

Tuesday, April 5, 2022

17th Annual CCTS Spring Conference

Gatton Student Center

Abstracts

CCTS Spring Conference

Posters 1 - 97

Oral Presentations Abstracts

Abstracts

Poster Number 1

Title: Study the Experiences of Isolated Elderly in Facilities and Their Use of Communication Technology during the COVID-19 Pandemic

Authors: Abigail Guidos, U of Kentucky, Ming-Yuan Chih, Department of Health and Clinical Sciences, U of Kentucky

Abstract: The COVID-19 pandemic has affected the elderly's mental health and way of life. Since they are the most vulnerable population to COVID-19, isolation has become the main defense to keep them safe. Isolation during lockdown has led to poor health outcomes, mentally and physically. Many existing mental illnesses can be exacerbated due to isolation, as well as lead to new mental health issues, such as, anxiety, depression, and worsening dementia among the elderly residents in healthcare facilities. Technology, such as smartphones, tablets, and laptops, have become a staple to communicate with those they have been isolated from. Fostering connectedness through technology can improve health outcomes for elderly patients, especially those living in a healthcare facility. This research project determines what types of technology that elderly patients use to help deal with social isolation due to the COVID-19 pandemic and if their social isolation has improved due to the technology. This mixed-method study consists of qualitative elderly patient interviews and quantitative surveys at one long-term care facility. The facility is Magnolia Springs Lexington, and there are 10 patient interviews. The purpose of this study focuses on social isolation experienced by the elderly residents during the pandemic, how the elderly utilize technology to connect with families and friends, how manageable technology has been to use, and their improvements in mental and physical health. This research is important to determine the impacts of social isolation on this vulnerable population that live in long-term care facilities in urban Kentucky.

Funding; Summer Undergraduate Research Fellowship Award

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Basic/Translational Research

Abstracts

Poster Number 2

Title: Analysis of Recurrent Methylation Changes as a Marker for Acute Lymphoblastic Leukemia-Associated Cell-Free DNA

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Abstract: Acute lymphoblastic leukemia (ALL) is the most common pediatric cancer. Recently, we have developed an assay that utilizes cell-free DNA (cfDNA), released by ALL cells, to monitor ALL burden and treatment response in patient blood and cerebrospinal fluid samples. While this assay is sensitive, a downside is that recombination events in genomic DNA from each patient's ALL must be identified, then those sequences used to identify ALL-specific cfDNA in the patient's biofluids. This was a time-consuming step and might not be ideal if this assay is to be translated to the clinic. Many cancers share similar hyper- or hypo-methylated profiles based on cancer type. We analyzed methylation profiles of ALL genomic DNA and found ~55 differentially methylated regions (DMRs) present in ALL and not normal lymphocytes. We hypothesize this methylation profile can be used to track ALL cfDNA across any patient. Realtime PCR primers were designed for these DMRs, and several were tested using gDNA and cfDNA from ALL and control samples. So far, results have successfully shown amplification in ALL DNA/cfDNA and no amplification in control DNA/cfDNA. After testing the remainder of the primers, we will use this established panel to assess cfDNA from patient bone marrow samples, plasma, and CSF, and correlate findings to clinical outcome. The end goal of our study is to develop a universal assay that can non-invasively assess ALL treatment response, minimal residual disease (MRD), and CNS disease by utilizing recurrent methylation changes in T-ALL and B-ALL, compared to normal PBMCs.

Funding: Kentucky Pediatric Research Trust Foundation.

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Basic/Translational Research

Abstracts

Poster Number 3

Title: Hydrogels, Magnetic Nanoparticles, and Hydrogel Nanocomposites for Environmental and Biomedical Applications

Authors: E. M. Frazar, Department of Chemical and Materials Engineering, U of Kentucky M. V. X. Klaus Department of Chemical and Materials Engineering, U of Kentucky P. Paul Department of Chemical and Materials Engineering, U of Kentucky J. Z. Hilt Department of Chemical and Materials Engineering, U of Kentucky

Abstract: Hydrogels, magnetic nanoparticles (MNPs), and their nanocomposites can provide unique solutions to environmental and biomedical problems. For example, decades of use of halogenated chemicals in product manufacturing and commercial applications and human exposures have been connected to detrimental health impacts. Additionally, the rapid global spread of SARS-CoV-2 has posed a significant threat to human health and developing a effective methods for inactivating virus has also become a critical issue. Here, we highlight example advanced materials to address these issues, including selective capture of contaminants from water and the body and then regenerating using an alternating magnetic field (AMF) as well as developing magnetic nanoparticles (MNPs) capable of inactivating viruses using an AMF.

Funding: NIH P42ES007380

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Abstracts

Poster Number 4

Title: SBRT for Lung Lesions: A Single-Center Experience

Authors: J. J. Grace, Second-Year Medical Student at the University of Kentucky College of Medicine, S. P. Saha MD, MBA, Medical Director PAS Chief of Transition to Practice and Advanced Training Programs, University of Kentucky College of Health Sciences

Abstract: **Introduction:** SBRT (stereotactic body radiation therapy) was first used in 1991 in Sweden. SBRT did not make its way to the United States until the late 90s and was not clinically studied in the US until 2003. Since that time, it has grown vastly in its application. This study aimed to review the outcomes of patients treated with SBRT in the University of Kentucky Healthcare system. **Clinical materials:** This study was conducted with IRB approval. We identified the first 100 consecutive patients treated with SBRT for lung lesions at the University of Kentucky Healthcare system. Comprehensive information was found on 51 of the 100 patients. Of the 51 patients, 20 were males vs. 31 females. Median age at treatment conclusion was 71 years (range 52-89 years). Needle biopsy was performed in 32 of the 51 patients. 9 others only had a bronchoscopy, while 10 patients were diagnosed clinically based on a PET scan. There were 26 cases of adenocarcinoma, 16 of squamous cell carcinoma, and 9 non-specific diagnoses. **Results:** Across all lesions, there was a median size reduction of 32% in the largest dimension. Median follow-up was 34 days (range 27-188 days). 5 patients reported complications from treatment. Those included esophagitis (1), anterior chest pain (1), fatigue (1), and increased coughing symptoms (2). **Conclusion:** SBRT is a valuable tool in treating confirmed and suspected lung cancer. It allows for highly focused radiation to be delivered quickly. SBRT is especially useful for high-risk patients or when other therapies are contraindicated.

Funding: No funding

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Abstracts

Poster Number 5

Title: Inhibition of de Novo and Salvage Pathways for dNTP Synthesis Enhances Sensitivity to Ionizing Radiation in Pancreatic Neuroendocrine Tumor Cells

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Abstract: Introduction: Ionizing radiation is a promising treatment for neuroendocrine tumors (NETs). However, these tumors confer radioresistance via DNA repair, which is dependent on the production of deoxynucleoside triphosphates (dNTPs). We investigated inhibitors of two enzymes in the production of dNTPs as radiosensitizers in NETs. **Methods:** CellTiter-Glo (Promega) luminescent assay established drug sensitivities of two pancreatic-NET cell-lines (BON and QGP-1) for triapine (ribonucleotide reductase inhibitor; RNRi) and three ataxia-telangiectasia-and-rad3-related inhibitors (ATRi: AZD6738, VX-970, and BAY1895344). Synergy models determined synergism of drug combinations with scores greater than zero. Clonogenic assays were performed with sulforhodamine B. Immunoblots were used to assess apoptosis and ATR activation following treatment. **Results:** BON cells are more sensitive to all agents compared to QGP-1 (BON vs QGP-1: triapine 2.8 μ M vs 6.3 μ M, AZD6738 0.9 μ M vs 6.1 μ M, VX-970 239nM vs 2.4 μ M, BAY1895344 81nM vs 1.1 μ M). Loewe synergy models found BAY1895344 and triapine to be synergistic with scores of 9.89 in BON and 15.91 in QGP-1 cells (p-values<0.0001). BAY1895344 is more efficacious when combined with IR in both BON (IC₅₀: 150nM 0Gy versus 19nM 2Gy) and QGP-1 cells (IC₅₀: 277nM 0Gy versus 93nM2Gy). Immunoblot demonstrated greater apoptosis with combination treatments as well as activation of the ATR pathway with IR and triapine and subsequent inhibition with an ATRi. **Conclusion:** The treatment of GEP-NET cell lines with inhibitors that block dNTP production markedly sensitize these cells to subsequent IR. The combination of IR with an ATRi and an RNRi is a potentially effective treatment modality for NETs.

Funding: NIH T32CA160003, UM1CA186712

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Basic/Translational Research

Abstracts

Poster Number 6

Title: Accelerating Colorectal Cancer Screening and follow-up through Implementation Science (ACCSIS) in Appalachia: Baseline County-level Colorectal Cancer Screening Rates and Behavioral Correlates

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Abstract: Background: The goal of ACCSIS Appalachia is to increase colorectal cancer (CRC) screening rates in underserved communities in Appalachian Kentucky and Ohio where CRC disparities are high. One measure of intervention effectiveness includes longitudinal estimates of county-level CRC screening rates collected through a series of random digit dialed telephone surveys of the 12-county study population, pre and post intervention implementation. **Methods:** Baseline data were collected between April and September 2019 with a random-digit-dialed sample of adults aged 50–74. The 30-item survey included socio-demographic characteristics, health care access, CRC screening and screening barriers. Logistic regression, weighted to account for stratified sampling by county, was used to estimate unadjusted and adjusted associations between demographic/clinical factors and screening status. **Results:** A total of 1221 responses were collected (18.7% response rate). Participants were an average of 63.2 years old and mostly non-Hispanic white (99.6%), married/cohabiting (65.8%), and female (65.6%). Nearly three-quarters (74.6%) self-reported being adherent to CRC screening guidelines, with having health insurance, a care provider, a previous cancer diagnosis, or a last-year check-up and being older, female, or ever married each significantly associated with greater screening adherence. **Conclusion:** Respondents reported higher screening adherence than 2018 statewide Kentucky (69.6%) and Ohio (67.2%) rates, a result consistent with prior research that could be partly explained by response bias. Additional research is needed to further explore CRC screening barriers using novel methods to reach non-responders to determine how possible differences in CRC screening behaviors or socio-demographic characteristics may contribute to disparities.

Funding: NCI 4UH3CA233282-02

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Clinical Research

Abstracts

Poster Number 7

Title: Black Louisville Residents' Colorectal Cancer Screening Knowledge, Beliefs, and Identified Needs

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Abstract: **Background:** Knowledge of colorectal cancer (CRC) screening options remains suboptimal in Black populations, contributing to screening disparities. We partnered with five Black churches in Louisville, a region of Kentucky with high Black-white CRC screening disparities, to explore screening barriers and perceptions of church-based CRC education and outreach. **Methods:** Project champions ($n = 5$) were trained to recruit church and community members ($n = 39$) to participate in semi-structured focus groups. Interview questions probed actual and perceived barriers to CRC screening, with focus on knowledge and perceptions of stool-based tests. Subsequent questions explored the feasibility of the church as a setting to adapt and implement a community-based CRC intervention. Focus group transcripts were analyzed iteratively, and codes were derived inductively and refined to develop overarching themes. **Results:** Participants listed multiple barriers to screening, including concerns about test messiness, perceptions of discomfort, and fear of discovering cancer. Inadequate medical care was frequently cited, with many participants having been solely offered colonoscopy; subsequently, knowledge of stool-based tests was low. Lastly, regarding a church-based screening intervention, participants suggested the inclusion of trusted sources of information to promote success, such as local Black medical providers, as well as CRC survivors to provide personal testimony and church leaders to increase buy-in. **Conclusion:** Members of Black churches in Louisville experienced multilevel barriers to completing CRC screening. Given the low knowledge of stool-based testing among participants and the identified inequities in receipt of clinical care, community-based CRC screening interventions may be feasible to reduce Black-white CRC screening disparities.

Funding: CCTS NIH UL1TR001998, P30CA177558

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Community Research

Abstracts

Poster Number 8

Title: Correlations Between Cellular-Level Contractile Properties and Echocardiographic-Based Measurements of Cardiac Function in Organ Donors and Patients With Heart Failure

Authors: G. N. Milburn, Department of Physiology, University of Kentucky, M. Zakharia, Department of Physiology, University of Kentucky, G. Hawk, Department of Statistics, University of Kentucky, K. S. Campbell, Department of Physiology, University of Kentucky

Abstracts: Clinical work-ups for patients with heart failure often use echocardiography to measure dimensions of the heart and assess cardiac function. Commonly reported parameters include ejection fraction and fractional shortening. Basic scientists can also use permeabilized myocardial preparations to measure cellular-level contraction. These experiments provide insight into the molecular mechanisms that regulate myocardial contraction and can be impaired in disease. Few studies have compared echo-based measurements with myofilament-level properties measured using cells from the same patients. We are currently mining previously-published contractile data to explore potential relationships between echo and cell-based measurements. Initial results suggest that the Ca²⁺-sensitivity of myofilament level contraction (pCa₅₀) is inversely correlated with echo-based ejection fraction in organ donors who do not have a history of heart failure (n=10). That is, high pCa₅₀ values are associated with lower ejection fractions. In contrast, there is no obvious relationship between ejection fraction and Ca²⁺-sensitivity in patients (n=27) who have ischemic or non-ischemic heart failure. We are continuing to explore these and other potential relationships in additional datasets. Our goal is to investigate how cell-level contraction translates to organ-level function.

Funding: NIH R01HL149164 and CCTS TL1TR001997

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Abstracts

Poster Number 9

Title: Prior Freezing has Minimal Impact on the Contractile Properties of Permeabilized Human Myocardium

Authors: N. Milburn, Department of Physiology, University of Kentucky, F. H. Moonschi, Department of Physiology, University of Kentucky, A. M. White, Department of Physiology, University of Kentucky, M. Thompson, Department of Physiology, University of Kentucky, E. J. Birks, Cardiology, University of Kentucky, K. S. Campbell, Department of Physiology, University of Kentucky

Abstract: Experiments measuring the contractile properties of human myocardium are important for translational research but complicated by the logistical difficulties of acquiring specimens. Accordingly, many groups perform contractile assays using samples that are acquired from patients at one institution and shipped to another institution for experiments. This necessitates freezing the samples and performing subsequent assays using chemically permeabilized preparations. It is unknown how prior freezing impacts the contractile function of these preparations. To examine the effects of freezing we measured the contractile function of never frozen and previously frozen myocardial samples. Samples of left ventricular tissue were obtained from 7 patients who were having a ventricular assist device implanted. Half of each sample was chemically permeabilized and used immediately for contractile assays. The other half of the sample was snap frozen in liquid nitrogen and maintained at -180 °C for at least 6 months before being thawed and tested in a second series of experiments. Maximum isometric force measured in pCa 4.5 solution, ktr measured in pCa 4.5 solution, passive force measured in pCa 9.0 solution, and Hill coefficients were not influenced by prior freezing ($p = 0.07$, $p = 0.977$, $p = 0.14$, and 0.27 respectively). pCa_{50} in never frozen samples (6.11 ± 0.04) was statistically greater ($p < 0.001$) than that measured after prior freezing (5.99 ± 0.04) but the magnitude of the effect was only ~ 0.1 pCa units. We conclude that prior freezing has minimal impact on the contractile properties that can be measured using chemically permeabilized human myocardium.

Funding: NIH R01HL149164, CCTS NIH TL1TR001997

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Abstracts

Poster Number 10

Title: Multiscale modeling of cardiac valve disease using cell-level signals to regulate concentric and eccentric myocardial growth

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Abstract: Multiscale models of the cardiovascular system are becoming effective tools for investigating the mechanisms that drive ventricular growth and biological remodeling. Some of these models can also predict how perturbations to molecular-level mechanisms impact organ-level function. This type of research might yield insights that lead to improved patient care. PyMyoVent is a multiscale computer model that bridges from molecular to organ-level function and simulates a left ventricle pumping blood around a systemic circulation. In previous work, we implemented baroreflex control of arterial pressure by using feedback to regulate heart rate, intracellular Ca^{2+} dynamics, the molecular-level function of both the thick and the thin myofilaments, and vascular tone. In this study, we extend PyMyoVent with concentric growth (wall thickening / thinning) and eccentric growth (chamber dilation / constriction) driven by cell-level signals. Specifically, concentric growth is controlled by the energy used by the myocytes for contraction (expressed as myosin ATPase normalized to myofibrillar volume) while eccentric growth responds to intracellular passive stress. The new framework reproduced clinical measures of left ventricular growth in three types of valvular disease, namely aortic stenosis, aortic insufficiency, and mitral insufficiency. Furthermore, simulations of each valvular disorder reversed growth, returning the ventricle to its default size, when the disease-mimicking perturbation was removed. In conclusion, these simulations suggest that myosin ATPase normalized to myofibrillar volume and intracellular passive stress can be used to drive concentric and eccentric growth in simulations of valve disease.

Funding: NIH HL133359, CCTS TR0001998, and AHA TP135689

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Basic/Translational Research

Abstracts

Poster Number 11

Title: Modeling Framework for Predicting the Dose-Dependent Effects on Contraction of Myotropes

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Abstract: Myotropes, such as omecamtiv mecarbil and mavacamten, are new therapeutics that bind to sarcomeric proteins. Their clinical development has reinforced the need for new quantitative understanding of sarcomere-level function. FiberSim (<https://campbell-muscle-lab.github.io/FiberSim/>) is a spatially-explicit computer model that simulates myofilament-level mechanics. The code tracks the position and status of each contractile protein within the half-sarcomere lattice. It can predict how modulating the function of a sarcomeric protein (e.g., due to a bound myotrope) will impact contractility. In particular, it can quantify sarcomere function modulation as a function of myotrope dose. In this study, we assessed the mavacamten dose-dependence of maximal isometric force. As suggested by experimental data (PMID: 32960449), we assume that mavacamten stabilizes the super-relaxed state of myosin dimers. The steady-state proportion of myosin heads bound by mavacamten can be calculated as a function of the mavacamten concentration using ATPase dose-dependent curve from the literature (PMID: 28808052). This prediction can then be integrated into FiberSim to predict a dose-response curve for maximum isometric force, which qualitatively compares to the experimental ATPase dose-dependent curve. FiberSim is a flexible and open-source software that can be used to study myofilament contraction. It is possible to evaluate a myotrope effect on force (or any other metrics, such as shortening velocity, or rate of force development) based on the target protein function modulation by the myotrope. Dose-dependent curves can be predicted. Combining this modeling approach with experimental data might to help develop new therapeutics and improve clinical care.

Funding: NIH awards: HL146676, HL148785, and TR001998 AHA awards: TP135689 and 829744

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Abstracts

Poster Number 12

Title: Late Chronotype in Young Sedentary Men, but Not Women, is Associated with Poor Cardiorespiratory Fitness

Authors: J. M. Thomas, Department of Biology, U of Kentucky, P. A. Kern, Department of Internal Medicine, Division of Endocrinology, U of Kentucky, H. M. Bush, Department of Biostatistics, U of Kentucky, W. S. Black, Lifestyle and Sports Medicine, Owensboro Health, J. S. Pendergast, Department of Biology, U of Kentucky, J. L. Clasey, Department of Kinesiology and Health Promotion, U of Kentucky

Abstract: Circadian rhythms differ between young adult men and women. For example, men tend to be later chronotypes, preferring later timing of sleep and activity, than women. Likewise, there are gender differences in body composition and cardiorespiratory fitness. Few studies have investigated gender differences in the relationship between circadian rhythms, cardiorespiratory fitness, and body composition measures that indicate metabolic risk. In this study, we sought to determine whether chronotype and circadian phase were associated with cardiorespiratory fitness, body composition, and anthropometric measures in young, sedentary men and women. Fifty-nine young adults (19 men, mean \pm SEM; 24.3 ± 0.74 years) participated in the study. Chronotype and circadian phase were measured using the Morningness-Eveningness Questionnaire (MEQ) score and dim light melatonin onset (DLMO). Actigraphy and sleep logs were collected to assess sleep timing and quality. We used peak oxygen uptake (VO_{2peak}) during a maximal graded exercise test to assess cardiorespiratory fitness. Body fat % (total body DXA scans), BMI, and abdominal circumference were collected as markers of adiposity and metabolic risk. We found that later chronotype by MEQ was associated with lower VO_{2peak} , an indicator of worse cardiorespiratory fitness, in our total dataset. A gender-stratified analysis demonstrated that in men, but not women, later chronotype, circadian phase, and sleep onset were associated with lower VO_{2peak} . Later circadian phase was also associated with increased body fat% and abdominal circumference in men, but not women. Together, these data demonstrate that young men who are later chronotypes may be at greater metabolic risk than women.

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Clinical Research

Abstracts

Poster Number 13

Title: Endovascular versus Open Surgical Techniques in the Management of Isolated Popliteal & Infrapopliteal Peripheral Vascular Disease: A Single Center Analysis

Authors: Davies, J.T., Davenport, D.L., Gurley, J.C., & Saha, S.P.

Abstract: **Introduction:** Peripheral artery disease (PAD) continues to be major health and economic burdens on many health care systems. The optimal surgical approach for the technically challenging occlusive lesions of the infra-femoral regions has yet to be described or substantiated. This study specifically aims to compare outcomes associated with endovascular versus open surgical treatment of popliteal and infrapopliteal occlusive disease. **Methods:** With IRB approval, we queried the institutional database for PAD interventions and reviewed patient records undergoing endovascular or open bypass intervention for PAD below the femoral artery anatomic region between 2010 and 2020. Patient records were reviewed for up to 2-years after the index procedure. **Results:** 45 endovascular and 22 open procedures involved specifically popliteal and/or infrapopliteal PAD met the inclusion criteria. For the surgical group (22): majority were male (16), with an average and median age at time of procedure of 62.49, and 63.98 years, respectively. For the endovascular group (45): majority were male (32), with an average and median age at time of procedure of 57.93, and 58 years, respectively. Most patients in this group were co-morbid with diabetes mellitus (29) or CKD (10). Commonest presenting symptom was nonhealing ulcer (22). Commonest complication was non-healing wound/ulcer. 4 and 10 patients required limb salvaging revascularization in the first 30 days and in the period from 31 days to 2 years following the index procedure, respectively. **Conclusions:** Endovascular interventions of isolated popliteal and infrapopliteal PAD was less costly, had better short-term outcomes, but was associated with higher rates of reintervention.

Funding: UK Cardiothoracic Surgery Department

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Clinical Research

Abstracts

Poster Number 14

Title: Factors that Affect Follow-up Completion Rates

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Abstract: Research has suggested that individual characteristics (e.g., sex, age and health status) may be associated with the choice to participate in research studies. However, findings are inconsistent. The purpose of this study is to examine the potential role of select personal characteristics and study condition in completing assessments in context of a longitudinal study of the effectiveness of an online game-based screening tool. Participants included 109 youth (ages 8-17; M = 11.8 years; 55 female) who presented for medical care in the emergency department and / or hospital and one caregiver per youth (98 female). Participants completed baseline measures, were randomized to study condition (n = 73 intervention; n = 36 usual care), and completed follow-up assessments 6 and 12 weeks later. Findings indicated that neither child nor parent sex, age, or child medical condition was associated with whether they completed follow-up assessments. However, those in the intervention condition were less likely to complete follow-up assessments at 6 (59.3% vs 80.6%; $\chi^2(1, 90) = 4.2, p < .05$) and 12 weeks (45.3% vs 70.4%; $\chi^2(1, 80) = 4.5, p < .05$). It may be that those in the intervention condition suffer from contact fatigue. Further research should examine what factors can help increase follow up completion and whether condition impacts follow up rates in other types of research studies.

Funding: NIH Grant: R42 HD087021-02

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Clinical Research

Abstracts

Poster Number 15

Title: Higher Levels of Cardiovascular Fatalism are Associated with Higher Levels of Anxiety in a Sample of Latinx Patients At-Risk for Cardiovascular Disease

Authors: M. Arce, University of Kentucky College of Medicine, U of Kentucky, K. V. Key, College of Nursing, U of Kentucky, G. Mudd-Martin, College of Nursing, U of Kentucky

Abstract: Anxiety has been linked to increased risk for cardiovascular disease (CVD). In the Latinx population, many believe that health outcomes are predetermined, known as fatalism. The purpose of this study was to examine whether increased cardiovascular fatalism among Latinx adults at-risk for CVD is associated with increased anxiety. **Methods:** Data were obtained from 125 Latinx participants in the *Corazon de la Familia* (Heart of the Family) study who were at-risk for CVD. Baseline data included self-reported sociodemographic information; and measures of fatalism using the Cardiovascular Fatalism Scale (range: 14-70) and anxiety using the PROMIS Anxiety scale (standardized to a mean of 50). We conducted linear regression modelling to examine if cardiovascular fatalism predicted anxiety controlling for age, sex, race, marital status, education level, financial comfort, health literacy, and family functioning. **Results:** The mean age of our sample was 41±9 years; 85.6% were female; 72.8% were married or cohabitating; 76.0% reported having a sufficient income to make ends meet each month; 34.4% had more than a high school degree; and 42.4% had adequate health literacy. Of those who self-identified race, 65.6% reported being White. The mean scores for fatalism and anxiety were 29.5±8.6 and 47.8±9.2, respectively. Higher levels of cardiovascular fatalism were associated with higher levels of anxiety ($p = .001$, $R^2 = .213$). **Conclusion:** The positive association between cardiovascular fatalism and anxiety in this sample of Latinx adults at-risk for CVD suggests the need for future research to better understand fatalism in Latinx populations and its impact on cardiovascular health.

Funding: Professional Student Mentored Research Fellowship (PSMRF) CCTS NIH UL1TR001998, UK HealthCare and the University of Kentucky College of Medicine; NIH R01NR01626

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Community Research

Abstracts

Poster Number 16

Title: Ternary Polypeptide Nanoparticles with Improved Encapsulation, Sustained Release, and Enhanced In Vitro Efficacy of Carfilzomib

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Abstract: Carfilzomib (CFZ) has been approved by the FDA for treatment of relapsed/refractory multiple myeloma (MM). Although it has been successful in treating patients with MM, CFZ has shown limited efficacy against solid tumors in the clinic. Clinical limitations include low half-life, rapid clearance and poor targetability. To address these limitations, we design ternary polypeptide nanoparticles (tPNPs) comprising Heptakis(6-amino-6-deoxy)- β CDheptahydrochloride (Ha β CD) and Azido-poly (ethylene glycol)-block-poly (L-glutamic acid sodium salt) (N₃-PEG-PLE). CFZ is entrapped within the core of Ha β CD which then ionically interacts with N₃-PEG-PLE to form CFZ/tPNPs. For targeted delivery, epithelial cell adhesion molecule (EpCAM) antibody was conjugated to N₃-PEG-PLE before drug loading to form (CFZ/EpCAM-tPNPs). All formulations (tPNPs, CFZ/tPNPs and CFZ/EpCAM-tPNPs) showed a uniform particle size of ~ 50 nm. tPNPs were also able to achieve high drug loading (>1 mg/mL). These formulations were tested in vitro in DLD-1 CFZ resistant cells. The EpCAM-tPNPs had significantly better cellular uptake than tPNPs and control. CFZ/tPNPs better sustained proteasome inhibition compared to free CFZ. Finally, CFZ/tPNPs and CFZ/EpCAM-tPNPs showed a greater cytotoxicity against DLD-1 CFZ resistant cells than free CFZ. These results suggest that CFZ/tPNPs and CFZ/EpCAM-tPNPs could be potentially useful for improving the efficacy of CFZ in solid tumors, hence, expanding its clinical utility.

Funding: Pharmaceutical sciences Excellence in Graduate Achievement Award and NIH R01 AG073122

Presenter: Agbana, Preye
Basic/Translational Research

Abstracts

Poster Number 17

Title: Investigation of polyene products of polyketide synthases and thioesterases that initiate biosynthesis of enediyne cores

Authors: Erome Daniel Hankore*,¹ Mitchell D. Miller,² Minakshi Bhardwaj,¹ Steven G. Van Lanen,¹ Jon S. Thorson,¹ George N. Phillips²

Abstract: Enediyne natural products like calicheamicin, C-1027, esperemycin, and dynemicin, are potent antitumor and antibacterial compounds. The iterative polyketide synthases (iPKSs) and cognate trans-thioesterases (TEs) involved in enediyne biosynthesis generate a 1,3,5,7,9,11,13-pentadecaheptaene intermediate that is thought to be the precursor for enediyne cores. However, other polyene products similar to the heptaene intermediate and which may also serve as precursors have been reported from biotransformations and *in vitro* assays with iPKSs and TEs of both 9- or 10-membered enediynes. To address the ambiguity surrounding the real precursor of the enediyne cores, we looked at products of iPKS and TE pairs SgcE/SgcE10 (C-1027 biosynthesis) and DynE8/DynE7 (dynemicin biosynthesis), including products generated when iPKSs and TEs of the 9- or 10-membered enediynes are cross paired. A TE from the esperemycin producing *Actinomodura verrucososora* strain, EspE7, was also studied alongside SgcE or DynE8. Finally, the crystal structure of EspE7 was solved and mutants were prepared and studied in *in vitro* assays to further clarify the catalytic mechanism of TEs.

Funding: NIH CA217255.

Presenter: Hankore, Erome\erome.daniel@uky.edu

Basic/translational research

Abstracts

Poster Number 18

Title: Development of Agents Against Stimulant Use Disorders: Synthesis and SAR studies of Protein Tyrosine Phosphatase Receptor Type D (PTPRD) Inhibitors

Authors: Nazmul H. Bhuiyan,¹ Ian M. Henderson,^{2,3} Fanxun Zeng,⁴ Dan Luo,¹ Maria Martinez,^{2,3} Fangchao Bi,⁴ Chamani Perera,⁵ David Johnson,⁵ Thomas E. Prisinzano,¹ Wei Wang,⁴ and George R. Uhl^{2,3,6-8}

Abstract: Stimulant abuse damages individuals and communities in the United States as well as across the world. It imposes not only a financial damage but also large societal costs. Deaths from stimulant use disorder is rising every year which compounded by the rise in abuse of synthetic opioids. Unfortunately, there is no Food and Drug Administration-approved medications for stimulant-use disorders. Genome wide association studies (GWAS), mouse models and studies with protein tyrosine phosphatase receptor type D (PTPRD) inhibitors suggest that PTPRD an attractive target to develop a medication for stimulant use disorder such as cocaine, methamphetamine. An illudalic acid analog, 7-butoxy illudalic acid (7-BIA) is a selective and small molecule inhibitor of PTPRD that reduces cocaine reward in self-administration and conditioned place-preference models. A set of analogs related to 7-BIA has been synthesized and evaluated for their activity at inhibiting PTPRD and related phosphatases. Analogues with improved activity compared to 7-BIA were identified. *In vivo* studies revealed there was no gross or behavioral toxicity up to 20 mg/kg in mice and rats with substantial intravenous, intraperitoneal and oral bioavailability of several of these compounds including 7-BIA. These encouraging data suggests investigating further in animal models relevant to substance use disorder and developing an agent toward use in human.

Funding: NIH U01047713 and CCTS NIH UL1TR001998

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Basic/translational research

Abstracts

Poster Number 19

Title: Design and synthesis of potential opioid rescue agents

Authors: Edem K. Onyameh,¹ Sidnee L. Hedrick,¹ Dan Luo,¹ and Thomas E. Prisinzano¹

Abstract: In 2020, exacerbated by the covid 19 pandemic, more than 69,000 deaths in the United States have been attributed to opioid overdose and 80% of these fatal deaths involves synthetics such as fentanyl (100 times more potent than morphine) and its analogs. Opioid induced fatalities result from respiratory depression that is the result of agonism at the mu opioid receptor. Currently, there are three opioid antagonists (naloxone, naltrexone and nalmefene) available clinically with the potential to reverse the effects of fentanyl. However, these antagonists are not optimal because of their short duration of action and weak potency compared to fentanyl. Thus, there is a need to develop higher potency and longer-acting opioid antagonists to reverse the respiratory depression of fentanyl and its analogues. Diprenorphine is an opioid partial agonist used in veterinary medicine for reversing the effects of super-potent opioid analgesics such as etorphine and carfentanil that are used for tranquilizing large animals. Due to its intriguing profile of reversing these highly potent opioid agonists, our laboratory has undertaken an optimization campaign to identify a diprenorphine analogue suitable for use in humans as an opioid rescue agent. Through a combination of multi-step organic synthesis and structure-activity relationships studies, we have identified MOR antagonists with enhanced potency compared to naloxone and greater antagonism than diprenorphine.

Funding: NIH U01DA051377 and CCTS NIH UL1TR001998

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Basic/translational research

Abstracts

Poster Number 20

Title: Analysis of Barriers and Facilitators to HIV PrEP in a Transgender Population

Authors: N. Dixon, Department of Pharmacy Practice and Science, U of Kentucky

Abstract: BACKGROUND: The transgender population is at high-risk for HIV, and yet often overlooked in studies on HIV pre-exposure prophylaxis, or PrEP. This population has its own unique barriers to health care, and how these barriers affect awareness and access of PrEP in at-risk transgender individuals is poorly understood. OBJECTIVES: To identify possible barriers and facilitators to PrEP use in a transgender population. METHODS: This retrospective observational study utilized a secondary analysis of quantitative survey results collected in ATN 130. R version 3.6.1 was used to analyze the survey responses of transgender youth aged 16-24 using chi-square and Fisher's exact tests to find variables that could predict the use of PrEP. RESULTS: No statistically significant relationship was found between mental health factors or gender affirmation factors and the use of PrEP. HIV programming was found to be strongly associated with the use of PrEP in transgender youth aged 16-24 ($p=0.01$). Research study participation was also found to be strongly associated with PrEP use ($p<0.01$). CONCLUSIONS: The strongest predictors of PrEP use in a young, transgender population appear to be involvement in either HIV preventative programs or HIV research studies. This is indicative that direct and HIV-focused approaches to care are by far the most effective way to improve HIV prevention and care in this population. Other factors hypothesized to predict PrEP use, such as mental health treatment and medical gender affirmation, were not found to be predictive of PrEP use.

Funding: NIH DASH, University of Kentucky College of Pharmacy

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Community Research

Abstracts

Poster Number 21

Title: The CLEVER Study: Implementing an Educational Intervention to Reduce Preterm Birth in Appalachian Kentucky

Authors: C. Jenkins, University of Kentucky College of Medicine J. Barnett, Perinatal Research and Wellness Center, College of Nursing, U of Kentucky A. McCubbin, Perinatal Research and Wellness Center, College of Nursing, U of Kentucky K. Ashford, Perinatal Research and Wellness Center, College of Nursing, U of Kentucky N. Chavan, Department of Obstetrics and Gynecology, Maternal Fetal Medicine, Saint Louis U

Abstract: **Purpose:** Preterm birth (PTB) represents a critical health disparity in Kentucky, particularly in rural Appalachia. In 2020, Kentucky's PTB rate was 11.05% making it the 9th highest in the United States, with some counties in Kentucky having over 1.5 times that rate. Online educational interventions have been shown to positively impact health outcomes and reduce health disparities; however effective online educational media targeting health disparate subgroups are lacking. The purpose of this study was to evaluate the impact of online educational videos on patient knowledge about PTB. **Methods:** Seven brief (3-5 minute) patient educational videos were created and implemented in two women's health clinics in Appalachian Kentucky – Hazard and Morehead, KY. Each video focused on a different topic related to PTB and PTB prevention. Pre- and post-test surveys were completed for each module, and rate of change calculations and t-tests were used to assess changes in knowledge ($p < 0.05$). **Results:** Out of 72 pregnant women that were recruited, 51 completed the videos and subsequent pre/post-test evaluations. Percentage change calculations indicated a positive increase in knowledge gained across each of the seven modules (range: 5.4% to 31.1%), while three of the seven modules yielded statistically significant differences from pre to post-test scores ($p < 0.001$; $p = 0.003$; $p = 0.02$). **Conclusions:** Patient education about PTB is a critical step for addressing knowledge-based barriers for strategies targeting PTB prevention. Online educational media serve as an effective tool for knowledge dissemination among health disparate populations in Appalachian Kentucky.

Funding: AMAG Pharmaceuticals, Inc., a Delaware Corporation

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Community Research

Abstracts

Poster Number 22

Title: Implications of the Gut Microbiota on Neonatal Abstinence Syndrome: Analysis of Finnegan Scores and Stool Outputs

Authors: E. S. Amrit, College of Medicine, U of Kentucky H. Bada, Department of Neonatology, U of Kentucky

Abstract: Neonatal Abstinence Syndrome (NAS) is a collection of symptoms that arises due to withdrawal from substances, such as opioids, from exposure during gestation. These behaviors are thought to be disorganized rather than adaptive. This study analyzed the Finnegan scores and stool outputs of infants in the Neonatal Intensive Care Unit at the University of Kentucky with various lengths of stay. An altered gut flora, known as dysbiosis, has been shown to play a role in various gastrointestinal conditions such as colic in infant and irritable bowel syndrome in young adults. The goal of this study was to see if dysbiosis also has an effect of NAS by comparing the stool samples against the Finnegan score, which is the most widely used tool in assessing NAS, and seeing if peaks of one correlated with a peak in the other. The infants were also divided into two groups a “short” group which was defined as 14–21-day hospital stay and a “long” group which was more than 21 days in the hospital. The cause of the extension of stay was also hypothesized. The main exposure of most of the infants was morphine. Examining the effects of the gut microbiome on NAS can help us understand if current pharmacologic interventions with NAS can utilize probiotics with treatment.

Funding: CCTS PSMRF Program

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Clinical Research

Abstracts

Poster Number 23

Title: Outcomes of Inpatient Palliative Care Consultations in Decompensated Cirrhosis at a Tertiary Care Center: A Descriptive Study

Authors: A. Matney, College of Medicine, U of Kentucky, A. Brenner, Department of Internal Medicine, U of Kentucky P. Abhyankar, Department of Internal Medicine, U of Kentucky K. Thakur, Department of Gastroenterology, U of Kentucky

Abstract: Introduction: Decompensated cirrhosis is associated with a high mortality rate, and poor health-related quality of life. Early intervention by palliative care can address symptoms, advanced care planning, and quality of life. We sought to characterize the patterns of use and outcomes in decompensated cirrhosis patients with inpatient palliative care consultation. Methods: We conducted a retrospective chart review of hospitalized patients with cirrhosis diagnosis and at least one of the four decompensating events i.e variceal bleeding, encephalopathy, ascites, or jaundice that received inpatient palliative care consultation between 2018 and 2019. We collected variables that identify key characteristics such as time to palliative care consult, complications of cirrhosis, and hospitalization outcome. This project was approved by the University of Kentucky IRB. Results: The cohort included 155 patients, and NASH was the most common cause of cirrhosis. The mean MELDNa for the cohort was 23. The mean time to PC consultation was 9 days from admission. Two thirds (68%) of patients had refractory ascites, and more than half (56%) had hepatic encephalopathy. Ninety percent of palliative care consultations addressed goals of care discussion and fifty-seven percent of consults addressed symptom management. One-fourth of the patients died in the hospital while more than half (52%) survived to discharge. Conclusion: Inpatient palliative care consultations often come at the end of life and focus on goals of care discussion. Most patients are discharged to hospice. We need interventional studies to implement a care pathway with early palliative care involvement to address unmet needs in these patients.

Funding: CCTS NIH UL1TR001998, and the Dean of the College of Medicine, University of Kentucky.

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Clinical Research

Abstracts

Poster Number 24

Title: Anti-inflammatory properties of new mPGES-1 inhibitors in gingival fibroblasts and Monocyte-derived Macrophages

Authors: V. T. E. Alves, Center for Oral Health Research, U of Kentucky M. Stewart, College of Pharmacy, U of Kentucky R. Danaher, Center for Oral Health Research, U of Kentucky C. Zhan, College of Pharmacy, U of Kentucky O. A. Gonzalez, Division of Periodontology, College of Dentistry, U of Kentucky

Abstract: Objective: Although non-steroidal anti-inflammatory drugs (NSAIDs) improve clinical outcome of periodontal treatment, their effect declines after drug withdrawal, and it is associated with adverse effects. The goal of this study was to test the ability of new microsomal prostaglandin E synthase 1 (mPGES-1) inhibitors to block oral bacteria-induced inflammation. mPGES-1 inhibitors are more specific for blocking newly synthesized prostaglandin E2 (PGE2) without affecting its basal levels or the production of other prostaglandins or thromboxanes, which avoid side effects. **Methods:** Cytotoxicity of mPGES-1 inhibitors UK4B and ISTZ (0.01, 0.1, 1, 10, and 20µM) was tested in human gingival fibroblasts (HGFs) and monocytes-derived macrophages (MDMs). Both HGFs and MDMs were treated with selected concentrations of UK4B or ISTZ inhibitor, followed by *P. gingivalis* infection and determination of prostaglandin E2 (PGE₂) levels by ELISA. mPGES-1 and COX-2 gene expression was evaluated in HGFs by qRT-PCR. **Results:** Cell viability was not significantly affected by UK4B or ISTZ inhibitor. UK4B and ISTZ inhibitors significantly decreased *P. gingivalis*-induced PGE2 levels in HGFs. Neither UK4B nor ISTZ decreased *P. gingivalis*-induced PGE₂ production in MDMs at the tested concentrations. mPGES-1 and COX-2 gene expression was also reduced by UK4B in *Pg*-exposed HGFs. **Conclusion:** Nanomolar concentrations of mPGES-1 inhibitor UK4B (and possibly ISTZ) decrease *P. gingivalis*-induced PGE₂ levels as well as mPGES-1 and COX2 gene expression in HGFs but not MDMs. Further studies testing higher concentrations or identifying mechanisms associated with potential failure of mPGES-1 inhibitors to block bacteria-induced PGE2 production in MDMs are needed.

Funding: UK Office of VPR - IRC 2021

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Basic/Translational Research

Abstracts

Poster Number 25

Title: The Dual Reporter Sensor Cell (DRSC) Assay: An Enhanced Tool for Measuring the HIV Viral Reservoir

Authors: S.Torabi, Department of Mechanical Engineering, U of Kentucky S. Backus, Department of Mechanical Engineering, U of Kentucky K. Eterovich, Department of Mechanical Engineering, U of Kentucky R. Striker, Department of Medicine, U of Wisconsin N. Sherer, Department of Oncology, U of Wisconsin S. Berry, Department of Mechanical Engineering and Biomedical Engineering, U of Kentucky

Abstract: A major barrier to the eradication of infection in HIV+ patients is the establishment of a “viral reservoir”, which consists of HIV-infected memory T-cells that have the ability to “activate” and produce infectious HIV virions. While many researchers are developing new therapeutic strategies to diminish this reservoir, existing tools to quantify reservoir reduction are either too inaccurate or too complex for widespread clinical implementation. Thus, there is an unmet need for an accurate (high sensitivity AND high specificity) assay to quantify the HIV viral reservoir that can be performed in 1-2 days. In this study, the high specificity is achieved by using dual reporter sensor cells (DRSCs) that have two independent HIV infection-linked reporter systems. A true positive signal is only obtained when both reporters are triggered simultaneously, therefore increasing the specificity. To improve the sensitivity of the assay, the cellular interactions are captured in a low-convection cell culture environment, which decreases the convective dilution of the secreted factors. This maintains a high local concentration of the virions that trigger the DRSCs, maximizing the sensitivity of the assay. To achieve those goals, polydimethylsiloxane (PDMS) microfluidic channels with different heights were designed, fabricated, and tested to capture the effects of a variety of low convective regimes. The viability of the DRSCs and their response to HIVs were examined in those microfluidic channels. The future work includes testing the system with HIV-positive patient samples to further verify the functionality of the assay.

Funding: NIH grant R21AI155008.

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Basic/Translational Research

Abstracts

Poster Number 26

Title: Incidence of Coinfection of Hepatitis A, B, and C in Southeastern Kentucky

Authors: U. Shankar, MD, Gastroenterology, Clark Regional Hospital, Winchester, KY M. Dignan, PhD, MPH, Director of Cancer Prevention Control Research Program, U of Kentucky S. Holla, College of Medicine, Ohio State University, Columbus, OH R. Munnolimath, Frederick Douglass High School, Lexington, KY

Abstract: Results: For hepatitis A, 56.25% were male, hepatitis B 58.3% male, and C 70.24% male. The median ages for males with hepatitis A was 43, females 56; hepatitis B 50, female 52; and C 43, female 40.5. Most (79.6%) patients were diagnosed with hepatitis C and of those, 70% were male. Five (13.2%) patients had more than one type of hepatitis; A and B 3.3%, A and C (3.3%), B and C (3.3%), and A, B, C (3.3%). Patients with hepatitis A, B and C were all male. Risk behaviors among the patients included reported IV drug use (35%), and alcohol abuse (12.5%). None of the patients had HIV infection. Tattoo users had a higher incidence of hepatitis B and hepatitis C than hepatitis A. Approximately 33% of drug users were associated with hepatitis A, B, and C. Overall, the incidence of coinfection was (13.2%). Finding: The incidence of coinfection is elevated in this population with hepatitis A, hepatitis B, and hepatitis C (13.2%) associated with increasing incidences of hepatitis A and B in a hepatitis C endemic area. In our findings, the incidence of hepatitis C (79.6%) was higher than A (10.5%) or B (7.9%). These incidence rates are higher in middle age groups (40-52). Further study with a higher number of patients might give more insight. Counseling and vaccination may prevent future incidents of hepatitis.

Funding: No Support

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Clinical Research

Abstracts

Poster Number 27

Title: KGDAL: Knowledge Graph Guided Double Attention LSTM for Rolling Mortality Prediction for AKI-D Patients

Authors: L.J. Liu, Department of Computer Science, U of Kentucky V. Ortiz-Soriano, Division of Nephrology, Bone and Mineral Metabolism, U of Kentucky J. A. Neyra, Division of Nephrology, Bone and Mineral Metabolism, U of Kentucky J. Chen, Department of Internal Medicine, Department of Computer Science, U of Kentucky

Abstract: With the rapid accumulation of electronic health record (EHR) data, deep learning (DL) models have exhibited promising performance on patient risk prediction. Recent advances have also demonstrated the effectiveness of knowledge graphs (KG) in providing valuable prior knowledge for further improving DL model performance. However, it is still unclear how KG can be utilized to encode high-order relations among clinical concepts and how DL models can make full use of the encoded concept relations to solve real-world healthcare problems and to interpret the outcomes. We propose a novel knowledge graph guided double attention LSTM model named KGDAL for rolling mortality prediction for critically ill patients with acute kidney injury requiring dialysis (AKI-D). KGDAL constructs a KG-based two-dimension attention in both time and feature spaces. In the experiment with two large healthcare datasets, we compared KGDAL with a variety of rolling mortality prediction models and conducted an ablation study to test the effectiveness, efficacy, and contribution of different attention mechanisms. The results showed that KGDAL clearly outperformed all the compared models. Also, KGDAL-derived patient risk trajectories may assist healthcare providers to make timely decisions and actions.

Funding: NIH NIDDK R56 DK126930 and P30 DK079337.

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Basic/Translational Research

Abstracts

Poster Number 28

Title: Impact of using different Acquisition Parameters on CT Image Radiomic Features

Authors: Md Selim, Institute for Biomedical Informatics, U of Kentucky Jie Zhang, Departments of Radiology, U of Kentucky Jin Chen, Institute for Biomedical Informatics, U of Kentucky

Abstract: Radiomics, a feature-based image analysis paradigm, shift the usages of CT images from a qualitative measure to quantitative analysis. However, the usages of different CT image acquisition parameters significantly influence the image features and make radiomic models unstable. The stability of the image features is essential for reliable correlation with the underlying pathology and potential applications in predicting clinical outcomes. The discrepancy in the underlying images also creates a limit for large-scale cross-center studies. Here we have studied the impacts of reconstruction kernels on the image features and how these differences influence a radiomic model for tumor staging prediction. We have used images from three different scanners, i.e. Siemens, General Electric, and Philips, for this study from a public dataset and an in-house phantom scanned dataset. The results show that each radiomic feature class has its unique level of impact due to the use of different reconstruction kernels. The radiomic model performance is also influenced by the selection of reconstruction kernels.

Funding: NIH NCI (grant no. 1R21CA231911) and Kentucky Lung Cancer Research (grant no. KLCR-3048113817).

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Basic/Translational Research

Abstracts

Poster Number 29

Title: Reproducing Solution NMR Protein Conformations Using Deep Learning and Molecular Dynamics Simulation

Authors: Qi Qiao, Department of Chemical and Materials Engineering, U of Kentucky, Qing Shao, Department of Chemical and Materials Engineering, U of Kentucky, Jin Chen, College of Medicine, U of Kentucky

Abstract: The recently announced alphaFold2 and RosettaFold, with their level of accuracy comparable to X-ray crystallography, spark the development of deep learning methods in predicting the 3D conformation of clinically important proteins. Nevertheless, due to the lack of data, deep learning tools cannot precisely predict the protein conformations in solvents, which are critical for inferring protein functions. Molecular dynamics (MD) simulations are traditional tools widely used to obtain protein conformations in solvents but the protein initial structures or constraints are difficult to obtain. It remains an open question whether MD simulations and deep learning combined can better predict protein conformation in solvents. This work compared the performance of alphaFold2 and MD simulations in reproducing the reported solution NMR protein conformations. We selected 30 proteins with their solution NMR conformations reported after the release of alphaFold2, meaning that none of the selected proteins were used to train alphaFold2. We first predicted the 3D conformations of the 30 proteins using the pretrained alphaFold2. Second, using the alphaFold2-predicted conformations as inputs, we obtained the conformations of the same proteins in explicit solvent using MD simulations with the default parameters. The reported solution NMR conformations for these proteins were served as the benchmark. The comparison was conducted based on the root means squared deviation of C_α atoms on proteins, the secondary structures of individual amino acid residues, and C_α-C_α contact distances. Our preliminary work based on the 30 preselected proteins confirmed that alphaFold2 presented a wide spectrum regarding their performance in predicting the NMR solution conformation of proteins. The results also showed MD simulations generated many results with their performance similar to alphaFold2 indicating that MD simulations can be used as an effective data augmentation tool to enhance protein conformation prediction using contractive learning.

Funding: Start-up Funds

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Basic/Translational Research

Abstracts

Poster Number 30

Title: Spontaneous Alignment of Myotubes through Satellite Cell Migration

Author: L. E. Mehanna, Department of Chemical and Materials Engineering, U of Kentucky, C. A. Peterson, Department of Rehabilitation Sciences, U of Kentucky, B. J. Berron, Department of Chemical and Materials Engineering, U of Kentucky

Abstract: In large volume muscle injuries, muscle fibers as well as the surrounding connective tissue are damaged, preventing therapeutic muscle stem cells, satellite cells (SCs), from reaching the injury site and initiating repair. There is a clinical need to rapidly fabricate in vitro muscle tissue constructs that mimic the native tissue organization, with aligned myotubes, for insertion and integration at the patient's injury site. Most strategies for myotube alignment require microfabricated structures or prolonged orientation times. We utilize the SC's natural propensity to close gaps across an injury site to guide alignment on collagen I, an extracellular matrix (ECM) protein substrate. Through the binding affinity of biotin and streptavidin molecules, we pre-position SCs in straight-line patterns separated with small gaps, mimicking small-scale muscle injuries. This temporary positioning initiates the migratory nature of the SCs to align and form myotubes across the gaps. There is a directional component to the SC migration perpendicular (90°) to the original biotin-streptavidin surface patterns. Cells migrate into the spaces between patterns towards other cells but do not migrate in directions where no cells were present. We use myosin heavy chain IHC to demonstrate that our patterning process does not impact SC viability or long-term functionality. The rapid and highly specific binding of biotin-streptavidin allows for quick formation of temporary patterns, with SC alignment based on natural regenerative behavior rather than complex fabrication techniques.

Funding: Igniting Research Collaboration (IRC) Pilot Grant, NSF Graduate Research Fellowship: Grant No. 1839289

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Basic/Translational Research

Abstracts

Poster Number 31

Title: Regenerative Peripheral Nerve Interface Versus Targeted Muscle Reinnervation for Prevention of Neuroma Formation Following Nerve Injury

Authors: J. C. Kluemper, College of Medicine, U of Kentucky A. J. Al Bayati, Department of Plastic Surgery, U of Kentucky E. Lynch, Department of Plastic Surgery, U of Kentucky B. Fink, Department of Plastic Surgery, U of Kentucky D. Bourne, Department of Plastic Surgery, U of Kentucky

Abstract: Targeted muscle reinnervation (TMR) and regenerative peripheral nerve interfaces (RPNI) have previously been shown to decrease neuroma (tumor or mass) formation following a nerve injury. However, the efficacy of these techniques has not been properly compared. The aim of this study is to assess the efficacy of TMR and RPNI in preventing neuroma formation. Three groups of 4 rats each were used during this study. All 3 groups would undergo a simulated nerve injury in which the common sciatic nerve is cut. One group would then undergo TMR in which the sciatic nerve is coapted to the transected motor nerve to the biceps femoris muscle. Another group would undergo RPNI in which the sciatic nerve is reattached to a free graft of extensor digitorum longus muscle. The final group was the control where the sciatic nerve was transected and not reattached in any way. After the operations the rats were given 16 weeks to recover and allow for any possible neuroma formation. After this time electromyography (EMG) studies were performed to assess nerve regeneration and muscle function. The rats were then euthanized and dissected to remove all relevant nerve and muscle tissue. These dissected samples underwent imaging via MRI and toluidine blue histology to determine the extent of any neuroma formation and nerve regeneration. Through our data we hope to determine whether RPNI and TMR are effective at preventing neuromas compared to the control group. We also hope to determine which method is most effective at preventing neuroma formation.

Funding: Startup Funds

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Basic/Translational Research

Abstracts

Poster Number 32

Title: Targeting Astrocytes improves hyperemic and brain function in a diet-based model of vascular contributions to cognitive impairment and dementia (VCID)

Authors: P. Sompol, Sanders-Brown Center on Aging and Department of Pharmacology and Nutritional Sciences, U of Kentucky J. Gollihue, Sanders-Brown Center on Aging, U of Kentucky B. Weiss, Department of Pharmacology and Nutritional Sciences, U of Kentucky C. J. Gant, Department of Pharmacology and Nutritional Sciences, U of Kentucky E. Weekman, Sanders-Brown Center on Aging and Department of Physiology, U of Kentucky S. Kraner, Department of Pharmacology and Nutritional Sciences, U of Kentucky D. Wilcock, Sanders-Brown Center on Aging and Department of Physiology, U of Kentucky R.-L. Lin, Department of Pharmacology and Nutritional Sciences, U of Kentucky O. Thibault, Sanders-Brown Center on Aging and Department of Pharmacology and Nutritional Sciences, U of Kentucky C. Norris, Sanders-Brown Center on Aging and Department of Pharmacology and Nutritional Sciences, U of Kentucky

Abstract: Vascular contributions to cognitive impairment and dementia (VCID) and other vascular diseases are highly related and comorbid with Alzheimer's disease (AD) pathology and may accelerate the progression of dementia and/or reduce the clinical efficacy of treatments. Astrocyte activation linked to aberrant calcineurin (CN)/NFAT signaling is a shared mechanism between VCID and AD. Here, we tested the hypothesis that blockage astrocytic CN/NFAT restrains astrocyte reactivity and preserves astrocyte-related vascular coupling in a mouse VCID model. Viral vectors to express control (AAV-Gfa-EGFP) or NFAT inhibitor, VIVIT peptide (AAV-Gfa-VIVIT-EGFP) were injected into barrel cortex of C57BL/6J mice. Transgene expression was regulated under the astrocyte specific, Gfa2, promoter. Then, glass window installation was performed for intravital imaging. After recovery, mice were fed for 12 weeks with control chow or chow with low levels of folate, vitamins B6 and B12 and enriched with methionine to induce hyperhomocysteinemia (HHcy) and cerebrovascular pathology. Astrocytic EGFP expression showed upregulation during HHcy diet, indicate astrocyte reactivity that was attenuated by VIVIT. Hyperemic responses including superficial blood flow and penetrating arteriole vasodilation were measured and VIVIT treatment rescued HHcy-impaired hyperemic function during whisker stimulation. To study memory and synaptic function, groups of mice were injected with AAV control vector or AAV-Gfa-VIVIT-EGFP into the hippocampus and then fed with control or HHcy diets. Synaptic deficits and reduced Y-maze alternation were found in HHcy diet group which could be alleviated by VIVIT treatment. Overall, findings suggest that HHcy, a major risk factor for VCID, may trigger an activated astrocyte phenotype leading to neurovascular impairment, and ultimately cognitive decline.

Funding: CCTS NIH UL1TR001998, NIH R01 AG027297

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Basic/Translational Research

Abstracts

Poster Number 33

Title: Development of a Monoclonal Antibody Specific for a Calpain-Generated Δ 48 kDa Calcineurin Fragment, a Marker of Distressed Astrocytes We would greatly appreciate it if the two posters from our lab could be put side-by-side. The other poster from our lab is: **Oxidative Stress-Associated Cerebrovascular Pathology in Alzheimer's Disease**

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Abstract: Background: Calcineurin (CN) is a Ca²⁺/calmodulin-dependent protein phosphatase expressed at high levels in brain. In healthy tissue, CN exists mainly as a full-length (~60 kDa) highly-regulated protein involved in essential cellular functions. However, in diseased or injured tissue, CN is proteolytically converted to a constitutively active fragment that has been causally linked to numerous pathophysiologic processes. This 48 kDa CN fragment (Δ CN) appears at high levels in human brain at early stages of cognitive decline associated with Alzheimer's disease. Δ CN tends to show-up in regions of frank amyloid and cerebrovascular pathology, especially in select subsets of astrocytes. Our goal was to develop monoclonal antibodies to this Δ CN for use in neuropathology research. **Methods:** A peptide encompassing the calpain sensitive region of the CN carboxyl terminus was used for antibody generation. Antibodies were screened in ELISAs against the immunizing peptide, but **decision-making screens** were carried out as a Western analysis of calpain-cleaved calcineurin, to show highest specificity towards the Δ 48 CN fragment. **Results:** We identified a monoclonal that was highly specific towards the Δ 48 CN fragment in Westerns, and then used this same antibody to determine that it was a marker of astrocytes surrounding amyloid plaques and other pathologies in human brain immunostaining analyses. This monoclonal will provide for ongoing analyses as a marker of distressed astrocytes.

Funding: NIH (AG027297), the Kentucky Spinal Cord and Head Injury Research Trust (12-10A), and The Hazel Embry Research Fund

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Basic/Translational Research

Abstracts

Poster Number 34

Title: Oxidative Stress-Associated Cerebrovascular Pathology in Alzheimer's Disease
We would greatly appreciate if the 2 posters from our labs could be put side-by-side. The title of the second poster from our lab is: Development of a Monoclonal Antibody Specific for a Calpain-Generated Δ 48 kDa Calcineurin Fragment, a Marker of Distressed Astrocytes

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Abstract: Oxidative stress is a key mechanism in pathogenesis and pathophysiology of neuronal disorders such as Alzheimer's disease (AD) and also plays roles on vascular injury. Cerebrovascular lesions highly comorbid with AD pathology and may worsen disease progression and reduce treatment efficacy. Oxidative stress markers including nitration of macromolecules are increased in AD. Here, we aim to investigate nitration status of fibronectin, a multifunction extracellular matrix protein that present in blood stream and brain parenchyma where it maintains vascular and perivascular integrity. Immunolabelling was performed to investigate levels of fibronectin and nitrotyrosine in postmortem AD brain specimens confirmed with vascular pathology obtained from UK-ADC brain bank. We found several lesions that link to different stages of vascular and brain pathology. Immunoreactivity of fibronectin and nitrotyrosine surrounding multiple arterioles and venules indicates acute vascular leakage. Levels of fibronectin and nitrotyrosine are increased in reactive astrocytes surrounding the vessels suggesting that oxidative stress is involve in astrocyte activation. Moreover, high levels of nitrotyrosine and fibronectin in stroke region shows impact of oxidative stress in cell death processes. Our results evidence oxidative damage of fibronectin that may be used as a new biomarker and strengthen association of oxidative stress and vascular complication in AD which could benefit future studies of the combined pathology.

Funding: UK CCTS NIH-UL1TR001998

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Abstracts

Poster Number 35

Title: Application of Multi-Analyte Assays with Algorithmic Analysis to Risk Identification and Early Detection of Alzheimer's Disease

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Abstract: Alzheimer's Disease (AD) ranks amongst the top ten leading causes of death in the United States and is expected to have an annual economic burden of 500 million USD by 2040. The use of multi-analyte assays with algorithmic analysis (MAAA) to detect pathologies at early intervenable stages has been an evolving field in recent decades. For example, OVERA is an FDA approved MAAA for early detection of ovarian cancer, which has been shown to have superior detection rates as opposed to single markers. The application of MAAA for detection of AD has been approached with small-scale studies that did not include biomarkers of metabolic dysfunction, which is a clear AD manifestation. Our project focuses on establishing an AD MAAA that is based on the metabolic derangement accepted in the literature. Furthermore, our novel approach to this topic includes hypothesizing and evaluating peroxisome involvement in AD. Prior studies have shown adequate evidence of a possible link between peroxisome dysfunction and AD stage, as well as genotypic status. Thus, peroxisome biomarkers may play a key role in our algorithm. The methodology includes in-house/send-out analysis of various metabolic biomarkers (e.g., TSH, Free T4, lipid panel, plasmalogens, plasma oxalate, CRP) for 300 established AD ante-mortem specimens from the Sanders-Brown Center on Aging Biospecimen Bank at the University of Kentucky, with a control comparison. After which, an algorithmic analysis will be performed. Preliminary results are within processing stages and will be available by the time of the CCTS Spring Conference.

Funding: CCTS PSMRF NIH UL1TR001998, Dean of the College of Medicine, University of Kentucky.

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Basic/Translational Research

Abstracts

Poster Number 36

Title: The HLA-A2, one of the most common human MHC class I molecule, is able to mediate the protective immunity against cerebral infection with *Toxoplasma gondii*

Authors: Rajesh Mani, and Yasuhiro Suzuki

Abstract: The reactivation of chronic infection with *T. gondii* can cause serious toxoplasmic encephalitis in immunocompromised individuals. CD8⁺ T cells play critical roles in the protective immunity against cerebral *T. gondii* infection, and the MHC class I molecules present target antigens to CD8⁺ T cells for their activation. However, the MHC class I molecules that activate the protective CD8⁺ T cells against cerebral *T. gondii* infection in humans remain unclear. Since the HLA-A2 is one of the most common MHC class I molecules in humans, we examine whether the HLA-A2 can mediate the protective immunity against cerebral *T. gondii* infection. C57BL/6-background HLA-A2-transgenic and wild-type (WT) control mice were infected and treated with sulfadiazine beginning at 7 days after infection for 10 days to control proliferation of tachyzoites and establish a chronic infection in their brain. Four to five weeks after discontinuation of sulfadiazine that initiates reactivation of the infection, we examined whether the presence of the human HLA-A2 molecule confers a protection against the reactivation of the infection. The amounts of mRNA for tachyzoite-specific SAG1 were significantly less in the brains of the HLA-A2-transgenic than WT control mice ($P<0.05$). Furthermore, the reactivation index, ratios of SAG1 mRNA levels to BAG1 mRNA levels were also significantly lower in the former than the latter ($P<0.01$). Relative expression levels of IFN- γ mRNA to SAG1 mRNA levels were significantly greater in the transgenic than WT mice ($P<0.05$). Thus, the human HLA-A2 is able to confer a protection against reactivation of cerebral *T. gondii* infection, and the protective effect is most likely mediated by activation of IFN- γ production by CD8⁺ T cells. Elucidating the mechanism in which the HLA A2 confers the protection against cerebral *T. gondii* infection could assist developing a method to prevent reactivation of the infection.

Funding: NIH R56AI152597, R01AI095032

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Basic/Translational Research

Abstracts

Poster Number 37

Title: Effector molecules responses in IFN- γ -mediated protective immunity against cerebral infection with *Toxoplasma gondii* differ between genetically resistant and susceptible strains of mice

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Abstract: Cerebral proliferation of tachyzoites can cause toxoplasmic encephalitis in immunocompromised individuals. IFN- γ is required for preventing proliferation of *T. gondii* tachyzoites in the brain. However, the effector mechanisms of the IFN- γ -mediated protective immunity against the cerebral tachyzoite growth are not well understood. We examined the roles of indoleamine-2, 3-dioxygenase 1 (IDO1), one of the effector molecules induced by IFN- γ , in controlling cerebral *T. gondii* infection in both genetically resistant and susceptible strains of mice. In susceptible C57BL/6 mice, IDO expression was immunohistochemically detected only in a minority (22.5 %) of tachyzoite-infected cells in their brains during the later stage of infection. When C57BL-6-background IDO1-deficient (IDO1^{-/-}) mice were infected, their cerebral tachyzoite burden was equivalent to those of wild-type (WT) animals. In contrast, in resistant BALB/c mice, IDO expression was detected in a majority (84.0%) of tachyzoite-infected cerebral cells. However, tachyzoite burden in BALB/c-background IDO1^{-/-} mice remained as low as that of WT BALB/c mice, which was 78 times less than those of C57BL/6 mice. Of interest, IDO1^{-/-} mice of only resistant BALB/c-background had markedly greater cerebral expressions of two other IFN- γ -mediated effector molecules, guanylate-binding protein 1 (Gbp1) and inducible nitric oxide synthase (NOS2), than their WT mice. Therefore, it would be possible that IDO1 deficiency was effectively compensated by the upregulated expression of Gbp1 and NOS2 to control cerebral tachyzoite growth in genetically resistant BALB/c mice, whereas IDO1 did not significantly contribute to controlling cerebral tachyzoite growth in genetically susceptible C57BL/6 mice because of its suppressed expression in infected cells.

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Abstracts

Poster Number 38

Title: Vitamin D Levels in Moyamoya Syndrome Patients

Authors: L. Whitnel, Department of Neurosurgery, U of Kentucky, J. F. Fraser, Department of Neurosurgery, U of Kentucky, J. Roberts, Department of Neurosurgery, U of Kentucky

Abstract: Moyamoya syndrome is a cerebrovascular condition that leads to stroke. While the etiology is unknown, blood vessel dysfunction and chronic inflammation are important contributors. Vitamin D plays a key role in endothelial cell function and is a known regulator of the immune system. What is not known is the vitamin D status of moyamoya syndrome patients. We evaluated 18 adult male and female moyamoya syndrome patients in our prospectively enrolling MASTER study. Demographic and comorbidity data were collected, along with blood samples. Plasma was isolated for vitamin D analysis via ELISA assay, all patients were assigned a Suzuki score of pathological severity, and correlation analysis between vitamin D levels and Suzuki score was performed. The median age of our moyamoya patient population was 46 years and 60% were female. Approximately 56% of the patients had bilateral pathology and 74% had a Suzuki score of 5-6 (most severe). Interestingly, 80% of the patients were either deficient (<20 µg/L) or at sub-optimal (<30 µg/L) levels of vitamin D. Data also indicate 75% of the patients with low levels of vitamin D had a Suzuki score of 5-6. Continued analysis of systemic inflammation (e.g., CRP, ESR, etc.) is anticipated to indicate increased inflammation and autoimmune disease. Our data indicate a large proportion of moyamoya syndrome patients are deficient in vitamin D, which we hypothesize contributes to pathological severity. Future studies incorporating vitamin D supplementation may act as a novel intervention for this patient population that currently has few treatment options.

Funding: CCTS NIH KL2TR001996

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Basic/Translational Research

Abstracts

Poster Number 39

Title: Kinetic Differences in α -Synuclein Aggregation Detected Via RT-QuIC in PD and MSA

Authors: L. Turcios, Department of Neurology, U of Kentucky S. Tadisetty, Department of Neurology, U of Kentucky T. Yamasaki, Department of Neurology, U of Kentucky

Abstract: Background: Nearly a million of people in the USA are affected with Parkinson's Disease (PD), a neurodegenerative movement disorder involving pathological aggregation of alpha-synuclein (α -syn). Multiple system atrophy (MSA) is a rare disorder presented with similar symptomatology to PD. This often results in the misdiagnosis of the disease with implications on proper treatment and prognosis. Recently, the development of the real-time quaking induced conversion assay (RT-QuIC) has allowed the detection of α -synuclein aggregation in patient biospecimens not only in the brain but in other GI-derived tissues including submandibular gland. In this assay, aggregation-prone α -syn present in samples induces further aggregation of recombinant α -syn monomer through cycles of shaking and rest as detected by fluorescence of Thioflavin T. **Objective:** Using RT-QuIC assay, we aimed to determine whether there are kinetic differences in the pathological aggregation of α -syn in PD and MSA derived from participant tissues and, explore the impact of familial α -syn mutations frequently involved in PD pathology. **Methods:** Soluble and insoluble fractions were obtained by serial homogenization of brain and submandibular tissues obtained from PD, MSA and non-synucleinopathy control patients. Fractions were tested for α -syn aggregation activity by RT-QuIC assay using a BMG CLARIOstar plate reader and represented as the time required to reach threshold values obtained using the MARS software. **Results:** We observed an increased α -synuclein activity in the PD cases in both soluble and insoluble fractions compared to MSA. These differences were observed in brain and submandibular tissue and suggest an underlying structural or conformational difference in α -syn between these synucleinopathies. **Conclusions:** We have successfully optimized the RT-QuIC assay in our lab using brain and submandibular tissue from PD and MSA cases. We further demonstrated the use of peripheral tissues as a potential tool to aid in the diagnosis of these synucleinopathies.

Funding: UK Neurology Department Pilot Grant and VA IK2 BX004883

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Basic/Translational Research

Abstracts

Poster Number 40

Title: A home-cage monitoring solution for non-invasive seizure screening in rodent models of epilepsy

Authors: Diane Iradukunda, Department of Biomedical Engineering, U of Kentucky Dillon Huffman, Signal Solutions Maxwell Lavin, Department of Biomedical Engineering, U of Kentucky Sydney Daniels, Department of Neuroscience, U of Kentucky Jasmine Perdeh, Department of Pharmaceutical sciences, U of Kentucky Pacifique Rukundo, Department of Biomedical Engineering, U of Kentucky Kevin Donohue, Departments of Electrical & Computer Engineering, U of Kentucky and Signal Solutions Bruce O'Hara, Department of Biology, U of Kentucky and Signal Solutions Bjoern Bauer, Department of Pharmaceutical sciences, U of Kentucky Sridhar Sunderam, Department of Biomedical Engineering, U of Kentucky

Abstract: Rationale: Epilepsy is a neurological disorder characterized by spontaneous, recurring seizures. Animal models serve a vital role in investigating disease mechanisms and screening potential treatment strategies. However, such investigations typically require validation via expensive, labor-intensive methods (i.e., electroencephalography) – limiting the pace and scale of experimentation. Previously, we have shown that piezoelectric technologies show great utility in non-invasive seizure detection. Here, we present further developments in this effort using an external sensor platform located beneath the home cage. **Methods:** 32 adult Wistar rats were treated with pilocarpine i.p. to induce acute status epilepticus. Following induction, rats were individually monitored in standard housing cages for a minimum of 8 weeks using piezoelectric sensors (Signal Solutions, LLC) alongside a continuous video record. Week-long recordings were processed to derive a seizure detection statistic time series, from which the 40 most intense events were identified. Event timestamps were written to a spreadsheet for inspection through the video record and were annotated according to observed behavior. **Results:** Piezoelectric sensors captured the essential dynamics of seizures, as well as pre- to post-ictal changes in physiological parameters. Derivation of a simple detection statistic was successful in discriminating seizure events with reasonable precision offering a great labor saving for identifying seizures compared to exhaustive video review. **Conclusions:** Overall, this approach shows great utility in identifying spontaneous seizures in chronic epilepsy monitoring. The signals generated by the piezo- sensors not only capture tonic-clonic behavior during seizures, but also other relevant behaviors such as breathing, freezing, and tremor.

Funding: NIH: NS107148, R01NS079507 and University of Kentucky Epilepsy Research Center (EpiC)

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Basic/Translational Research

Abstracts

Poster Number 41

Title: Laser Speckle Contrast Imaging of Cerebral Blood Flow Using Picosecond Pulsed Laser Illumination

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Abstract: Background: Conventional laser speckle contrast imaging (LSCI) technique illuminates continuous-wave (CW) laser light on tissue surface. A CCD/CMOS camera captures the temporal/spatial speckle pattern fluctuations, resulting from motions of red blood cells (i.e., blood flow). In this study, we tested a picosecond-pulsed laser as the LSCI source for 2D imaging of cerebral blood flow (CBF) in mice. This new system has the potential to be integrated with other imaging techniques using pulsed illumination such as photoacoustic imaging (PAI) and fluorescence angiography (FA). **Methods:** We assembled an integrated LSCI system combining a CW laser (DL785-120-SO, CrystaLaser) at 785 nm and a picosecond pulsed laser (KATANA-08 HP, NKT photonics) at 775 nm. The glass and engineered diffusers were placed in front of the lasers for uniform illuminations. A 12-bit CMOS camera (BFS-U3-16S2M-CS, PointGray, pixels: 1440x1080, pixel size: 3.45 μ m) collected images from the mouse head with intact skull using varied exposure times from 1 to 5 milliseconds. A mouse model of transient global ischemia was used to test the integrated imaging system. **Results:** The picosecond pulsed laser with the engineered diffuser and 5 ms exposure time captured more details of cerebral blood vessels compared to the CW laser with glass diffusers. The consecutive ligations of left and right common carotid arteries resulted in significant CBF reductions, which agreed with clinical expectations. **Conclusions:** This research lays the ground for future work to develop multimodal imaging systems integrating LSCI, PAI, FA, and other time-resolved imaging systems with shared pulse illuminations.

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Basic/Translational Research

Abstracts

Poster Number 42

Title: A Fast Algorithm Towards Real-Time Laser Speckle Contrast Imaging

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Abstract: Background: Laser speckle contrast imaging (LSCI) technology illuminates laser light on tissue surface to produce interference speckle patterns. A CCD/CMOS camera captures the spatial/temporal speckle pattern fluctuations, resulting from motions of red blood cells (i.e., blood flow). With recent advancements in computational technologies, developing a real-time flow-mapping algorithm has gained significant attention. This study developed a parallel computing technology with more efficient functions in the MATLAB. **Methods:** We built a MATLAB-based algorithm that takes advantage of its Parallel Computing Toolbox along with Image Processing Toolbox functions. Traditionally, two for-loops are defined for calculating LSCI statistical variance on an N by N pixel window. Instead, we reduced the window's dimension to a column of length N×N, which MATLAB handles at ease. The codes were executed on a desktop with Intel(R) Core (TM) i9-10900K CPU @ 3.70GHz configuration. Three hundred images were collected by a customized LSCI device from a mouse head with intact skull. The efficacy of our new algorithm for mapping of cerebral blood flow was compared with a MATLAB-based traditional script. **Results:** The traditional script took several hours while our new algorithm clocked 12.68, 51.80, and 103.77 seconds for the pixel windows of 3×3, 5×5 and 7×7, respectively. The flow image qualities from all pixel windows were comparable. **Conclusions:** The analysis proved the possibility of obtaining close to real-time flow-mapping speed of ~24 fps (i.e., 300/12.68) for the 3×3 pixel window. Running this code on a more powerful computer may facilitate even faster flow-mapping on par with high-speed cameras.

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Basic/Translational Research

Abstracts

Poster Number 43

Title: Repurposing FDA-approved PI3K/Akt Inhibitors to Improve Brain Uptake of Anticancer Drugs in Glioblastoma Resection Models

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Abstract: Objective/Goals: Our laboratory has shown that glioblastoma upregulates blood-brain barrier drug efflux transporters via TNF α and PI3K/Akt, limiting brain drug delivery. Our goal is to repurpose FDA-approved PI3K/Akt inhibitors to downregulate drug efflux transporters and increase anticancer drug brain concentrations. This therapeutic strategy holds the potential for translation into the neuro-oncology clinic. **Methods:** GL261 Red-FLuc cells (2.5K cells/ μ l; 2 μ l/2min) were injected into 8-week-old female J:NU mice (coordinates relative to bregma: AP -2 mm, ML -2 mm, DV -3 mm). Tumor burden, volume and invasiveness were assessed with IVIS[®] Spectrum imaging, MRI and histopathology, respectively. On day 14 post-injection, mice received 5-aminolevulinic acid (200 mg/kg ip), and tumors were resected with a 2mm punch biopsy tool and surgical fluorescence microscope (ex/em: 405/635nm). Drug efflux transporter expression and activity in isolated brain capillaries were determined by Western blotting and substrate fluorescence assays, respectively. Cytotoxicity was assessed after 48-hour drug incubation using CyQuant MTT Cell Viability Assays. **Results/Anticipated Results:** For GL261 Red-FLuc cells, IC₅₀ values from cell viability assays with temozolomide, lapatinib, alpelisib, and miltefosine were N/A, 32, 20, and 190 μ M, respectively. Median survival of glioblastoma mice was 26.5d and resecting the tumor significantly increased survival to 34d (p=0.0116). Drug efflux transporter expression and activity levels in contralateral brain capillaries were significantly upregulated compared to sham controls. Based on preliminary data, we expect the FDA-approved PI3K/Akt inhibitors, alpelisib and miltefosine, to significantly reduce drug efflux transporter expression and activity levels, increase brain uptake of anticancer drugs, and prolong glioblastoma mouse survival.

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Basic/Translational Research

Abstracts

Poster Number 44

Title: Estrogen Receptor Alpha Regulates Circadian Organization in Female Mice

Authors: O.B. Omotola, Department of Biology, U of Kentucky, J.S. Pendergast, Department of Biology, U of Kentucky

Abstract: The circadian system is a critical regulator of obesity, but its role in females is poorly understood. In previous studies, we found that estrogen regulates daily rhythms in female mice to confer resistance to diet-induced obesity. High-fat feeding disrupts circadian organization in ovariectomized females by advancing the phase of the liver clock. Here, we studied estrogen signaling mechanisms that regulates circadian organization in female mice. Estrogen signals via estrogen receptor alpha (ER α) to regulate metabolism and obesity. We tested whether ER α was necessary to regulate internal circadian alignment using global ER α -KO mice. Female C57BL/6J ER α -KO and WT mice heterozygous for PERIOD2::LUCIFERASE were fed standard chow or high-fat diet (HFD). We measured PER2::LUC rhythms in ER α -KO SCN and peripheral tissues and found the phase relationship between tissue clocks was not affected during chow feeding. In contrast, the liver PER2::LUC rhythm was advanced in HFD-fed ER α -KO females compared to WT, resulting in internal circadian misalignment. We also tested whether ER α signaling was sufficient to confer circadian organization during high-fat feeding in females. Ovariectomized females were implanted with pellets containing ER α -specific agonist, propyl-pyrazole triol (PPT), or vehicle and fed low-fat diet or HFD. Consistent with our prior results, high-fat feeding phase-advanced the liver circadian clock in ovariectomized mice with control pellets but had no effect in females treated with PPT. These data show that estrogens are critical regulators of circadian organization in females during nutritional challenge. Circulating estrogens signal via ER α to protect the liver circadian clock from HFD-induced disruption in female mice.

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Basic/Translational Research

Abstracts

Poster Number 45

Title: Differential Effects of Short and Extended Cocaine Exposure on Astrocytes in Rat Nucleus Accumbens

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Abstract: Nucleus accumbens is involved in motivational and affective behavioral processing, playing a significant role in development and maintenance of substance use. Astrocyte morphology has been shown to be affected by cocaine, but the functional role of astrocytic signaling in cocaine use remains unknown. The goal is to address astrocytic adaptations within nucleus accumbens using two different cocaine exposure regimes. Rat self-administration model was used to study the effects of cocaine exposure. Two groups of animals went through short- (1h/day) and extended- (6h/day) access cocaine self-administration for 14 days. To identify functional adaptations of astrocytes, calcium imaging with GCaMP6fs was performed, labelling the endoplasmic reticulum or cell membrane. To isolate astrocyte membrane properties adaptations to dopaminergic changes, whole-cell patch clamp was performed, whole cell currents and potassium channels currents were recorded. Intracellular level of calcium within NAc astrocytes is differentially affected by short- or extended- access cocaine self-administration. Calcium transients reported by indicators targeting the endoplasmic reticulum and cell membrane were distinct, suggesting compartmentalized sensitivity to history of cocaine exposure. Electrophysiologically, dopamine treated astrocytes generated larger amplitude currents compared to naïve ones, dose-dependently. 4AP reduced recorded currents in the control slices, while dopamine pre-incubated astrocytes were not affected. Astrocytes adapt to cocaine exposure differently through short- and extended- access self-administration, both morphologically and functionally. Our results indicate a potential regulatory role of astrocytic signaling in the NAc on neural mechanisms underlying substance use. Future studies will examine the specific relationship between astrocytic and neuronal signaling following exposure to cocaine.

Funding: NIH: DA04041513

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Basic/Translational Research

Abstracts

Poster Number 46

Title: A Wearable Optical Sensor for Continuous Monitoring of Cerebral Ischemia in Rodents and Piglets

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Abstract: **Background:** Wearable technologies are needed for continuous monitoring and management of cerebral ischemia. Currently existing cerebral monitoring techniques are either too invasive, too large/heavy to carry, too shallow in detection depth, or too costly. This presentation reports an innovative, inexpensive, wearable, multi-scale diffuse speckle contrast flowmetry (DSCF) probe for transcranial imaging of cerebral blood flow (CBF) in rodents and a neonatal piglet. **Methods:** The DSCF uses small laser diodes as focused point sources for deep tissue penetration and a tiny CMOS camera as a high-density 2D detector array to detect spontaneous spatial fluctuations of diffuse laser speckles, resulting from red blood cell motions in the deep brain (i.e., CBF). CBF variations during sequentially transient ligations of left and right common carotid arteries (CCA) were concurrently monitored by the DSCF and an established diffuse correlation spectroscopy (DCS) with an integrated hybrid probe fixed on the animal head. **Results:** Significant reductions in CBF during transient bilateral CCA were detected by the DSCF ($-35\pm 13\%$ in two mice and -59% in a piglet), which meet clinical expectations. Results from the DSCF and DCS were consistent and significantly correlated. **Conclusions:** Based on the promising results from this pilot study, we are currently developing a wireless, wearable DSCF probe for continuous cerebral monitoring in freely behaving subjects, including rodents, piglets and human neonates. Ultimately, we expect to offer a unique, noninvasive, low-cost, fast, multiscale brain imaging tool for basic neuroscience research and clinical applications.

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Basic/Translational Research

Abstracts

Poster Number 47

Title: The intraspinal adaptive immune response in pigs varies between males and females after spinal cord injury

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Abstract: The incidence of spinal cord injury (SCI) among females is increasing, however, sex is understudied in SCI pathophysiology. Further, responses in rodents may not predict human conditions. Here, we examined intraspinal inflammatory responses between male and female pigs after T10 contusion injury. The pig SCI model has important similarities to humans in anatomic and physiologic characteristics including inflammation. Briefly, adult (gonad-intact) male and female Yucatan miniature swine were subjected to either a SCI or laminectomy only control. Females were injured on proestrus, estrus and diestrus stages to consider the effects of estrous cycle. Animals were sacrificed at 48hr or 6 weeks after SCI and spinal cord sections analyzed for astrocytes, microglia, macrophages, and T-lymphocytes (T cells) by immunohistochemistry. Neutrophils were counted based on H&E morphology. No histopathological abnormalities were identified in control cases. All data was analyzed on Halo v2.2.1870. No differences were seen for astrocytes, microglia, macrophages and neutrophil infiltration between males and females. Individual intraspinal T cell counts and T cell microclusters were significantly higher in females (independent of estrus stage) and in females injured at proestrus (in case of T cell counts only) compared to males by Welch's t test. Our observation indicates that sex is a potential biological variable for T cell infiltration and may contribute to difference in sex-based differences in SCI pathophysiology and recovery outcomes. The adaptive immune response is implicated in a number of SCI complications (pain, autoimmunity, neural repair); our data implicates sex as a potential factor for immune-focused SCI therapies.

Funding: University of Kentucky and Utah Centers for Clinical and Translational Science: NIH CTSA Grants: UL1TR001998 & UL1TR002538

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Basic/Translational Research

Abstracts

Poster Number 48

Title: Fibroblast Growth Factors Indicate Type of Hemorrhagic Conversion in Patients Following Mechanical Thrombectomy

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Abstract: Background: Emergent Large Vessel Occlusion (ELVO), often treated with mechanical thrombectomy (MT), can lead to complications such as hemorrhagic conversion (HC). Fibroblast growth factors (FGF) 21 and 23 are angiogenic proteins that are independent factors for overall risk of stroke and intracranial hemorrhage (PMID: 33967812), and levels of which are affected by comorbidities. This study analyzes the possible association between FGFs and HC in patients with acute ischemic stroke following MT. **Methods:** The Center for Advanced Translational Stroke Science at the University of Kentucky utilizes the Blood and Clot Thrombectomy Registry and Collaboration (BACTRAC) protocol (www.clinicaltrials.gov NCT03153683) for collection of systemic arterial blood during MT procedure. Proteomic analysis was completed by Olink Proteomics. Logistic regressions were used to determine the association of FGF with subtypes of HC. Data analyses were performed using IBM SPSS Statistics. **Results:** FGF-21 and FGF-23 were significantly higher in patients with HI versus PH-type HC ($p=0.043$ and $p=0.004$). Logistic regression yielded a significant model for only FGF-21 ($\chi^2= 5.196$, $p=0.023$). Increasing levels of FGF-21 were associated with decreased likelihood of having PH-type HC. Most patients receiving TPA had decreased levels of FGF-21 ($p=0.04$). **Discussion:** The data indicates that lower levels of FGF-21 increase the odds for a worse type of hemorrhagic transformation and have been associated with hypercholesterolemia and hypertension. Our study found TPA correlated with lower levels of FGF-21. Taken together, patients at risk for decreased FGF-21 levels should be monitored more carefully following thrombectomy. FGF-21 should be evaluated further as a potential biomarker for hemorrhagic transformation to administer adjunctive therapies to MT.

Funding: CCTS NIH UL1TR001998 Pilot Award

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Basic/Translational Research

Abstracts

Poster Number 49

Title: Noncontact Optical Assessment of Disrupted Cerebral Functional Connectivity in a Piglet Model of Transient Ischemic Stroke

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Abstract: Perinatal ischemic stroke results from the lack of blood supply to brain tissue, possibly leading to cerebral ischemic/hypoxic stress, neurological disorder, and brain network impairment. Preterm infants with ischemic stroke are prone to alterations in cerebral blood flow (CBF) and associated spontaneous low-frequency oscillations (LFOs). However, there are no established noninvasive imaging methods for continuous monitoring of CBF alterations at the bedside in neonatal intensive care units (NICUs). An innovative camera-based speckle contrast diffuse correlation tomography (scDCT) technology has been recently developed in our laboratory, which enables noncontact, noninvasive, and high-density 3D imaging of CBF distributions in cerebral cortex. In the present study, the capability of scDCT technique for 3D imaging of CBF distributions in a neonatal piglet model of transient ischemic stroke was demonstrated. Moreover, power spectral density analyses of LFOs and the network connections over the brain were assessed before and after the induction of acute ischemic stroke. The stroke resulted in a substantial decrease in CBF, attenuations in resting-state LFOs over the LFO frequency band (0.01–0.08 Hz), and functional connectivity disruptions in motor and somatosensory cortices. This pilot study demonstrated the feasibility and safety of scDCT for noninvasive detection of resting-state LFO alteration and functional connectivity disruption after stroke. We are currently testing this fully noncontact scDCT technology for 3D imaging of brain hemodynamics in the NICU, with the ultimate goal of instantly evaluating and managing brain injury/health to improve the clinical decision and outcome.

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Basic/Translational Research

Abstracts

Poster Number 50

Title: Effects on Gait in Participants with Parkinson's Disease Receiving an Investigational Peripheral-Nerve-Cell Therapy and Deep Brain Stimulation.

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Abstract: The objective of this observational study is to determine how gait is affected in people with Parkinson's disease, who received a peripheral nerve tissue (PNT) delivery to the substantia nigra as an adjuvant to the deep brain stimulation (DBS) and levodopa therapy. Gait parameters measured using the GAITrite software included step length for the less and more affected sides, gait velocity, and cadence. Clinical assessment incorporated Unified Parkinson's Disease Rating Scale (UPDRS) part III. Data for 10 participants [7M/3F, 60±8 yr.], was collected in the OFF state and ON state at baseline, 6 and 24 months. At baseline, the OFF state received no treatment and the ON state received levodopa only. At six and 24 months, the OFF state was the PNT only, and the ON state was the best medical therapy (BMT), which included levodopa, DBS and the PNT. Gait cadence, velocity and UPDRS III in both OFF and ON states, significantly improved from baseline to 6 months ($p < 0.05$). Over time, improvements in gait and clinical parameters measured at 6 months were sustained through 24 months. Also, over the course of two years, participants with PNT did not show worsening of gait and clinical outcome measures. Our data provides preliminary evidence that the addition of PNT in conjunction with DBS and levodopa could provide improvements in gait and clinical outcome measures in the long term. In a population with progressive degenerative disease, participants who received PNT and DBS did not show worsening of gait after two years.

Funding: Brain Restoration Center, Ann Hanley Parkinson's Research Fund, Tom Dupree for Parkinson's Disease Research, Pro's Players Fore Parkinson's, the Werner Schmitt endowment for Neurobehavior and Aging, UK Startup Funds, CCTS NIH UL1TR001998

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Clinical Research

Abstracts

Poster Number 51

Title: Electroencephalogram Features Predict Motor Effort Associated with Graded Finger Extension in Individuals with Chronic Hemiparetic Stroke

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Abstract: Brain-computer interfaces (BCIs) offer disabled individuals the means to interact with external devices by decoding neural signals such as the electroencephalogram (EEG). However, the ability to extract EEG features associated with fine motor control may be limited, especially in stroke victims with large cortical lesions. Here we investigate the feasibility of predicting motor effort associated with graded finger extension from the EEG in stroke patients with left-hand paresis and healthy controls of similar age. Participants extended their fingers in response to visual cues to one of four levels: low, medium, high, or “no-go” (i.e., none). Hand, muscle, and brain activity were monitored using a pair of motion capture gloves, electromyography (EMG), and EEG (32 channels), respectively. Task-related modulation of sensorimotor EEG (8-30 Hz) was measured in terms of the mean-squared power at each location relative to a pre-trial reference period. A quadratic classifier was trained on this EEG feature vector and its accuracy assessed using out-of-sample cross-validation. In both stroke and control groups, the EEG classifier predicted graded finger extension with accuracies of 46-67% on either hand, much greater than chance (25%) despite severe spasticity in the stroke-impaired hand. In contrast, an EMG power classifier gave only 40% accuracy on the paretic hand in the stroke group but 80% in the unimpaired hand and in controls. Hence, EEG features predict the effort associated with attempted finger extension in individuals with chronic hemiparetic stroke. This could be useful in rehabilitative BCI protocols that emphasize fine control.

Funding: NSF 1849213, Halcomb Fellowship in Engineering and Medicine from the University of Kentucky

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Clinical Research

Abstracts

Poster Number 52

Title: "Neurobank sample collection at the EMU: Building a Unique Resource for Epilepsy Research."

Abstract: A. Sindhura Tadisetty, Dept of Neurology, U of Kentucky. b. Marlee Kelley, Dept of Neurology, U of Kentucky. c. Susannah Stitzer, Dept of Neurology, U of Kentucky. d. Shelby McCubbin, Dept of Neurology, U of Kentucky. e. Mohammed Abdelsalam, Dept of Neurology, U of Kentucky. f. Tritia Yamasaki, Dept of Neurology, U of Kentucky.

Abstract: Introduction: The University of Kentucky NeuroBank commenced operations in 2020. Under the VPR-funded Neuroscience Research Priority Area, Neurobank aims to support neurologic researchers in better understanding the disease process by providing access to relevant human biospecimens and accelerating translational and innovative research. The Epilepsy Monitoring Unit at University of Kentucky is located on the 7th floor West wing, has six private rooms, helps provide prolonged combined data from the EEG and concomitant video monitoring of epileptic patients. This information helps clinicians judge where the seizure originates in the brain and helps clinicians produce a diagnosis. Utilizing the clinical resource of the EMU, UK (University of Kentucky), Neurobank developed a unique workflow to aid researchers studying epilepsy.

Funding: No Funding

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Abstracts

Poster Number 53

Title: The estrous cycle coordinates the daily eating behavior rhythm in mice

Authors: V.M. Alvord, Department of Biology, U of Kentucky, J.S. Pendergast, Department of Biology, U of Kentucky

Abstract: The estrous cycle regulates daily rhythms of locomotor activity, body temperature, and circadian gene expression. In mice and rats, wheel-running activity is greatest on the night of proestrus into estrus, when elevated estrogens cause ovulation. High activity level at the time of ovulation could increase the likelihood of finding a mate and thus fitness. Exogenous estrogen regulates eating behavior rhythms in female mice fed high-fat diet but it is not known whether endogenous estrogens regulate daily rhythms of eating. The goal of this study was to determine whether daily eating behavior rhythms change systematically across the estrous cycle. Female C57BL/6J mice were housed in 12L:12D with running wheels and fed standard chow diet. Estrous cycle stages were determined by vaginal cytology. Eating behavior and wheel revolutions were continuously measured. The mice had regular 4- or 5-day estrous cycles that were abolished after ovariectomy. The magnitude of daily wheel-running activity fluctuated in 4- or 5-day cycles. The greatest number of wheel revolutions occurred during proestrus into estrus, when estrogens peak. We found that amplitude, or robustness, of eating behavior rhythms fluctuated in 4- or 5-day cycles. Like wheel-running activity, peak amplitude of the eating behavior rhythm occurred primarily during proestrus or estrus. After removal of cycling hormones with ovariectomy, the amplitude of the eating behavior rhythm peaked at irregular intervals. Together, these data suggest that ovarian hormones fluctuations across the estrous cycle temporally organize daily eating behavior rhythms.

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Basic/Translational Research

Abstracts

Poster Number 54

Title: Deletion of *Period* genes exacerbates diet-induced obesity in female, but not male, mice

Authors: Elizabeth J. Kantra, Department of Biology, University of Kentucky Julie S. Pendergast, Department of Biology, University of Kentucky

Abstract: Obesity differs in men and women. Sex differences in obesity in mice are mediated by circadian responses to high-fat feeding. Additionally, the circadian *Period* genes regulate obesity in mice. In this study, we sought to investigate the role of the *Period* genes in regulating sex differences in obesity. *Period1* and *Period2* have primary roles in the circadian timekeeping mechanism, while *Period3* regulates rhythms in peripheral tissues. Male and female C57BL/6J WT, *Per1/2* KO, and *Per1/2/3* KO mice were fed high-fat diet (45% kcal fat) for 12 weeks. We measured eating behavior and locomotor activity rhythms as well as adiposity, food intake, and glucose tolerance. We found adiposity was exacerbated in female, but not male, mice. Adiposity was doubled in *Per1/2* KO females and tripled in *Per1/2/3* KO females compared to WT females. Increased adiposity in female *Period* KO mice was not due to increased energy intake since they ate fewer calories than WT females. Both male and female *Period* KO mice had advanced phases and reduced amplitudes of locomotor activity compared to WT mice. Since locomotor activity rhythms were similarly disrupted in male and female *Period* KO mice, this may not account for their sex difference in obesity. Our preliminary results suggest *Per1/2/3* KO females had disrupted eating rhythms on high-fat diet due to more daytime eating behavior than WT females. These results reveal a sex difference in *Period* regulation of diet-induced obesity and that sex is a critical factor when studying the interplay between circadian rhythms and metabolic risk.

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Basic/Translational Research

Abstracts

Poster Number 55

Title: High-fat feeding disrupts eating behavior rhythms in pregnant female mice and increases offspring mortality

Authors: Cameron R. Rostron, Department of Biology, U of Kentucky Josie D. Llanora, Department of Biology, U of Kentucky Julie S. Pendergast, Department of Biology, U of Kentucky

Abstract: Maternal obesity increases the risk of pregnancy complications. The circadian system regulates diet-induced obesity in non-pregnant mice, but the effects of high-fat feeding on circadian rhythms during pregnancy are not known. Here we investigated daily rhythms and pregnancy outcomes of female mice fed high-fat diet. Female mice were fed high-fat/high-sucrose or low-fat diet for 6 weeks prior to breeding, during pregnancy, and after pups were born. Body weight, energy intake, and activity and eating behavior rhythms were measured. We assessed pregnancy outcomes by measuring the number of litters and pups that survived to weaning. We found that females fed high-fat diet weighed more than low-fat-fed dams at breeding, during pregnancy, and after giving birth. Maternal high-fat feeding had detrimental effects on pregnancy outcomes. Only one-third of litters born to dams fed high-fat diet survived to weaning, while 80% of litters from low-fat-fed dams survived. Among surviving litters, dams fed low-fat diet had twice as many pups survive per litter compared to dams fed high-fat diet. We next determined whether daily rhythms were differentially affected by diet in pregnant females. The amplitude of activity rhythms decreased during pregnancy, but did not differ with diet. Before breeding, both high-fat- and low-fat-fed females had robust, high-amplitude daily rhythms of eating behavior. Pregnant females fed low-fat diet maintained high-amplitude eating behavior rhythms throughout pregnancy, but high-fat feeding disrupted the eating behavior rhythm in pregnant mothers. Together these data show that high-fat feeding disrupts eating behavior rhythms during pregnancy, which could contribute to offspring mortality.

Funding: NIH R01DK124774, NSF IOS-2045267, UK College of Arts and Science Summer Undergraduate Research Fellowship, University of Kentucky.

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Basic/Translational Research

Abstracts

Poster Number 56

Title: COVID-19 ICU Survivors: How Nutritional Status Impacts Physical Function

Abstract: A. Locke, Human Nutrition, U of Kentucky, L. E. Jubina, Rehabilitative Services PhD Program, U of Kentucky, K. P. Mayer, Department of Physical Therapy, U of Kentucky A. Montgomery-Yates, Division of Pulmonary, Critical Care and Sleep Medicine, U of Kentucky A. G. Kalema, Division of Pulmonary, Critical Care and Sleep Medicine, U of Kentucky

Abstract: Background: Patients surviving an intensive care unit (ICU) admission develop significant impairments in physical function. The relationship between nutritional status and physical function in patients with critical COVID-19 is unclear. We hypothesized that patients who report poor nutritional intake early in recovery have muscle weakness and physical dysfunction. **Methods:** Prospective observational study in patients who survived admission to ICU due to critical COVID-19 and attended the ICU Recovery Clinic. Demographic and clinical variables including days without nutritional intake and days on tube-feeds while in ICU were extracted from the EHR. Two-months after hospital discharge, patients completed questionnaires about nutrition status, participated in muscle strength testing (MRC-ss), and performed the Short Physical Performance Battery. Patients were grouped according to self-reported nutritional intake and independent t-tests and correlative testing were performed. **Results:** Twenty-six patients with a mean age of 48 ± 15.5 years, 54% male, and BMI of 33.7 kg/m^2 with a mean 1.8 days without food in the hospital (range 0-11) participated. Patients who subjectively report poor nutritional status ($n = 9$, 36%) had more muscle weakness (51 vs 56.5 on MRC-ss, $t = 1.3$, $p = 0.13$) and worse physical function on SPPB (7.5 vs 9.5, $t = 1.26$, $p = 0.18$). SPPB scores at follow-up were associated with age ($r = -0.499$, $p = 0.009$), tube feed duration ($r = -0.40$, $p = 0.10$), and self-reported access to food ($r = -0.51$, $p = 0.008$). **Conclusion:** Patients surviving critical COVID-19 who self-reported poor nutritional status have muscle weakness and poor physical function.

Funding: No funding

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Clinical Research

Abstracts

Poster Number 57

Title: Attentional Bias towards Food Cues Varies According to Weight Status

Authors: K. D. Flack, Department of Dietetics and Human Nutrition, U of Kentucky C. R. Rush, Department of Behavioral Science and Psychiatry, U of Kentucky J. A. Colella, U of Kentucky N. B. Wheeler, U of Kentucky K. F. McFee, Department of Dietetics and Human Nutrition, U of Kentucky R. E. Anderson, Department of Dietetics and Human Nutrition, U of Kentucky

Abstract: The United States food environment has become increasingly obesogenic over the past three decades, with rates of obesity and related conditions continuing to rise. Advertisements capitalize on an individuals' attentional bias towards food cues, a cognitive process resulting from the sensitization of highly reinforcing food promoting a compulsive "wanting" to eat. Individuals classified as overweight or obese may be more susceptible to overconsumption of energy dense foods due to greater food cue reactivity than normal weight individuals. The current study hypothesized the attentional bias towards food cues is greater among individuals classified as overweight to obese than those classified as normal weight. A cross-sectional design was used to test attentional bias towards food cues using the visual probe procedure task with eye tracking modified for food cues. Nineteen (19) overweight/obese (BMI ≥ 25) and 47 normal weight (BMI < 25) participants were recruited and completed the study. Attentional bias was conceptualized as the percentage of time fixated on food cues when both food and neutral images were presented during the visual probe procedure modified for food cues. Differences in attentional bias between groups was tested through one-way ANOVA. Individuals classified as overweight to obese demonstrated greater attentional bias towards food cues compared to normal weight individuals. This underscores another aspect of our food environment contributing to the obesity epidemic and establishes an important factor influencing energy intake that may be modified in future clinical trials for obesity treatment.

Funding: No Funding

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Community Research

Abstracts

Poster Number 58

Title: Direct and Indirect Relationships between Economic Hardships, Family Interactions, and Obesogenic Behaviors among Hispanic/Latinx Youth.

Authors: Barnhart, Shelia

Abstract: **Background:** Prevalence of overweight status and obesity among Hispanic/Latinx children and youth is a major health concern in the US. Further, Hispanic/Latinx families experience disproportionately high rates of poverty and low income, a known risk factor for obesogenic behaviors including screen time and low physical activity. The family is an important context for understanding child and youth obesogenic behaviors in Hispanic/Latinx populations, yet, relationships between economic strains, family interactions, and youth obesogenic behaviors among Hispanic/Latinx families are not fully understood. **Method:** The current exploratory study used an analytic subset of 1,469 Hispanic/Latinx youth (10–13 years old) from the combined 2018 and 2019 National Survey of Children’s Health (NSCH) to examine if 1) family economic hardship was directly associated with higher levels of obesogenic behaviors (screen time and physical inactivity), and 2) family economic hardship indirectly associated with obesogenic behaviors due to increased levels of family disengagement and parenting stress. **Results:** Results from the structural equation modeling evidenced that Family economic hardship was positively associated with obesogenic behaviors ($\beta=0.149$, $p<.05$), parenting stress ($\beta=0.243$, $p<.001$), and familial disengagement ($\beta=0.293$, $p<.001$). Family economic hardship was indirectly associated with obesogenic behaviors via family disengagement ($\Sigma_{ind}=0.127$, $p<.001$), but not via parenting stress. **Discussion:** Families play an important role in their children’s health. Results from this exploratory study support that economic hardships may negatively affect levels of family engagement which may behave as a potential mechanism by which economic hardships relate to obesogenic behaviors in early adolescent Hispanic/Latinx youth.

Funding: CCTS DREAM Scholars Program, CCTS NIH UL1TR001998

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Community Research

Abstracts

Poster Number 59

Title: Comparison of Treatment Patterns and Disease Impact Between Those with Posttraumatic Versus Idiopathic Knee Osteoarthritis

Authors: L. Steele, College of Medicine, U of Kentucky, C. Jacobs, Department of Orthopedics, U of Kentucky C. Conley, Department of Orthopedics, U of Kentucky

Abstract: There is increasing evidence that the pathophysiological mechanisms underlying posttraumatic osteoarthritis (PTOA) may differ from those of idiopathic knee OA. Anecdotally though, these patients are usually treated the same. The purpose of this study was to compare patient demographics, self-reported emotional wellbeing, and the treatments utilized by PTOA and OA patient populations. We hypothesized that PTOA patients will be significantly younger, will have sought a greater number of knee treatments, and will report that their emotional wellbeing has been more greatly impacted by their condition than those with idiopathic OA. For this study, we collected and analyzed questionnaire data utilizing a REDcap survey that was administered through ResearchMatch. To qualify for this study, participants had to be between 18 and 95 years old, have a self-reported physician-diagnosed knee osteoarthritis, and be a member of ResearchMatch. 84 people fully completed the survey and were included in the analyses, with 36 reporting that their knee OA was the result of a previous injury. The survey looked at demographic data, knee injury or surgery history, utilized treatments and their characteristics (duration & cost), and whether the participants felt that their knee has impacted their emotional wellbeing. Demographically we saw no differences but did see a greater percentage of the PTOA group utilized self-directed exercise, acetaminophen, and knee braces. As a result, these patients may be better suited for combination therapies that pair intra-articular treatments with exercise modification to help slow the progression of PTOA pain and the associated structural changes.

Funding: CCTS NIH UL1TR001998 Professional Student Mentored Research Fellowship (PSMRF) Program and the University College of Medicine

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Basic/Translational Research

Abstracts

Poster Number 60

Title: Retrograde Femur Intramedullary Nailing: Identifying the True Anatomic Axis for the Ideal Start Point

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Abstract: *Background:* Retrograde femoral intramedullary nailing (IMN) is a common method to treat distal femur fractures. There are inconsistencies in the trauma literature regarding the ideal starting point in the coronal plane. The objective of this study is to clarify the ideal starting point relative to the intercondylar notch. *Methods:* A series of 48 patients with anteroposterior long-leg radiographs prior to elective knee arthroplasty from 2017-2021 were used to illustrate the anatomic axis. The center of the femoral isthmus was marked. Another point 3cm distal from the isthmus was marked in the center of the canal. A line was drawn connecting the points and extended along the canal through the knee. The distance from the center of the intercondylar notch to the point where the anatomic axis of the femur intersects the distal femur was measured. *Results:* The distance from the intercondylar notch to where the femoral axis intersects the distal femur was normally distributed with an average distance of 4.1mm (SD, 1.7mm) medial to the intercondylar notch, with no points at or lateral to the intercondylar notch. The ratio of this distance against the bicondylar width was also normally distributed with a mean of 0.06 (SD, 0.02). *Conclusion:* The ideal start point for retrograde femur IMN is medial to the intercondylar notch with a mean distance of 4mm. Medialization of the starting point in the coronal plane aligns with the anatomic axis. Incorporating this into surgical planning is one way to help avoid the 10% chance of coronal plane malalignment.

Funding: No Funding

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Clinical Research

Abstracts

Poster Number 61

Title: Dynamic Knee Joint Stiffness is Impaired during a Drop Vertical Jump after an ACL Reconstruction

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Abstract: Purpose/hypothesis: Dynamic joint stiffness is the ability to store and transmit elastic energy, which has not been reported after anterior cruciate reconstruction (ACL) surgery. We hypothesized that knee joint stiffness (KJS) in the injured limb would be lower than the uninjured limb during landing from a jump, and that knee stiffness symmetry would be positively associated with symmetry of quadriceps peak torque and rate of torque development (RTD). **Subjects:** 30 (13 female) subjects (20.5±5.8 years) 6-months post ACL reconstruction. **Materials/Methods:** Kinematic and kinetic analysis was performed on drop vertical jumps. Knee joint stiffness (KJS) is the slope of the change in the knee joint moment over the change in the knee joint angle during early-phase landing. Peak torque is the mean of the maximum torques and RTD is the initial slope of the torque-time curve of maximal isometric contractions. Paired T-tests and Pearson's correlations determined between-limb differences and the association between knee stiffness symmetry and quadriceps symmetry respectively. **Results:** Significant differences in KJS were present during landing (INJ = 0.02±0.01 Nm/kg/°, UNI = 0.05±0.01 Nm/kg/°, p<.01). Knee joint stiffness symmetry was a significant positive correlated RTD symmetry (r=0.42, p=0.02), but not peak torque symmetry (r = 0.34, p=0.08). **Conclusion:** Surgical-limb KJS is significantly lower during the early phase landing. Greater KJS symmetry was associated with better quadriceps RTD symmetry. **Clinical Relevance:** Impaired KJS during landing may predispose patients to future injury risk. Quadriceps RTD may be as important as strength for restoring jump performance and improving long-term outcomes.

Funding: No Funding

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Clinical Research

Abstracts

Poster Number 62

Title: Optimizing Radiographic Techniques for Imaging of the Thumb Carpometacarpal Joint

Authors: M. A. O'Shaughnessy, Assistant Professor, Chief of Orthopedic Hand and Upper Extremity Surgery, University of Kentucky, Dept of Orthopedic Surgery M. F. Walker, University of Kentucky College of Medicine

Abstract: The carpometacarpal (CMC) joint of the base of the thumb exists as a bi-concave, convex saddle joint between the trapezium and the first metacarpal. Because of its unique anatomical orientation, movements of precision pinch, grip strength, cylindrical grasp and object positioning are implicated in the instances of osteoarthritis, a common pathology of the CMC joint. Proper diagnosis is imperative to allow accurate staging to appropriately formulate a patient treatment plan. Radiographs remain the mainstay of imaging for thumb joint pathology. However standard radiographic views do not appropriately visualize the CMC joint of the thumb due to the trapezium's unique anatomy. In order to accurately classify and treat OA at the CMCJ, an accurate, precise, and reproducible standard imaging protocol is necessary. We have compiled an expanded set of described radiographic views which more accurately image the joint. These views include anteroposterior (Robert's), posteroanterior (PA), lateral, Bett's, basal joint stress, pinch lateral and oblique views. We propose this new imaging protocol believed to optimize CMC joint visibility required for OA diagnosis. Future plans include testing our hypothesis that our expanded radiographic protocol will lead to improved inter- and intra-rater reliability staging of thumb arthritis.

Funding: No Funding

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Clinical Research

Abstracts

Poster Number 63

Title: Occupational Stress Exposure, Sleep Quality, and Musculoskeletal Injury in Urban Firefighters

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Abstract: **BACKGROUND:** The physical demand of firefighting is detrimental on sleep quality, but also may increase occupational stress exposure. However, it remains unclear how other elements, such as emergency call volume and/or frequency of emergency response calls also may effect on- or off-duty sleep quality and occupational stress exposure. **PURPOSE:** To determine the effect of emergency call volume on stress exposure and sleep quality among urban career firefighters. **METHODS:** Twenty-four firefighters will volunteer for the current study. Participants will be excluded if they are not over 18 years of age and/or not active-duty firefighters from a professional fire department. A physiological monitor that captures sleep and heart rate variability (HRV) will be given at the beginning of the study and worn throughout the duration of data collection. Participants will also complete surveys related to sleep, rate of perceived exertion (RPE), and quality of life (QoL) throughout the duration of the study. Previous call log data will be used to determine “high” versus “low” call volume fire stations. **RESULTS:** Based on the study’s working hypothesis, a significant difference in sleep quality and HRV is expected between high and low call volume stations. In addition, we expect participants at high call volume stations will subjectively report poorer sleep quality, increased RPE, and poorer QoL compared to participants at low call volume stations. The results will provide critical data reflecting the potential impact of physiological monitoring in a firefighter model and will quantify sleep and occupational stress exposure and their influence on musculoskeletal injury.

Funding: CDC/NIOSH Central Appalachian Regional Education and Research Center (CARERC)

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Clinical Research

Abstracts

Poster Number 64

Title: Post Admission, What Modifiable and Non-Modifiable Factors Lead to Delayed Administration of Antibiotics in Open Fractures?

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Abstract: Purpose: Early antibiotic administration has been shown to be associated with decreased risk of infection in open fractures. Delays of antibiotic administration may be in part due to hospital and patient/injury factors, and our goal was to determine which factors may be associated with delayed administration after patient arrival to the hospital. We hypothesized that isolated injuries, patients with dorsal locations of wounds, and polytrauma would be associated with an increased risk of antibiotic delay. Methods: This retrospective review examined 963 patients with open fractures treated at a level 1 trauma center. Patients were excluded if the administration of antibiotics occurred prior to arrival. Overall delay in antibiotic administration was defined using a previously published threshold of 66 minutes between patient arrival and antibiotic administration. Pharmacy and nursing-related delay was defined as greater than 1 interquartile range above the median number of minutes between the time antibiotics were ordered and administered (median 20 minutes; IQR 58 minutes; total 78 minutes). We used multivariable logistic regression to assess age, gender (male/female), isolated injury, transfer from another facility, wound location (anterior/posterior), trauma team activation, day vs. night presentation (7pm vs 7am), Body Mass Index, Charleston Comorbidity Index, and Injury Severity Score (ISS). Results: 963 records of patients with open fractures were reviewed, with a median time to antibiotic administration of 33 minutes and IQR of 108 minutes. Patient transfer from another facility ($P < 0.001$), isolated injury ($P = 0.046$), and increasing CCI ($P = 0.018$) were associated with a delay in administration (>66 minutes). A delay due to pharmacy/nursing preparation was associated with trauma team activation ($P < 0.0001$), higher ISS ($P = 0.015$), and transfer from another facility ($P = 0.004$). Discussion and Conclusion: Reducing delays of antibiotic administration may reduce infections among patients with open fractures. In our study, factors associated with delays in antibiotic administration include transfer from outside facilities, isolated injuries, CCI, and delays in antibiotic preparation. Dramatic delays in antibiotic preparation (> 1 hour) are associated with trauma team activation, higher ISS, and transfer from another facility. Delays could potentially be addressed by modifying trauma activation protocols, highlighting the importance of assessing low-acuity transfers, and the use of premixed antibiotics or pre-hospital antibiotics. Traumatologists can utilize these findings to implement change at their institution.

Funding: CCTS NIH UL1TR001998 Professional Student Mentored Research Fellowship (PSMRF) Program, College of Medicine

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Abstracts

Poster Number 65

Title: Lower extremity kinematics are altered during walking in people with Marfan syndrome

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Abstract: Marfan syndrome (MFS) is an autosomal dominant connective tissue disorder that affects approximately 1 in 5,000 people. MFS is caused by a mutation of the fibrillin-1 (FBN-1) gene, resulting in decreased deposition of fibrillin microfibrils in the extracellular matrix and leads to decreased FBN-1 production within skeletal muscle resulting in quadricep and hamstring muscle weakness. People with MFS self-report severe pain and disability during activities of daily living i.e., walking, and have a 9% higher incidence rate and earlier onset of hip and knee osteoarthritis (OA) than people without MFS. To our knowledge, there is no prior work in assessing gait mechanics in individuals with MFS. Therefore, understanding the effects of MFS on gait mechanics will allow insight into the link between joint health and pain in the MFS population. Five participants with MFS and 5 age, sex, and BMI-matched healthy individuals underwent 3D gait analysis at a walking speed of 1.35 m/s. A custom MATLAB algorithm was used to analyze peak sagittal and frontal plane hip, knee, and ankle joint kinematics. There were no between group differences in sagittal plane kinematics at the hip, knee, or ankle joints. People with MFS ambulate with more hip abduction ($p=0.02$) and knee adduction ($p=0.04$) compared to healthy individuals. These altered gait patterns in the MFS population may lead to abnormal hip, knee, and ankle joint loading patterns during walking, which may be associated with the high severity of joint pain and incidence of OA in the MFS population.

Funding: Marfan Foundation and CCTS NIH KL2-TR001996

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Clinical Research

Abstracts

Poster Number 66

Title: Masquelet Technique for the Tibia: A Systematic Review and Meta-Analysis of Contemporary Outcomes

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Abstract: Introduction: The Masquelet Technique (MT) is used by orthopaedic surgeons to treat segmental bone loss. There is concern that the MT may have less favorable outcomes in the tibia, especially with larger defects, due to higher rates of open fractures, limited soft tissue coverage, and poor vascularity. The purpose of this study is to systematically review outcomes of the MT in the tibia, and to assess whether defect size is associated with union. **Methods:** A systematic search was performed on PubMed, EBSCO, and Cochrane for studies published from 2010-2019 that included more than 5 cases of the MT applied to the tibia in adult patients. Meta-analysis with random-effects models was used to produce a summary estimate for union rate when the MT is applied to the tibia irrespective of defect size. Additionally, meta-regression was used to assess for association between defect size and union rate. **Results:** A total of 30 studies with 643 tibiae were included in the meta-analysis. A meta-analytic estimate of union rate regardless of defect size when employing the MT in the tibia was 84% (95% C.I. 79-88%). Meta-regression revealed that union rate did not vary by defect size in a statistically significant manner ($\beta=0.35$, $p=0.10$). **Conclusions:** The MT can be an effective technique to treat segmental bone loss in the tibia, even in patients with large bone defects. To better define and understand what patient factors are associated with treatment success and complications when employing the MT at the tibia, large, randomized multi-center trials are required.

Funding: No funding

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Clinical Research

Abstracts

Poster Number 67

Title: Prophylactic Tobramycin Injection Reduces Infection Following Internal Fixation of Open Fractures

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Abstract: Introduction: Open fractures are at an increased risk of infection compared to closed fractures despite early administration of systemic antibiotics and prompt surgical debridement. These fracture-related infections (FRI) result in significant morbidity and need for additional intervention. That said, increasing evidence has suggested that local antibiotics may improve infection rates following surgical fixation. Therefore, we hypothesized that local administration of tobramycin in open fractures lowers rates of infection. Methods: A retrospective, case-control study was performed at our institution of all patients with an open fracture treated with internal fixation and local tobramycin over a one-year time period by a single surgeon. A control group was created by reviewing randomly selected, similar patients that did not receive local tobramycin. Patient demographics, smoking history, injury characteristics, infection, and fracture union were reviewed. Results: In total, 156 patients were included, 79 in the tobramycin group and 77 in the control group. Both groups were similar with respect to demographics, diabetes, smoking, and injury characteristics. The FRI rate was 10% in the tobramycin group compared to 25% in the control group ($P=.02$). The nonunion rate was 13% in the tobramycin group compared to 18% in the control group ($P=.38$). Conclusion: Local tobramycin injection at the time of definitive closure in open fractures treated with internal fixation significantly reduced FRI. No significant difference in union rate was appreciated. The limitations in this retrospective study have prompted a single-blinded randomized control trial to further evaluate the efficacy of this adjunct therapy.

Funding: CCTS NIH UL1TR001998

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Clinical Research

Abstracts

Poster Number 68

Title: Bladder oxidative stress and ERK signaling contribute to bladder pain mediated by macrophage migration inhibitory factor and High Mobility Group Box 1

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Abstract: Intravesical PAR4 induced bladder hyperalgesia (BHA) in mice through release of urothelial macrophage migration inhibitory factor (MIF) and High Mobility Group Box 1 (HMGB1). We aimed to confirm our observations using transgenic strains and examine downstream mechanisms at the level of the bladder involved in BHA. BHA was induced in C57BL/6 with intravesical PAR4 or in MIF knockout with di-sulfide HMGB1 (dsHMGB1). Lower abdominal von Frey (VF) mechanical threshold (index of BHA) was measured before and 24 hr after treatment. Intravesical pre-treatments included: PBS; ethyl pyruvate (EP); N-acetylcysteine amide (NACA); FR180204 (FR; methylcellulose as solvent); LY294002 (LY; DMSO as solvent). Awake micturition parameters and bladder histology were assessed 24 hr after treatment. R was used for all analyses. Scrambled peptide did not induce BHA while intravesical PAR4 induced BHA in WT mice. Pre-treatment with EP nearly blocked BHA while NACA significantly reduced it and FR had no effect. PAR4 did not induce BHA in MIF KO mice while intravesical dsHMGB1 elicited BHA. Pre-treatment with NACA and FR but not LY significantly prevented HMGB1-induced bladder pain in MIF KO mice. No significant effects were noted on micturition volume, frequency, inflammation, or edema. MIF mediates bladder pain through the release of intravesical (likely urothelial) HMGB1. Downstream of HMGB1, ROS production and ERK1/2 activation at the level of the bladder mediate bladder pain. Further dissecting HMGB1 downstream signaling pathway may lead to novel potential therapeutic strategies to treat non-inflammatory bladder pain.

Funding: NIH R01 DK121695 and R01 AR049610

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Basic/Translational Research

Abstracts

Poster Number 69

Title: Assessing Functional Impairments, Structural Abnormalities, and Clinical Outcomes in People with Chronic Hip Pain

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Abstract: Chronic hip pain (CHP) is common in the aging population and impacts activities of daily living and quality of life (QOL). The purpose of this study was to assess the structural and functional differences between subjects with CHP and asymptomatic controls. We hypothesized that subjects with CHP would exhibit weaker knee and hip musculature, decreased bone mineral density (BMD) of the femoral head, and worse clinical outcomes compared to healthy controls. This is a controlled laboratory study with ongoing recruitment. Five subjects with CHP (6 hips; 4 females, age: 57 ± 17.4 years, BMI: 26.8 ± 3.3 kg·m⁻²) and 15 healthy controls (15 hips; 8 females, age 30.5 ± 9.6 years, BMI: 25.6 ± 2.1 kg·m⁻²) were tested. The affected limb within the CHP group was tested while the dominant limb was tested for controls. Isometric strength of the knee and hip musculature, normalized by body mass, was assessed via an isokinetic dynamometer. The BMD of the femoral head was measured via Dual-energy X-ray absorptiometry (DXA). The Hip disability Osteoarthritis Outcome Score (HOOS) was used to assess hip-related clinical outcomes. Despite similar BMI and sex distribution ($p > 0.05$), the CHP group was significantly older than the controls ($p < 0.01$). After adjusting for age, the CHP group had lower femoral head BMD ($p = 0.04$) yet similar hip and knee muscle strength compared to controls. The CHP group also reported worse hip-related pain, symptoms, function, and QOL ($p < 0.001$). Our future work will assess the role of hip and knee muscle rate of torque development on femoral head BMD within the CHP group.

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Basic/Translational Research

Abstracts

Poster Number 70

Title: Hematological Outcomes of Delayed Umbilical Cord Clamping in Preterm Infants

Authors: A. Porter BS, UK College of Medicine MS3 Student, P. Giannone MD, UK Healthcare, Chief of Neonatology, H. Huang MD PhD, Research Protocol Manager/Clinical/UK Healthcare, A. Schadler PhD, UK Healthcare, Department of Statistics, J. Bauer PhD, UK College of Medicine, Department of Pediatrics-Neonatology

Abstract: **Background:** Extremely preterm neonates are infants born at <28 weeks gestational age. Prematurity is a major risk factor of neonatal morbidity and mortality. Historically it has been debated when is appropriate to clamp the umbilical cord: delayed cord clamping (DCC) or immediate cord clamping (ICC). DCC refers to the delay of 30-60 seconds after birth before clamping and cutting the umbilical cord. Recent studies support the safety and beneficence of this practice in all infants as it has been shown to increase hemoglobin and iron storage as well as provide significant reductions in risk of morbidities namely intraventricular hemorrhage (IVH). However, IVH prevention is rarely studied in research literature. **Purpose of research:** Thus, we aim to study the hematological effects of DCC in extremely preterm, low birthweight neonates in comparison to immediate cord clamp (ICC) for potential mechanistic insights of DCC. We believe DCC infants will exhibit better hematological factors and lower levels of inflammatory factors, therefore reduced risk of IVH. **Methods:** Mothers and infants were identified for this study primarily based on gestational age: admission <30wks. Neonates (n=216) in this study ranged from 22-30 weeks gestation. This study compared DCC and ICC cohorts of tiny babies at various time points. Data was collected from blood samples from umbilical cord blood, indwelling arterial catheters, and/or heel sticks.

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Basic/Translational Research

Abstracts

Poster Number 71

Title: Inhaled Antibiotics and Resistance Patterns in Pediatric Cystic Fibrosis

Authors: L. Disney, U of Kentucky College of Medicine, M. Wurth, Department of Pediatric Pulmonology, U of Kentucky E. Autry, Department of Pediatric Pulmonology, U of Kentucky

Abstract: Progressive respiratory disease is the primary driver of morbidity and mortality in cystic fibrosis, largely driven by infection with opportunistic pathogens. *Pseudomonas aeruginosa* is a leading cause of chronic respiratory infection in patients with cystic fibrosis and is associated with accelerated decline in lung function and death. Management of *Pseudomonas aeruginosa* is notoriously challenging due to its tendency to develop resistance to antibiotics. Inhaled antibiotics are used in the management of *Pseudomonas aeruginosa*, both to help clear new infections and to reduce bacterial burden in chronic infections. Inhaled tobramycin has long been the first-line and most commonly prescribed inhaled antibiotic for management of *Pseudomonas aeruginosa*, followed by the relatively newer aztreonam lysine. There remains limited data comparing these inhaled antibiotics with respect to drug resistance, and clinical trials addressing this topic are currently underway. This retrospective study compared the outcomes of respiratory cultures and pulmonary function tests in pediatric cystic fibrosis patients prescribed inhaled tobramycin and inhaled aztreonam at the University of Kentucky Cystic Fibrosis Center. No difference was detected between aztreonam users and tobramycin users in development of drug-resistant *Pseudomonas aeruginosa* or in rate of lung function decline, although the study was not sufficiently powered to evaluate these outcomes. There was a non-significant trend toward increased rates of drug-resistant gram-negative infections largely driven by pathogens with less clinical significance than *Pseudomonas aeruginosa*.

Funding: CCTS NIH UL1TR001998

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Clinical Research

Abstracts

Poster Number 72

Title: Advantages of Management by Pediatric Headache Specialists: A Pediatric Headache Database Initial Review

Authors: E. Touma, U of Kentucky College of Medicine, S. Qaiser, Department of Child Neurology, U of Kentucky

Abstract: **OBJECTIVE:** To assess the health outcomes and care matrices in children managed by a headache specialist. **BACKGROUND:** In the era of precision medicine, sub-specialty clinicians emphasize an individualized care approach. Recently, it was argued that there is *no* change in patient outcomes in children seen by headache specialists compared to non-headache specialists. Our study aims to provide a nuanced perspective of the advantages of care when treated by headache specialists. **METHODS:** A RedCAP database was utilized to record and measure variables that assess health outcomes and the Healthcare Matrix framework. Children and their parents were provided with IRB-approved questionnaires based upon NIH-guided research. The data from 200 time-points of patients (0 - 17 years of age) seen at the UK Headache Clinic was then analyzed. **RESULTS:** The analysis demonstrates an exponential improvement in patient outcomes over their course of care. Over 96% of patients reported understanding of the diagnosis and treatment at the first follow-up . 71.6% of patients reported feeling better at first follow-up. Finally, frequency scores dropped dramatically from the first visit to first follow-up: A 27% decrease in patients experiencing 1+ headaches per week. **CONCLUSION;** Children seen by pediatric headache specialists have undeniably positive outcomes. Patients understand their headaches and treatment at high rates, likely a product of education- focused approach by headache specialists. Patients also were likely to feel better at first follow-up, and have a general decrease in headache frequency. Further analysis will provide insight into variables such as education barriers and treatment regimen patterns.

Funding: CCTS NIH UL1TR001998 Professional Student Mentored Research Fellowship (PSMRF) Program, College of Medicine

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Clinical Research

Abstracts

Poster Number 73

Title: Understanding Appalachian Perspectives on Asthma in Children

Authors: Joslyn Isaac, University of Kentucky College of Medicine, MD Candidate Nancy Schoenberg PhD, University of Kentucky College of Medicine, Center for Health Equity Transformation and Department of Behavioral Science Steven Browning PhD, University of Kentucky College of Public Health, Department of Epidemiology

Abstract: The central Appalachia sub-region of the United States, which includes eastern Kentucky, suffers from the highest respiratory disease rates in the nation. The Mountain Air Project (R01ES024771, Browning & Schoenberg) sought to investigate risk factors for respiratory disease and implement an intervention to mitigate such risks. Set in two rural Appalachian counties, MAP investigators and staff trained community members to enumerate and interview 972 household and individuals, assessing health and behavioral and environmental exposures. With extensive encouragement from community members, we conducted a sub-study that focused on the experiences of Appalachian children with asthma. The “Asthma in Kids” sub-study engaged 17 children (age, 6-17) and their parents in in-depth interviews to better understand their perspectives on this respiratory disease. An Appalachian native (JI) conducted an ethnomedical in-depth interview with children diagnosed with asthma and their family member(s), focusing on asthma diagnoses, knowledge of risk factors, the lived experience of asthma, and treatment. Twenty-eight audio recorded interviews were conducted, interviews were transcribed, and transcripts were coded to identify overarching themes. We found that asthma significantly restricts physical activity in a community burdened with obesity. We also found that patients treat and follow up with providers on a symptomatic basis, rather than preventatively. We also discovered the family’s personal experience/history with asthma influences treatment mechanisms and emotional components to the disease. It was also noted that the knowledge of risk factors varies widely from family to family. These findings are important for healthcare providers to consider cultural components of disease management.

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Community Research

Abstracts

Poster Number 74

Title: Analysis of Pediatric Dentistry Patient Education Materials on Google

Authors: J. Martin, Department of Pediatric Dentistry, U of Kentucky, K. Dingrando, Department of Pediatric Dentistry, U of Kentucky, G. Hawk, Department of Statistics, U of Kentucky

Abstract: Purpose: As Internet usage has become commonplace in today's society, so has the reliability of the general population on utilizing it to obtain information. Google (the most popular search engine) provides ample results for each query entered. While healthcare providers cannot control the information provided, they recognize the influence it has on healthcare decisions made by patients (and their parents). The purpose of this study is to obtain a list of commonly searched keywords related to Pediatric Dentistry using Google AdWords Planner and to assess the Top Level Domain and Readability of the top 20 websites for each keyword. The readability level will then be compared to the recommended readability level of the American Medical Association (AMA) and the National Institute of Health (NIH). **Methods:** Google AdWords planner was utilized to determine commonly searched keywords relating to Pediatric Dentistry. The keywords were then categorized into 7 groups: prevention, diagnosis, sedation, emergency care, invasive treatment, noninvasive treatment, and oral habits. Each keyword was entered into Google search engine utilizing Incognito Mode (to prevent locational and search biases). The Top Level Domain was recorded and the Readability level was calculated using four validated formulae. **Results:** Results Pending. **Conclusions:** Conclusions pending. It is predicted that search results will likely exceed the recommended reading level recommended by the AMA and NIH and the most common Top Level Domain will be .com.

Funding: No Funding

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Policy & Education Research

Abstracts

Poster Number 75

Title: Rural Women and Substance Use Disorder: Availability of SUD Treatment Services, Facilitating Factors, and Barriers to Receiving Treatment

Authors: K. I. Flores, College of Social Work, U of Kentucky

Abstract: The literature surrounding substance use disorder (SUD) and SUD treatments has, until the 1980's, largely revolved around the specific needs and use patterns of men. Incongruence between the unique treatment needs of women and current available SUD treatments is further exacerbated by unaddressed needs along geographical lines. Women in rural areas exhibit different use patterns (e.g., substance preference, daily use, age of first use) and have sparser access to SUD treatments than women in urban areas. The following study examines the intersection of urban and rural culture and geography with barriers and facilitating factors women encounter while seeking treatment. A systematic literature review was conducted using Academic Search Complete. Seventeen articles met the inclusion-exclusion criteria for this study. Eight overarching factors affecting women's access to SUD treatment were identified: availability of gender-specific SUD treatments, quality of healthcare provider relationships, responsibility to family, gendered roles and expectations, lack of general healthcare and specialized treatment options, lack of transportation/geographical spread, availability of childcare, and lack of community anonymity. The latter five are especially impactful for rural women with SUD. These factors delineate the need for rural-specific and urban-specific SUD treatment approaches beyond the scope of gender-based lines. This study discusses how specialized training for healthcare providers, emphasis on building positive professional relationships, and integration of general healthcare systems with treatment systems may mitigate, if not completely remove, barriers that women, especially in rural areas, face when seeking SUD treatment.

Funding: No Funding

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Basic/Translational Research

Abstracts

Poster Number 76

Title: Recruitment in Substance Abuse Research: An Analysis of the Efficiency of Several Recruitment Strategies

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Abstract: Purpose: 40.3 million people Americans aged 12 or older had a substance use disorder in 2020. This high prevalence creates an unprecedented need for research to recruit participants to develop interventions and understand factors that contribute to substance use disorders. Unsuccessful recruitment can increase study costs and delay completing important projects. The purpose of this analysis was to explore the efficacy of several recruitment strategies on enrollment for inpatient and outpatient studies at UK's Laboratory of Human Behavioral Pharmacology. Methods: 444 initial phone screens conducted in 2021 were analyzed based on referral source and outcome. The efficiency of each source was calculated by dividing the number of callers from each source by the number of participants from each source that were 1) eligible for further screening following the phone screen and 2) enrolled in a study. Results: The four recruitment strategies that produced the most phone screens were radio advertisement, past participants returning, word of mouth, and online advertising. Forty-six percent of phone screens returned for further screening across all referral methods, which was balanced across all methods. Eligible individuals referred from flyers were most likely to enroll across multiple studies. Conclusion: There are a variety of recruitment methods that can successfully produce eligible participants. However, it is recommended to first attempt less expensive recruitment strategies (e.g., past participant referrals) prior to more expensive methods that may be less efficient (e.g., radio advertising).

Funding: NIH R01DA048617, R01DA047368, T32DA035200

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Clinical Research

Abstracts

Poster Number 77

Title: Eye Tracking to Measure Attentional Bias in Smokers

Authors: R. Khanal, College of Medicine, U of Kentucky, R. Gopalkumar, Department of Psychiatry, U of Kentucky

Abstract: Background: Incentive salience encompasses classical conditioning causing the brain to pay more attention toward stimuli with greater emotional valence or reward compared to neutral stimuli. Quantifying time spent by the eyes on stimuli of interest compared to neutral stimuli helps to what is called attentional bias. This is done using eye tracking. Eye tracking can quantify attention given to stimuli using gaze fixation metrics and by monitoring saccades. We examined various metrics, to identify the relationship between them in a patient sample with tobacco use disorder. We also examined how these metrics would differ between smoking versus neutral stimuli in these patients. Methods: We compiled eye tracking data from 60 participants with tobacco use disorder, using Tobii Pro Fusion. We used 20 pairs of smoking (S)- nonsmoking neutral (N) images. Each recording had 32 metrics and we examined correlations between these metrics. We also examined the differences between these metrics for smoking versus neutral stimuli. Results: Correlation between total duration of fixations and total duration of whole fixations was 0.55 ($P < 0.05$). Correlation increased to 0.9 ($P < 0.05$) with total duration of glances and 0.44 ($p > 0.05$) for total duration of visits. Smoking and neutral stimuli showed significant differences on all metrics except for average pupil diameter and time to first whole fixation/glance/visit. Conclusion: Glances could be a plausible surrogate metric for total duration of fixations. More studies and analyses are needed to identify an optimal metric to quantify attentional bias for stimuli of interest.

Funding: Substance use research priority area (SUPRA) Pilot Award; CCTS NIH UL1TR001998 Professional Student Mentored Research Fellowship (PSMRF) Program, College of Medicine

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Clinical Research

Abstracts

Poster Number 78

Title: Preoperative Opioid Use as a Predictor of Postoperative Opioid Use in Ventral and Incisional Hernia Repair

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Abstract: Introduction: Previous research has shown that nearly one in two ventral and incisional hernia repair (VIHR) patients have preoperative opioid use within a year before procedure. The purpose of the study was to investigate the association of preoperative opioid use on postoperative use and identify risk factors of increased postoperative use in VIHR patients. **Methods:** With IRB approval, a retrospective review was conducted on open VIHR cases performed over four years. Kentucky All Schedule Prescription Electronic Reporting (KASPER) data was linked to patient records to obtain opioid use, dose, and prescription length. Opioid naivety was defined as no active opioid prescription during the 45-day pre-admission period. Morphine milligram equivalent (MME) was used for uniform comparison of dose. **Results:** 205 patients were included in the analyses (average age = 53.5 ± SD 12.0; 49.3% were female.) Over 35% met criteria for preoperative opioid use; 64% of patients had postoperative opioid days dispensed greater than 10 and cumulative dose greater than 450 MME over 45 days post-discharge. Any 45-day preoperative opioid use (OR 13.62, 95% CI 4.0-46.4, p<.001), smoking status (OR 8.81 95% CI 1.68-46.1, p<0.01), and history of two or more hernia repairs (OR 4.73 95% CI 1.41-15.90, p<0.012) were the strongest risk factors for increased postoperative opioid utilization. **Conclusion:** Preoperative opioid use during 45-day pre-admission correlated strongly with postoperative use in VIHR patients. Several independent preoperative risk factors associated with increased postoperative opioid use were identified, and further research exploring the impact of these elements is needed.

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Clinical Research

Abstracts

Poster Number 79

Title: Alcohol Use, Sleep, and Depression Among Family Caregivers in the Time of COVID-19

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Abstract: The COVID-19 pandemic has substantially altered daily life around the world, resulting in significant impacts on health behaviors. The additional burdens imposed by family caregiving (i.e., providing unpaid care for children and/or adults) may further exacerbate negative effects of the pandemic on health and health behaviors, including increased alcohol consumption, poor sleep, and increased depressive symptoms. The current study examined this possibility. Participants (N = 320, mean age = 35.11 years) completed an online questionnaire assessing alcohol use, sleep, and depression during the COVID-19 pandemic (June-August 2020) and retrospectively assessed the same health behaviors in the months prior to the pandemic. Insomnia severity increased, sleep quality decreased, and depressive symptoms increased for both caregivers and non-caregivers during the pandemic ($p < 0.001$). By contrast, alcohol consumption increased among caregivers only ($p < 0.05$). Further, increased alcohol use was associated with decreased sleep quality and increased insomnia symptoms among caregivers, but not non-caregivers. While additional longitudinal research is warranted in this population, our findings offer important insight on self-reported changes in alcohol consumption, sleep patterns, and mood among family caregivers during the COVID-19 pandemic.

Funding: CCTS NIH Grant UL1TR001998

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Community Research

Abstracts

Poster Number 80

Title: Breast Implant Illness: Correlation Between Explantation and Symptom Relief

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Abstract: Breast Implant Illness (BII) is a relatively new term used to describe a wide array of symptoms seen in a select group of patients with breast implants. The symptom set is not well defined, and the cause of the symptoms is not well understood. It has been theorized that breast implants act as an adjuvant in this population and cause an immune response resulting in symptoms similar to those seen in an autoimmune disease.¹ The aim of this study then is twofold: to document the symptoms observed in BII and to analyze the relationship between explantation and symptom relief. Ten patients seen through the UK Department of Plastic Surgery for consultation regarding BII opted to participate in the study. Symptoms were recorded via questionnaires distributed through REDCap. The initial questionnaire recorded symptoms experienced preoperatively, and a subsequent questionnaire recorded symptoms experienced 1-month postoperatively. Patients reported if each symptom was experienced monthly, weekly, or daily or if it was never experienced. A numerical value was assigned to each of these frequencies for ease of data analysis (never=0, monthly=1, weekly=2, daily=3). The most experienced preoperative symptoms included fatigue, difficulty concentrating, mood changes, insomnia, joint pain, and muscle aches. The average frequency of symptoms preoperatively was 1.99 (SD, 0.72), and the average frequency of symptoms after explantation was 0.72 (SD, 0.47). The average decrease in symptom frequency was highly statistically significant with a P value <0.001. These results suggest that explantation is effective for symptomatic relief as it relates to BII.

Funding: No Funding

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Clinical Research

Abstracts

Poster Number 81

Title: Comparison of Automated and Manual Segmentation of the Foveal Avascular Zone in Patients with and Without Diabetic Macular Edema Using Optical Coherence Tomography Angiography

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Abstract: Purpose: Enlarged foveal avascular zone (FAZ) has been associated with lower visual acuity in diabetic patients. Accurate and automatic FAZ measurements could be a valuable tool in the management of diabetic macular edema. Here, we compare manual (MS) and automated segmentation (AS) FAZ tracings from 3 x 3mm optical coherence tomography angiography (OCTA) scans in healthy and diabetic macular edema (DME) patients. **Methods:** This IRB approved study prospectively collected OCTA images in patients evaluated in a tertiary care center where 43 eyes from 43 healthy individuals and 36 eyes from 36 DME patients were included. The FAZ superficial vascular plexus was traced by three masked, trained graders using ImageJ. The raw images were analyzed with the Advanced Retinal Imaging (ARI) network algorithm. All images were analyzed for perimeter, circularity, and area. Paired t-tests were used to compare the manual and automated methods. **Results:** For the healthy subjects, the FAZ area was $0.267 \pm 0.149 \text{ mm}^2$, and $0.244 \pm 0.189 \text{ mm}^2$ by MS and AS respectively ($P=0.25$). In DME patients, the FAZ area was $0.428 \pm 0.222 \text{ mm}^2$ and $0.347 \pm 0.217 \text{ mm}^2$ by MS and AS respectively ($P=0.024$). There was a statistically significant difference between the two methods for both perimeter and circularity in both cohorts of patients with AS underestimating perimeter ($P<0.001$) and overestimating circularity ($P<0.001$). **Conclusions:** Our study shows that while automatic FAZ segmentation is reliable in healthy subjects, the reliability is reduced when estimating FAZ area in patients with DME.

Funding: No funding

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Abstracts

Poster Number 82

Title: Fetal Skull Fracture Detection in Pregnant Trauma Patient with Multiple Pelvic Fractures Using Computed Tomography

Authors: D. House, University of Kentucky College of Medicine, E. Ahmed, Department of Radiology, University of Kentucky College of Medicine A. Chishti, University of Kentucky College of Medicine, J. Lee, Department of Radiology, University of Kentucky College of Medicine

Abstract: Background: Although fetal injuries are generally uncommon due to the protection provided by the maternal body, fetal injury may occur following maternal body compromise. Trauma is the leading mechanism of non-obstetric maternal mortality and fetal injury resulting in fetal loss. Motor vehicle collision (MVC) is the most common mechanism of traumatic injury in pregnant patients. Depending on severity and mechanism of injury, spontaneous abortion may become more likely. Ultrasound is the primary method of fetal evaluation during pregnancy. Though not the first-line imaging modality, computed tomography (CT) may reveal fetal injuries that would otherwise go undetected when evaluating the extent of maternal injury. **Case Presentation:** An 18-year-old female G1P0 at 38 weeks gestational age with no significant medical history and stable vital signs presented to the emergency department following an MVC. She was an unrestrained passenger, traveling 60 MPH, when she was ejected from the vehicle, sustaining multiple pelvic fractures. She was unconscious at time of admission. A full body CT was performed to evaluate the extent of maternal injury, where a fetal skull fracture was detected. Following imaging, the patient underwent an exploratory laparotomy to resolve current trauma and prevent additional damage. The fetus was non-viable due to the extent of the skull damage, but the mother survived to hospital discharge. **Discussion:** Although fetal injuries are uncommon, they often present in the setting of maternal pelvic fractures. This case demonstrates the potential for detecting fetal skull fractures and cranial injuries by utilizing CT when evaluating pregnant trauma patients.

Funding: No Funding

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Abstracts

Poster Number 83

Title: Treatment and Outcomes of Uncomplicated Hyperglycemia in the Emergency Department

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Abstract: Background: Patients with hyperglycemia have longer hospital stays and an increased risk of mortality. Hyperglycemia is commonly encountered in the emergency department (ED). We examined if treatment of uncomplicated hyperglycemia in the ED is associated with hospitalization and mortality. **Methods:** We conducted a retrospective cohort study among adults (aged ≥ 18) seen at University of Kentucky emergency departments between 11/1/2015-12/31/2020 with an initial blood glucose (BG) value ≥ 180 mg/dl. We excluded patients with a BG > 600 mg/dl, diagnosis of DKA, HHS, stroke, myocardial infarction, pregnancy, and sepsis. Severity of illness was controlled for by using the National Early Warning Score (NEWS). Logistic regression models estimated associations between receipt of insulin and saline and odds of hospitalization and mortality. Models were adjusted for race, ethnicity, diabetes type, NEWS, gender, degree of hyperglycemia and age. **Results:** In our sample of 19,626 patients (mean (SD) age=54.5 (15.0); 52.5% male) 2,281(11.6%) received insulin or saline, 300(1.53%) died, and 8,249(42.0%) were hospitalized. A higher BG was associated with higher odds of mortality (OR=1.061 per 10-unit increase in BG; 95% CI: 1.001, 1.031) and lower odds of admission (OR=0.982 per 10-unit increase in BG; 95% CI: 0.979, 0.986). Treatment resulted in lower odds of mortality (OR=0.085; 95% CI: 0.56, 1.30) and higher odds of admission (OR=2.15; 95% CI: 1.95, 2.38). **Conclusions:** Hyperglycemia in the ED had increased odds of mortality; however, treatment with insulin or saline attenuated the risk. More research is needed to understand the optimal management of uncomplicated hyperglycemia in the ED.

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Clinical Research

Abstracts

Poster Number 84

Title: Impact of Per-and Poly-Fluorinated Alkyl Substances (PFAS) on PPAR Receptors

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Abstract: Per- and poly- fluorinated alkyl substances (PFAS) are man-made surfactant chemicals of concern to human health due to their detectable levels in most individuals, their persistent nature and ubiquitous presence in our environment. The long-term consequences of human exposure to PFAS are difficult to assess due to their diverse chemical structures, regional differences in human exposures and poorly understood mechanisms of action. One possible deleterious consequence of exposure to PFAS is suggested by studies in humans and laboratory animals that associate elevated circulating levels of certain PFAS surfactants, such as PFOA (perfluorooctanoic acid **1**), with lipid dysfunction and liver steatosis. Our goal is to identify the molecular mechanism(s) by which PFOA alters hepatic lipid homeostasis. *We hypothesize that exposure to PFOA inappropriately activates PPAR γ in the liver which subsequently enhances lipid accumulation and inflammation in the liver.* To test this, we synthesized a novel fluorescent, carboxamide derivative of PFOA that retained the heteroatom-hydrogen bond found in PFOA. A similar fluorescent derivative of octanoic lacking fluorines was also synthesized to serve as a control. Use of purified PPAR α and PPAR γ indicated that fluorescent PFOA, but not the control, interacted with both receptors. Additional experiments performed in cultured cells indicated that PFOA interfered with the ability of rosiglitazone to activate PPAR γ mediated reporter genes. These results support the idea that PFAS surfactants inappropriately interact with PPARs to mediate events that ultimately contribute to lipid dysfunction and liver steatosis.

Funding: NIH P30ES026529

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Basic/Translational Research

Abstracts

Poster Number 85

Title: Comparison of Active and Passive Sampling of Nursing Home Wastewater for COVID Surveillance

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Abstract: Timely and accurate information on the status of infection has been crucial to data-driven management of the COVID pandemic. Wastewater surveillance techniques, typically employed for environmental health surveillance, have found increased application in the surveillance of large human health populations for COVID. The current technique for sampling wastewater is achieved via “active” sampling methods, which require expensive programmable pumps and other ancillary equipment, thus severely limiting implementation in remote, low-resource settings. In this work, we compare the sampling capabilities of a passive sampling technique (known as a Moore swab, which is simply a bundle of porous material (e.g., gauze) suspended within a wastewater flow) with the standard composite sample collected via active sampling. Two nursing home effluent wastewater streams were sampled concurrently using both passive and active sampling for 24 hours over a period of 2 months, and SARS-CoV-2 and CrAssphage (an omnipresent bacterial virus present in the gut of most people) were quantified in the samples using RT-PCR. We observed that there was no significant difference in the detection of SARS-CoV-2 between the Moore swab and the composite samples, although the CrAssphage count was generally significantly higher in the Moore swab samples. Notably, SARS-CoV-2 was detected in passive samples in cases in which there was zero detection in the active sample, suggesting that the passive sample methodology has the potential to be a more sensitive sampling tool than active sampling, while significantly improving both cost and simplicity.

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Basic/Translational Research

Abstracts

Poster Number 86

Title: Inhibitory Effect of Sulfur Dioxide Inhalation on Hering-Breuer Inflation Reflex in Mice: Role of 4-AP-sensitive Potassium Channels

Authors: N. Chan, Department of Physiology, University of Kentucky Medical Center, Lexington, KY, United States, C. Hsu, School of Respiratory Therapy, College of Medicine, Taipei Medical University, Taipei, Taiwan, Y. Lin, Department of Physiology, School of Medicine, College of Medicine, Taipei Medical University, Taipei, Taiwan, L. Lee, Department of Physiology, University of Kentucky Medical Center, Lexington, KY, United States

Abstract: Rationale: Vagal bronchopulmonary sensory receptors play a critical role in maintaining normal airway functions; among them, slowly adapting receptors (SARs) are primarily responsible for regulating the breathing pattern and Hering-Breuer inflation reflex (HBIR). Our recent study has shown that breathing of high concentration of sulfur dioxide (SO₂) blocked the SAR activity in mice, suggesting a possible involvement of voltage-gated K⁺ channels. This study was carried out to test the hypothesis that inhalation of SO₂ changes the breathing pattern and inhibits the HBIR, and this inhibitory effect can be altered by pretreatment with 4-aminopyridine (4-AP, a non-selective voltage-gated K⁺ channel blocker). **Methods:** In anesthetized, spontaneously breathing mice, we measured the HBIR and compared the responses between before and after termination of SO₂ inhalation. 4-AP and its vehicle were infused separately, in alternating sequence between animals, 5 min prior to the SO₂ inhalations in the same animal. **Results:** The HBIR response was blocked by the inhalation of SO₂. In addition, inhalation of SO₂ induced slow and deep breathing. These changes emerged immediately after the termination of SO₂ inhalation and returned toward baseline approximately 30 min later. Pretreatment with 4-AP, but not its vehicle, completely blocked the SO₂-induced inhibitory effect on HBIR and significantly reversed the changes in breathing patterns. **Conclusions:** Inhalation of SO₂ inhibited the HBIR and induced slow and deep breathing; these responses were reversible and reproducible in the same animals. This inhibitory effect was probably mediated through an action of SO₂ on 4-AP-sensitive K⁺ channels in vagal SAR sensory nerves.

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Basic/Translational Research

Abstracts

Poster Number 87

Title: **Stabilization of SARS-CoV-2 in ESP-Extracted Wastewater Samples**

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Abstract: Wastewater surveillance has become popular during the SARS-CoV-2 pandemic as a means to estimate prevalence within a population. Despite this growth in implementation, logistical challenges have limited wastewater surveillance rollout to urban areas in regions with advanced laboratory infrastructure. Specifically, SARS-CoV-2 RNA is affected by factors that promote degradation of viral RNA (e.g., variable temperatures, RNA-degrading enzymes). Initial experiments quantifying this degradation illustrated significant and variable decay of viral RNA signal, with signal half-lives ranging from days to two weeks. Thus, to preserve both accuracy and precision in wastewater surveillance, there is an unmet need for a rapid, field-compatible method to stabilize viral RNA. Further, given the paucity of cold-chain (refrigerated) transportation in many parts of the world, a method that provides ambient stability would be particularly valuable. Here, we utilize Exclusion-based Sample Preparation (ESP) to extract and stabilize SARS-CoV-2 RNA from wastewater via the rapid separation of labile viral RNA from the bulk of the degradation-promoting wastewater. ESP is a fast and electricity-free method of manipulating RNA with paramagnetic microparticles. Raw wastewater and ESP-stabilized aliquots were aged at room temperature and refrigerated conditions to assess degradation over time using RT-qPCR. The half-life of SARS-CoV-2 RNA in room-temperature wastewater was 2-7 days; this increased to 5.9-14.1 days with refrigeration (4°C). ESP-extracted aliquots exhibited a half-life of 21 days, even with room temperature storage. Thus, ESP provides a rapid and inexpensive process for room temperature stabilization of SARS-CoV-2 RNA, potentially enabling wastewater surveillance in regions that are currently not feasible.

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Basic/Translational Research

Abstracts

Poster Number 88

Title: Primary Care Provider Beliefs and Tobacco and Radon Risk Messaging with High-Risk Individuals in Kentucky

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Abstract: An estimated 2,660 Kentuckians will lose their lives this year to lung cancer, yet the disease is highly preventable. Prevention of tobacco smoke and radon co-exposure and early lung cancer screening will lower new lung cancer cases and deaths. The scientific premise is that the lung cancer screening sharing decision-making (SDM) is an ideal teachable moment to promote home radon testing and mitigation and smoking cessation treatment among high-risk adults. Using stratified random sampling by ADD, we will invite 1,000 PCPs from across Kentucky to participate in a mailed survey assessing beliefs and practices related to lung cancer prevention and explore current tobacco and radon risk messaging during lung cancer screening SDM visits. We will present preliminary findings examining PCP beliefs, self-efficacy and practices related to tobacco and radon exposure messaging, controlling for urban-rural status and county radon risk potential. We hypothesize that PCPs with higher scores on beliefs, and self-efficacy related to tobacco and radon exposure will use more proactive tobacco and radon risk reduction practices when counseling their high-risk patients.

Funding: NIH UL1TR001998

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Abstracts

Poster Number 89

Title: Engaging High School Students as Citizen Scientist in Assessing the Effects of Waste Water Run-off in Rural Appalachian Waterways

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Abstract: Residents of urban areas take public wastewater sanitation for granted because of city or county run sanitation infrastructure. The lack of municipal sanitation in large areas of Appalachia creates a situation where many people must provide their own means of wastewater sanitation such as traditional septic systems. Wastewater sanitation is a problem for many homeowners in Appalachia because of poverty, topography of the land and a lack of education about the detrimental effects of inadequate wastewater sanitation. Inadequate wastewater sanitation, such as “straight piping” of wastewater directly into local creeks often leads to large amounts of wastewater making it into local waterways. This influx of wastewater can increase bacterial concentrations and harmful chemicals. One of the waterways that has not received much attention is the Middle Fork of the Kentucky River. The Middle Fork of the Kentucky River runs through Leslie, Western Perry, Breathitt and Lee counties and it confluences with the North and South Forks of the Kentucky River. Students quantified the amount *E. coli* and total coliform bacteria by determining the most probably number (MPN) and nutrient analysis was conducted at the University of Kentucky. Biochemical oxygen demand (BOD), and other water quality measurements including conductivity, pH, temperature and dissolved oxygen (DO) were also examined. While a couple of streams had elevated *E. coli* levels there was not a strong indicator that wastewater run-off from “straight-piping” was contaminating streams. Additional research is warranted to determine the causes of the high conductivity in two of the streams sampled.

Funding: NIH P30 ES026529-02S1

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Community Research

Abstracts

Poster Number 90

Title: Summarizing Air Pollution Health Consequences: Emphasizing Traffic Pollution Effects

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Abstract: Our goal is to review the literature on health effects of air pollution, with special emphasis on air pollution caused by automobile and truck traffic. We highlight epidemiology studies with quasi-experimental design or difference-in-difference design. Such studies provide evidence of causality. Human epidemiology literature is being complemented by studies of human secondary endpoints, which correlate with disease or death. These studies are further complemented by studies with experimental animals. Although we are not creating new knowledge, we will synthesis the literature and review the effects of air pollution on human health, identifying gaps in the current body of knowledge.

Funding: UK Department of Pathology and Laboratory Medicine

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Community Research

Abstracts

Poster Number 91

Title: Implications to Tap and Stream Water Chemistry Due to Variations in Sampling Location and Watershed Land Use

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Abstract: Heavy metals and sulfate are persistent environmental contaminants in Appalachian communities. Exposure to heavy metals and sulfate has been associated with human health impacts including nervous system disorders, birth defects, and various forms of cancer. To date, there is limited information regarding the potential exposure and introduction of heavy metals and sulfate entering rural water treatment plants, resulting in a notable and concerning knowledge gap in these regions. Therefore, the following research objectives included: 1. Conducting a citizen science tap water campaign, including 70 residential homes, with a variety of water outlets (indoor faucet vs. outdoor spigot), source water (well, spring, water treatment plant), and counties; 2. Complete an in-stream monitoring campaign at nine field sites. Heavy metals were found to be statistically higher in outdoor spigot samples compared to water samples collected at indoor faucets, with many outdoor spigot samples exceeding human health limits. However, after allowing water to flush from outdoor spigots for five minutes, no differences were observed between indoor faucets and outdoor spigot heavy metal concentrations. Significant differences in sulfate, aluminum, and iron concentrations were also observed in residential tap water samples depending on source water. Surface water monitoring sites had significantly different heavy metal and sulfate concentrations depending on monthly precipitation and watershed land use. Findings from this work provide guidance on metal accumulation in tap water pipes along with guidance on heavy metal and sulfate concentration environmental exceedances depending on watershed land use.

Funding: NIH P30ES026529.

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Community Research

Abstracts

Poster Number 92

Title: Plasma Protein Analysis of Stroke vs Non-stroke patients utilizing the BACTRAC Tissue Bank

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Abstract: Stroke is the fifth leading cause of death and first in causes of disability in the United States. Mechanical thrombectomy and tissue plasminogen activator are the current treatments for ischemic stroke, which have improved clinical outcomes. Despite these treatments, functional and cognitive deficits still occur demonstrating a need for predictive biomarkers for these clinical outcomes, which then are also potential pharmacological targets for treatments. The BACTRAC Tissue Bank collects blood distal and proximal to a thrombus from ischemic stroke patients. For control comparisons, arteriolar blood samples from patients undergoing diagnostic angiogram are collected and banked. Demographic and comorbidity data from these patients are amassed in a database. The aim of this study was to compare the proteomic expression of proximal blood from stroke patients to those in blood from control patients in which patients were matched for age, sex, BMI and other comorbidities. Proteomic analyses of 184 proteins from proximal stroke plasma samples and control plasma samples were performed by Olink. Proteomic levels between matched patients were analyzed using a paired T-test. Overall, protein expression associated with inflammation increased while proteins related to growth and survival decreased in plasma samples from stroke patients. CXCL1, chemoattractant for immune cells, and IL6, a major inflammatory cytokine, showed a significant increase in stroke patients. TWEAK, which is involved in angiogenesis, and ARTN, which has neurotrophic properties, showed a significant decrease in plasma from stroke patients. Further analysis will be used to elucidate the proteomic signaling pathway related to clinical outcomes in the stroke patients.

Funding: CCTS NIH UL1TR001998

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Clinical Research

Abstracts

Oral Presentation /Poster Number 93

Title: An Automated RNA extraction method for wastewater analysis of SARS-CoV-2

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Abstract: Wastewater monitoring has emerged as a promising method for detecting and quantifying SARS-CoV-2 within a population. As implementation of wastewater monitoring increases in scope and scale, there is a need to make the process simpler, faster, and more reliable. Current methods are labor intensive and include several complex filtration and centrifugation steps, which are difficult/expensive to automate. Recently, an RNA extraction method based on Exclusion-based Sample Preparation (ESP) has been developed to extract, concentrate and stabilize RNA from wastewater. This study advances the usability of this method via the development of an automated version of this RNA extraction method based on the simple PIPETMAX® liquid handling robot. Following the loading of samples, reagents, and consumables, the robot automatically performs viral lysis (via heat and chemical lysis), RNA capture, and RNA purification. The automated version of ESP takes 26 minutes (45% faster than the manual process), including lysis, binding, and washing steps for four samples/replicates. A confirmed SARS-CoV-2 negative wastewater sample spiked with the heat-inactivated virus is used to optimize different parameters of the process. In total, 12 samples in September -October 2021 from 9 different wastewater treatment plants in central and eastern Kentucky were collected and processed with both manual and automated protocol. The automated extraction process captures either equal or a greater number of SARS-CoV-2 copies from each sample, demonstrating the feasibility of this new automated protocol. This method also shows less variability in the number of RNA copies among replicates of each sample, resulting in a higher precision.

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Abstracts

Oral Presentation/ Poster Number 94

Title: Comparison of post-ARDS fibrosis in patients with COVID-19 and non-COVID etiologies

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Abstract: Objective: to examine the patient-centered outcomes and the occurrence of lung fibrotic changes on Chest CT imaging following pneumonia-related ARDS. We sought to investigate outpatient clinic chest CT imaging survivors of COVID19-related ARDS and non-COVID-related ARDS, to determine group differences and explore relationship between lung fibrotic changes and limitations in six-minute walk distances and pulmonary function. **Design:** retrospective practice analysis; **Setting:** ICU Recovery Clinic in academic medical center; **Patients:** adult patients surviving ARDS due to COVID-19 and non-COVID etiologies; **Measurements and Main Results:** One-hundred four patients with mean age 54 ± 13 and 52% male were included (n=74 COVID-19 and n=30 non-COVID groups). There were no differences for age, sex, mechanical ventilation duration, tracheotomy, or SOFA scores between two groups. Six-weeks after hospital discharge fibrotic changes visualized on CT imaging occurred in a higher proportion of COVID-19 survivors (69%) compared to non-COVID (43%, $\chi^2 = 5.6$, $p = 0.018$). Patients with fibrotic changes (n=64) regardless of group were older, had a lower BMI, and had longer time requiring ventilation. Patients performed poorly on six-minute walk test ($44 \pm 27\%$ of predictive distance), had poor respiratory function ($FEV1\% = 66 \pm 27\%$ and $FVC\% = 65 \pm 20\%$), and had high occurrences of anxiety, depression, distress, and mild cognitive impairment regardless of presence of fibrotic changes. **Conclusions:** Patients surviving pneumonia-ARDS are at high risk of impairments in physical, emotional, and cognitive health related to Post-Intensive Care Syndrome. Of clinical importance, pulmonary fibrosis occurred in a higher proportion in COVID-ARDS group.

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Basic/Translational Research

Abstracts

Oral Presentation /Poster Number 95

Title: A Machine Learning Approach for the Prediction of Retinopathy of Prematurity (ROP) in Preterm Infants

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Abstract: Background: Retinopathy of prematurity (ROP) is a leading cause of visual impairment in preterm infants. Predicting ROP plays a vital role in preventing vision loss. The objective of this study is to employ a machine learning algorithm with influencing factors (e.g., gestational age, birth weight, small for gestational age) as inputs to predict ROP. **Methods:** Data were collected from 230 preterm infants (23 0/7 to 34 6/7 weeks gestation) at the Kentucky Children's Hospital, including 200 infants without ROP and 30 infants with ROP. A logistic regression-based model for predictive analysis was used to predict ROP. Model training was performed using seven independent variables including gestational age, birth weight, small for gestational age, gender, prenatal steroids, cesarean section, and multiple gestation. All analyses were performed using Python program and a *data analysis tool* of Pandas. The model performance was examined using a metrics including the sensitivity, specificity, area under the receiver operating characteristic curve (ROC), and harmonic mean of the model's precision (F-score). **Results:** Our logistic regression model predicts the ROP with the sensitivity of 0.74, specificity of 0.83, area under ROC of 0.86, and F-score of 0.52. Among seven independent variables, gestational age is the most significant factor for ROP prediction, which meets the clinical expectation. **Conclusions:** With the promising logistic regression model established in this pilot study, we are now adding other influencing factors such as intermittent hypoxemia for better prediction and management of ROP.

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Abstracts

Oral Presentation /Poster Number 96

Title: Developing Cancer Education Curriculum to Enhance Cancer Literacy in Appalachian Kentucky Middle and High School Students

Authors: L. Hudson, Markey Cancer Center, U of Kentucky, N. Vanderford, Department of Toxicology and Cancer Biology, College of Medicine, U of Kentucky

Abstract: *Background:* Cancer is the 2nd leading cause of death in the United States. Kentucky has the highest cancer incidence and mortality rates in the U.S., and Appalachian residents are disproportionately affected. Poor health behaviors and inequities in social determinants of health contribute to this disparity, including obesity, tobacco use, poverty, and low education attainment. Cancer literacy, which is defined as a person's ability to make appropriate healthcare decisions, is essential to reducing Kentucky's cancer burden. *Methods:* A Markey Cancer Center team traveled to 6 middle and high schools in central and eastern Kentucky, 5 of which were in the Appalachian region. Upon arrival, students were given a 10-question cancer-related pretest. Immediately after the pretest, a 30-minute presentation covering cancer basics was given, followed by an identical 10-question posttest. 3 months after the intervention, a follow-up survey was sent via email to all participants. *Results:* The results show that a brief, cancer-related intervention significantly improved students' cancer literacy. To influence long-term cancer literacy, we created cancer education curriculum for Appalachian Kentucky middle and high school students. This curriculum contains 3 lessons that cover cancer basics, risk factors, and treatments. The lessons, which are culturally tailored to Appalachian Kentucky students, are equipped with teachers' guides, instructional PowerPoints, pre/posttests, and guided recordings. *Discussion:* By educating students at a formative age, we are motivating them to adopt healthy habits and encouraging them to share this information. Increased cancer education through classroom curriculum can increase cancer literacy, which can reduce Appalachian Kentucky's cancer disparity.

Funding: NIH NCI R25CA221765, P30CA17755; UK VPR Summer Fellowship Program; UK Appalachian Center Eller and Billings Student Research Award.

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Policy & Education Research

Abstracts

Oral Presentation/Poster Number 97

Title: Low-Dose Short-Term Ketorolac Reduces Opioid Use and Pain Scores in Orthopaedic Polytrauma Patients

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Abstract: **Introduction:** The posttraumatic inflammatory response is a complex process associated with several complications including post-traumatic pain. We conducted a double-blinded randomized controlled trial to determine whether scheduled short-term use of a low-dose, non-steroidal anti-inflammatory (NSAID), ketorolac, affects opioid intake and pain in orthopaedic polytrauma patients. **Methods:** Patients 18-70 years old, with a New Injury Severity Score (NISS) greater than 9, and no contraindication to NSAIDs were recruited. Patients were randomized to ketorolac or placebo. The ketorolac group received 15mg of IV ketorolac every 6 hours for up to five inpatient days. The placebo group received 2mL of IV saline in a similar fashion. At enrollment and every 24 hours of stay, morphine milligram equivalent (MME) intake and visual analog scale (VAS) for pain were recorded. Repeated-measures ANOVA was used to estimate differences in MME intake and VAS pain scores across groups over time. **Results:** Overall, 43 participants were included with 22 randomized to the ketorolac group and 21 to the placebo group. There were no significant differences between groups in age, BMI, and NISS. Over the five-day treatment period, mean opioid intake and pain were reduced in the ketorolac group compared to the placebo group (p -values = <0.0001 and 0.022 , respectively). **Conclusion:** Scheduled, short-term use of low-dose ketorolac reduced opioid use and pain in orthopedic polytrauma patients with no apparent short-term adverse effects. These results suggest that ketorolac can be a vital component in a multi-modal pain pathway.

Funding: Orthopaedic Trauma Association (OTA) Research Grant

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Abstracts

Oral Presentation

Title: Comparison of Hemostatic Dysregulation in HIV-1 and SARS-CoV-2 Infection

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Abstract: Systemic and local infections, such as HIV-1 and SARS-CoV-2, increase the risk of potentially fatal thrombotic events. We compared HIV-1 and SARS-CoV-2-associated hemostatic dysregulations, to understand the mechanisms of thrombosis in these populations. Citrated plasma was collected from consenting HIV-1+ (17 naïve/ prior to therapy, and 13 on antiretroviral treatment/ART) or SARS-CoV-2+ (29 inpatients, 49 outpatients) adults and healthy controls for both populations (10, 36, respectively), and hemostatic markers were measured. HIV-1 infection was associated with depletion of anticoagulant protein S (PS), as total protein S (TPS) was reduced ($p=0.007$), with similar trends in the free PS pool (FPS) and protein C (PC), another anticoagulant. No difference was seen in plasma Tissue Factor (TF), a procoagulant marker. TPS deficiency was associated with increased plasma thrombin generation *ex vivo*, indicating hypercoagulability. By contrast, SARS-CoV-2+ inpatients and outpatients had normal TPS and PC, but reduced FPS ($p=0.001$), suggesting a shift in the PS plasma pools. Inpatients also had higher plasma TF activity ($p=0.009$) and monocyte TF expression ($p<0.0001$) compared to controls. As global hemostatic markers, SARS-CoV-2+ individuals had elevated D-dimer ($p=0.02$) and comparable TG to controls, despite prophylactic anticoagulation in the inpatients, indicating hypercoagulability. They also had higher von Willebrand Factor ($p<0.0001$) (a marker of endothelial activation), and IL-6 ($p<0.0001$), soluble Mer ($p=0.021$), and complement C5a ($p<0.0001$) (inflammatory markers). In summary, while both HIV-1 and SARS-CoV-2 are associated with thrombosis, the mechanisms are very different. HIV-1 infection is associated with anticoagulant dysregulation, whereas in SARS-CoV-2, acute inflammation and TF upregulation are predominant.

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Basic/Translational Research

Abstracts

Oral Presentation

Title: Cerebrovascular Reactivity is Related to Enlarged Perivascular Spaces in the Basal Ganglia Among Cognitively Normal Older Adults

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Abstract: Enlarged perivascular spaces (ePVS) are a neuroimaging biomarker of cerebral small vessel disease. Arterial pulsatility drives waste removal through the PVS. Thus, arterial stiffness, a common feature of brain aging, may lead to waste accumulation and perivascular space enlargement. We explored the relationship between arterial stiffness and ePVS burden in 80 cognitively normal older adults ranging in age from 60-85. Participants were scanned on a 3T Siemens Prisma scanner. Arterial stiffness was assessed using cerebrovascular reactivity (CVR), a measure of the ability of cerebrovasculature to dilate in response to hypoxia. BOLD-fMRI was used in conjunction with blocked administration of hypercapnic gas. CVR was computed by dividing change in BOLD signal by change in end-tidal CO₂. All ePVS counts were performed on T1 and FLAIR images. ePVS were defined as regions of hypointensity <3mm in diameter. ePVS were individually and manually counted in a representative axial slice of the basal ganglia (BGePVS), centrum semiovale, hippocampus, and midbrain. Regression analyses controlling for age, sex, intracranial volume, and education demonstrated a negative relationship between whole brain CVR and BGePVS ($P = 0.003$). Moreover, CVR in the left basal ganglia was negatively related to BGePVS in the left basal ganglia ($P < 0.001$), and CVR in the right basal ganglia was negatively related to BGePVS in the right basal ganglia ($P < 0.001$). Our findings indicate a regional relationship between decreased CVR and greater ePVS burden. Future work should compare other potential mechanisms of PVS enlargement to strengthen the hypothesis that arterial stiffness leads to ePVS.

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Basic/Translational Research

Abstracts

Oral Presentation

Title: Carnitine Palmitoyltransferase 1a Modulates Lipoprotein and Hepatic Lipid Metabolism in a Sex-Specific Manner

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Abstract: Background: Nonalcoholic fatty liver disease (NAFLD) affects ~1 billion people worldwide. Epigenome-wide association studies have associated methylation status of carnitine palmitoyltransferase 1a (CPT1a) to perturbations in very low-density lipoprotein (VLDL) cholesterol and triglyceride levels. We demonstrate that hepatocyte-specific deletion of CPT1a in mice lowers serum lipids but exacerbates NAFLD and hepatic inflammation in a sex-specific manner. **Methods:** 8-week-old *Cpt1a* floxed mice carrying the human apoB100 transgene (*Cpt1a^{fl/fl}/B100^{Tg}*) were administered control adenoassociated virus (AAV) or AAV encoding Cre-recombinase under control of a liver specific promoter (TBG-Cre). Control and *Cpt1a* liver-specific knock out (LKO) mice were placed on low-fat control or western-type diet (WTD; 42% kcal fat, 0.2% cholesterol) for 16 weeks. Tissues and plasma were collected, and analyzed for lipid composition and gene and protein expression by QPCR and immunoblotting, respectively. **Results:** Male and female LKO mice displayed lower plasma triglycerides and LDL-cholesterol irrespective of diet. Hepatic triglycerides were elevated in mice fed WTD and exacerbated in LKO mice. Loss of hepatic *Cpt1a* had no effect on hepatic cholesterol in male mice, but increased total and unesterified cholesterol by 2- and 2.5-fold, respectively, in females. These sex-specific differences were also observed in bile acid and inflammatory gene expression, where female LKO mice exhibited increased *Cyp8b1*, and Kupffer cell (*Clec4f*) and collagen (*Col1a1*) gene expression markers. **Conclusions:** CPT1a LKO reduces plasma LDL-cholesterol and triglycerides in male and female mice. Female LKO mice exhibit increases in hepatic cholesterol levels which is associated with changes in expression of bile acid and inflammatory genes.

Funding: NIH K01DK128022; CCTS NIH UL1TR001998

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Basic/Translational Research

Abstracts

Oral Presentation

Title: Primary Results of a Platform-Based Clinical Trial for Persons Diagnosed with MCI

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Abstract: The process of receiving a diagnosis of mild cognitive impairment (MCI) is overwhelming. Individuals may experience adaptive or maladaptive responses to the diagnosis. Five specific areas of maladaptive response were previously identified, including: 1) failure to plan for future decline, 2) decreased compliance and interaction with medical care providers, 3) decreased confidence and reduced social engagement, 4) increased physical limitations and mobility, and 5) decreased medication compliance. This pilot study reports on the delivery of the platform-based trial for persons diagnosed with MCI with survey data and qualitative focus groups data (N=38). The study consisted of a single-site platform trial examining the intervention group. Using this approach allowed the participants to explore different arms of the intervention. Second, the platform design allowed researchers to determine the effects of the interventions on patient help-seeking and adherence behavior in real-world care. Feasibility, opportunities, and challenges will be discussed. Opportunities include the group's cohesion with the group-based intervention, which increased engagement for study group participation. Additionally, participants were most susceptible to intervention components that were novel (i.e., mindfulness) and administered by a professional (i.e., pharmacist, physical therapist) as opposed to self-facilitated activities. Challenges include frequency of study visits, the study partner requirement, and the in-person delivery of the intervention. These challenges were further compounded by the COVID-19 pandemic. Findings from this study offer specific aspects to consider when implementing support programming and clinical research for persons diagnosed with MCI. The presentation will also discuss COVID-19 pandemic-related protocol modifications of this intervention study.

Funding: CCTS NIH UL1TR001998

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Clinical Research

Abstracts

Oral Presentation

Title: A cross-sectional examination of the early-onset hypertensive disorders of pregnancy and industrial emissions of toxic metals using Kentucky birth records, 2008-2017

Authors: C. J. Walker, Department of Behavioral Science, U of Kentucky, W. J. Christian, Department of Epidemiology, U of Kentucky, A. Kucharska-Newton, Department of Epidemiology, U of Kentucky, S. R. Browning, Department of Epidemiology, U of Kentucky

Abstract: Using geocoded residential information from Kentucky live and still birth records (2008-2017) and census micro block group estimates of aerosol concentration of arsenic (As), cadmium (Cd), chromium (Cr), lead (Pb), mercury (Hg), selenium (Se), and zinc (Zi) from the Risk Screening Environmental Indicators (RSEI) model (2007-2017), this exploratory cross-sectional study assessed geospatial patterns of early-onset hypertensive disorders of pregnancy (eHDP) in primiparous mothers and exposure to industrial emissions. Employing a latent class analysis to assess overlaps in exposure, this study identified four district classes – As, Cd, and Pb (12.6%); Se and Zi (21.4%); Pb and Cr (8%); and low or no exposures (57.9%). Women classified as having a high probability of exposure to both Pb and Cr had a statistically significantly greater prevalence of eHDP after adjusting for demographic factors (aPR=1.22, 95% CI: 1.04, 1.44), relative to those with low or no exposure. Our findings contribute to the emerging literature on the association of metal exposures with pregnancy outcomes.

Funding: Education Research Center (ERC) 6U54OH007547; Berea College Olive Ruth Russel Fellowship

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Community Research

Abstracts

Oral Presentation

Title: What is the association between quality of life and weight change at 6 months among African American Diabetes Prevention Program participants?

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Abstract: Background: According to the Centers for Disease Control and Prevention, the US, obesity prevalence among adults is 42.4%; with the prevalence among African Americans 49.6%. Annually, 2/3 adults with obesity report attempting weight loss. Previous research has determined factors such as one's perception of their weight, stigma, and body dissatisfaction as mediators of weight loss efforts. Research suggests that African American adults with overweight have positive body image and weight satisfaction and report higher health related quality of life than African Americans in other BMI categories and white adults. Perceptions of weight satisfaction and high QOL despite having overweight may be a disincentive to actively strive for healthy weight. Several studies have assessed how quality of life improves after weight loss. However, there is a literature gap regarding how quality of life prior to weight loss may be a predictor of weight loss success. **Objective:** To examine whether baseline quality of life using IWQoL influences weight change in African Americans in the Fit and Faithful program.

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