 million patients for a period of 3 years. The research has been approved by the institutional review board at the University of Kentucky. Prescriptions for oxycodone, oxycodone with acetaminophen, and hydrocodone with acetaminophen were included. Patients without baseline ALF events prior to the index date (defined as first prescription date) were included. Data collection included: age, sex, dose of acetaminophen and opioid prescribed, prescription quantity and day supply, and presence of ALF by ICD 9 code. Results: To be presented.

Supported by:
Primary Presenter / e-mail: Sowell, A. J. / amanda.sowell@uky.edu
Mentor or Senior Author / e-mail: Lewis, D. A. / dalewi2@uky.edu

181 **Abstract Title:** **Complete Edentulism and Associated Co-morbid Factors-A Literature Review**

Author(s): D.A. Felton, Department of Restorative Dentistry, West Virginia University School of Dentistry

Abstract:
Complete edentulism, or loss of all teeth, continues to plague the Appalachian region, with nearly 42% of adults over the age of 65 in Kentucky and West Virginia being edentulous. People with no teeth meet the World Health Organization's definitions for being handicapped, disabled, and physically impaired. Tooth loss can result in reduction in one's ability to properly masticate foods, and the denture wearing population often suffer from poor systemic health. Recently, complete tooth loss has been shown to be associated with other co-morbid conditions, including coronary artery disease, asthma, diabetes, obesity, certain types of cancer, dementia, and an increased incidence of mortality. Whether the relationship between loss of all teeth and general systemic health is a causal or a casual relationship is purely speculative at this time. This literature review will focus on the condition of complete edentulism, and will review the relationship between tooth loss and various co-morbid conditions. Tooth loss, and replacement with prosthetic equivalents, will be discussed in light of emerging concerns about general systemic health.

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Primary Presenter / e-mail: Felton, D. A. / dafelton@hsc.wvu.edu
Mentor or Senior Author / e-mail: Felton, D. A. / dafelton@hsc.wvu.edu

182 **Abstract Title:** **Long-term Outcome of High-dose Gamma Knife Radiosurgery in Treatment of Trigeminal Neuralgia**

Author(s):
A. Shivazad, College of Medicine, University of Kentucky
B. Young, Department of Neurosurgery, University of Kentucky
W. St. Clair, Department of Radiation Medicine, University of Kentucky
R. Kryscio, Department of Statistics, University of Kentucky

Abstract:
Purpose: The safest and most effective dose and target for stereotactic radiosurgery for treating Trigeminal Neuralgia remains unresolved. Methods: We report the long-term results of Gamma Knife Radiosurgery in treatment of Trigeminal Neuralgia in 315 patients treated with a maximum dose of 90 Gy to the trigeminal nerve with the 20% isodose line tangential to the pontine surface (18 Gy). Results: One-hundred-eighty-five (85.6%) patients reported pain intensity was decreased compared to before treatment. MMS Pain-classification after GKS at last follow-up was reported as follows: Class I (pain-free without medications) in 104 (43.7%), Class II (pain-free with medications) in 66 (27.7%), Class III (> 90% decrease in pain-intensity) in 23 (9.7%), Class IV (50-90% decrease in pain intensity) in 20 (8.4%), Class V (< 50% decrease in pain intensity) in 11 (4.6%), and Class VI (pain becoming worse) in 14 (5.9%), respectively. Therefore, 170 (71.4%) patients were pain-free after radiosurgery (including those with and without medications (Class I-II)).Two-hundred-thirteen (89.5%) patients had at least 50% pain-relief after GKS. Categorizing the patients into Excellent – Class I-II (no pain), Good – Class III-IV (at least 50% reduction in pain), and Poor – Class V-VI (less than 50% reduction in pain or repeat GKS/another procedure) the outcomes were: Excellent – 170 (71.4%) patients; Good – 43 (18.1%) patients; and Poor – 25 (10.5%) patients. Conclusion: GKS using 90 Gy maximum dose to the TN and 18 Gy to the pontine surface provides long-term pain control, enables reduction of medications, and improves quality-of-life.

Supported by:
Primary Presenter / e-mail: Shivazad, A. / ashiv2@uky.edu
Mentor or Senior Author / e-mail: Young, B. / byronyoung@uky.edu

183 **Abstract Title:** **Restoring Equity: The Effect of Patient's Competence As a Spouse on Caregiver's Psychological Well-Being in Couples Living With ALS**

Author(s):
I. A. Boggero, Department of Psychology, U of Kentucky
E. J. Kasarskis, Department of Neurology, U of Kentucky
S. C. Segerstrom, Department of Psychology, U of Kentucky

Abstract:
Equity theory proposes that optimal relationship functioning is achieved when partners perceive equal contributions to the relationship. In couples living with Amyotrophic Lateral Sclerosis (ALS), the requirements of care giving may result in spouses of patients feeling under-benefited, leading them to experience increased depressive symptoms and decreased psychosocial well-being. While the progression of ALS leads to decreased physical functioning in patients, these individuals can help restore the equity of the relationship by demonstrating their competence as a spouse in non-physical ways, such as providing support. In the current study, multilevel modeling was used to analyze a pre-existing longitudinal dataset tracking 103 couples living with ALS over 1.5 years. The aim was to test whether 1) patient's self-rated competence as a spouse, 2) patient's self-rated competence as a lover, 3) spousal ratings of patient as loving and 4) spousal rating of patient as sexy could be used to predict spousal depressive symptoms and spousal psychosocial well-being between and within couples. Changes in patient's self-ratings of competence as lovers predicted spousal depression over time within couples, even when ALS severity was included in the model ($g = -.021$, $SE = .010$, $t(303) = -2.07$, $p < .05$). Similarly, changes in spousal ratings of how sexy he or she found the patient predicted spouse's psychosocial well-being over time within couples with and without ALS severity in the model ($g = .170$, $SE = .083$, $t(339) = 2.06$, $p < .05$). Examining contributions from the patient to the spouse could be helpful in developing interventions to increase the well-being of spousal caregivers.

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Primary Presenter / e-mail: Boggero, I. A. / iboggero@gmail.com
Mentor or Senior Author / e-mail: Segerstrom, S. C. / scsege0@uky.edu

184 **Abstract Title:** **Stability of Affinity Based Multilayered Polymeric Self-assemblies for Oral Wound Applications**

Author(s): S. P. Authimoolam, Department of Chemical and Materials Engineering, U of Kentucky
D. A. Puleo, Center for Biomedical Engineering, U of Kentucky
T. D. Dziubla, Department of Chemical and Materials Engineering, U of Kentucky

Abstract:
Oral mucositis is a painful and debilitating chronic inflammatory condition that can result from chemo- and/or radiotherapy. While current treatment strategies (e.g., gels and mouth rinses) provide temporary relief, there is still an unmet clinical need for a robust, long-acting barrier strategy that can simultaneously provide protection and release drug to enhance wound healing. It is proposed that an affinity based layer-by-layer self-assembled barrier administered as a series of mouth rinses can allow for wound-specific drug delivery, providing an effective regenerative therapy. In this work, biotinylated poly(acrylic acid) was used to develop LBL assemblies based upon biotin-streptavidin affinity interactions. To explore the ability of developed LBL assemblies to resist the harsh intraoral environment, in vitro chemical and ex vivo mechanical tests are performed. The stability results demonstrate significant LBL barrier stability with wear resistance. From principal component regression analysis, factors such as polymer MW and number of layers in assemblies contributed significantly to chemical barrier stability. Also it is observed that the extent of biotin conjugation plays a significant role in LBL development and in mechanical stability. Thus, the proposed affinity-based multilayered assemblies with their excellent barrier properties offer a modular treatment approach in oral mucosal injuries.

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Primary Presenter / e-mail: Authimoolam, S. P. / sundarprasanth86@gmail.com
Mentor or Senior Author / e-mail: Dziubla, T. D. / dziubla@engr.uky.edu

185 **Abstract Title:** **Sub-Second Direct Measurements of Nitric Oxide Formation in the Corpus Cavernosum**

Author(s): V.A. Davis, Center for Microelectrode Technology, Dept of Anatomy & Neurobiology, U of Kentucky
S.R. Batten, Center for Microelectrode Technology, Dept of Anatomy & Neurobiology, U of Kentucky
J.E. Quintero, Center for Microelectrode Technology, Dept of Anatomy & Neurobiology, U of Kentucky
F. Pomerleau, Center for Microelectrode Technology, Dept of Anatomy & Neurobiology, U of Kentucky
P. Huettl, Center for Microelectrode Technology, Dept of Anatomy & Neurobiology, U of Kentucky
G.A. Gerhardt, Center for Microelectrode Technology, Dept of Anatomy & Neurobiology, U of Kentucky

Abstract:
In recent years, development of drugs that affect the nitric oxide (N0)-cyclic guanosine monophosphate (cGMP) pathway have become very popular due to their potential to treat erectile dysfunction (ED). The most popular ED drugs act as phosphodiesterase type 5 (PDE-5) inhibitors which block the degradation of NO-generated cGMP. However, not all patients respond to PDE-5 inhibitors, therefore other therapies are being investigated. A wealth of pharmacological studies suggests that NO generated in the corpus cavernosum is the main molecular mediator of penile erection. However, the physiological levels of NO in the corpora and their possible (phasic) changes during penile erection have remained unknown because suitable methodologies to measure NO directly at the source were lacking; NO is difficult to measure as it is a short lived, labile, and gaseous molecule. These studies employ in vivo electrochemistry to assess sub-second NO level changes in the corpus cavernosum following a variety of experimental manipulations in an effort to better understand the role of NO in erection. Carbon fiber electrodes were prepared for NO detection and placed in the corpus cavernosum. NO precursor L-Arginine and NO synthase inhibitor L-NG-Nitroarginine methyl ester (L-NAME) were applied locally and systemically, both alone and in concert with electrical stimulation. Preliminary results indicate that NO and nitrite, and oxidation product of NO, can be measured directly in the corpus cavernosum using in vivo electrochemistry. Because NO is an important molecule in the cardiovascular system, the ability to measure it in peripheral tissue could have an impact in cardiovascular research as well as offer potential erectile dysfunction treatments. In future studies we plan to investigate the correlation between NO neurotransmission in the CNS and NO levels in corpus cavernosum.

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Primary Presenter / e-mail: Batten, S. R. / seth.batten@uky.edu
Mentor or Senior Author / e-mail: Gerhardt, G. A. / gregg@uky.edu

186 **Abstract Title:** **Synthesis and Characterization of Antioxidant based Poly (β-amino ester) Nanoparticle to Control Cellular Oxidative Stress**

Author(s):
P. Gupta, Chemical and Material Engineering Department, U of Kentucky
P. Wattamwar, Chemical and Material Engineering Department, U of Kentucky
D. Chochran, Chemical and Material Engineering Department, U of Kentucky
J. Z. Hilt, Chemical and Material Engineering Department, U of Kentucky
T.D. Dziubla, Chemical and Material Engineering Department, U of Kentucky

Abstract:
Oxidative stress is a pathophysiological condition defined by an increased production of reactive oxygen species (ROS, e.g.,DPPH radical, singlet oxygen (1O2), superoxide radicals O2._, peroxyl radical CCL3O2.), which react with and damage cell membranes, DNA, proteins, impairing normal cellular functioning. A number of antioxidants (e.g. curcumin, quercetin) are capable of intercepting ROS, thereby short-circuiting this self-propagating disease state. Despite this advantage, these antioxidants possess very poor water solubility and hence low bioavailability making their usage in medical applications more difficult. In order to overcome this pharmacological limitation, we have developed a method for synthesizing polyphenolic antioxidants into degradable polymers using poly(β-amino ester) chemistry (PBAE). PBAE's are hydrolytically degradable biopolymers capable of releasing non-toxic alcohols and acids as degradation products. Here, these hydrophobic biodegradable polymers were shown to degrade (i.e., hydrolytic cleaving the ester bond) within endothelial cells resulting in the controlled release of free antioxidant molecule, which in turn performs its anti-oxidant function. The ability to synthesize these polymers into nanoparticle was explored as a way of providing long term drug delivery to desired sites of action. Antioxidant release profiles were studied in acidic, basic, and neutral pH in aqueous buffer system with time dependence, which helped in tuning the rate of antioxidant release.

Supported by: DEPSCoR
Primary Presenter / e-mail: Gupta, P. / prachi.gupta@uky.edu
Mentor or Senior Author / e-mail: Dziubla, T. D. / dziubla@engr.uky.edu

187 **Abstract Title:** **Transfusion of Red Blood Cells Suppresses T Cell Function**

Author(s):
C. Meier, Department of Surgery, U of Kentucky
A. Bernard, Department of Surgery, U of Kentucky
M. Ward, Departemtnt of Immunology and Molecular Genetics, U of Kentucky
J. Woodward, Departemtnt of Immunology and Molecular Genetics, U of Kentucky

Abstract:
Introduction: Transfusion related immunomodulation (TRIM) is a clinical phenomenon of both pro- and anti-inflammatory immune derangement that occurs with transfusion of packed red blood cells (PRBCs). While the existence of TRIM is recognized, the mechanisms triggering these events are unknown. We have recently identified a potent T cell suppressive property inherent in stored RBC from the blood bank. We hypothesized that this property is acquired during blood banking and storage. Methods: We compared freshly drawn human blood with stored blood from the blood bank for the ability to suppress T cell responses. To determine whether stored RBC were inducing apoptosis or necrosis of T cells in culture, we harvested T cells after 72h of culture with or without RBC and stained with propidium iodide and annexin V. Results: While there was almost complete inhibition of T cell proliferation with blood bank RBC, there was only a slight inhibition of proliferation with fresh. Cultures undergoing active proliferation in the absence of RBC showed about 18% apoptotic cells and about 6% necrotic cells which is typical of T cell cultures undergoing robust proliferation. In contrast, T cells cultured in the presence of stored RBC showed no apoptosis nor necrosis, typical of a resting, unactivated T cell population. Conclusion: Our data show that RBC acquire their suppressive phenotype as a result of storage under blood bank conditions. Intact RBC are required at ratios of about 5:1 or greater RBC:T cell, and must be in contact with the T cells. Alloantigens are not involved as syngeneic RBC suppress equally well. Suppression is not associated with cell death nor apoptosis. RBC may become suppressive to T cells as a consequence of storage under blood bank conditions.

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Primary Presenter / e-mail: Woodward, J. / jwood1@email.uky.edu
Mentor or Senior Author / e-mail: Woodward, J. / jwood1@email.uky.edu

188 **Abstract Title:** **Use of Fenoldopam in the Treatment of Calcineurin Inhibitor Induced Renal Failure**

Author(s): M. L. Thompson, UK HealthCare Pharmacy Services, Lexington, KY
T. E. Macaulay, UK HealthCare Pharmacy Services, Lexington, KY
T. Clifford, UK HealthCare Pharmacy Services, Lexington, KY
W. McKeown, UK HealthCare Department of Internal Medicine and Transplant Nephrology
J. Gokun, Department of Pharmacy Practice and Science, College of Pharmacy, U of Kentucky, Lexington, KY

Abstract:
Background: Chronic allograft nephropathy is the primary cause of late graft dysfunction in the renal transplant population. The causes are multi-factorial including: chronic rejection, alloantigen-independent factors (like diabetes or hypertension) and calcineurin inhibitor nephrotoxicity. Calcineurin inhibitors (CNI), such as tacrolimus and cyclosporine are commonly used in solid organ transplant patients to prevent allograft rejection. They contribute to chronic allograft nephropathy and cause nephrotoxicity in all solid organ transplant populations through a variety of mechanisms, the most prominent one being afferent arteriolar vasoconstriction. These mechanisms work together to cause a dose dependent decrease in renal blood flow, a side effect which is considered reversible upon discontinuation of the drug. Dopamine and fenoldopam have been used to delay renal failure in patients with acute kidney injury. Fenoldopam is a dopamine receptor-1 agonist, which causes vasodilatation in the proximal tubule. Methods: A retrospective chart review was performed on transplant patients, in acute renal failure, admitted to the University of Kentucky medical center from 2004- 2011. Our hypothesis is that fenoldopam will be effective in prolonging renal function in transplant patients with CNI. Our primary objective was to compare changes in renal function values of patients admitted with acute renal failure due to calcineurin inhibitors who receive either fenoldopam or another agent. Secondary objectives will evaluate use of renal replacement therapies, rejection rates, changes in immunosuppression regimens, length of hospital stay and 28d mortality. Results: Data collection is in progress.

Supported by:

Primary Presenter / e-mail: Thompson, M. / mth226@uky.edu
Mentor or Senior Author / e-mail: Clifford, T. / tim.clifford@uky.edu