INDIANA CLINICAL AND
TRANSLATIONAL SCIENCES INSTITUTE

2024 Annual Meeting

Precision to Population

ABSTRACT BOOKLET

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SCIENTIFIC ABSTRACTS

EDUCATION:
INDIANA CTSI TRAINEES

K12 Scholars

 # 1

Poster Title: Targeting Negative-Self Referential Processing with Transcranial Magnetic Stimulation: Feasibility Studies

Poster Presenter: Conroy, Susan
Poster Presenter Institution: Indiana University School of Medicine

Poster Authors: Susan K. Conroy, Indiana University School of Medicine; Ho-Ching (Shawn) Wang, Indiana University School of Medicine; Yu-Chien Wu, Indiana University School of Medicine; Stephen Strakowski, Indiana University School of Medicine; Paul Holtzheimer, Geisel School of Medicine at Dartmouth and National Center for PTSD

Abstract:
Background/Significance/Rationale: Major Depressive Disorder (MDD) is common, debilitating, and often difficult to treat. Neuromodulation strategies such as Transcranial Magnetic Stimulation (TMS) can target specific neural circuits underlying particular symptoms, potentially 1) enhancing our understanding of neural mechanisms of illness and recovery, and 2) acting as novel therapeutics. We hypothesize that targeting the ventromedial prefrontal cortex (VMPFC) in the brain's Default-Mode Network may normalize aberrant VMPFC activity seen in MDD, thereby improving excessive negative self-referential processing. Several methods needed to test such hypotheses, including an fMRI task and image guided TMS to VMPFC had not been used previously at IUSM.

Methods: Four healthy volunteers completed structural and functional MRI (fMRI). fMRI included a Trait-Adjective Task, a negative self-referential processing task known to activate VMPFC. During the task, participants respond on a task pad whether they feel that each of a series of displayed adjectives (positive, negative, or neutral) applies to them. Three participants then participated in a simulated image-guided TMS session using their structural MRI data. Three-dimensional tracking of the participant's head and the TMS coil were used to position the coil for peak stimulation of the targeted brain region.

Results/Findings: Our team collected quality neural and behavioral data on the fMRI task; participants reported a tolerable experience. Simulated neuronavigated TMS showed feasibility and tolerability of positioning the device to stimulate VMPFC.

Conclusions/Discussion: The fMRI task activated the VMPFC as predicted. The MRI and TMS protocols were replicable and tolerable. These procedures can now be used experimentally by our team with confidence.

Translational/Human Health Impact: This project lays essential groundwork for my K12 project, "Targeting Negative-Self Referential Processing in Depression with TMS," a longitudinal neuroimaging and behavioral study using these methods in the MDD population. We are hopeful that targeting aberrant VMPFC activity underlying excessive self-referential processing seen in MDD will result in symptom improvement.

 # 2

Poster Title: Parental Involvement is related to Parental Resilience & Offspring Neural Reward Prediction Error Signaling

Poster Presenter: Crum, Kathleen
Poster Presenter Institution: Indiana University School of Medicine

Poster Authors: Kathleen I. Crum, PhD, Indiana University School of Medicine, Medical University of South Carolina; Joseph Aloi, MD, PHD, Indiana University School of Medicine; Katherine LeFevre, Indiana University School of Medicine; Mario Dzemidzic, PhD, Indiana University School of Medicine; Leslie Hulvershorn, MD, MSc, Indiana University School of Medicine

Abstract:
Background/Significance/Rationale: Parent mental health is related to children's mental health across development. Intervention efforts for youth psychopathology often leverage parental involvement. However, parents of offspring with psychopathology often struggle with psychiatric risk factors themselves, such as difficulty with resilience following adversity. Reduced resilience in parents increases risk for psychopathology and dysfunctional parenting behaviors. In turn, dysfunctional parenting behaviors place offspring at risk for psychopathology. Our goal was to investigate the associations between parental resilience and parenting behaviors, and their relationship to their offspring's reward neurocircuitry function; in particular, the reward prediction error (RPE) circuit, a transdiagnostic marker of psychopathology.

Methods: N=26 parent-child dyads (child ages 10-14) were recruited. Parents reported on parenting behaviors using the Alabama Parenting Questionnaire (APQ), and resilience using the Connor-Davidson Resilience Scale (CD-RISC). Children performed the Novelty task, a reward learning task, during fMRI scanning. Trial-by-trial RPEs were calculated based on a reinforcement learning model. Brain Regions of Interest (ROIs) including the nucleus accumbens, anterior putamen, and ventromedial prefrontal cortex were created (regions implicated in RPE representation).

Results/Findings: The APQ parental involvement subscale was associated with increased negative affect tolerance (r=0.40, p<.05), personal competence (r=0.37, p=.06), and sense of control on the CD-RISC (r=0.37, p=.06). Parental involvement was also associated with increased *offspring* neural RPE representation within anterior putamen and nucleus accumbens (rs=0.44-0.61, ps<.05) during the Novelty task.

Conclusions/Discussion: Parental resilience is associated with increased parental involvement. Parental involvement is associated with greater offspring neural RPE representation within bilateral striatum. However, findings must be replicated in larger samples with a formal mediation model. Overall, findings suggest that parental factors may impact neurocircuitries underlying psychopathology in offspring, and consequently, risk for offspring psychopathology.

Translational/Human Health Impact: Interventions designed to increase *parental* resiliency may be helpful for reducing risk for psychopathology in *offspring*, perhaps by increasing parental involvement and neural RPE sensitivity in offspring.

 # 3

Poster Title: A pilot study to explore the effects of red meat intake on gut-derived uremic toxins in people with chronic kidney disease

Poster Presenter: Kistler, Brandon
Poster Presenter Institution: Purdue University

Poster Authors: Brandon Kistler, Department of Nutrition Science, Purdue University; Annabel Biruete, Department of Nutrition Science, Purdue University; Wayne Campbell, Department of Nutrition Science, Purdue University; Sharon Moe, Division of Nephrology, Indiana University School of Medicine

Abstract:
Background/Significance/Rationale: Chronic kidney disease (CKD) affects 14% of adults in the United States. Among people with CKD, cardiovascular disease (CVD) is the leading cause of death. Traditional risk factors do not fully explain the increased risk of CVD in people with CKD. Uremic toxins, substances that build up with reductions in kidney function, are one potential non-traditional cause of increased CVD. Importantly, many uremic toxins associated with CVD are derived from the diet by the gut microbiome. Epidemiological data suggests red meat is of particular concern potentially due to shifts in the microbiome or higher amounts of uremic toxin precursors. Therefore, the purpose of this pilot study will be to examine the effects of red meat intake on the gut microbiome and gut-derived uremic toxins.

Methods: This study will be a crossover, complete feeding study that will examine the effects of three weeks of a lacto-ovo vegetarian diet with or without the isonitrogenous replacement of 25% of total protein with red meat. We will recruit twelve people with CKD (age 30-70, eGFR between 30 and 59 ml/min/1.73m^2, without recent hospitalization or antibiotic use). Blood and urine uremic toxins (including trimethylamine N-oxide, p-cresyl sulfate, and indoxyl sulfate) will be measured by Bindley Biosciences Research Institute at Purdue University and fecal microbiome (alpha and beta diversity) in collaboration with the Purdue Applied Microbiome Sciences (PAMS) on consecutive weeks before and after each intervention period.

Results/Findings: Inter and intra-person variabilities will be compared, and outcomes will be analyzed by linear mixed-effects models.

Conclusion: No conclusion presented.

Translational/Human Health Impact: Results of this study will help inform a larger trial and provide novel data on food-based dietary guidance for people with CKD.

 # 4

Poster Title: The Impact of Preoperative Glucagon-Like Peptide-1 Receptor Agonists (GLP-1RA) Utilization on Bariatric Surgery Outcomes

Poster Presenter: Yuce, Tarik
Poster Presenter Institution: Indiana University School of Medicine

Poster Authors: Qais AbuHasan, MD, Department of Surgery, Indiana University School of Medicine, Indianapolis, IN; Daniel E Kpormegbey, PhD, School of Public Health, Indiana University, Bloomington, IN; Luke M Funk, MD, MPH, Department of Surgery, University of Wisconsin, Madison, WI; David B Allison, PhD, School of Public Health, Indiana University, Bloomington, IN; Jane L Holl, MD, MPH, Department of Surgery, Indiana University School of Medicine, Indianapolis, IN, Department of Neurology and Center for Healthcare Delivery and Science Innovation, University of Chicago, Chicago, IL; Dimitrios Stefanidis, MD, PhD, Department of

Surgery, Indiana University School of Medicine, Indianapolis, IN; Tarik K Yuce, MD, MS, Department of Surgery, Indiana University School of Medicine, Indianapolis, IN

Abstract:

Background/Significance/Rationale: The efficacy of GLP1RA for the treatment of obesity has led to considerably increased demand for GLP1RA. GLP1RA use prior to bariatric surgery may represent a novel approach to treating obesity. The objectives of this study were to (1) describe trends in pre-bariatric GLP1RA use, (2) investigate social and clinical factors associated with their use, and (3) evaluate differences in clinical outcomes based on preoperative GLP1RA use.

Methods: Patients who underwent bariatric surgery at three Indiana hospitals from 2018-2023, were identified. Patients who utilized GLP1RA in the year preceding surgery were compared to those who did not. Social determinants of health included insurance, income, and unemployment. Outcomes included rates of GLP1RA use, 30-day postoperative readmissions, ED visits, and percent total weight lost (%TWL) at one year. Associations between preoperative GLP1RA use and outcomes of interest were evaluated using multivariable logistic and linear regressions.

Results/Findings: Of 2,169 patients who underwent surgery, 293 (13.5%) utilized GLP1RA preoperatively. The rate of GLP1RA utilization increased threefold from 2018-2023. Males were more likely to receive preoperative GLP1RA (20.1% vs, 12.2%, $p<0.001$). There were no significant differences in social determinants of health or 30-day postoperative outcomes between patients who did and did not use GLP1RA preoperatively. Similarly, there were no significant differences in %TWL at one year postoperatively between groups (median 25.5% vs. 27.3%, coefficient: -0.78, 95%CI: -2.26-0.70).

Conclusions/Discussion: Utilization of GLP1RA in the year prior to bariatric surgery has significantly increased. Preoperative GLP1RA use is not associated with worse 30-day outcomes or differences in %TWL at one year postoperatively. Further work is needed to evaluate whether GLP1RA dosing and duration of treatment impact postoperative outcomes.

Translation/Human Health Impact: The use of GLP1RA prior to bariatric surgery may represent a novel method for preoperative optimization, lending further support to efforts seeking to improve access to these medications for the treatment of obesity.

T32 Post-Doctoral Trainees

 # 5

Poster Title: Characterizing Liver Transplant Waitlist Disparities: Candidates Initially Listed as Inactive

Poster Presenter: Huber, Sarah
Poster Presenter Institution: Indiana University School of Medicine

Poster Authors: Sarah, Huber, Department of Surgery, Indiana University School of Medicine; Katie Ross-Driscoll, PhD, MPH, Department of Surgery, Indiana University School of Medicine

Abstract:
Background/Significance/Rationale: Liver transplantation is the only curative treatment for end-stage liver disease. Disparities have been documented in access to the transplant waitlist, yet little is known regarding disparities in changes in status once listed. Inactive status on the waitlist prevents candidates from receiving any organ offers and may be the initial listing status or due to a change from active status. Candidates are reactivated if the underlying reason for inactivation is resolved. Our objectives were to describe the characteristics of patients initially listed with inactive status and compare the prevalence of initial inactive status listings across transplant centers.

Methods: This was a retrospective cohort study of candidates waitlisted for liver transplant between 01/03/2023 and 12/02/23, utilizing the Scientific Registry of Transplant Recipients, a national database including all solid organ transplant candidates. 224,736 candidates were included in analysis, and covariates included race, ethnicity, sex, age, BMI, primary payer, MELD at listing, and etiology of liver disease.

Results/Findings: 8,131 (3.62%) candidates were initially listed for liver transplant with inactive status. Although there were statistically significant differences between those listed initially with active status and those listed initially with inactive status in each covariate, these differences did not reach clinical significance. Of the 151 transplant centers, 128 listed any patients with an initial inactive status, with inactive status listings compromising 0 to 49.36% of total listings by transplant center.

Conclusions/Discussion: Despite no significant clinical difference in the characteristics of patients listed with initial inactive status, there is significant variation across transplant centers of the prevalence of listing with initial inactive status. Subsequent investigations will focus on understanding these differences in listing practices between centers.

Translation/Human Health Impact: For the liver transplant process to be equitable each stage of the transplant process must be investigated to identify disparities and potential targets for future interventions to mitigate these disparities.

 # 6

Poster Title: Adjuvants for the Potentiation of the Activity of β-Lactam Antibiotics Against Methicillin-Resistant Staphylococcus aureus

Poster Presenter: Thomas, Caitlyn
Poster Presenter Institution: University of Notre Dame

Poster Authors: Caitlyn A. Thomas, Choon Kim, Amr M. El-Araby, Biruk T. Birhanu, Mayland Chang, Shahriar Mobashery, Department of Chemistry and Biochemistry, University of Notre Dame

Abstract:

Background/Significance/Rationale: Methicillin-resistant *Staphylococcus aureus* (MRSA) causes serious infections in humans and emerged in response to treatment with second-generation penicillins. A common resistance mechanism is by the functions of the *bla* and *mec* operons, which encode a β-lactam sensor/signal transducer protein BlaR/MecR, a gene repressor BlaI/MecI and a resistant determinant BlaZ or PBP2a. BlaR/MecR is responsible for sensing a β-lactam and transducing a signal to its cytoplasmic domain. Without a β-lactam, *blaZ* (gene encoding serine-β-lactamase BlaZ) is down-regulated by the transcriptional repressor BlaI. Upon β-lactam binding to the sensor domain of BlaR (BlaR-SD), BlaI is hydrolyzed and allows for transcription of *blaZ*.

Methods: A fluorescence-reporter assay was used to screen a compound library. Minimum inhibitory concentration experiments were used to determine the activity of compounds against various MSSA and MRSA strains. These methods were used to determine the mechanism of inhibition of compound **1:** nano-differential scanning fluorimetry (nanoDSF); surface plasmon resonance (SPR); PBP anti-sense experiments; and scanning electron microscopy (SEM). In preparation for animal experiments a time-kill assay was performed.

Results/Findings: A fluorescence-reporter assay identified 80 compounds from a 1,974-compound library as potential antibiotic adjuvants. We performed assays for potentiation of the activity of oxacillin against MSSA and MRSA strains. Twenty-four compounds showed promising potentiating ability (2- to 4,096-fold decrease in MIC). Seven compounds exhibited melting temperature shifts using nanoDSF, suggesting binding to BlaR-SD. SPR determined compound **1** has a binding affinity of 31 µM to BlaR-SD. Growth curves showing hypersusceptibility of *S. aureus* penicillin-binding proteins (PBP) antisense strains show Compound **1** targets PBP2 and PBP2a. SEM images showed severe disruption in the *S. aureus* cell wall. The time-kill assay showed 3-log reduction in bacterial count when N315 MRSA was treated with compound **1** and oxacillin.

Conclusions/Discussion: In conclusion, compound **1** targets BlaR-SD, PBP2, and PBP2a, which restores *S. aureus* susceptibility to treatment by oxacillin.

Translation/Human Health Impact: There are currently few antibiotics available in the clinic capable of treating MRSA infections. These findings open new treatment options for patients infected with MRSA.

STUDENT / TRAINEE CATEGORIES

CTSI Student Research Program

 # 7

Poster Title: Cognitive Deficits in Acute Opioid Withdrawal: A Review

Poster Presenter: Khan, Faizan
Poster Presenter Institution: CTSI Student Research Program

Poster Authors: Faizan Khan, CTSI Undergraduate Summer Research Intern, RA Chambers, MD, Professor of Psychiatry, Indiana University School of Medicine, Indianapolis, IN, Laboratory for Translational Neuroscience of Dual Diagnosis & Development; Brett Montieth, MD, MS, Laboratory for Translational Neuroscience of Dual Diagnosis & Development

Abstract:
Background/Significance/Rationale: Opioid addiction can be characterized by a cycle of use, withdrawal, and relapse. Cognitive deficits during opioid use, maintenance, and long-term abstinence are consistently found in studies. Due to the debilitating withdrawal experience, it is necessary to define the cognitive effects there are to pave the way to a solution.

Methods: A literature review using Google Scholar, PubMed, and a reference list search was conducted for studies on the cognitive effects of opioid withdrawal.

Results/Findings: Cognitive deficits were found during opioid withdrawal. Little research was found; less using human subjects.

Conclusions/Discussion: This lack of literature calls for intentional future research. Due to the many causes of cognitive decline and its intersection with other mental illness, lifestyle choices, and withdrawal effects, it is important to isolate opioid withdrawal in order discern its real impact on cognition.

Translation/Human Health Impact: From this review of this topic, it has become clear that not enough intentional research has been done. Researchers need to dive deeper into cognition and opioid withdrawal to identify the extent of the impairment and the best away to address it.

IMPRS

 # 8

Poster Title: Impact of Social Determinants of Health on Stroke Severity in Northwest Indiana

Poster Presenter: Barnard, Jacobus and Lin, David
Poster Presenter Institution: Indiana University School of Medicine

Poster Authors: Jacobus Barnard*****, Indiana University School of Medicine – Northwest (IUSM-NW); David Lin*****, Indiana University School of Medicine – Northwest (IUSM-NW); Miranda Cash, Indiana University School of Medicine – Northwest (IUSM-NW);Grace Armstrong, Indiana University School of Medicine – Northwest (IUSM-NW); Neon Calumpang, Indiana University School of Medicine – Northwest (IUSM-NW); Amy Han, Indiana University School of Medicine – Northwest (IUSM-NW), Department of Psychiatry, Indiana University School of Medicine; *****Shared First Authorship

Abstract:
Background/Significance/Rationale: Stroke significantly contributes to mortality and disability in the United States, yet geographical disparities exist across regions like Northwest Indiana, where stroke incidences and mortality rates are 2-4 times higher than the national average. Social and demographic determinants of health are known factors of stroke risk and outcomes. This study aims to investigate the associations between specific determinants and stroke severity of Stroke Center patients from Lake County, Indiana.

Methods: Data elements were extracted from patients hospitalized at Community Hospital, St. Mary's Medical Center, and St. Catherine Hospital under Powers Health between January 2022 and May 2024. Data was recorded with the AHA's GWTG Stroke Case Record Form. Our retrospective study conducted bivariate analysis, using R, on predictor variables of age, sex, race, Hispanic ethnicity, ZIP code, payment sources, and mode of arrival to the ordinal scores of the modified Rankin Scale (mRS) and the National Institutes of Health Stroke Scale (NIHSS).

Results/Findings: Analysis of 1563 patients, excluding non-residents and transfer patients, revealed notable variations in social and demographic characteristics. Patients from certain urban ZIP codes with comparatively lower median household incomes and secondary education attainment had higher, more severe, mean NIHSS and discharge mRS scores ($p<0.05$). When age-adjusted, Black patients had a 2.5 point higher mean initial and 1.9-point higher mean discharge NIHSS score than White patients ($p<0.001$, $p<0.01$). Patients with higher mean scores across all measures were those associated with using Medicare versus private insurance ($p<0.0001$) and those arriving to the hospital via EMS versus private transport ($p<0.01$).

Conclusions/Discussion: This research addresses the significance of surveying region-specific social determinants of health for its insight into clinical stroke care and future preventative and quality improvement initiatives.

Translation/Human Health Impact: Implementation of interventions and policies can mitigate disparities and impact overall stroke management and prevention strategies.

 # 9

Poster Title: From Birth to Practice: An Analysis of Migration Patterns Among U.S. Orthopaedic Surgeons

Poster Presenter: Duffett, Bryce
Poster Presenter Institution: Indiana University School of Medicine

Poster Authors: Bryce E. Duffett, Indiana University School of Medicine, Department of Orthopaedic Surgery, Indiana University School of Medicine/Indiana University Health, Indianapolis, IN; Samuel T. Jines, Indiana University School of Medicine, Department of Orthopaedic Surgery, Indiana University School of Medicine/Indiana University Health, Indianapolis, IN; Christopher D. Collier, MD, Indiana University School of Medicine, Department of Orthopaedic Surgery, Indiana University School of Medicine/Indiana University Health, Indianapolis, IN

Abstract:
Background/Significance/Rationale: The purpose of this study is to understand the geographic migration of orthopaedic surgeons from birth, through training, to final practice location, and determine what predicts where orthopaedic surgeons practice.

Methods: This retrospective observational study analyzed data gathered by the American Medical Association (AMA) on 8,676 orthopaedic surgeons who completed residency training between 2004 and 2017 and had over 5 years in practice. Data extracted included location of birth, medical school, residency, and final attending practice location as of January 1st, 2023. Relationships were determined using chi-squared analysis and logistic regression.

Results/Findings: Residency location was the most predictive of attending location, with 96.52% of residents from 2008 – 2017 represented. Attending surgeons located where they completed residency training was census division (CD) dependent and ranged from 16.37% (Mountain West) to 71.59% (Middle Atlantic Northeast) with an average of 49.34%. Significant associations ($p<0.00001$) were observed between attending location and birth, medical school, and residency locations for all CDs. Heatmapping of ACGME data showcased that residency allocation across the US is not predicated by the population of the given state.

Conclusions/Discussion: This study suggests that birth and training location are highly predictive of where orthopaedic surgeons will practice in the United States. These relationships are stronger in some areas of the country than others. Residency location was most predictive of practice location, and therefore, the geographic allocation of residency positions is likely to influence the distribution of practicing orthopaedic surgeons. Residency allocation and retention is highly variable across the United States, further impacting the distribution. This information should guide decision makers in graduate medical education to ensure that future expansion and/or reallocation of orthopaedic residency positions serves population needs and provides equitable access to orthopaedic care in the United States.

Translation/Human Health Impact: Included in Conclusions/Discussion section.

 # 10

Poster Title: Kidney Function and Mortality Following Two-Stage Revision Total Joint Arthroplasty for Periprosthetic Joint Infection

Poster Presenter: Epley, Rilee
Poster Presenter Institution: Indiana University School of Medicine

Poster Authors: Rilee L. Epley, Indiana University School of Medicine, South Bend, Indiana; T. Kyle Stoops, Indiana Joint Replacement Institute, Indianapolis, Indiana; Leonard T. Buller, Indiana University School of Medicine, Department of Orthopaedic Surgery, Indianapolis, Indiana; Evan R. Deckard, Indiana Joint Replacement Institute, Indianapolis, Indiana; Peter Caccavallo, Indiana Joint Replacement Institute, Indianapolis, Indiana; R. Michael Meneghini, Indiana Joint Replacement Institute, Indianapolis, Indiana, Indiana University School of Medicine, Department of Orthopaedic Surgery, Indianapolis, Indiana

Abstract:
Background/Significance/Rationale: Periprosthetic joint infection (PJI) after total hip and knee arthroplasty (THA, TKA) is reported in up to 2% of cases yet remains a serious complication. The current gold standard of treatment consists of a two-stage surgery involving intravenous antibiotic therapy between stages of implant resection and reimplantation. In addition, studies on the effects of these antibiotics on kidney function after two-stage treatment for PJI are limited. This study evaluated kidney function and mortality before, during, and after two-stage revision for PJI. The hypothesis of the study was that the antibiotics part of the treatment course would not lead to an increased risk of kidney injury.

Methods: Clinical data on 160 THAs and TKAs undergoing two-stage treatment for PJI were retrospectively reviewed. Standardized protocols were used for all cases consisting of robust medical optimization by a dedicated perioperative medicine specialist and 6-weeks of intravenous antibiotics prior to reimplantation. Kidney function metrics of serum creatinine (Cr), estimated glomerular filtration rate (eGFR), and blood urea nitrogen (BUN) were collected from routine labs in the electronic medical record along with mortality data. A *P*-value of 0.05 was considered statistically significant.

Results/Findings: No significant differences were observed in mean serum Cr (1.10, 1.12, 1.13 mg/dL), eGFR (78.6, 77.7, 74.8 mL/min/1.73m^2), or BUN levels (19.8, 18.9, 19.0 mg/dL) between pre-resection, the inter-stage period, or post-reimplant, respectively ($P \geq 0.432$; Power ≥ 85.3%). Mortality was 0% within 90-days of resection and 1.4% (2/138) within 1-year of resection (both cardiac events unrelated to kidney function). Kaplan-Meier survivorship estimates were 98% at 2-years and 86% at 5-years post-resection.

Conclusions/Discussion: Kidney function was not adversely impacted by the antibiotics associated with the two-stage revision procedure for PJI.

Translation/Human Health Impact: With proper medical management, the two-stage revision for PJI remains the preeminent treatment for PJI following TJA.

 # 11

Poster Title: 0.5% Bupivacaine Provides Additional Analgesia Than 0.25% Bupivacaine In Fascia Iliaca Blocks For Periacetabular Osteotomy

Poster Presenter: Kular, Amol
Poster Presenter Institution: Indiana University School of Medicine

Poster Authors: Amol Kular, Indiana University School of Medicine; Yar Yeap, Department of Anesthesia, Indiana University School of Medicine

Abstract:
Background/Significance/Rationale: Periacetabular osteotomy (PAO) is an incredibly painful surgical procedure to correct hip dysplasia resulting from a deformity in the acetabulum. Current protocols for controlling perioperative pain have no consensus and include the use of nerve blocks, lumbar epidural-based protocols, and local anesthetic wound infiltration. This study aims to gather information regarding the efficacy of 0.25% Bupivacaine vs 0.5% Bupivacaine in fascia iliaca nerve blocks.

Methods: A retrospective chart review was conducted encompassing PAO patients from June 2023-June 2024. Patients were grouped according to concentration and volume of local anesthetic. Outcomes included pain scores in the post anesthesia care unit (PACU), 24-, 48-, and 72-hours post-op, duration of hospital admission and use of opioid medications. The data was sorted by concentration and volume of Bupivacaine administered.

Results/Findings: Comparisons between pain scores of those receiving 0.25% and 0.5% Bupivacaine showed similar scores in the PACU and at 24 hours post-op. At 48 hours post-op, pain scores were significantly lower (p=0.052) for the 0.5% Bupivacaine group (4.52) than the 0.25% Bupivacaine group (5.21). At 72 hours post-op, pain scores were slightly lower (p=0.11) for the 0.5% Bupivacaine group (3.91) than the 0.25% Bupivacaine group (4.62). Duration of hospital admission was similar. Analyzing pain scores by volume demonstrates that 40-60 mL of Bupivacaine had lower pain scores (average=4.15, p=0.060) than those receiving 20-30 mL of Bupivacaine (average=5.22) in the PACU. Opioid usage at PACU, 24-, 48-, and 72-hour time frames showed similar milliequivalents of PO morphine needed when compared by concentration.

Conclusions/Discussion: We conclude that if local anesthetic toxicity is not a problem, anesthesiologists should use 0.5% Bupivacaine 40 mL for fascia iliaca nerve blocks to provide patients with the maximum benefit from their regional anesthesia.

Translation/Human Health Impact: These findings will directly alter current regimens used for PAO patients at IU Health.

 # 12

Poster Title: Assessing Mouse Model Based Femur mRUST Scores via Intelligent Fracture Detection and Deep Learning Neural Networks

Poster Presenter: Parish, Cooper
Poster Presenter Institution: Indiana University School of Medicine

Poster Authors: Cooper R. Parish, Department of Orthopaedic Surgery, Indiana University School of Medicine, Indianapolis, IN, Richard L. Roudebush VA Medical Center, Indianapolis, IN; Jie Chen, Advanced Imaging Research Center, University of Texas Southwestern Medical Center, Dallas, TX; Sarah L. Mostardo, Department of Orthopaedic Surgery, Indiana University School of Medicine, Indianapolis, IN, Richard L. Roudebush VA Medical Center, Indianapolis, IN; Sonali, J. Karnik, Department of Orthopaedic Surgery, Indiana University School of Medicine, Indianapolis, IN, Richard L. Roudebush VA Medical Center, Indianapolis, IN; Rachel J. Blosser, Department of Orthopaedic Surgery, Indiana University School of Medicine, Indianapolis, IN, Richard L. Roudebush VA Medical Center, Indianapolis, IN; Istvan Gergely, Department of Orthopaedic Surgery, Indiana University School of Medicine, Indianapolis, IN; Nian Wang, Advanced Imaging Research Center, University of Texas Southwestern Medical Center, Dallas, TX, Department of Biomedical Engineering, University of Texas Southwestern Medical Center, Dallas, TX; Roman M. Natoli, Department of Orthopaedic Surgery, Indiana University School of Medicine, Indianapolis, IN; Melissa A. Kacena, Cooper R. Parish, Department of Orthopaedic Surgery, Indiana University School of Medicine, Indianapolis, IN, Richard L. Roudebush VA Medical Center, Indianapolis, IN

Abstract:
Background/Significance/Rationale: Bone fractures are a major issue worldwide. Beyond the physical affects, fractures may result in substantial economic burden due to hospitalization costs, surgical procedures, and rehabilitation. Modified Radiographic Union Score for Tibia fractures (mRUST) is a method for evaluating long bone fracture healing in humans using plain radiographs. Preliminary data from mRUST scored femoral midshaft mouse femurs proved the utility of mRUST in murine models. While mRUST is a reliable technique, it is a time consuming and labor-intensive process. Additionally, there are concerns about inter-rater reliability.

Methods: Radiographs are taken twice weekly for 42 days, and each radiograph must be prepared by cropping the image to include the femurs only for assessment. We proposed that artificial intelligence (AI) can be used to expedite the scoring of radiographic images and create uniformity throughout the process to enhance the consistency of the analysis of mRUST scores and produce results faster than humans. Using an AI/machine learning (ML) algorithm we allowed AI to analyze femoral shaft fracture radiographs that previously received an mRUST score by our orthopaedic surgeons. Following analysis, mRUST scores generated from AI were compared to the scores generated from the orthopaedic surgeons.

Results/Findings: Following analysis, mRUST scores generated from AI were compared to the scores generated from the orthopaedic surgeons. Results indicated that the mRUST scores generated by AI matched the scores produced by the surgeons with 96% accuracy.

Conclusions/Discussion: Based on these findings, our team was able to enhance the production of mRUST scores by limiting the time and cost that is required to score radiographs.

Translation/Human Health Impact: Future studies will determine whether comparable results can be obtained for different skeletal sites and with human x-rays. Eventually, we hope to predict early after surgery who is likely to heal or go on to nonunion. Early intervention could substantially decrease pain, morbidity, and healthcare costs.

 # 13

Poster Title: MRI Prediction of Surgical Treatment for Juvenile Osteochondritis Dissecans

Poster Presenter: Puthran, Andrew
Poster Presenter Institution: Indiana University School of Medicine

Poster Authors: Andrew Puthran, Department of Radiology & Imaging Sciences, Indiana University School of Medicine, Indiana University School of Medicine; Deva Chan, Weldon School of Biomedical Engineering, Purdue University; Christopher Newman, Department of Radiology & Imaging Sciences, Indiana University School of Medicine, Indiana University School of Medicine

Abstract:
Background/Significance/Rationale: Juvenile osteochondritis dissecans (OCD) is an abnormality of joint cartilage and its underlying bone. It is a leading cause of joint pain in children (affecting approximately 1 in every 1,000 children) and predisposes patients to early osteoarthritis and osteonecrosis. Its precise cause remains unknown, though repetitive trauma and multiple other factors have been implicated. Magnetic resonance imaging (MRI) aids patient management by assessing the mechanical stability of the bone and cartilage defects. Unfortunately, imaging criteria established for adults do not translate well to juvenile patients. This study aimed to determine whether quantitative analysis of standard MRI sequences of knee, elbow, and ankle joints could predict the need for surgery. The proposed hypothesis was that signal intensity could distinguish between those receiving conservative management and those requiring surgery.

Methods: Using pretreatment MRI sequences from the IU Health Radiology Information Systems, 41 skeletally immature patients with OCD were analyzed retrospectively to quantify the cartilage signal on standard anatomy and fluid-sensitive sequences. The entire cartilage portion of the lesion was quantified using manual segmentation (with signal intensity normalized to the opposite condyle as an internal control). Logistic regression assessed whether lesion signal intensity could discriminate surgical or non-surgical management with receiver operator characteristic (ROC) curves obtained to identify the optimal signal intensity threshold.

Results/Findings: Unfortunately, neither type of sequence could discriminate between surgical and non-surgical patients. Likewise, signal intensity was not a good predictor of surgical stability in patients undergoing surgery.

Conclusions/Discussion: Future studies are needed to assess individual joints and evaluate cartilage-specific sequences to determine if quantitative cartilage analysis can improve diagnostic accuracy in these patients.

Translation/Human Health Impact: The study found that MRI signal intensity of juvenile OCD lesions could not reliably predict the need for surgery, highlighting the need for better imaging methods to guide treatment.

 # 14

Poster Title: Three-Dimensional Modeling of Anterior Communicating Artery Aneurysm for Surgical Simulation

Poster Presenter: Ravikumar, Aditi
Poster Presenter Institution: Indiana University School of Medicine

Poster Authors: Aditi Ravikumar, Indiana University School of Medicine; Matthew Tobin, Department of Neurosurgery, Indiana University School of Medicine; Bradley Bohnstedt, Department of Neurosurgery, Indiana University School of Medicine

Abstract:
Background/Significance/Rationale: A ruptured cerebral aneurysm is a common cause of life-threatening subarachnoid hemorrhage and can be treated using open surgical clipping or endovascular coiling and stenting. The recent shift towards endovascular procedures has decreased the frequency of open surgical aneurysm clipping resulting in less opportunities for neurosurgical residents to develop procedural skills needed to successfully clip an aneurysm. To fill the gap, three-dimensional (3D) modeling and printing can be adapted to create a surgical simulator.

Methods: A preexisting model of a skull was remodeled to print with a pre-cut pterional craniotomy. A 3D model of a circle of Willis with an anterior communicating artery aneurysm was constructed using a patient's computed tomography angiography data. The model was prepared for 3D printing. A prototype was printed using acrylonitrile-butadiene-styrene and coated with silicone containing red pigment. The ABS was dissolved using acetone to create a hollow silicone cast of the aneurysm and the circle of Willis.

Results/Findings: Following successful printing and casting, the hollow vascular model was positioned within the skull and a simulation was assembled. Comparing the similarity between the view of the aneurysm model through the pterional craniotomy window and the actual surgical perspective, suggested the necessity to move the craniotomy window more anteriorly.

Conclusions/Discussion: 3D printing and silicone casting of cerebrovascular models is a feasible method to create surgical simulators as it can approximate the anatomy and tactile characteristics of vasculature.

Translation/Human Health Impact: 3D printed simulators can enhance surgical training by increasing exposure to rare cases and open procedures. A low-acuity teaching and practice environment can be created at no risk to the patient. By allowing the attending physicians to focus on teaching and trainees to focus on incorporating feedback and practicing, 3D printed simulators can improve outcomes for future patients.

 # 15

Poster Title: Investigating the Impacts of Estrogen Receptor Alpha (ERα) Deficiency on Dynamics of the Ovarian Immune Microenvironment

Poster Presenter: Salter, Lucy
Poster Presenter Institution: Indiana University School of Medicine

Poster Authors: Lucy Salter, Indiana University School of Medicine; Tia Brodeur, Department of Obstetrics and Gynecology, Division of Reproductive Endocrinology and Infertility, Indiana University School of Medicine

Abstract:
Background/Significance/Rationale: The ovary is a dynamic reproductive organ with an immune microenvironment that allows for continual remodeling following monthly tissue damage. While it is understood that M1 and M2 macrophages play roles in folliculogenesis and mediating vital cyclic remodeling, the role of natural killer (NK) cells is less characterized. Utilizing an ERα deficient experimental group, this study aims to examine differences in macrophage and NK cell trafficking, inflammation, follicle number, and to novelly elucidate an NK cell role. We hypothesize that ERα deficient tissues will have an influx of macrophages and NK cells and increased inflammation which will impair follicular development.

Methods: ERα deficient mice created utilizing the Cre-Lox system were exposed to 48 hours of exogenous gonadotropins or saline before ovarian cells were isolated for flow cytometric analysis of NK cell activation upon ovarian stimulation. Next, ovarian tissues were sectioned and stained for IHC analysis and quantification of follicle number. Finally, tissues were stained with NK1.1/CD161 or CD206/MRC1 primary antibodies for immunofluorescent evaluation of macrophage and NK cell trafficking.

Results/Findings: Flow cytometry demonstrated that ovarian stimulation led to a significant increase in NK cell activation. Additionally, immunohistochemistry revealed that ERα deficiency led to a significant increase in inflammation. However, ERα deficiency did not lead to defective ovulation, with no significant changes in corpora lutea number, and did not cause deficient follicular development. Finally, immunofluorescence showed that NK cells are present in both ERα deficient and control ovarian tissues with presence mainly surrounding graafian follicles.

Conclusion: No conclusion presented.

Translation/Human Health Impact: The results from this study help to better understand the impacts of estrogen on the ovarian immune microenvironment and demonstrate a presence of NK cells in ovarian tissue. Further research looking into distinct patterns of NK activation in specific locations will aim to further elucidate NK role in ovarian disease.

 # 16

Poster Title: Assessment of the Toxicological Impact of Gold Nanoparticles on Retinal Tissue Health in Mice

Poster Presenter: Robinson, Kelsey
Poster Presenter Institution: Indiana University School of Medicine

Poster Authors: Kelsey Robinson, Glick Eye Institute, Indiana University School of Medicine; Ben McCall, Department of Engineering and Technology, Purdue University; Sunland L. Gong, Glick Eye Institute, Indiana University School of Medicine; Yong Gao, Glick Eye Institute, Indiana University School of Medicine; Afshin Izadian, Glick Eye Institute, Indiana University School of Medicine; Amir Reza Hajrasouliha, Glick Eye Institute, Indiana University School of Medicine

Abstract:
Background/Significance/Rationale: Retinal degeneration stands as a leading cause of blindness, impacting millions in the United States. Currently, no principal treatment exists for the loss of these photoreceptors. Gold nanoparticles (AuNPs) have garnered significant interest in retinal research due to their distinctive properties. Despite their promising applications, concerns have been raised regarding the safety of AuNPs, particularly in the context of ocular tissues. Therefore, evaluating their toxicity is essential to understanding the interactions between AuNPs and retinal cells.

Methods: This study utilized Scanning electron microscope (SEM), UV-Vis spectroscopy, and dynamic light scattering (DLS) to characterize the AuNPs, Nanocomposites (NC), and Barium Titrate NC (BTNC) that were synthesized and injected into WT C57 mice. Optical Coherence Tomography (OCT) was conducted to determine the AuNPs presence post-injection into the mice. Average retinal thickness was analyzed and compared pre-injection (day 0) and post-injection on days 1, 3, and 7. Electroretinography (ERG) was also conducted to determine the retinal cell's response to light stimulus. Lastly, Isolectin B4 (IB4) immunostaining was conducted, and the cross sections of blood vessels were analyzed to monitor angiogenesis.

Results/Findings: Nanoparticle characterization revealed no abnormalities in size, morphology, or charge. Using OCT to examine the average retinal thickness over 7 days after IVI in WT, results reveal that at a concentration of 1000µg/m, retinal thickness decreased but returned to a nearly normal baseline by day 7. Overall, AuNPs do not cause a decrease in the average retinal thickness in all concentrations. Retinal ERG analysis revealed no significant changes in function following treatment, indicating that the procedure had no adverse effects. When compared to the total retinal area, the IB4 immunostaining showed no significant decrease in angiogenesis in all concentrations.

Conclusions/Discussion: All studies show little to no toxicity of the AuNPs, demonstrating their safety and efficacy. These findings further support the use of AuNPs to restore vision in patients with retinal degeneration.

Translation/Human Health Impact: AuNPs will now be sub-retinally and used for their regenerative properties with hopes of building an artificial retina, enable these patients to regain sight.

 # 17

Poster Title: Clomiphene Citrate Therapy Effects on Lipid Panels in Men with Hypogonadism

Poster Presenter: Siddiqui, Ahsan
Poster Presenter Institution: Indiana University School of Medicine

Poster Authors: Ahsan, Siddiqui, Indiana University School of Medicine; Thairo, Pereira MD, Indiana University Department of Urology; Helen, Bernie DO MPH, Indiana University Department of Urology

Abstract:
Background/Significance/Rationale: Clomiphene citrate (CC) is a selective estrogen receptor modulator FDA approved for women with ovulatory dysfunction yet used to improve testosterone production in men with hypogonadism. CC is contraindicated in patients with high triglyceride (TG) lab values, but little data exists evaluating the impact of CC on lipid panels in men with hypogonadism treated with CC. This study aims to provide information on the effects of CC on TG lab values.

Methods: We conducted a retrospective chart review on hypogonadism patients from January 2020 - August 2024. Pre-treatment endocrine and lipid profiles collected before 11am fasting was compared to panels collected 4 weeks after beginning treatment. A paired t-test was performed to determine statistically significant differences in lipid profiles before and after CC therapy.

Results/Findings: 52 men with a mean age of 42.4 had complete data and were included in this study. Mean testosterone levels were 322 ng/dl pre-CC and 502 ng/dl post-CC treatment. Pre-CC Triglyceride (TG), Total Cholesterol (TC), HDL, and LDL means were 141.9, 172.4, 43.3, and 100.9, respectively. Post-CC TG, TC, HDL, and LDL means were 140.9, 171.5, 40.1, and 103.2, respectively. We found no statistically significant difference in the change of triglyceride ($p = 0.903$, SD = 39.3), total cholesterol ($p = 0.783$, SD = 14.01), and low-density lipoprotein ($p = 0.447$, SD = 24.3) lab values before and after treatment with CC. We observed a statistically significant decrease in high-density lipoprotein lab values ($p < 0.001$, SD = 12.95).

Conclusions/Discussion: CC therapy for male hypogonadism decreases HDL levels. CC does not seem to significantly affect other parameters in the lipid profile of patients.

Translation/Human Health Impact: Lipid profiles of patients on CC therapy should be monitored, especially if there are risk factors such as cardiovascular disease, obesity, HTN, old age etc.

 # 18

Poster Title: Accuracy of Imaging Compared to Biopsy for Diagnosis of Pediatric Liver Tumors

Poster Presenter: Wright, Andrea
Poster Presenter Institution: Indiana University School of Medicine

Poster Authors: Andrea Wright Indiana University School of Medicine; Chao Jarasvaraparn Indiana University School of Medicine, Indiana University Division of Pediatric Gastroenterology, Hepatology and Nutrition; Jean Molleston Indiana University School of Medicine, Indiana University Division of Pediatric Gastroenterology, Hepatology and Nutrition

Abstract:
Background/Significance/Rationale: Pediatric liver tumors, though uncommon, are the third most frequent type of abdominal tumors in children. These tumors encompass a diverse group of neoplasms, such as hepatoblastoma, hepatocellular carcinoma, focal nodular hyperplasia, hemangiomas, and hepatic abscesses. Pediatric liver tumors etiology often differs from adults, with genetic predispositions and developmental

anomalies playing significant roles. Traditionally, diagnosis is made through imaging and tissue sampling; however, technological advancements may reduce the need for tissue sampling through improved imaging accuracy.

Methods: Using DoRIS, an online software tool, 78 patients from 2010-2024 were identified as having a liver biopsy for suspected tumors. Twenty-eight were excluded for not having a liver tumor or not undergoing imaging prior to biopsy, leaving 50 patients. In this retrospective study, imaging reports were compared to biopsy reports to assess diagnostic accuracy. The number and size of lesions were reviewed, and statistical analysis determined if these factors impacted diagnostic accuracy.

Results/Findings: The study included 11 tumors from cancer metastasis, 7 hepatic abscesses, 7 other types of tumors, 6 hepatoblastomas, 6 hepatocellular adenomas, 4 vascular tumors, 2 hepatocellular carcinomas, and 1 rhabdoid tumor. The overall accuracy using one imaging modality was 73%. CT accuracy was 71%, MRI accuracy was 77%, and ultrasound accuracy was 33%. The average largest lesion size was 55.3 mm, and tumor size did not correlate with imaging accuracy ($p=0.8$).

Conclusions/Discussion: Overall, 27% showed a different diagnosis between imaging and biopsy. MRI demonstrated the highest accuracy in matching biopsy diagnoses. Tumor size did not impact diagnostic accuracy; rather, accuracy was more likely dependent on the type of tumor.

Translation/Human Health Impact: Biopsy poses risks of pain, bleeding, infection, and hematoma. With research and advancements in imaging, the need for biopsy may be limited to certain types of pediatric liver tumors.

IVY TECH FELLOWSHIP

 # 19

Poster Title: Assessing Expression Profile of Adrenergic Receptors in Human Hearts from Patients with CKD

Poster Presenter: Alarcon, Leonardo
Poster Presenter Institution: Ivy Tech Community College

Poster Authors: Leonardo Alarcon, Ivy Tech CTSI Fellowship; Arvin Halim, Division of Nephrology and Hypertension, Indiana University School of Medicine; Monique Campos, Division of Nephrology and Hypertension, Indiana University School of Medicine; Kenneth Lim, Division of Nephrology and Hypertension, Indiana University School of Medicine

Abstract:
Background/Significance/Rationale: Chronotropic incompetence (CI), defined as an impaired heart rate (HR) response to exercise, leads to a higher risk of mortality in patients with chronic kidney disease (CKD). In individuals without CKD, elevated catecholamines from autonomic dysfunction leads to downregulation of β1-adrenergic receptors (β1-ARs), which are essential for regulating HR. Moreover, decreased β1-ARs function is associated with upregulation of α1-ARs, which is purported to be a cardioprotective and compensatory response to chronic stress. In CKD, catecholamines are also elevated, but how cardiac ARs are affected in CKD is unknown. Therefore, we aim to comprehensively phenotype the ARs expression in the donor hearts of patients with CKD.

Methods: A cross-sectional study was conducted involving 45 donated human left ventricular (LV) tissue samples of patients with advanced CKD (Hemodialysis, HD; n=18), hypertensive controls with preserved kidney function (HTN; n=10), and healthy controls (CON; n=17), from the Cardiovascular Aging in CKD (CAIN) cohort. Tissues were subjected to immunoblotting and bulk RNA sequencing.

Results/Findings: β1-AR protein expression was similar across all groups. Two α1a-AR isoforms were detected at 50kDa and 32kDa. 32 kDa α1a-AR was elevated in both HD and HTN groups compared to the CON group ($P<0.05$, $P<0.001$), but there was no difference between HTN and HD groups. 50 kDa α1a-AR expression was similar across all groups. Additionally, RNAseq showed no differential expression of AR signaling-related genes (FDR > 0.05).

Conclusions/Discussion: Our data suggests β1-AR expression is unchanged in hearts from HD patients in our cohort. Additionally, upregulation of the 32kDa α1a-AR isoform in CKD hearts suggests CKD hearts also undergo compensatory mechanisms. Further studies are needed to validate these findings and whether CI in CKD may originate from impaired downstream β1-AR signaling.

Translation/Human Health Impact: Elucidating the expression profile of ARs in CKD hearts will provide further insight into the underlying mechanisms of and possible therapeutic targets for CI in patients with CKD.

 # 20

Poster Title: Examination of Diabetes Research Models

Poster Presenter: Badami, Julie
Poster Presenter Institution: Ivy Tech CTSI Fellowship

Poster Authors: Julia D. Badami, Department of Diabetes, Indiana University School of Medicine; Mallory A. Oswalt, , Department of Diabetes, Indiana University School of Medicine; Anthony Acton, , Department of Diabetes, Indiana University School of Medicine; Robert V. Considine, Department of Diabetes, Indiana University School of Medicine

Abstract:
Background/Significance/Rationale: Obesity is a chronic disease associated with numerous health conditions, one being type 2 diabetes. Type 2 diabetics have an increased amount of adipose tissue. This summer I composed an experiment using mouse 3T3L1 cells that resemble similar characteristics to adipose tissue cells. I measured growth and gene expression for seven days. I also ran various ELISAs and observed two clinical experiences.

Methods: Throughout my seven-day experiment, I used cell culture techniques, isolated RNA, and ran a real-time PCR. There were six time points I used to compose my experiment marked at 0 hours, 12 hours, 24 hours, 48 hours, 72 hours, and 7 days. I also learned how to run various ELISAs and use a clinical analyzer. Two of the things I observed were the glucose tolerance test and the bariatric surgery.

Results/Findings: Our experiment demonstrates that the cells matured into adipocytes, as evidenced by microscopic photos taken over the 7 days. We observed increased growth and number of lipid droplets in these images. The changes we observed in the levels of mPPar-γ and LPLm indicate a shift in gene expression patterns, providing evidence that our cells have differentiated into mature adipocytes.

Conclusions/Discussion: Obesity is a rising chronic disease that requires multifaceted approaches, encompassing the use of tissue cell culture, assay procedures, and clinical settings. Methods such as these provide valuable insight into potential treatments.

Translation/Human Health Impact: There is a lot of value in research when it comes to potential treatments. By utilizing these methods, patients with chronic diseases may be able to live longer.

 # 21

Poster Title: Effects of LAMZ on Skeletal Muscle Function, Blood Biochemistry, and Cardiovascular Calcification in a rat model of CKD

Poster Presenter: Burton, Sydney
Poster Presenter Institution: Ivy Tech CTSI Fellowship

Poster Authors: Sydney E.Burton, Ivy Tech Community College; Ashley D. Troutman, Department of Physical Therapy, Indiana University; Shruthi Srinivasan, Division of Nephrology, Indiana University School of Medicine; Neal X. Chen, Division of Nephrology, Indiana University School of Medicine; Kalisha D. O'Neill, Division of Nephrology, Indiana University School of Medicine; Sharon M. Moe, Division of Nephrology, Indiana University School of Medicine; Keith G. Avin, Division of Nephrology, Indiana University School of Medicine, Department of Physical Therapy, Indiana University

Abstract:
Background/Significance/Rationale: Chronic Kidney Disease (CKD) is a progressive disease that's often coupled with Mineral Bone Disorder (MBD). CKD-MBD can cause impaired function of skeletal muscle, cardiovascular calcification, and abnormal mineral metabolism in blood. Exercise is known to alleviate these symptoms, but CKD-MBD can leave patients bedridden. Locamidazole (LAMZ) is a drug that mimics the effects of exercise with documented effects on muscle and bone, possibly by increasing cytosolic calcium and altering cell signaling in skeletal muscle.

Methods: We used a rat model of progressive CKD (Cy/+ rats, n=10-12 groups). LAMZ was administered via subcutaneous injections, twice daily at 0.625mg/kg for 5 weeks, beginning at 27 weeks (CKD stage 3). At 33 weeks (CKD stage 5), we used electrical stimulation to measure muscle strength. Blood and aorta were collected for biochemistry and calcification after euthanasia.

Results/Findings: The results demonstrated that the LAMZ partially normalized the muscle strength and decreased plasma parathyroid hormone (PTH) levels in CKD rats. However, LAMZ didn't have an effect on kidney function and vascular calcification in CKD rats.

Conclusions/Discussion: Our future studies will focus on optimizing LAMZ dosage and starting treatment in earlier stages of CKD to induce therapeutic benefit.

Translation/Human Health Impact: Studying LAMZ's impact on common CKD symptoms may provide CKD patients a future full of the benefits of exercise with none of the risks.

 # 22

Poster Title: Activation Of The Mitochondrial Unfolded Protein Response (uprMt) Promotes Vascular Remodeling In Pulmonary Arterial Hypertension.

Poster Presenter: Ssendawula, Arthur
Poster Presenter Institution: Ivy Tech CTSI Fellowship

Poster Authors: Arthur Ssendawula, Ivy Tech CTSI Fellowship; Robert F. Machado, Division of Pulmonary, Sleep and Critical Care Division, Indiana University School of Medicine; Angelia Lockett, Department of Medicine – Pulmonary, Sleep and Critical Care Division, Indiana University School of Medicine; Aaron Snow, Department of Pulmonary Medicine, Indiana University School of Medicine; Tendo Mubuuke, Department of Pulmonary Medicine, Indiana University School of Medicine

Abstract:
Background/Significance/Rationale: Pulmonary Arterial Hypertension (PAH) is a severe and progressive disease which results in death due to increased pulmonary vascular resistance that leads to right heart failure. Increased vascular resistance occurs as a result of pulmonary arterial smooth muscle cells (PASMCs) and endothelial cells (PAECs) undergoing changes in intracellular signaling that leads to a proliferative, apoptosis resistant phenotype that causes remodeling and occlusion of the pulmonary vasculature. We demonstrated that the sphingosine-1-phosphate (S1P)/sphingosine kinase 1(SPHK1) signaling pathway promotes vascular remodeling, that it is upregulated in PAH patients and that inhibition of S1P mitigates PAH *in vivo*. Preliminary data from our lab demonstrates that the mitochondrial unfolded protein response (UPRmt) is activated by the S1P pathway. Hence, we hypothesized that the UPRmt induces vascular remodeling to promote PAH development.

Methods: Human PASMCs and PAECs were treated with S1P up to 6h or Lentiviral-Sphk1 was overexpressed for 48h at MOI 20. Western blotting was performed on whole cell extracts to assess regulation of the UPRmt pathway. Activation of UPRmt mediators was assessed by immunoblotting for mtHSP70, HSP60, ClpP and LonP1. The effect of UPRmt inhibition on proliferation was assessed by Western blotting for PCNA and Ki67 expression level.

Results/Findings: Activation of the Sphk1-S1P signaling axis promoted activation of the UPRmt pathway as we observed increased expression of UPRmt pathway mediators (mtHSP70, HSP60, ClpP and LonP1). There was also an increase in vascular remodeling as expression of proliferation markers was elevated. Inhibition of the UPRmt using the mtHSP70 inhibitor, MKT-077, mitigated the increase in proliferation.

Conclusions/Discussion: Aberrant regulation of mitochondrial function leading to activation of the UPRmt pathway promotes vascular remodeling.

Translation/Human Health Impact: Currently, no therapeutic interventions exist to treat vascular remodeling in PAH. These studies suggest that pharmacological interventions targeting the UPRmt pathway may improve PAH outcomes.

MedSTAR

 # 23

Poster Title: Loss of *NF2* Disrupts Differentiation in Neuroepithelial Stem Cells

Poster Presenter: Burket, Noah
Poster Presenter Institution: Indiana University School of Medicine

Poster Authors: Noah Burket, Department of Neurosurgery, Indiana University School of Medicine, Indiana; Scott Cooper, Department of Neurosurgery, Indiana University School of Medicine, Indiana; Victoria Dershem, Department of Neurosurgery, Indiana University School of Medicine, Indiana; Jingnesh Tailor, MD, PhD, Department of Neurosurgery, Indiana University School of Medicine, Indiana, Indiana University Melvin and Bren Simon Comprehensive Cancer Center, Department of Pediatrics and Herman B Wells Center for Pediatric Research, Indiana University School of Medicine

Abstract:

Background/Significance/Rationale: *NF2*-related schwannomatosis is a tumor predisposition syndrome caused by mutations in the *NF2* gene and associated with spinal ependymomas (SP-EPN). These tumors are suspected to originate from mutations in the radial glia (RG) cell lineage. They are only effectively treated through high-risk surgical resection, emphasizing the critical need for identification of targets for medical therapy. Yet, the role of NF2-dependent disruption in RG cell development is poorly understood. We hypothesize that a loss of the NF2 gene in NES cells will prevent normal differentiation and promote a RG-like progenitor state.

Methods: An NF2-knockout was generated in neuroepithelial stem (NES) cells using CRISPR/Cas9. Knockouts were validated using Western blot and Sanger sequencing. In vitro differentiation was induced with removal of growth factors. NF2-knockout phenotypes were assessed with polymerase chain reaction and compared with wildtype NES cells.

Results/Findings: Preliminary data has shown that NF2-knockout cells express similar levels of early pan-neural and neural stem cell genes compared to wildtype after CRISPR editing. The NF2-knockodown cells retain this stem cell-like gene expression following attempted differentiation, whereas wildtype cells take on a primarily neural phenotype. The knockout cells also form what appears to be pre-neoplastic spheres when allowed to differentiate. Two clones that were identified as having NF2 mutations on each allele still retain *NF2* protein expression.

Conclusions/Discussion: NF2-knockout NES cells fail to differentiate normally compared to wildtype NES cells. They retain early stem cell-like markers, including DACH1, HES1, and PLZF. Furthermore, formation of spheres when growth factors were removed hints at NF2 loss being relevant to formation of pre-neoplastic growths. Future work will include investigating downstream effects of NF2 loss in this model.

Translation/Human Health Impact: The long-term goal of this project is to use this model to study potential therapies for medical treatment of SP-EPN.

SEED/STEM

 # 24

Poster Title: Applications of Machine Learning in Tissue Image Analysis

Poster Presenter: White, Annabelle
Poster Presenter Institution: Whiteland Community High School

Poster Authors: Annabelle White, Whiteland Community High School, Whiteland, IN; Takashi Hato, PhD, Hato Lab, IU School of Medicine (Nephrology Division), Indiana University, Indianapolis, IN

Abstract:
Background/Significance/Rationale: Determining effects of experimental procedures on tissue involves careful observation of microscopic images. Human observation has potential for bias. In this project, I used three unsupervised machine learning methods to analyze H&E stained kidney tissue.

Methods: I built an autoencoder for anomaly detection using Keras. The model includes an encoder that reduces dimensionality and a decoder that reconstructs the original input from the compressed representation. After training with H&E stained kidney tissue images, I calculated image reconstruction errors and set an error threshold for detecting anomalies. To use the Anomalib library for anomaly localization, I split the images into training, testing, and validation sets. I created a Reverse Distillation model, instantiated an engine, and trained the model. This process generates a heatmap for an image, with anomalies highlighted. The Histomorphological Phenotype Learning framework begins with training a self-supervised model. Then, I used the model to create vector representations for each tile. Tiles are clustered using Leiden Clustering. This process outputs clustering configuration files as well as cluster assignments for individual tiles.

Results/Findings: The autoencoder approach was ineffective. Reconstructed tissue images did not contain the necessary level of detail to be used for meaningful analysis. The Anomalib library showed moderate success in identifying features of the kidney tissue. However, the generated heatmaps did not provide any insights. The Histomorphological Phenotype Learning (HPL) framework presented challenges due to technical issues. I am in the process of using the trained model to cluster images.

Conclusions/Discussion: Each method had its strengths and limitations in detecting anomalies and identifying distinct features within the tissue images.

Translation/Human Health Impact: Considering its ability to provide unbiased assessments and find patterns, the potential of unsupervised machine learning techniques for analyzing tissue images is significant.

INDIANA CTSI
AFFILIATED RESEARCH

 # 25

Poster Title: Müller cell Kir4.1 channel dysfunction in *APOE4*-KI model of Alzheimer's disease

Poster Presenter: Abhyankar, Surabhi
Poster Presenter Institution: Eugene and Marilyn Glick Eye Institute

Poster Authors: Surabhi D. Abhyankar, Department of Ophthalmology, Eugene and Marilyn Glick Eye Institute, Indianapolis, Indiana, Department of Biochemistry and Molecular Biology, Indiana University, Indianapolis, Indiana; Xiao Yucheng, Department of Biology, Indiana University, Indianapolis, Indiana; Neha Mahajan, Department of Ophthalmology, Eugene and Marilyn Glick Eye Institute, Indianapolis, Indiana; Qianyi Luo, Department of Ophthalmology, Eugene and Marilyn Glick Eye Institute, Indianapolis, Indiana; Theodore R. Cummings, Department of Biology, Indiana University, Indianapolis, Indiana; Adrian L. Oblak, Stark Neurosciences Research Institute, Indianapolis, Indiana; Bruce T. Lamb, Stark Neurosciences Research Institute, Indianapolis, Indiana; Ashay Bhatwadekar, Department of Ophthalmology, Eugene and Marilyn Glick Eye Institute, Indianapolis, Indiana, Department of Biochemistry and Molecular Biology, Indiana University, Indianapolis, Indiana, Stark Neurosciences Research Institute, Indianapolis, Indiana

Abstract:

Background/Significance/Rationale: Worldwide, at least 55 million individuals have Alzheimer's disease (AD). The most prevalent form of AD is late-onset AD (LOAD), and apolipoprotein *E4* (*APOE4*) is the major genetic component in the pathogenesis of LOAD. As a central nervous system component, the eye displays a variety of abnormalities in AD. Müller cell (MC), a principal glia of the eye, possesses specialized functions such as neurotransmitter uptake and glycogen storage, thus serving as a metabolic powerhouse; however, in LOAD, the MCs are dysfunctional. While MCs regulate water and K+ balance via inwardly rectifying Kir4.1 channels, it remains unknown how *APOE4* affects Kir4.1 channels and overall MC health in AD. Therefore, in this study, we assess the effect of *APOE4* on Müller cell Kir4.1 channel in both animal and *in vitro* studies.

Methods: Immunofluorescence staining for Kir4.1 and glutamate synthase-1 (GS-1) was performed on the retinas of 52-57-week-old *APOE3* knock-in (KI, neutral for AD) and *APOE4*-KI mice. A whole-cell voltage-gated patch clamp was performed on the MCs isolated from the retinas of these mice. The *in vitro* experiments were performed on Rat MC (RMC-1) transfected with *APOE2*/ *APOE3*/ *APOE4* plasmids. qRT-PCR and western blotting were performed to check Kir4.1 expression. Flow cytometry was used to check mitochondrial membrane potential (MMP) using JC-1 and mitochondrial reactive oxygen species (ROS) levels using MitoSOX-Red.

Results/Findings: 52-57-weeks-old *APOE4*-KI mice showed decreased Kir4.1 and GS-1 expression and reduced Kir4.1 current densities compared to *APOE3*-KI mice. RMC-1 expressing *APOE4* showed a reduction in the Kir4.1 gene and protein expression. Flow cytometry analysis showed *APOE4* decreased MMP and increased mitochondrial ROS.

Conclusions/Discussion: *APOE4* causes structural and functional deficits in the MCs, potentially via mitochondrial dysfunction.

Translation/Human Health Impact: These discoveries shed light on the mechanisms behind MC dysfunction in LOAD and help better understand whether enhancing mitochondrial health improves retinal health.

 # 26

Poster Title: Ferroptosis Regulation by Fatty Acid Synthase-Derived Lipid Droplets in Model of Breast Cancer Metastasis

Poster Presenter: Andolino, Chaylen
Poster Presenter Institution: Purdue University

Poster Authors: Chaylen, Andolino, Department of Nutrition Science, Purdue University, West Lafayette, IN; Kimberly K. Buhman, Department of Nutrition Science, Purdue University, West Lafayette, IN; Michael F. Coleman, Department of Nutrition, University of North Carolina, Chapel Hill, NC; Stephen D. Hursting, Department of Nutrition, University of North Carolina, Chapel Hill, NC; Marjorie Layosa, Department of Nutrition Science, Purdue University, West Lafayette, IN; Michael K. Wendt, Department of Medicinal Chemistry and Molecular Pharmacology, Purdue University, West Lafayette, IN; Dorothy Teegarden, Department of Nutrition Science, Purdue University, West Lafayette, IN

Abstract:

Background/Significance/Rationale: Dysregulated metabolism, including lipid droplet (LD) accumulation, is associated with breast cancer progression. Given that breast cancer metastasis accounts for majority of patient deaths, we sought to identify novel mechanisms by which LDs may promote metastasis.

Methods: Whole cell lysates (WCLs) and LDs from vehicle-treated and FASN-inhibited (3d, 20 μM TVB-3166) human metastatic MCF10CA1a cells were prepared for untargeted proteomics analysis. Tryptic/Lys-C peptides were analyzed by reverse-phase LC-ESI-MS/MS by data-dependent acquisition.

Results/Findings: Over 60% of the total proteins identified from LD fractions were unique to vehicle-treated cells (1,571), whereas only 19 proteins were unique to LDs from FASN-inhibited cells. Proteins unique to LDs from vehicle-treated cells include those known to reduce cancer cell survival and progression, such as cadherin-binding and cell cycle regulation proteins. The association of these proteins to LDs might prevent them from functioning at their normal sites of action. Pro-ferroptotic proteins were more abundant on LDs of the more migratory cells, despite similar levels between WCLs, suggesting that the machinery for ferroptosis may be mislocalized in TAG-rich cells, thereby protecting them from ferroptosis. Indeed, FASN-inhibited cells had nearly 30% more intracellular iron compared to the vehicle-treated cells, indicating higher levels of ferroptotic stress. Vehicle-treated cells were 25% more readily rescued by N-acetylcysteine from ferroptosis induced by erastin than were FASN-inhibited cells, despite comparable sensitivity to erastin.

Conclusions/Discussion: These findings indicate that FASN-derived LDs in metastatic cells may aid in protecting against ferroptosis to promote breast cancer progression.

Translation/Human Health Impact: Identifying a role of FASN-derived LD accumulation in modulating protein localization involved in the novel cell death mechanism of ferroptosis in metastatic breast cancer cells provides leverage to further explore the clinical relevance of inhibiting FA synthesis of lipid-rich breast cancers in an effort to induce cancer-specific ferroptosis lethality.

 # 27

Poster Title: Intelligent Healthcare Data Analytics for Hepatic Steatosis Prediction

Poster Presenter: Castro, Heiner
Poster Presenter Institution: Purdue University

Poster Authors: Heiner Castro, School of Engineering Technology, Purdue University; Suranjan Panigrahi, School of Engineering Technology, Purdue University

Abstract:
Background/Significance/Rationale: The increasing prevalence of Hepatic Steatosis (HS) necessitates the development of effective screening tools to aid clinical decision-making. This study builds upon the work of Deo (2022), which proposed a set of machine learning (ML) algorithms for HS detection using the NHANES III survey dataset. While Deo's algorithms demonstrated promising performance, they did not incorporate the sample weights recommended for analysis. Our research aims to evaluate the impact of these sample weights on the performance of an HS screening model, utilizing physiological and liver biochemistry parameters.

Methods: We employed a methodology that retained key predictors, including age, BMI, HDL, plasma glucose, AST, ALT, and ASP, while excluding samples from individuals outside specified demographic criteria. To address the imbalanced nature of the dataset, we implemented under-sampling and SMOTE techniques. We trained Support Vector Machine (SVM) models with linear, quadratic, and Gaussian kernels, assessing their performance metrics, including accuracy, sensitivity, and specificity.

Results/Findings: Our findings indicate that while the quadratic kernel SVM with weights achieved comparable performance to models without weights, the introduction of sample weights improved sensitivity but reduced specificity.

Conclusions/Discussion: Overall, the sample weights did not enhance the performance of the SVM models significantly. Future work will explore additional algorithms tested by Deo (2022) to further improve HS prediction outcomes.

Translation/Human Health Impact: This research contributes to the ongoing efforts to refine clinical decision support tools for the early detection of Hepatic Steatosis, ultimately aiming to improve patient outcomes in healthcare settings.

 # 28

Poster Title: Bitter taste dysfunction and salivary gustin in long-COVID

Poster Presenter: Chowdary, Harika
Poster Presenter Institution: Indiana University School of Dentistry

Poster Authors: Harika Chowdary, Indiana University School of Dentistry; Parul Patel, Indiana University School of Dentistry; Naomi Riley, Indiana University School of Dentistry; Shveta Jaishankar, Indiana University School of Dentistry; Mythily Srinivasan, Indiana University School of Dentistry

Abstract:
Background/Significance/Rationale: Taste dysfunction was reported by nearly 40%-60% of coronavirus disease (COVID)-19 patients during the acute phase of the infection. While majority reported improvement and recovery over time, a subset of patients suffers from persistent taste dysfunction post-infection. Several studies estimate that 5-10% report taste dysfunction as persistent symptom of long-COVID syndrome. Gustation is an integrated event of multiple physiological processes occurring concurrently through activation

of continuous renewing specialized taste cells. A balance between the cell generation and cell death maintains the homeostatic turnover. We hypothesized that a disruption of this homeostasis contributes to the taste dysfunction in long-COVID. Specifically, we postulated that an increase in taste cell exfoliation in long-COVID will be associated with reduced levels proteins associated with taste bud cell renewal including sonic hedgehog protein and gustin will be decreased.

Methods: Individuals with long-COVID were recruited with the help of the Indiana CTSI Research Network (ResNet) services. The control included archived saliva samples catalogued prior to 2019. Objective assessment of taste perception was determined by the waterless empirical taste test. The SHH, gustin and inflammatory cytokines in unstimulated whole saliva were determined by ELISA. The expressions of epithelial and taste cell specific markers were assessed by immunoflurorescence.

Results/Findings: Taste dysfunction was predominantly related to that of bitter taste. Salivary SHH and gustin were lower in long-COVID as compared to that in pre-COVID, although the difference was significant only with gustin. Interestingly, the decrease in gustin correlated with the lower bitter taste score. The salivary epithelial cell included cells positive for occludin, gustin and SHH as representative markers for taste bud cell.

Conclusions/Discussion: The reduced salivary SHH and gustin suggest that the taste bud cell renewal is lowered and could constitute a potential mechanism of taste dysfunction in long-COVID.

Translation/Human Health Impact: Salivary gustin could be a marker for taste dysfunction in long-COVID.

 # 29

Poster Title: Circadian Rhythm Types in Individuals with Diabetic Macular Edema

Poster Presenter: Davé, Nikhil
Poster Presenter Institution: Indiana University School of Medicine

Poster Authors: Nikhil Davé, Indiana University School of Medicine; Matthew T. Cory, Indiana University School of Medicine; Janvi S. Patel, Indiana University Indianapolis; Denis Jusufbegovic, Department of Ophthalmology, Indiana University School of Medicine; Ashay Bhatwadekar, Department of Ophthalmology, Indiana University School of Medicine

Abstract:
Background/Significance/Rationale: Diabetic Retinopathy (DR) is the leading cause of vision loss in patients with diabetes. Diabetic macular edema (DME) can be associated with any stage of DR, causing thickening and swelling of the macula, leading to vision impairment. Circadian rhythm, the body's natural clock that governs physiological processes and dictates our sleep-wake cycle, is known to be affected by DR and DME. This study hypothesizes that DME will be associated with a more extreme circadian rhythm type.

Methods: Individuals 18 years or older with a diagnosis of type I or type II diabetes complicated by DME were given a 19-item Morningness-Eveningness Questionnaire (MEQ) to determine their circadian rhythm and sleep patterns. Information regarding demographics, metabolic parameters, diabetes, visual acuity and DME severity was collected.

Results/Findings: In this ongoing study, we compiled data from 64 individuals out of a targeted enrollment of 160. Overall, the MEQ scores characterized more individuals as morning types, followed by intermediate and evening types. The preliminary analysis shows a weak, insignificant positive correlation with retinal thickness in the right eye and a weak, insignificant negative in the left eye. In addition, a weak, insignificant negative correlation was also observed between MEQ and right eye visual acuity, with the opposite trend occurring in the left eye. DME variables such as mean central foveal thickness decreased insignificantly in right eyes from morning to evening groups but increased in the left eye.

Conclusions/Discussion: Our study suggests DME individuals are mostly morning type instead of evening type. However, there is no strong relationship between MEQ scores and DME parameters.

Translation/Human Health Impact: As we recruit more individuals in the future, we hope to establish a more significant relationship that could improve our understanding of how circadian rhythms and DME are interconnected and could lead to new treatments.

 # 30

Poster Title: Evaluation of Lead Screening in Indiana Populations

Poster Presenter: Doherty, Sarah
Poster Presenter Institution: Indiana University School of Medicine

Poster Authors: Sarah Doherty, Indiana University School of Medicine; Dr. Alyson Alde, Indiana University Bloomington; Dr. Kara Garcia, Indiana University School of Medicine; Dr. Michelle Del Rio, Indiana University Bloomington

Abstract:
Background/Significance/Rationale: Lead is known to have negative health impacts, and screening for lead toxicity is imperative for preserving cognitive development in pediatric populations. The impact of lead on adult populations also holds significant chronic health consequences, with symptom presentation that is often non-specific and easily overlooked. Though many changes have been enacted to minimize exposures, lead still leads to disproportionate health burdens in lower socioeconomic communities and minority populations within the US. In this study, we address current lead screening regulations and assess the level of lead exposure in the population of Vanderburgh County (VC). We aim to address, and re-educate, on specific aspects of lead exposure, and opportunities for screening improvement.

Methods: Participants with variable degrees of home lead exposure throughout Indiana and North Carolina collected soil, water, and dust samples from their homes which were then tested for lead composition. The data from VC was used for comparison with federal and local legislation on lead screening.

Results/Findings: The VC data was limited to eight participants, four from an area with a higher risk of lead exposure and four from an area with a lower risk. One of the high-risk participants out of four was found to have high soil and dust lead levels. Conversely, two of the four participants with low risk of lead exposure had water lead levels below the CDC action level, but above the recommended level for pediatric exposure.

Conclusions/Discussion: Current screening for lead within Indiana, exemplified by VC, may be inadequate at accurately identifying populations at risk of lead exposure.

Translation/Human Health Impact: Improving clinical understanding of lead exposure and public health lead screening in adult and adolescent populations is likely to improve identification of populations with lead exposure. This would reduce the chronic health outcomes, and inordinate financial strain of healthcare costs, placed on lower socioeconomic groups and minority populations.

 # 31

Poster Title: "We had no idea what to ask": Development and Co-Design of Osteosarcoma Surgical Discussion Cards for Use at Diagnosis

Poster Presenter: Hicks, Clayton
Poster Presenter Institution: Indiana University School of Medicine

Poster Authors: Clayton Hicks, Indiana University School of Medicine; Janet Panoch, Indiana University School of Medicine, Chris Collier, Indiana University School of Medicine

Abstract:
Background/Significance/Rationale: Osteosarcoma is a rare bone cancer that often occurs around the knee. Options for surgery include amputation, limb salvage, and rotationplasty. With funding from a CTSI grant, a set of discussion cards is being developed with patient, caregiver, and provider input. The cards would be used at the time of diagnosis to introduce the surgical options prior to receiving the more comprehensive Osteosarcoma Decision Aid.

Methods: Study 1: One parent focus group (n=9) and one patient focus group (n=6) focus group provided initial card conceptualization. A prototype was discussed and designed in four meetings total.
Study 2: The prototype cards were reviewed by attendees (n=24) at the 2024 Osteosarcoma conference. They were asked what they liked and what improvements could be made. Content analysis was conducted and organized by two coders.
Study 3: A stakeholder focus group of parents and patients (n=7) met to discuss and resolve conflicting recommendations Study 2.

Results/Findings: Study 1: Cards should include questions to help families frame their values, focus on function rather than appearance, pros/cons of options, and resources for further information.
Study 2: Recommendations included: providing images, better quality images, removing acronyms, clarifying wording, and reorganizing the order of the cards.
Study 3: Recommendations included: setting up QR code for additional images to allow families to choose what they see and reframing the pros/cons to avoid good/bad labels.

Conclusions/Discussion: This study suggests these conversations are not happening in ways that optimally benefit families. The first prototype was well received, and the recommendations provided guide development. A second prototype will be reviewed at the 2024 Musculoskeletal and Tumor Society for usability feedback from orthopedic oncologists.

Translation/Human Health Impact: The discussion cards translate patient, parent, and provider needs into a tangible communication tool. The final version of the cards will be pilot tested in multiple institutions by early 2025.

 # 32

Poster Title: Age-dependent changes in the molecular signatures of mouse brain elucidated by multi-protease proteomic and phosphoproteomic analyses

Poster Presenter: Mohallem, Rodrigo
Poster Presenter Institution: Purdue University

Poster Authors: Rodrigo Mohallem, Purdue University; Allison Schaser, Purdue University; Uma K. Aryal, Purdue University

Abstract:

Background/Significance/Rationale: With the growing elderly population, aging and age-related diseases are at the forefront of the medical challenges faced in the 21st century. The prevalence of age-related diseases, in particular neurodegenerative illnesses, is currently at an all-time high. It is estimated that one fourth of Americans over the age of 55 suffer from a mental disorder, and worldwide one person is diagnosed with dementia worldwide in every 3 seconds. Despite the increasing numbers of patients suffering from dementia, there are currently no treatments or therapeutic strategies available. In fact, the process of neurodegeneration remains poorly understood, and the mechanisms underlying the pathobiology of aging brains are complex yet not fully explored. In this study, we focus on unveiling the changes in the proteome, kinome and phosphoproteome of aging mice brains to elucidate the molecular signatures of age-related neurodegenerative processes.

Methods: The brain from Adult (3–4-month-old), Middle-aged (10-month-old) and Old (19-2-month-old) wild-type mice were harvested, homogenized and separetely digested with Trypsin, Chymotrypsin, AspN and GluC (Sigma-Aldrich, USA). Peptides from each enzyme digestion were desalted using C18 spin columns (Thermo Fisher Scientific, USA) before the enrichment of phosphopeptides using the PolyMaC spin tips. (Phospho)peptides were then separated with a reverse phase column and analyzed with the Orbitrap Fusion Lumos mass spectrometer. Data was analyzed with the MaxQuant and Perseus software.

Results/Findings: Our multi-protease digestion strategy greatly improved the sequence coverage of identified proteins, and, by extent, drastically increased the number of quantified phosphosites. Using this approach, we were able to identify 18492 phosphorylated peptides, from which 10474 were class I phosphosites (phosphosites with probability >0.75). By employing a wider range of enzymatic digestions, including Chymotrypsin, AspN, and GluC, we were able to map 40% of all identified class I phosphosites that would have been entirely missed in studies relying solely on Trypsin. This underscores the significant advantages of this approach for comprehensively surveying phosphorylation events relevant to aging research. Our global proteomics results suggested a marked increase in proteins involved in neuroinflammation, synaptic functions and protein folding were among the top enriched terms for clusters in which protein levels were significantly elevated in old mice. All of these pathways' underly neurodegeneration and declined synaptic functions. Furthermore, "Post-Translational protein phosphorylation" were among the top upregulated pathways in old mice, prompting the exploration of the age-associated changes in the mouse kinome and phosphoproteome.

Conclusions/Discussion: We found an upregulation of the PI3K-AKT-mTOR-p53 signaling pathway, further corroborated with hyperphosphorylation of several proteins, including key proteins in the onset of Alzheimer's and Parkinson's diseases, such as Mapt and Dpysl2. Our results further suggest an interplay between Cdk5 and Gsk3b signaling pathways in the brain of old mice, a crosstalk which has been previously suggested to underline AD pathogenesis.

Translation/Human Health Impact: Our data provides a new perspective of age-related changes in the brain kinome and phosphoproteome.

 # 33

Poster Title: Age-dependent changes in mouse brain and liver lipidomes

Poster Presenter: Panda, Punyatoya
Poster Presenter Institution: Purdue University

Poster Authors: Punyatoya Panda, Department of Comparative Pathobiology, Purdue University, West Lafayette, IN; Christina R. Ferreira, Bindley Bioscience Center, Purdue University, West Lafayette, IN; Allison Schaser, Department of Speech, Language, and Hearing Sciences, Purdue University; Uma Aryal, Department of Comparative Pathobiology, Purdue University, West Lafayette, IN

Abstract:

Background/Significance/Rationale: Aging is a major risk factor for various diseases such as cancer and neurological disorders including Alzheimer's disease. However, the mechanisms of aging are complex and remain elusive. Like genes and proteins, lipids play key structural, regulatory, and signaling roles within the cells. Therefore, characterizing lipids in various organs provides useful information for understanding their functions under different physiological or disease states. However, relatively very little is known about the composition and age-dependent changes of lipids in the brain and liver, the two most lipid-rich organs after adipose tissues. In this work, we characterized the brain and liver lipidome using two complementary analytical approaches: targeted shotgun profiling using Multiple Reaction Monitoring and untargeted Liquid Chromatography-tandem mass spectrometry (LC-MS/MS).

Methods: The brain and liver tissues collected from three age groups of mice-young adult(3–5-month-old), middle-aged (10–12-month-old) and old-aged mice(19–21-month-old) were homogenized and lipids were extracted by Bligh-Dyer method. For MRM-profiling, these were administered directly without any chromatographic separation into the ESI-source of an Agilent QqQ 6410 and samples were screened for specific ion transitions corresponding to different lipid classes and fatty acid composition based on LIPID MAPS database. For untargeted lipidomics, samples were analyzed using an Agilent 6545 Q-TOF MS coupled with Agilent 1290 Infinity II UPLC System. The untargeted LC-MS/MS-data were searched against MONA-database for lipid identification and relative quantitation. For DESI Imaging, the tissue sections were embedded in Carboxy-methyl-cellulose and subjected to ambient mass spectrometry in Waters Synapt XS. Statistical analysis of identified lipid species or lipid classes was performed by Perseus using ANOVA to identify the significantly changing lipids.

Results/Findings: The MRM profiling analysis focused on specific ion transitions corresponding to different lipid classes and fatty acid composition based on LIPID MAPS database. Using MRM profiling without LC, the samples were screened for 3246 MRMs comprising of 24 different lipid classes and fatty acid composition including different phospholipid classes like phosphatidylcholines (PCs), phosphatidylethanolamines (PEs), ceramides, di- and tri-acylglycerols, acylcarnitines. In the brain, phosphatidylcholines (PCs), phosphatidylethanolamines (PEs) and free fatty acids (FFAs) were among the most abundant classes of lipids, while in the liver, tri- and di-acylglycerols were among the most abundant ones, apart from PCs and FFAs. Statistical analysis revealed age-dependent changes in sphingomyelins, TGs and FFA in the brain, and TGs, DGs, and phospholipids classes in the liver.

Conclusions/Discussion: Lipids detected in the MRM and LC-MS/MS data showed a high degree of overlap (100% in the brain and 98% in the liver)) indicating consistency and agreement between the two analytical methods. In conclusion, the shotgun profiling using MRM enables simpler, faster, sensitive, and cost-effective exploratory lipid analysis workflow for characterizing the lipidome in diverse biological samples. Understanding age-dependent changes in lipid composition using this MRM method can shed light on potential biomarkers and mechanisms associated with aging.

Translation/Human Health Impact: Identification of lipid biomarkers of aging and their spatial mapping will help us understand the biology of aging and age-associated diseases better.

 # 34

Poster Title: A Tailored Approach to Increase Engagement in Lifestyle Change Programs in Women with Previous Gestational Diabetes

Poster Presenter: Pike, Julie
Poster Presenter Institution: Indiana University School of Medicine

Poster Authors: Julie M. Pike, Department of Pediatrics, Indiana University School of Medicine, Indianapolis, IN, Department of Biostatics and Health Data Science, Indiana University School of Medicine, Indiana University Health, Indianapolis, IN; Kathryn M. Haberlin-Pittz, Department of Pediatrics, Indiana University School of Medicine, Indianapolis, IN, Department of Biostatics and Health Data Science, Indiana University School of Medicine, Indiana University Health, Indianapolis, IN; Luz A. Machuca, Department of Pediatrics, Indiana University School of Medicine, Indianapolis, IN; Brett M. McKinney, Department of Pediatrics, Indiana University School of Medicine, Indianapolis, IN; Lisa G. Yazel, Department of Pediatrics, Indiana University School of Medicine, Indianapolis, IN; Aric Kotarski, Department of Pediatrics, Indiana University School of Medicine, Indianapolis, IN; Tamara S. Hannon, Department of Pediatrics, Indiana University School of Medicine, Indianapolis, IN, Department of Biostatics and Health Data Science, Indiana University School of Medicine, Indiana University Health, Indianapolis, IN

Abstract:

Background/Significance/Rationale: Women with previous GDM (pGDM) are at increased risk for type 2 diabetes. Yet, engagement of this population in lifestyle change programs is low. We evaluated the effect of a tailored diabetes prevention approach on engagement and health outcomes in women with pGDM.

Methods: This unrandomized cohort study engaged women with pGDM in an informed decision-making process to discuss type 2 diabetes risk, explore preferences for a lifestyle change program, and select a program aligned with individual priorities. Seven evidence-based lifestyle change programs with a variety of delivery modes, duration, time of day, and childcare availability were offered free of charge. The primary outcome was program engagement. Secondary outcomes were psychosocial questionnaires and clinical measures at baseline, 6 months (T1), and 12 months (T2). Statistical analysis included repeated measures ANCOVA.

Results/Findings: We consented 116 women (34.9 ± 5.7 y; 57.3% white; college degree 47.3%). Ninety-two participants were included in data analysis after exclusions due to pregnancy (n=9), baseline BMI <25 (n=11), baseline HbA1c ≥6.5 (n=3), and illness (n=1). Almost half selected WW (41%), followed by Habit Nu (22%), health coaching (11%), Encourage (10%), the dietitian consult (9%), Healthy Me (5%), and the YMCA NDPP (1%). Most participants who selected WW (84%) remained engaged in the study at T1 and/or T2. BMI, HbA1c, and questionnaires were stable from baseline to T1 and T2.

Conclusions/Discussion: A tailored diabetes prevention strategy is feasible and acceptable in women with pGDM, even during the COVID-19 pandemic and shutdown, which impacted the outcomes. Lifestyle change programs that meet the unique priorities and needs of women with pGDM are needed to optimize engagement and outcomes.

Translation/Human Health Impact: Offering a choice of lifestyle change programs and completing program enrollment at the time of type 2 diabetes risk discussion may enhance engagement in diabetes prevention efforts among women with pGDM.

 # 35

Poster Title: Exploring novel insights into alcohol use disorder and related traits: A functional polygenic score approach

Poster Presenter: Robins, Melissa
Poster Presenter Institution: Indiana University School of Medicine

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Abstract:

Background/Significance/Rationale: Polygenic Scores (PGS) have evolved into powerful tools for assessing genetic predisposition to complex traits. Recent studies suggest that integrating functional information to select SNPs to calculate PGS (referred to as functional PGS) both enhances predictive accuracy and improves portability across populations. In this study, we use a functional PGS to uncover mechanisms underlying Alcohol Use Disorder (AUD) and related traits.

Methods: We developed an innovative approach to construct functional PGS by integrating a diverse range of multi-modal functional genomics data, including the effects of genetic variants on gene expression measured in Massively Parallel Reporter Assays (MPRA) in neuronal and glial cells, chromosomal conformation data, and chromatin accessibility data derived from single-cell multiome analyses of postmortem brain tissues.

Results/Findings: We designed MPRA to evaluate the impacts of 23,232 variants (11,564 enhancer and 7,936 3'-untranslated region variants) on gene expression in human neuroblastoma (SH-SY5Y), oligodendroglioma (HOG), and astrocytoma (CCF-STTG1) cell lines. These variants are associated with a broad spectrum of substance use disorders including problematic alcohol use, opioid use disorder and cannabis use disorder. Our results suggest that 25% of the enhancer and 22% of the 3'UTR variants impact gene expression in at least one cell type. These functional variants were used to train a machine learning model to predict the potential impacts of variants that have not been measured. Using the functional variants identified in our analysis and an interpretable machine learning framework, we built PGS for AUD.

Conclusions/Discussion: Our analyses point to key genes and pathways related to neuroinflammation, responses to oxidative stress and neurodegeneration. Integrating functional data into PGS analysis can go beyond risk assessment and enhance our understanding of genetic mechanisms affecting AUD and related traits.

Translation/Human Health Impact: Our results also suggest that functional PGS can provide greater insight into the heterogeneity of AUD risk and lead to better treatment personalization.

 # 36

Poster Title: Miniaturized Manual Renal Replacement Therapy: Pre-clinical Model for Neonatal Applications

Poster Presenter: Russell III, Carl
Poster Presenter Institution: Indiana University School of Medicine, Purdue University School of Biomedical Engineering

Poster Authors: Carl Russell III, Indiana University School of Medicine, Department of Pediatrics, Indianapolis, IN, Purdue University Weldon School of Biomedical Engineering, West Lafayette, IN; Angus, Stergar, Indiana University School of Medicine, Department of Pediatrics, Indianapolis, IN; Giovanni Ceschia, Cincinnati Children's Hospital and Indiana University Health, Cincinnati, OH; Rose Odom, Indiana University School of Medicine, Department of Pediatrics, Indianapolis, IN; Michelle C. Starr, Indiana University School of Medicine, Department of Pediatrics, Indianapolis, IN, Riley Hospital for Children, Indianapolis, IN; Jolyn Morgan, Cincinnati Children's Hospital, Cincinnati, OH; Amanda Snyder, Cincinnati Children's Hospital, Cincinnati, OH; Denise Hasson, New York University Langone Health, New York, NY; Ed Pulte, ExThera Medical Inc, Martinez, CA; Apaara K. Chawla, George Washington University, Washington, DC; Stuart Goldstein, Cincinnati Children's Hospital and Indiana University Health, Cincinnati, OH, University of Cincinnati College of Medicine, Department of Pediatrics, Cincinnati, OH; Danielle E. Soranno, Indiana University School of Medicine, Department of Pediatrics, Indianapolis, IN, Purdue University Weldon School of Biomedical Engineering, West Lafayette, IN, Riley Hospital for Children, Indianapolis, IN; Cara L. Slagle, Indiana University School of Medicine, Department of Pediatrics, Indianapolis, IN, Riley Hospital for Children, Indianapolis, IN

Abstract:
Background/Significance/Rationale: Neonates weighing <2.5 kg with fluid overload (FO) and/or acute kidney injury (AKI) have limited treatment options. Peritoneal dialysis is constrained by skin integrity and reliable ultrafiltration (UF) challenges, whereas extracorporeal devices are expensive and hindered by the need for large-bore dual-lumen vascular access. The Brophy Kit™ (BK), a manual, single-lumen, low-cost dialysis kit is designed for <2.5 kg patients.

Methods: Healthy male 600–800-gram rats had 3 French central venous catheters placed. The BK was primed with heparinized crystalloid. Blood aspiration and infusion (3mL) marked one cycle. Four cycles were performed before ultrafiltration (UF) to determine prime tolerance. Replacement infusion (PlasmaLyte™) was initiated at 0.5 mL/min to account for anticipated UF (0.5 mL per cycle/1 min). Goal UF cycles equaled the number of cycles required to UF 10% total blood volume (TBV). Respiratory rate (RR) was recorded at baseline, 5% TBV UF, and 10% TBV UF. Blood was collected during central line placement (baseline), pre-ultrafiltration, and at sacrifice. UF was weighed at experiment completion to compare expected vs. observed.

Results/Findings: Nine rodents underwent the procedure; one was terminated before UF (loss of access). RRs demonstrated no difference at experimental milestones. All eight rodents remained hemodynamically stable. Percent difference between serum electrolytes vs. PlasmaLyte™ was minimal (Na {4.1%}; K {5.15%}, Cl {0.25%}). Prescribed vs actual UF volume differed by 11.4% (day 1) and 12.0% (day 2).

Conclusions/Discussion: Initial rodent experiments using small-caliber vascular access demonstrate feasibility and procedural tolerance, electrolyte stability, and device reliability. A two-person user approach might be preferred to achieve prescribed UF volumes. Passive clearance and normalization to PlasmaLyte™ were observed.

Translation/Human Health Impact: Results are encouraging. The Brophy Kit™ could support ultrafiltration in infants weighing less than 2.5 kg.

 # 37

Poster Title: Sex-specific topological structure associated with dementia identified via latent space network analysis

Poster Presenter: Wang, Selena
Poster Presenter Institution: Indiana University School of Medicine

Poster Authors: Selena Wang, Indiana University School of Medicine; Yiting Wang, Indiana University School of Medicine; Frederick Xu, Bioengineering PhD Student and Research Fellow at the University of Pennsylvania; Li Shen, Indiana University School of Medicine; Yize Zhao, Associate Professor Biostatistics and Health Data Sciences, Indiana University School of Medicine

Abstract:
Background/Significance/Rationale: We investigate sex-specific topological structure associated with typical Alzheimer's disease (AD) dementia using a novel state-of-the-art latent space estimation technique.

Methods: This study applies a probabilistic approach for latent space estimation that extends current multiplex network modeling approaches and captures the higher-order dependence in functional connectomes by preserving transitivity and modularity structures.

Results/Findings: We find sex differences in network topology with females showing more default mode network (DMN)-centered hyperactivity whereas males showing more limbic system (LS)-centered hyperactivity while both show DMN-centered hypoactivity. We find that centrality plays an important role in dementia-related dysfunction with stronger association between connectivity changes and regional centrality in females than in males.

Conclusions/Discussion: The study contributes to the current literature by providing a more comprehensive picture of dementia-related neurodegeneration linking centrality, network segregation and DMN-centered changes in functional connectomes, and how these components of neurodegeneration differ between the sexes.

Translation/Human Health Impact: No impact presented.

 # 38

Poster Title: Peripheral Monoacylglycerol Lipase Inhibition Prevents Neuropathy While Enhancing Tumor-Killing Efficacy of Chemotherapeutic Treatment in a Mouse Breast Cancer Model

Poster Presenter: Wirt, Jonah
Poster Presenter Institution: Indiana University Bloomington

Poster Authors: Jonah Wirt, Dept. of Psychological and Brain Sciences, Indiana University, Bloomington, IN; Program in Neuroscience, Indiana University, Bloomington, IN; Emily Fender-Sizemore, Dept. of Psychological and Brain Sciences, Indiana University, Bloomington, IN; Mirjam Huizenga, Department of Molecular Physiology, Leiden University & Oncode Institute, Netherlands; Mario Van Der Stelt, Department of Molecular Physiology, Leiden University & Oncode Institute, Netherlands; Andrea G. Hohmann, Dept. of Psychological and Brain Sciences, Indiana University, Bloomington, IN; Program in Neuroscience, Indiana University, Bloomington, IN, Gill Center for Biomolecular Science, Indiana University, Bloomington, IN

Abstract:
Background/Significance/Rationale: Chemotherapeutic treatment for breast cancer produces anti-cancer effects but also produces dose-limiting toxicities such as neuropathic pain [1-3]. Inhibition of the primary

enzymes that degrade endogenous cannabinoids 2-arachidonoylglycerol (2-AG) and anandamide (AEA) suppress neuropathic nociception in models of chemotherapy-induced peripheral neuropathy (CIPN) and show anti-cancer properties [4-7]. 2-AG is degraded by the enzyme monoacylglycerol lipase (MGL) whereas AEA is degraded by fatty-acid Amide Hydrolase (FAAH), respectively. In the current studies, we compared a CNS-impermeable MGL inhibitor LEI-515, global MGL inhibitor JZL184, and peripheral FAAH inhibitor URB937 in their abilities to suppress development of CIPN and reduce tumor size in a mouse model of breast cancer.

Methods: LEI-515, JZL184, URB937, or vehicle were administered prophylactically before and during administration of chemotherapeutic agent paclitaxel to assess the development of paclitaxel-induced mechanical (assessed by von Frey) and cold (assessed by the acetone test) hypersensitivities in non-tumor bearing and 4T1 breast cancer tumor-bearing mice. Tumor volumes were measured daily. At the terminal endpoint, colonic content weights were assessed.

Results/Findings: LEI-515 and URB937 prevented the development of paclitaxel-induced mechanical and cold hypersensitivity in non-tumor bearing mice, and only LEI-515 fully suppressed hypersensitivities in tumor-bearing mice. JZL184 did not prevent the development of mechanical or cold hypersensitivity; tolerance developed to antinociceptive effects of JZL184. Peripheral MGL inhibitor LEI-515 and Global MGL inhibitor JZL184 reduced tumor size compared to chemotherapy alone when combined with paclitaxel. Paclitaxel-treated mice that received LEI-515 showed reduced tumor weights. Colonic weights of all paclitaxel groups increased.

Conclusions/Discussion: Peripheral MGL and FAAH inhibition hold therapeutic potential for suppressing development of CIPN in breast cancer patients.

Translational/Human Health Impact: Finding therapeutic treatment options that improve cancer patient quality of life through CIPN suppression without sacrificing anti-cancer efficacy remains a clinical imperative. These studies provide a rationale for the use of peripheral endogenous cannabinoid enzyme inhibition for breast cancer patients.

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