INDIANA CTSI Clinical and Translational Sciences Institute

Celebrating 15 Years of Improving Health through Research

Annual Meeting

Speaker Biographies
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September 22, 2023

Welcome to the 2023
Indiana Clinical and Translational Sciences Institute's (CTSI)
Annual Meeting

Dear Friends and Colleagues,

Thank you for joining us for the 2023 Annual Meeting. This year, our theme is "Translational Neuroscience: Transforming Health through Innovative Research." This theme is a jumping off point for a day of learning, rigorous inquiry, and interdisciplinary problem-solving—all of which are at the heart of what we do in clinical and translational science.

We are proud to deliver a dynamic line-up of events and speakers representing unique strengths, contributions, and perspectives from each of our partner institutions. Additionally, we are delighted to complement those perspectives with discussions led by brilliant speakers from beyond Indiana. Keynote speaker Huda Y. Zoghbi, MD, of Baylor College of Medicine, the winner of the 2023 August M. Watanabe Award, will share her cutting-edge work on the ***Pathogenesis Studies of Neurodegenerative Diseases*** and Peggye Dilworth-Anderson, PhD, of the University of North Carolina – Chapel Hill, will deliver the plenary address on ***Inclusivity and Intersectionality in Dementia Research.***

Additionally, our poster session will give you the opportunity to engage with colleagues across career stages on a dynamic range of topics in translational science.

If you are able to attend in person, we invite you to connect with one another, share ideas, and have conversations that may lead to future collaboration and discovery. If you are attending virtually, we invite you to connect with us via the Q&A function during the presentations, learn additional ways to connect with us and our services during the lunch presentation, and review the research posters online to learn about exciting new projects and potential future collaborations. It is our hope that the multiplicity of our research, expertise, and perspectives will lead us together toward a collectively healthier Indiana.

Please take a moment to review this booklet, and familiarize yourself with our poster presenters, our speakers, the Indiana CTSI's programs and our 80-plus research service cores from across our campuses, all of which enable translational research throughout the state.

Enjoy the meeting!

Sarah Wiehe, MD, MPH and Sharon Moe, MD
Co-Directors, Indiana CTSI

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SPEAKER BIOGRAPHIES

Huda Y. Zoghbi, MD

Investigator, Howard Hughes Medical Institute

Distinguished Service Professor
Baylor College of Medicine

Director, Jan and Dan Duncan Neurological Research Institute Texas Children's Hospital

Dr. Zoghbi's research focuses on patients who are suffering from rare and mysterious disorders, including Rett syndrome. Rett syndrome is a neurodevelopmental disorder caused by a genetic mutation which leads to serious impairment, affecting a child's ability to walk, talk, eat and breathe. The disorder is usually recognized in girls under the age of two. Her research has also contributed to the understanding of a wide variety of neurological disorders and other diseases including deafness, pediatric brain tumors and sudden infant death syndrome.

Dr. Zoghbi has received many honors and awards, including election to the National Academy of Sciences (2004), Bristol Myers-Squibb Neuroscience Distinguished Achievement Award (2006), election to the Lebanese Academy of Sciences (2013), Breakthrough Prize in Life Sciences (2017), election to the American Academy of Arts and Sciences (2018), election to the National Academy of Inventors (2019), the Brain Prize (2020) and Kavli Prize in Neuroscience (2022).

In addition to her other achievements, Dr. Zoghbi co-discovered the gene for spinocerebellar ataxia type 1 (SCA1), a progressive condition which affects a person's ability to move and balance. As an investigator at the Howard Hughes Medical Institute, a nonprofit research organization which aims to advance basic biomedical research and science education to benefit humanity, her team is looking for ways to reduce abnormal proteins that accumulate in degenerative conditions, such as Alzheimer's disease.

Peggye Dilworth-Anderson, PhD

Professor, Department of Health Policy and Management
Gillings School of Global Public Health
University of North Carolina – Chapel Hill

Head of Patient Strategies, Society of Improve Diagnosis in Medicine (SIDM

Dr. Dilworth-Anderson's research focus is on health disparities and Alzheimer's disease with an emphasis on building knowledge for the scientific and lay community to inform conducting culturally relevant research and disseminating information about Alzheimer's disease and related disorders in medically underserved diverse populations. Her research bridges community engagement activities on empowering patients and families in seeking diagnoses for chronic diseases, accompanying care, and needed support.

Dr. Dilworth- Anderson is the recipient of numerous wards that include the Alzheimer's Association International Conference 2022 Bengt Winblad Lifetime Achievement Award in Alzheimer's Research, UNC Diversity Award in 2018 in recognition of her commitment to diversity and inclusion in research, teaching, and leadership, 2010 recipient of the Ronald & Nancy Reagan Alzheimer's Research Award from the Alzheimer's Association, 2018 Pearmain Prize for Excellence in Research on Aging from the University of Southern California (USC) Roybal Institute on Aging, UNC Faculty- to- Faculty Mentoring Award in 2012 from the Carolina Women's Leadership Council, and 2006 Minority Task Force Mentor Award from the Gerontological Society of America.

She is former President of Gerontological Society, member of the National Advisory Council on Aging of NIA, former Board member of the National Borad of Directors of the Alzheimer's Association and is currently a member of the Global Council on Brain Health and Board of Directors of the Alzheimer's Association Eastern North Carolina Chapter
A graduate of Tuskegee Institute, Dr. Dilworth-Anderson received her master's and doctorate degrees in sociology from Northwestern University, with further training in family therapy from the Family Institute at Northwestern University. She received post-doctoral training in aging from the Midwest Council of Social Research in Aging. She is a fellow of the Gerontological Society and National Council on Family Relations.

Maria Dadarlat, PhD

Assistant Professor
Weldon School of Biomedical Engineering
Purdue University

Dr. Dadarlat completed her BS in Biomedical Engineering from Purdue in 2008. She then went on to complete a PhD in Bioengineering at the UC Berkeley/UCSF Joint PhD program in Bioengineering, where she worked on developing artificial sensation for neural prostheses. Next, as a Simons Foundation Post-Doctoral Fellow, she worked in the lab of Michael Stryker at UCSF studying state-dependent encoding of sensory information and neural activity patterns evoked by electrical stimulation. She joined Purdue as an Assistant Professor of Biomedical Engineering in the fall of 2019, where her lab uses a combination of electrophysiology, 2-photon imaging, and animal behavior to study natural and artificial sensory processing.

Jeff Dage, PhD

Senior Research Professor
Stark Neurosciences Research Institute
Indiana Univesity School of Medicine

Dr. Jeffrey Dage is a Senior Research Professor of Neurology at Indiana University School of Medicine and primary member of the Stark Neurosciences Research Institute. He received his PhD from the University of Cincinnati in Ohio where he worked in the area of protein characterization using mass spectrometry. He has been in the pharmaceutical industry for the last 28 years and has contributed to many therapeutic discovery programs through analytical measurement of biologically relevant molecules in cell culture, preclinical models, and human clinical samples. His research at Indiana University is focused on the discovery and development of biomarkers for Alzheimer's disease and related dementias. Over the last several years he led the discovery and development of ultrasensitive immunoassays to measure phosphorylated tau in blood for use in Alzheimer's disease diagnosis, prognosis, and clinical trials. These blood-based biomarker assays have led to a dramatic change in AD research and clinical development.

Tatiana Foroud, PhD

Executive Associate Dean for Research Affairs
August M. Watanabe Professor for Medical Research
Distinguished Professor, Medical and Molecular Genetics
Chancellor's Professor, IUPUI
Indiana University School of Medicine

Tatiana Foroud, PhD, is the Executive Associate Dean for Research Affairs and the August M. Watanabe Professor for Medical Research. Dr. Foroud is also a Distinguished Professor and a Chancellor's Professor, IUPUI. She is a faculty member in the Department of Medical and Molecular Genetics. Over the course of her more than 25 years with IU School of Medicine, Dr. Foroud has been actively involved in the genetics of neurodegenerative disorders such as Alzheimer's disease and Parkinson's disease as well as studies of alcoholism. A statistical geneticist by training, she leads several large NIH-funded biorepositories focused on the development of effective biomarkers of disease onset and progression.

Shaun Grannis, MD, MS

Vice President, Data and Analytics
Research Scientist, Center for Biomedical Informatics
Regenstrief Institute, Inc

Regenstrief Chair in Medical Informatics
Professor of Family Medicine
Indiana University School of Medicine

Dr. Shaun Grannis collaborates closely with national and international public and population health stakeholders to advance the technical infrastructure and data-sharing capabilities in varying settings. His research is focused on improving discovery and decision support in a variety of contexts by developing, testing, and implementing innovative approaches for data integration, patient matching, predictive modeling and other novel data science use cases, including developing novel population health data frameworks supporting fusion of community and social determinants of health with clinical data, as well as leveraging machine learning-based models to improve discovery and decision support in a variety of contexts.

Dustin Hammers, PhD, MS

Associate Professor of Neurology
Lead Neuropsychologist
Indiana University School of Medicine

Dr. Hammers is a board-certified clinical neuropsychologist and Associate Professor in the Department of Neurology at Indiana University. Joining the Department in 2021, he was previously faculty at the University of Utah starting in 2011. Dr. Hammers is the lead neuropsychologist involved in the NIA-funded *Longitudinal Early-Onset Alzheimer's Disease Study* (LEADS), and he is currently the Principal Investigator on the NIA- and Alzheimer's Association- funded study *Lifestyle Interventions for the Treatment of Early-Onset AD Study* (LITES). He is also affiliated with the Indiana Alzheimer's Disease Research Center (IADRC). His research has emphasized the evaluation of diagnostic consistency between cognitive and advanced AD biomarkers (β-amyloid and tau) in an effort to improve diagnostic accuracy. Additional areas of interest have included examining the assessment of cognitive change over time, teleneuropsychology, and the detection of early memory decline in elderly and dementia populations through computerized batteries and novel learning measures. He currently serves as Associate Editor of *Developmental Neuropsychology* and Grand Rounds Editor of *The Clinical Neuropsychologist* and has recently served as the Guest Editor for the *Journal of Clinical and Experimental Neuropsychology*. In addition to being the lead neuropsychologist for the multi-center NIA-funded *Anti-NMDA Receptor Encephalitis ExTINGUISH* trial, he is the past Chair of the American Psychological Association's (APA) Committee on Rural Health and is currently a Liaison for the Public Interest Advisory Committee, APA Society for Clinical Neuropsychology.

Jay L. Hess, MD, PhD, MHSA

Dean, Indiana University School of Medicine
Executive Vice President, University Clinical Affairs

Dr. Hess joined Indiana University School of Medicine in 2013 as its 10th dean. He leads the largest medical school in the United States, with nine campuses and approximately 11,000 faculty, staff and learners throughout Indiana. During his tenure, he has overseen a doubling in research funding from the National Institutes of Health, led the school through a comprehensive curriculum reform, and strengthened the relationship with IU Health, the school's primary clinical partner and one of the nation's premier academic medical centers.

Keisuke Kawata, PhD

Assistant Professor
Clinical Neuroscientist
School of Public Health
Indiana University Bloomington

Dr. Kawata is a clinical neuroscientist and sports medicine practitioner. He is an Associate Professor in the Department of Kinesiology and Program in Neuroscience at Indiana University Bloomington. Dr. Kawata has experience working in various sports settings, such as NFL Detroit Lions, MLS Sporting Kansas City, ESPN Wide World of Sports, and MLB Atlanta Braves. His undergraduate days were dedicated to sports medicine/athletic training while his Master's and Ph.D. at Temple University focused on molecular and clinical neuroscience to understand cellular and functional consequences of traumatic brain injury, especially subconcussive neurodegeneration. He currently conducts diverse research projects related to brain resiliency and vulnerability using fluid biomarkers, cognitive/sensor function, and advanced neuroimaging approaches.
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Bruce Lamb, PhD

Indiana University Distinguished Professor
Executive Director, Paul and Carole Stark Neurosciences Research Institute
Roberts Family Professor of Alzheimer's Disease Research
Indiana University School of Medicine

Co-Director, IUH/IUSM Neuroscience Institute
Professor of Medical & Molecular Genetics
Professor of Psychiatry
Adjunct Professor of Pharmacology & Toxicology
Stark Neuroscience Research Institute

Dr. Lamb received his bachelor's degree from Swarthmore College and his PhD from the University of Pennsylvania, prior to a post-doctoral fellowship at Johns Hopkins University. In 1996, Dr. Lamb was recruited to Case Western Reserve University, where he rose from Assistant to Associate Professor and finally moved to the Cleveland Clinic in 2005. At the Cleveland Clinic, Dr. Lamb was promoted from Associate Professor to Full Professor in 2011. Dr. Lamb was recruited to become the Executive Director of the Stark Neuroscience Research Institute in January of 2016 and is Co-Director of the Indiana University Health Neuroscience Institute since 2020. Dr. Lamb's laboratory works on the basic science of Alzheimer's disease, with a focus on: 1) genetic modifiers identified from both mouse and human studies, 2) microglia and neuronal-microglial communication in the development and progression of AD pathologies; and 3) traumatic brain injury as an environmental modifier for the development of AD pathologies. Dr. Lamb is Director of the Indiana University/Jackson Laboratory/University of Pittsburgh Model Organism Development and Evaluation for Late-onset Alzheimer's Disease (MODEL-AD) Center and Co-Director of the IUSM/Purdue Target Enablement to Accelerate Therapy Development for Alzheimer's Disease (TREAT-AD) Center, both funded by the NIH. In addition, Dr. Lamb is actively involved in advocacy for increased research funding for the disease. Dr. Lamb was the Leader of the Alzheimer's Breakthrough Ride in 2010, a cross-country bicycle event supported by the Alzheimer's Association that featured researchers cycling from California to Capitol Hill to draw attention to the cause. Dr. Lamb has received numerous awards and honors including the Jennifer B. Langston Award from the Cleveland Chapter of the Alzheimer's Association and the National Civic Award and Zaven Khachaturian Lifetime Achievement Award from the National Alzheimer's Association, is a Fellow in the American Association for the Advancement of Science, and Chair of the Medical and Scientific Advisory Group and member of the Board of Directors of the National Alzheimer's Association.

Nancy Michael, PhD

Rev. John A. Zahm, C.S.C. Associatge Teaching Professor
Department of Biological Sciences
University of Notre Dame

Since December of 2014, Nancy Michael has served as the Director of Undergraduate Studies for the Neuroscience and Behavior major at the University of Notre Dame. During her time as faculty, Michael's dedication to excellence, innovation in education and commitment to community wellness have earned her numerous teaching, advising and community awards. In collaboration with multiple community organizations, Michael works in partnership to cultivate engagement with Self-Healing Communities of Greater Michiana; a collective impact, community-capacity building model aimed at mitigating the impact of toxic stress on individuals and communities through elevating the neuroscience of human resilience. Michael's primary role in this coalition is to spearhead the collaborative development of population-specific NEAR (neuroscience, epigenetics, adverse childhood experiences, resilience) science resources and professional development strategies to support individual, organizational and community capacity-building.

Sharon Moe, MD, FASN

Stuart A. Kleit Distinguished Professor of Medicine
Associate Dean for Clinical and Translational Research
Director, Division of Nephrology and Hypertension
Co-Director Indiana CTSI
Indiana University School of Medicine

Dr. Moe is the Associate Dean for Clinical and Translational Medicine, and the Co-Director for the Indiana Clinical Translational Sciences Institute. She is also Director of the Division of Nephrology and Stuart A. Kleit Professor of Medicine for the Indiana University School of Medicine. She has been a faculty member at Indiana University since 1992, and in 2019 was named Distinguished Professor at IU. Dr. Moe is the principal investigator for several ongoing basic and clinical research studies in the field of Chronic Kidney Disease-Mineral Bone Disorder (CKD-MBD), including studies on vascular calcification, mineral metabolism and bone metabolism in kidney disease. Her research has been funded by the NIH and Veterans Affairs for over 25 years, in addition to funding from Foundations and Pharmaceutical companies. She has authored over 200 scientific manuscripts, teaching manuscripts and textbook chapters and has mentored over 29 pre/post docs and clinical fellows on NIH awards. Dr. Moe served on the National Kidney Foundation's Bone and Mineral metabolism K/DOQI clinical practice guidelines in 2003, was co-chair of the international KDIGO Mineral and Bone guidelines released in 2009, and a member of the 2017 update committee. She has serves on numerous ad hoc NIH study sections and was recently named as a standing member to the AMSC study section. Key Honors include election to the American Society for Clinical Research in 2005; the National Kidney Foundation in Gareb Eknoyan Award for exceptional contributions to key initiatives of the such as the Kidney Disease Outcomes Quality Initiative (KDOQI) in 2009; Councilor to the AHA Kidney Council (2002-2004), Councilor for the International Society of Nephrology (2005-2007), Councilor for the American Society of Nephrology from 2008- 2015; President of the American Society of Nephrology from 2013-2014, and election to the American Association of Physicians (AAP) in 2017.

Alan Palkowitz, PhD

President and CEO
Indiana Biosciences Research Institute

Senior Research Professor of Medicine
Division of Clinical Pharmacology
Indiana University School of Medicine

Dr. Palkowitz currently leads the IUSM-Purdue TREAT-AD Center, an NIH-NIA funded initiative focused on discovering potential new therapies for Alzheimer's disease. Prior to to this, Dr. Palkowitz served as the vice president of Discovery Chemistry Research and Technologies at Eli Lilly and Company, where he worked for 28 years. In his role as vice president, Dr. Palkowitz was responsible for the global small molecule drug discovery strategy and delivery of clinical candidates in disease areas including cancer, diabetes, immunology, pain and neurodegenerative disorders. As a member of the Lilly Research Laboratories leadership team, Dr. Palkowitz participated in setting strategic direction for the company along with governance of the discovery and early clinical development pipeline. Additionally, Dr. Palkowitz has served on several prominent advisory committees including most recently the NIH NCATS Advisory Council and the National Academy of Sciences Board on Chemical Sciences and Technologies. He has published numerous research articles and is an inventor on almost 60 US patents. Dr. Palkowitz obtained his PhD in synthetic organic chemistry from the Massachusetts Institute of Technology and his bachelor's degree in chemistry from the University of California at Berkeley.

Michelle Shwery, MSc, MBA

Chief Operating Officer
Indiana Clinical and Translational Sciences Institute (CTSI)

Michelle Shwery joined the Indiana CTSI in July 2021 as Chief Operating Officer following more than 30 years in a range of industry roles and active community engagement. Prior to joining the Indiana CTSI, Shwery worked as an independent consultant in biotech following her retirement from Eli Lilly and Company. During her 27-year Lilly career, Shwery held a wide range of global leadership roles in research and development, enterprise risk management, and ethics and compliance, working across Lilly's research sites and affiliates. She is pleased to now be applying her experience, expertise and perspective to the Indiana CTSI to advance innovation and health through research.

Shwery holds a Master of Business Administration from the University of Chicago Booth School of Business, a Master of Science from the University of Toronto, Canada, and a Bachelor of Science from the University of Guelph, Canada. Her community involvement has included engagement with the United Way of Central Indiana as member of the Women United Steering Committee and of the Tocqueville Society. Shwery served as Board President of Dress For Success Indianapolis where she remains an Emeritus Member.

Brielle Stark, PhD

Assistant Professor
Speech, Language and Hearing Sciences Department
Indiana University Bloomington

Dr. Stark is an Assistant Professor in the Speech, Language and Hearing Sciences Department and Program in Neuroscience faculty at Indiana University Bloomington. Dr. Stark completed her doctoral research in Clinical Neuroscience at the University of Cambridge (UK) as a Gates Cambridge Trust Scholar and a postdoctoral fellowship at the Center for the Study of Aphasia Recovery at the University of South Carolina prior to joining the IUB faculty in 2018. Dr. Stark's research characterizes language and communication using neuropsychological and neuroimaging methodologies post-stroke, in typical aging, and in neurodegenerative disease. She is particularly interested in spoken discourse, manual gesture, and inner speech (the experience of speaking to ourselves in our head). Dr. Stark was honored with the 2021 IU Faculty Excellence in Mentoring Award from the Center for Women & Technology and the 2021 IU Trustees Teaching Award, evidencing her commitment to teaching and mentoring. In 2021, she was named one of four Distinguished Aphasia Scholars USA, a national award given by the Tavistock Trust UK, and was one of six pre-tenure faculty awarded the Outstanding Junior Faculty Award (2022-2023) from Indiana University Bloomington.

Sarah Wiehe, MD, MPH

Dean for Community and Translational Research
Co-Director of Indiana Clinical and Translational Sciences Institute (CTSI)
Director of Community Health Partnerships, Indiana CTSI
Associate Professor of Pediatrics
Indiana University School of Medicine

Dr. Wiehe is Co-Director of the Indiana Clinical and Translational Sciences Institute and its Community Health Partnerships program, Patient Engagement Core, and the Monon Collaborative initiative. She is a pediatrician and public health researcher.

Dr. Wiehe is an Investigator at the Regenstrief Institute and serves as Division Chief of Children's Health Services Research in Pediatrics and Associate Dean of Community and Translational Research at Indiana University School of Medicine as well as adjunct faculty of Geography at the School of Liberal Arts and Epidemiology at the Richard M. Fairbanks School of Public Health at IUPUI.

Dr. Wiehe's research focuses on health equity issues among children, adolescents, and young adults. Specifically, she engages community stakeholders and leverages existing data to identify mechanisms and opportunities for intervention in order to improve health among vulnerable populations. She partners with patients and community stakeholders to strengthen the relevance, the impact and the sustainability to her work.

SCIENTIFIC ABSTRACTS

EDUCATION:
INDIANA CTSI TRAINEES

KL2/K12 Scholars

 # 1

Poster Title: The effects of dietary fiber based on fermentability and viscosity on mineral balance and the gut microbiome in a rat model of CKD

Poster Presenter: Biruete, Annabel
Poster Presenter Institution: Purdue University

Poster Authors: Neal X. Chen- Indiana University School of Medicine; Shruthi Srinivasan- Indiana University School of Medicine; Kalisha O'Neill- Indiana University School of Medicine; David Nelson- Indiana University School of Medicine; Kathleen Hill Gallant- University of Minnesota; Sharon M. Moe- Indiana University School of Medicine

Abstract:
Background/Significance/Rationale: Hyperphosphatemia, or high circulating phosphorus, is a major factor in the pathogenesis of chronic kidney disease-mineral and bone disorder (CKD-MBD). Available therapies vary in their efficacy and focus on phosphorus absorption in the small intestine, ignoring the possible impact of the large intestine. Fiber supplementation based on their physicochemical properties may help us understand the impact of the large intestine on mineral absorption and balance via mechanisms dependent and independent of the gut microbiome.

Methods: 22-week-old male CKD rats were randomly assigned to receive one of four fiber treatments (10% w/w each) based on fermentability and viscosity: 1) Cellulose (-fermentability, -viscosity), 2) inulin (+fermentability, -viscosity), 3) psyllium husk (-fermentability, +viscosity), or 4) pectin (+ fermentability, +viscosity). Treatments lasted 10 weeks, and rats were euthanized at 32 weeks of age (kidney failure). Mineral balance will be assessed by placing rats in metabolic cages for 3 consecutive days during the last week. Cecal/fecal metagenomics and plasma for circulating gut-derived uremic toxins will be assessed at 32 weeks. Tissue collection included all intestinal segments, kidneys, heart, muscle, and bone.

Results/Findings: 70% of the animals have completed the study. Our preliminary data indicates that weight trajectories were similar between treatment groups. The length of the small intestine and the colon were significantly larger in the psyllium-treated rats. Survival at 32 weeks was not statistically significant between groups.

Conclusions/Discussion: In our preliminary analyses, the supplementation of psyllium increased the length of the small and large intestines possibly related to an increased surface area to correct for limiting absorption of nutrients.

Translational/Human Health Impact: The results from this study will help us understand the impact of fiber on mineral balance and develop interventions to be trialed in people with CKD with the goal of improving outcomes in this clinical population.

 # 2

Poster Title: Piloting a functional MRI emotion regulation task in youth with parental alcohol use disorder histories

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

Poster Authors: Kathleen I. Crum, Indiana University School of Medicine, Medical University of South Carolina; Joseph Aloi, Indiana University School of Medicine; Leslie Hulvershorn, Indiana University School of Medicine

Abstract:
Background/Significance/Rationale: Youth alcohol use disorder (AUD) is a serious public health problem. Emotion dysregulation is one potential pathway to AUD. Risk for youth AUD is also affected by *parental* AUD, which likely influences youth neurobiology and in turn, youths' emotion regulation. Indeed, emotion dysregulation is associated with AUD family history. However, associations between parental AUD, youths' neurodevelopment, and youths' alcohol use have been minimally examined. Addressing this gap would support AUD prevention. Therefore, my objective is to pilot a functional MRI task eliciting *implicit emotion regulation*, or youths' ability to modulate negative emotions when performing a cognitive task, among youth whose parents have AUD histories.

Methods: Six alcohol/substance-naïve youth ages 10-12, whose parents had AUD histories, performed the Emotional N-Back task during functional MRI scanning. Parents reported on their alcohol/substance use. Youth confirmed alcohol/substance-naïve status by self-report. A 4x2 whole-brain ANOVA was conducted with the following within-subject independent variables: emotional valence (fearful, angry, neutral faces; places); cognitive task difficulty (high, low working memory load); valence x difficulty.

Results/Findings: At a threshold of $p<.02$, the ANOVA identified brain regions whose activation differed by emotional valence and cognitive task difficulty. I found significant effects of valence (ventromedial prefrontal cortex, angular gyrus) and difficulty (dorsomedial prefrontal cortex/anterior cingulate cortex, anterior insula) in brain regions associated with salience and attention networks.

Conclusions/Discussion: Findings indicate that the fMRI task elicits activation from the expected large-scale, brain-level systems, and is functioning as intended in this specialized sample of youth. Regarding feasibility, data quality was promising despite the motion concerns accompanying a young age range.

Translational/Human Health Impact: Findings will inform sample sizes estimates in impending NIH grant applications; they support the feasibility of recruiting and scanning youth at IU. This pilot project is pivotal to launching my program of research to identify youth for early, targeted intervention and mitigate risk for AUD.

 # 3

Poster Title: Content Variability in Vaccine Education Clinic Messaging in Nigeria

Poster Presenter: Ekhaguere, Osayame
Poster Presenter Institution: Indiana University School of Medicine

Poster Authors: Rosena O. Oluwafemi, Mother and Child Hospital, Akure, Ondo, Nigeria; Eneida A. Mendonca, University of Cincinnati; Paul Biondich, Indiana University School of Medicine

Abstract:

Background/Significance/Rationale: In Nigeria, vaccine clinics are the primary location parents receive vaccine health education (vaccine talk). The current delivery format is for a health worker to deliver an unscripted vaccine talk to an assembly of parents. There is limited data on the content of the vaccine talk to inform interventions to improve vaccine communication. In this study we evaluated content of the vaccine talk within providers.

Methods: A prospective observational study conducted in a routine vaccine clinic representing a semi-urban setting located in government-run hospital in Akure, Ondo State, Nigeria. Two routine vaccine talks delivered by the same nurse to clients was audio recorded at least one week apart and transcribed. We performed content analysis on the vaccine talks based on these minimal standards pertaining to vaccines: name, benefit, administrative site, common expected side effect and management, next appointment, need for vaccines even when sick, and importance of keeping the vaccine records.

Results/Findings:

Visit 1	Visit 2
Vaccine topics discussed: • Names of vaccines • Benefits of vaccines	**Vaccine topics discussed:** • Names of vaccines • Benefits of vaccines • Administration site • Next appointment
Vaccine topics NOT discussed: • Administration site • Common side effect and their management • Next appointment • Vaccinate even when sick. • Safekeeping vaccine records.	**Vaccine topics NOT discussed**: • Common side effect and their management • Vaccinate even when sick. • Safekeeping vaccine records.

Conclusions/Discussion: Parents receive incomplete vaccine health education information during clinic visit and within provider variation exist.

Translational/Human Health Impact: Innovative ways to standardize the vaccine talk is required.

 # 4

Poster Title: Central Apnea Severity is Related to Changes in Natriuretic Peptide Levels During Decongestive Treatment of Acute Decompensated Heart Failure

Poster Presenter: Harrison, Nicholas
Poster Presenter Institution: Indiana University School of Medicine

Poster Authors: Shalini Manchanda, Department of Medicine, Division of Sleep Medicine, Indiana University School of Medicine; Henry Ludwig, Department of Emergency Medicine, Indiana University School of Medicine; Peter Pang, Department of Emergency Medicine, Indiana University School of Medicine; Ankit Desai, Department of Medicine, Division of Cardiology, Indiana University School of Medicine

Abstract:
Background/Significance/Rationale: Cheyne-Stokes Central Apnea (CS-CA), is common in heart failure (HF) and associated with morbidity and mortality. The pathophysiology of CA-CS is unknown. We tested whether brain natriuretic peptide (BNP), a biomarker secreted specifically by myocardial cells under stress from congestion, was associated with severity of CS-CA during acute HF (AHF) decongestive treatment.

Methods: We analyzed 85 consecutive hospital days from 30 prospectively-enrolled patients with cardiologist-adjudicated AHF and echocardiographic evidence of elevated cardiac pressures at admission. Daily data collected included biomarkers (BNP, troponin, electrolytes, renal/hepatic function), vitals, treatments, physical exam, pulmonary edema quantification by lung ultrasound, demographics, medical history, and continuous central-apnea monitoring. Central apnea index (CAI), scored by a blinded Board-Certified sleep medicine physician, was compared to BNP and other covariates through time by linear mixed modeling.

Results/Findings: The final model explained 95% of variance in CAI between treatment days and patients (i.e. adjusted R^2 = 0.953). BNP steadily declined in response to decongestive treatment through hospitalization. Each 10% daily change in BNP was associated with a concordant 4.7% change in CAI ($p<0.01$), after adjusting for covariates. Other significant ($p<0.05$) daily predictors of CAI were diuretic dosing, tachycardia, serum albumin, anion gap, high-flow oxygen, and history of central sleep apnea.

Conclusions/Discussion: For the first time in humans we show that CS-CA is directly associated with treatment-responsive changes in myocardial cellular stress after adjusting for biomarkers and measures of alternative proposed pathophysiologic mechanisms (e.g. metabolic alkalosis, pulmonary edema severity and pulmonary gas exchange, renal dysfunction, et al.).

Translational/Human Health Impact: While efforts to develop treatment strategies for CS-CA in HF have largely focused on ventilatory support and/or acid base status as potential physiologic targets, our results point to the importance of relieving underlying myocardial dysfunction with aggressive decongestive therapy. Future research should focus on identifying the specific molecular targets linking CS-CA and myocardial cellular stress.

 # 5

Poster Title: Diagnostic Accuracy of Primary Care Clinicians Across a Statewide System of Autism Evaluation

Poster Presenter: McNally Keehn, Rebecca
Poster Presenter Institution: Indiana University School of Medicine

Poster Authors: Rebecca McNally Keehn, Department of Pediatrics, Indiana University School of Medicine; Nancy Swigonski, Department of Pediatrics, Indiana University School of Medicine; Brett Enneking, Department of Pediatrics, Indiana University School of Medicine; Tybytha Ryan, Department of Pediatrics, Indiana University School of Medicine; Patrick Monahan, Department of Biostatistics and Health Data Science, Indiana University School of Medicine; Ann Marie Martin, Department of Pediatrics, Indiana University School of Medicine; Lisa Hamrick, Department of Psychological Sciences, Purdue University; Girija Kadlaskar, Department of Speech, Language and Hearing Sciences, Purdue University, MIND Institute, University of California Davis; Angela Paxton, Department of Pediatrics, Indiana University School of Medicine; Mary Ciccarelli, Department of Pediatrics, Indiana University School of Medicine; Brandon Keehn, Department of Speech, Language and Hearing Sciences, Purdue University

Abstract:
Background/Significance/Rationale: Our objective was to evaluate the diagnostic accuracy of the Early Autism Evaluation (EAE) Hub system, a statewide network that provides specialized training and ongoing collaborative support to community primary care providers (PCP) in the diagnosis of young children at risk for autism spectrum disorder (ASD).

Methods: EAE Hub clinicians referred a consecutive sample of children, ages 14-48 months, to this prospective diagnostic study for blinded follow-up expert evaluation including assessment of developmental level, adaptive behavior, and ASD symptom severity. The primary outcome was agreement on categorical ASD diagnosis (present/absent) between EAE Hub clinician (index diagnosis) and ASD expert (reference standard).

Results/Findings: Among 126 children (mean age: 2.6 years; 77% male; 14% Latinx; 66% non-Latinx White), 82% (n=103) had consistent ASD outcomes between the index and reference evaluation. Sensitivity was 81.5%, specificity was 82.4%, positive predictive value was 92.6%, and negative predictive value was 62.2%. There was no difference in accuracy by EAE Hub clinician or site. Across measures of developmental and adaptive skills, there were significant differences between true positive (TP) and false negative (FN) cases (all *P*s<0.001; Cohens *d*=1.1-1.4), with TP cases evidencing greater impairment.

Conclusions/Discussion: Community-based primary care clinicians who receive specialty training can make accurate ASD diagnoses in most cases. Diagnostic disagreements were predominately FN cases in which EAE Hub clinicians had difficulty differentiating ASD and global developmental delay. FN cases were associated with a differential diagnostic and phenotypic profile.

Translational/Human Health Impact: This research has significant implications for the development of future population health solutions that address ASD diagnostic delays. Our findings suggest that

most young children can be served within the primary care setting, potentially leading to improved access to specialists for children who require a higher level of diagnostic expertise.

 # 6

Poster Title: Psychological, Physical, and Relational Health in Breast Cancer Survivors and their Partners

Poster Presenter: Shrout, Rosie
Poster Presenter Institution: Purdue University

Poster Authors: Elliot Friedman, Purdue University; Kathy Miller, Indiana University School of Medicine and Comprehensive Cancer Center; James Tisdale, Purdue University; Rasheedah Adisa, Purdue University

Abstract:
Background/Significance/Rationale: Breast cancer survivors who experience psychological and physical symptoms well after treatment ends have an increased risk for comorbid disease development, reduced quality of life, and premature mortality. However, survivors in satisfying marriages report lower stress and better health than those in dissatisfying marriages. Research is needed to identify how survivors' marriages provide these health benefits across the cancer continuum. Including both survivors and their partners' perspectives can identify key pathways connecting relationships to better health.

Methods: This study examined survivors' and their partners' psychological, physical, and relational health. Breast cancer survivors (stage 0-III) and their partners (n=34 individuals, 17 couples) completed an online survey. Questionnaires assessed their cancer-related communication, relationship distress, and psychological and physical symptoms.

Results/Findings: Survivors reported poorer sleep quality and greater fatigue than their partners. Survivors also reported disclosing more thoughts, feelings, and information about cancer compared to their partners. For both survivors and partners, feeling more satisfied with each other's cancer-related discussions and reporting lower relational distress correlated with fewer physical symptoms, sleep problems, fatigue, and psychological distress.

Conclusions/Discussion: Breast cancer survivors experienced greater sleep problems and fatigue than their partners, and those reporting greater relational distress had even greater psychological and physical health symptoms. However, for both survivors and their partners, feeling more satisfied with how often they talked about survivorship and the cancer experience was associated with better psychological and physical health. This research demonstrates the health benefits and importance of open communication for both survivors and their partners across the cancer continuum.

Translational/Human Health Impact: Open communication and talking about cancer-related thoughts, feelings, and information can promote better psychological and physical health in both survivors and partners. These findings highlight the importance of screening for relational distress and enhancing both survivors' and partners' communication. This study identified intervention points for couple education and cancer programming across survivorship.

TL1 Pre-Doctoral Trainees

 # 7

Poster Title: Stool microbiome in Ugandan children is associated with differential malaria outcomes

Poster Presenter: Bednarski, Olivia
Poster Presenter Institution: Indiana University School of Medicine

Poster Authors: Olivia Bednarski, Department of Microbiology and Immunology, Indiana University School of Medicine, Indianapolis, Indiana; Ruth Namazzi, Department of Pediatrics and Child Health, Makerere University, Kampala, Uganda; Robert Opoka, Department of Pediatrics and Child Health, Makerere University, Kampala, Uganda; Chandy John, Ryan White Center for Pediatric Infectious Diseases and Global Health, Department of Pediatrics, Indiana University, Indianapolis, Indiana; Nathan Schmidt, Ryan White Center for Pediatric Infectious Diseases and Global Health, Department of Pediatrics, Indiana University, Indianapolis, Indiana

Abstract:
Background/Significance/Rationale: Gut microbiota in mice modulates the severity of malaria by regulating the humoral immune response to Plasmodium. It is presently unknown if gut microbiota also impacts the severity of malaria in humans. This study sought to assess if the composition of the gut microbiota differentially affects the development of severe malaria in Ugandan children infected with *P. falciparum.*

Methods: We sequenced the bacterial 16S rRNA gene in over 500 stool samples from <5-year-old Ugandan children with five clinically distinct severe malaria presentations (prostration, severe malaria anemia, multiple seizures, respiratory distress, and cerebral malaria), and healthy community children (consisting of both *P. falciparum* negative and asymptomatic *P. falciparum* positive children).

Results/Findings: When assessing alpha diversity, asymptomatic and community children had greater richness and evenness compared to children that developed severe malaria. Beta diversity analysis demonstrated significant dissimilarity in stool bacteria communities between each severe malaria subgroup and asymptomatic children. Differential abundance testing revealed a single bacteria species as consistently enriched in all severe malaria subgroups. Additionally, longitudinal analysis over twelve months revealed specific bacteria were enriched in the community children that subsequently developed severe malaria.

Conclusions/Discussion: Our data provide the first demonstration that specific gut bacteria are associated with the severity of malaria in African children. With this preliminary evidence, it is substantiated to investigate further the connection between the gut microbiota as another risk factor for the development of severe disease in malaria. Ongoing experiments include metagenomic sequencing of stool samples and causative experiments with mice.

Translational/Human Health Impact: This may lay the groundwork for the development of probiotic or oral antibiotic therapies to better control *P. falciparum* infection in African children.

 # 8

Poster Title: 3D printed guided bone regeneration (GBR) graft optimized through finite element analysis (FEA)

Poster Presenter: Benito Alston, Claudia
Poster Presenter Institution: Purdue University

Poster Authors: Claudia Benito Alston, Weldon School of Biomedical Engineering, Purdue University; Nicanor Moldovan, Richard L. Roudebush VA Medical Center; Clark Barco, Richard L. Roudebush VA Medical Center; Luis Solario, Weldon School of Biomedical Engineering, Purdue University

Abstract:

Background/Significance/Rationale: Guided bone regeneration utilizes bone particulates surrounded by titanium or collagen mesh encasing in order to reconstruct bone defects. In this study, we explored dual-component constructs through a pre-surgical 3D printed patient specific design. Finite element analysis (FEA) was utilized to compare the impact of screws, cover porosity and core material during mastication. The end goal was to design a cover and core construct that could sustain mastication, limit stress shielding, and allow for cell infiltration early in the regeneration cascade.

Methods: A graft was designed to fit an open source mandible model with a defect. Simulations utilized a downward 250N masticatory force, and a 24N bolt preload while fixed along the mandible's inferior edge. The graft was assumed to be bonded. Outputs included stress, strain, von mises stress and deformation.

Results/Findings: Results show that porous covers with a hydrogel core, which allow for cell infiltration, could sustain mastication without yielding but also begin to fall within the region of limiting stress shielding which is 20 – 60 MPa. Comparing hydrogel and solid cores, significant differences across all parameters can be seen. Furthermore, increasing the elastic modulus of hydrogel cores will allow the cover to transmit further stress to the core, improving bone regeneration through Wolff's law. Comparing lingual screws to buccal screws, showed little to no effect on parameter outputs.

Conclusions/Discussion: Through FEA the viability of a porous 3D printed cover and core graft with buccal screws was demonstrated. The large effect that a solid core had on the model demonstrated the importance of a softer core for modulating stress shielding while ensuring the cover would minimally deform.

Translational/Human Health Impact: The current standard of care is designed *in vivo* leading to longer surgical times, unreproducible porosities, requiring the core material to be structurally sound to sustain possible mastication. Pre-surgically tuning a cover and core construct and 3D printing remedy these problems, while improving bone regeneration.

 # 9

Poster Title: Agent based model of latent and naïve *in vitro M. Tuberculosis* early infection dynamics shows synergistic interactions between CD4+ T cell and macrophage activation

Poster Presenter: Hoerter, Alexis
Poster Presenter Institution: Purdue University

Poster Authors: Alexa Petrucciani, Purdue University; Israel Guerrero, Texas Biomedical Research Institute; Charles Renshaw, Texas Biomedical Research Institute; Maria Montoya, Texas Biomedical Research Institute; Eusondia Arnett, Texas Biomedical Research Institute; Larry S. Schlesinger, Texas Biomedical Research Institute; Elsje Pienaar, Purdue University; Regenstrief Center for Healthcare Engineering

Abstract:
Background/Significance/Rationale: Tuberculosis (TB) remains a prevalent global health challenge with 10.6 million infections and 1.6 million deaths in 2021. Granulomas – clusters of immune cells and bacteria – are the hallmark of TB infection. Early infection interactions during granuloma formation have been shown to be impacted by the host immune status. Cells from individuals with latent TB infection (LTBI) have improved bacterial growth control and cellular proliferation and faster granuloma formation compared to cells from unexposed (naïve) individuals.

Methods: We developed a computational agent-based model to analyze mechanistic differences in early infection dynamics between LTBI and naïve individuals. We simulate macrophages, bacteria, and CD4+ T cells as agents along with TNFα and IFNγ. Virtual interactions between our agents include bacterial growth, macrophage phagocytosis and infection, CD4+ T cell and macrophage activation, bacterial killing, cytokine secretion, diffusion and degradation. We calibrate the model to published experimental data for bacterial and total cell fold change and timing of first granuloma appearance.

Results/Findings: Our results indicate that the earliest interactions between activated CD4+ T cells and activated infected macrophages in LTBI cells inhibit bacterial growth by seeding granuloma-like structures with fewer bacteria. The granulomas produced in the simulations promote TB-specific CD4+ T cell proliferation, macrophage activation and continue to inhibit bacterial growth. Differences in baseline killing rates (reminiscent of trained immunity) between LTBI and naïve cells also contribute significantly to bacterial control.

Conclusions/Discussion: Our findings suggest that LTBI cells have quicker macrophage activation, better bacterial clearance and higher chance to promote rapid T cell proliferation. These findings support the use of host directed therapies that promote macrophage activation such as IFNγ and enhanced macrophage autophagy before infection to support innate immune clearance of the bacteria.

Translational/Human Health Impact: This work highlights the need for more research into the initial interactions between macrophages and *Mtb* to identify preventative strategies in TB endemic regions.

 # 10

Poster Title: Behavioral activation as an unguided single-session intervention

Poster Presenter: Peipert, Allison
Poster Presenter Institution: Indiana University Bloomington

Poster Authors: Lauren Rutter, Indiana University Bloomington; Lorenzo Lorenzo-Luaces, Indiana University Bloomington

Abstract:

Background/Significance/Rationale: Behavioral activation (BA) is an empirically supported treatment for depression. However, traditional mental health care (e.g., one-on-one psychotherapy with a professional) cannot address the public health burden of untreated mental disorders. Single session interventions (SSIs), which may not require the use of a professional, have the potential to address the public health burden of mental disorders by serving as a more accessible tool for mental health care. The Common Elements Toolbox (COMET) is an SSI delivered online and self-guided (e.g., without the guidance of a professional or paraprofessional). COMET contains CBT and positive psychology elements, including BA. It is unclear, however, how patients' complete BA delivered as an unguided SSI.

Methods: Using data from an 8-week randomized controlled trial of COMET-SSI with online workers, we conducted a content analysis of the activities generated from the BA portion of the intervention. 409 participants brainstormed three possible activities, then choose one to schedule. Two experts in CBT used qualitative content analysis to code activity types into established BA themes. Discrepancies between raters were resolved through discussion until complete consensus was achieved. Additionally, we compared the self-generated activities to a BA dictionary using Linguistic Inquiry and Word Count (LIWC), an established natural language processing tool, to quantify the similarity of the self-guided BA content to those used in online text-based counseling sessions.

Results/Findings: Results yielded 9 different activity types, including sedentary hobbies (41%), physical (29%), active hobbies (18%), social (6%), task-oriented (3%), psychological/emotional (1%), spiritual (0.6%), volunteering (0.2%), and academic (0.1%). LIWC analysis found an average lexicon overlap of 17% between the self-guided BA activities and those in the BA dictionary.

Conclusions/Discussion: Implications of this work include providing more psychoeducation and specificity in what constitutes BA.

Translational/Human Health Impact: Results suggest that there may be considerable differences between self-guided BA compared to traditional BA psychotherapy.

 # 11

Poster Title: Racial-Ethnic Differences in Antipsychotic Initiation Among Youth with Diagnosed ADHD, Depression, or Conduct Disorder

Poster Presenter: Sepe-Forrest, Linnea
Poster Presenter Institution: Indiana University Bloomington

Poster Authors: Linnea Sepe-Forrest, Department of Psychological and Brain Sciences, Program in Neuroscience, Indiana University Bloomington; Richard Meraz, Department of Psychological and Brain Sciences, Indiana University Bloomington; Sydney Adams, Department of Psychological and Brain Sciences, Indiana University Bloomington; Brian M. D'Onofrio, Department of Psychological and Brain Sciences, Program in Neuroscience, Indiana University Bloomington; Patrick D. Quinn, Department of Psychological and Brain Sciences, Program in Neuroscience, School of Public Health, Indiana University Bloomington

Abstract:
Background/Significance/Rationale: An up-to-date characterization of the commercially insured pediatric antipsychotic user population is important for evaluating whether such medications are prescribed according to evidence-based guidelines, especially among marginalized groups. This study examined racial-ethnic differences in antipsychotic initiation within psychiatric diagnostic groups as a follow-up to our prior work, which reported that, overall, youth from minority backgrounds had lower odds of initiating antipsychotics compared to White youth.

Methods: This study used 2009-2021 data from Optum's® Clinformatics® Data Mart, a database containing longitudinal patient information from nationwide commercial insurance claims. We created three separate samples of antipsychotic users and matched non-user controls between the ages of 6-17 years old. These groups contained individuals with clinically diagnosed ADHD, conduct disorder, and depressive disorder, respectively. We used conditional logistic regression to estimate the odds of antipsychotic initiation based on race-ethnicity within each diagnostic group.

Results/Findings: There were no racial-ethnic differences in the odds of antipsychotic initiation among youth diagnosed with ADHD. Among youth with depression diagnoses, Asian youth had 20% lower odds of initiating antipsychotics and Hispanic youth had 10% lower odds compared with White youth. Similar results were observed for conduct disorders, with Asian and Black youth having 10% lower odds of initiating antipsychotic treatment and Hispanic youth having 20% lower odds relative to White youth.

Conclusions/Discussion: Previously observed lower rates of antipsychotic initiation among racial-ethnic minority groups may be at least partially attributable to factors leading to disparities in diagnosis. Further research is needed to evaluate factors, such as clinical recognition and healthcare access, that may lead to differential antipsychotic use, as the disparities may occur upstream of receiving clinical diagnoses.

Translational/Human Health Impact: This study can inform efforts to promote equitable and safe antipsychotic prescribing among youth from all racial-ethnic backgrounds in the United States by highlighting the role of upstream disparities associated with antipsychotic initiation rates

TL1 Post-Doctoral Trainees

#12

Poster Title: Imaging fine structures of the human trabecular meshwork in vivo using a custom design goniolens and OCT gonioscopy

Poster Presenter: Carmichael-Martins, Alessandra
Poster Presenter Institution: Indiana University Bloomington

Poster Authors: Alessandra Carmichael-Martins, Indiana University Bloomington; Thomas J. Gast, Indiana University Bloomington; Brett J. King, Indiana University Bloomington; Brittany R. Walker, Indiana University Bloomington; Marcelina Sobczak, Indiana University Bloomington; Stephen A. Burns, Indiana University Bloomington

Abstract:
Background/Significance/Rationale: The trabecular meshwork (TM), located within the iridocorneal angle (ICA), is a target for many glaucoma treatments aimed at controlling intraocular pressure. Structural variations between individuals are poorly understood. We propose a newly designed gonioscopic lens optimized for high-resolution imaging for fine structures of the human TM *in vivo*.

Methods: The body of the new lens is index-matched to the human cornea. The new design allows a diffraction-limited image plane at the ICA. The goniolens design was 3D printed and manufactured in house. The lens is then placed on the subjects´ eyes coupled to the cornea with goniogel. Images were obtained and analyzed using a commercially available Optical Coherence Tomography (OCT) device (Heidelberg™ Spectralis).

Results/Findings: The optical resolution was measured in a model eye to be 11.05 µm. Dense OCT scans with minimum spacing oriented tangential to the iris and ICA were performed on 7 healthy subjects (23-73 yrs). The TM was successfully imaged in all subjects. The custom goniolens improved the contrast of the uveoscleral meshwork structures and corneoscleral meshwork revealing limbus parallel striations, not visible with previous goniolens designs. Transverse OCT images were constructed segmented along the anterior TM, providing an enface image of the TM structures including corneoscleral beams, previously only imaged in vivo using custom adaptive optics systems.

Conclusions/Discussion: A new optimized goniolens design has successfully been used to image the human TM with sufficient resolution to depict fine structural features. This high-resolution gonioscopic OCT allows imaging of fine collagenous structures within the TM that are not resolvable with commercially available systems using a clinically feasible approach.

Translational/Human Health Impact: The clinical feasibility and cost-efficient gonioscopic OCT imaging of the TM at high-resolution in vivo, allows us to study the structural changes with age and disease. This will increase insight into the development of high intraocular pressure and glaucoma by imaging such patients.

STUDENT TRAINEE CATEGORIES

 # 13

Poster Title: Neonatal Outcomes of Children who are HIV Exposed and Uninfected Compared with HIV Unexposed in Western Kenya

Poster Presenter: Etling, Mary Ann
Poster Presenter Institution: Indiana University School of Medicine, Richard M. Fairbanks School of Public Health

Poster Authors: Mary Ann Etling, Indiana University School of Medicine, Richard M. Fairbanks School of Public Health, Indianapolis, Indiana; Eren Oyungu, Academic Model Providing Access to Healthcare (AMPATH), Eldoret, Kenya, Department of Child Health, College of Health Sciences, Moi University School of Medicine, Eldoret, Kenya; Ziyi Yang, Indiana University School of Medicine, Indianapolis, Indiana; Emily Abuonji, Academic Model Providing Access to Healthcare (AMPATH), Eldoret, Kenya; Carolyne Jerop, Academic Model Providing Access to Healthcare (AMPATH), Eldoret, Kenya; Roselyne Ombitsa, Academic Model Providing Access to Healthcare (AMPATH), Eldoret, Kenya; Cleophas Cherop, Academic Model Providing Access to Healthcare (AMPATH), Eldoret, Kenya; Wanzhu Tu, Indiana University School of Medicine, Indianapolis, Indiana; Megan S. McHenry, Indiana University School of Medicine, Richard M. Fairbanks School of Public Health, Indianapolis, Indiana

Abstract

Background/Significance/Rationale: Nearly 16 million children are born to mothers with HIV globally and emerging literature suggests that those who are HIV-exposed and uninfected (HEU) are at an increased risk for adverse neonatal outcomes compared to their HIV unexposed, uninfected (HUU) peers. This study is among the first to further investigate whether maternal HIV exposure is associated with newborn unit (NBU) admission in Kenya.

Methods: This is an interim analysis of a longitudinal cohort study of infants born to women living with HIV who are maternally age-matched to those born unexposed to HIV in western Kenya within the Academic Model for Providing Access to Healthcare (AMPATH) Partnership. Both maternal and infant characteristics were prospectively collected, and infants were followed for the first 28 days of life. Multivariable logistic regression was used to determine the associations between HIV exposure and NBU, adjusting for birthweight.

Results/Findings: A total of 511 infants and their mothers were included for analysis, including 253 infants who are HEU and 258 unexposed infants. Eleven infants died prior to 28 days of life (n=7 HIV-exposed, n=4 HIV-unexposed; p=0.521). Maternal anemia and other maternal chronic disease (non-HIV) were significantly higher in the HEU cohort (24.5% vs. 8.1%, p<0.001; 4.0% vs 8.5%, p=0.047). Infants who are HEU had a significantly higher rate of NBU admission compared to HUU peers (13.0% vs. 2.7%, p<0.001), as well as higher rates of low birthweight (<2500 g), preterm birth (<37 weeks gestation), supportive care in 24 hours, and respiratory distress (21.3% vs. 10.9%, p=0.002; 23.7% vs. 13.2%, p<0.001; 10.3% vs. 3.9%, p<0.001; 6.7% vs. 1.2%, p=0.003.) When adjusting for birth weight, odds of NBU admission remained higher for infants who were HEU (aOR=4.55, 95% CI 2.06-11.5, p<0.001).

Conclusions/Discussion: Conclusions/Discussion: Infants who are HEU had increased odds of NBU admission, even after adjusting for birth weight. They also have higher rates of preterm birth, NBU admission, low birthweight, supportive care in 24 hours, and respiratory distress compared to unexposed infants.

Translational/Human Health Impact: Close follow-up and medical management of pregnant women living with HIV is critical for improving care for infants exposed to HIV in Kenya.

 # 14

Poster Title: Early Changes in Porcine Larynges Following Injection of Motor-Endplate Expressing Muscle Cells for the Treatment of Unilateral Vocal Fold Paralysis

Poster Presenter: Kaefer, Samuel
Poster Presenter Institution: Indiana University School of Medicine

Poster Authors: Samuel L. Kaefer, Indiana University School of Medicine, Indianapolis, Indiana, Weldon School of Biomedical Engineering, Purdue University, West Lafayette, Indiana; Lujuan Zhang, Indiana University School of Medicine, Department of Otolaryngology-Head and Neck Surgery, Indianapolis, Indiana; Rachel A. Morrison, Weldon School of Biomedical Engineering, Purdue University, West Lafayette, Indiana ; Sarah Brookes, Weldon School of Biomedical Engineering, Purdue University, West Lafayette, Indiana; Oluwaseyi Awonusi, Indiana University School of Medicine; Elizabeth Shay, Indiana University School of Medicine, Department of Otolaryngology-Head and Neck Surgery, Indianapolis, Indiana; Orlando S. Hoilett, Weldon School of Biomedical Engineering, Purdue University, West Lafayette, Indiana, Department of Biomedical Engineering, University of Cincinnati, Cincinnati, Ohio; Jennifer L. Anderson, Weldon School of Biomedical Engineering, Purdue University, West Lafayette, Indiana; Craig J. Goergen, Weldon School of Biomedical Engineering, Purdue University, West Lafayette, Indiana; Sherry Voytik-Harbin, Weldon School of Biomedical Engineering, Department of Basic Medical Sciences, Purdue University, West Lafayette, Indiana; Stacey Halum, Indiana University School of Medicine, Department of Otolaryngology-Head and Neck Surgery, Indianapolis, Indiana, Department of Speech, Language and Hearing Sciences, Purdue University, West Lafayette, Indiana

Abstract

Background/Significance/Rationale: No curative injectable therapy exists for unilateral vocal fold paralysis. Herein, we explore the early implications of muscle-derived motor-endplate expressing cells (MEEs) for injectable vocal fold medialization after recurrent laryngeal nerve (RLN) injury.

Methods: Yucatan minipigs underwent right RLN transection (without repair) and muscle biopsies. Autologous muscle progenitor cells were isolated, cultured, differentiated, and induced to form MEEs. Three weeks after the injury, MEEs or saline were injected into the paralyzed right vocal fold. Outcomes including evoked laryngeal electromyography (LEMG), laryngeal adductor pressure, and acoustic vocalization data were analyzed up to 7 weeks post-injury. Harvested porcine larynges were examined for volume, gene expression, and histology.

Results/Findings: Results/Findings:
MEE injections were tolerated well, with all pigs demonstrating continued weight gain. Blinded analysis of video- laryngoscopy post-injection revealed infraglottic fullness, and no inflammatory changes. Four weeks after injection, LEMG revealed on average higher right distal RLN activity retention in MEE pigs. MEE-injected pigs on average had vocalization durations, frequencies, and intensities higher than saline pigs. Post-mortem, the MEE-injected larynges revealed statistically greater volume on quantitative 3D ultrasound, and statistically increased expression of neurotrophic factors (BDNF, NGF, NTF3, NTF4, NTN1) on quantitative PCR.

Conclusions/Discussion: Minimally invasive MEE injection appears to establish an early molecular and microenvironmental frame- work to encourage innate RLN regeneration. Longer follow-up is needed to determine if early findings will translate into functional contraction.

Translational/Human Health Impact: With the porcine larynx being comparable in size to that of humans, this study encapsulates an effective translational model for studying unilateral vocal fold paralysis. Herein, we demonstrate the molecular potential of MEEs and show a successful step in preclinical study of this biotherapeutic technique.

 # 15

Poster Title: Exploring the DNA repair mechanism of the APE1/Ref-1 protein

Poster Presenter: Kpenu, Eyram
Poster Presenter Institution: Indiana University School of Medicine

Poster Authors: Eyram Kpenu, Indiana University School of Medicine; Mark R. Kelley, Indiana University School of Medicine; Randall Wireman, Indiana University School of Medicine

Abstract:
Background/Significance/Rationale: Pancreatic Ductal Adenocarcinoma (PDAC) is inherently resistant to therapy and can proliferate under conditions of hypoxia and nutrient deprivation. Innovative approaches against new targets are needed. Redox factor-1 (APE1/Ref-1) is a regulator of multiple transcriptional factors involved in cancer cell signaling through its redox signaling activity. Ref-1 redox status is itself regulated by other redox proteins such as peroxiredoxin (PRDX) and thioredoxin (TRX). Studies have demonstrated an interaction of peroxiredoxin-1 (PRDX1) and Ref-1. PRDX1 is a member of a family of peroxidases comprising six isoforms that differ in their H2O2 scavenging, organelle/conditional expressions, and chaperone activity; yet their relationship with Ref-1 is largely unknown.

Methods: Using siRNA knock-down of PRDX1 ($PRDX1^{KD}$) or TRX (TRX^{KD}) in combination with our second-generation Ref-1 inhibitor APX2014, we explored the PRDX-Ref-1-TRX axis in a human patient PDAC cell line, Pa03c. We then engineered CRISPR/Cas9 PRDX1 knock-out cells ($PRDX1^{KO}$) and tested APX2014.

Results/Findings: We found that both $PRDX1^{KD}$ and TRX^{KD} conditions resulted in significant sensitivity to Ref-1 inhibition. $PRDX1^{KO}$ cells were even more sensitive to Ref-1 inhibition compared to the $PRDX1^{KD}$ cells. Ref-1's second major function as a DNA repair protein apurinic/apyrimidinic

endonuclease was not impacted by PRDX1^{KO}. We measured growth and cell-colony formation and confirmed statistical distinctions. Initial studies with PRDX2 knockdown (PRDX2^{KD}) had no increased effect in combination with Ref-1 inhibition.

Conclusions/Discussion: Our hypothesis is that the activity of Ref-1 and interplaying redox proteins such as PRDX1 in PDAC tumor microenvironment (TME) correlates with resistance to treatment and thus could be a biomarker of response to the currently available standard of care regimens.

Translational/Human Health Impact: The eventual goal is to select the subset of patients who could benefit most from APX compounds, which are currently in clinical development and could be an important addition to the current arsenal of treatments either in the upfront setting or upon failure.

IMPRS

 # 16

Poster Title: Differentiation of Retinal Ganglion Cell Subtypes from Human Induced Pluripotent Stem Cells

Poster Presenter: Kumar, Chaman
Poster Presenter Institution: Indiana University School of Medicine

Poster Authors: Chaman Kumar, Indiana University School of Medicine; Melody Hernandez, Indiana University School of Medicine, Department of Medical and Molecular Genetics, Stark Neurosciences Research Institute; Kang-Chieh Huang, Indiana University School of Medicine; Jason S. Meyer, Indiana University School of Medicine, Department of Medical and Molecular Genetics, Stark Neurosciences Research Institute, Department of Ophthalmology

Abstract:
Background/Significance/Rationale: Intrinsically photosensitive retinal ganglion cells (ipRGCs) are a subset of retinal ganglion cells that respond to light independently from rod and cone photoreceptor input. ipRGCs are non-image forming but are integral for regulating metabolic functions, such as circadian rhythms and pupillary reflexes, through the use of the photopigment melanopsin. However, the developmental processes that lead to the generation of ipRGCs over other subtypes of RGCs are unclear. Additionally, previous studies have suggested that some RGC subtypes, including ipRGCs, are more resilient to disease-associated stressors, yet the mechanisms that confer this increased resilience remain incompletely understood.

Methods: To address these questions, particularly in a human-relevant system, we have focused upon the use of human induced pluripotent stem cells (iPSCs) to assess their ability to give rise to RGCs, with a particular emphasis upon ipRGC differentiation. Cells were initially edited by the CRISPR/Cas9 system to express the Thy1 gene at the Brn3b locus and the tdTomato gene at the melanopsin locus. The former edit allows for the purification of RGCs from retinal organoids derived from iPSCs, while the latter edit allows for the identification of ipRGCs among the broader RGC population. Cells were grown in a directed, stepwise manner following established protocols.

Results/Findings: By immunostaining for cell type specific markers**,** I have documented the different stages of retinal differentiation and provided insight into the mechanisms of ipRGC differentiation.

Conclusions/Discussion: We found that iPSCs can be effectively differentiated into retinal cells, including the formation of 3D retinal organoids. Retinal ganglion cells can be purified and matured in vitro to generate models for optic neuropathies. Within the RGC population, evidence demonstrates the presence of distinct RGC subtypes.

Translational/Human Health Impact: My project will highlight how differentiating iPSCs into functional ipRGCs will allow for more accurate ophthalmological disease modeling in vitro. This process is also essential to study the spatial and temporal characteristics of retinal development that

can inform models of retinogenesis and may be integral for future RGC transplants and disease modeling.

 # 17

Poster Title: Reduced Endocochlear Potential *in vivo* Prevents Hair Cell Degeneration in *Tmprss3*-deficient Mice

Poster Presenter: Libiran, Nicole Bianca
Poster Presenter Institution: Indiana University School of Medicine

Poster Authors: Nicole Bianca Libiran, Indiana University School of Medicine; Ernesto Cabrera, Indiana University School of Medicine; Yuan-Siao Chen, Indiana University School of Medicine; Rick Nelson, Indiana University School of Medicine, Department of Otolaryngology

Abstract:
Background/Significance/Rationale: Transmembrane serine protease 3 (TMPRSS3) is a transmembrane serine protease with proteolytic activity essential for normal auditory function in mice and humans. *Tmprss3*-mutant mice exhibit normal hair cell (HC) development until postnatal day 12 (P12), followed by rapid HC degeneration within 48 hours, resulting in deafness. The HC degeneration temporally correlates with the rapid rise in endocochlear potential (EP) that is required for hearing. This phenotype mirrors other mouse models with defects in genes expressing tight junctions (TJs). Thus, we hypothesize that TMPRSS3 regulates tight junctions and cell death is mediated through high EP.

Methods: Here we investigated the role of EP in *Tmprss3*-deficient mice using *in vivo* experiments. We crossed the *Tmprss3*-mutant mice with *Pou3f4*-mutant mice, which fail to generate EP. Cochlear whole mounts were dissected, fixed, and stained for four groups of mice: wild-type, *Tmprss3*-mutant, *Pou3f4*-mutant, and double-mutant mice. Inner and outer hair cells were quantified within a span of 125 µm and compared between groups.

Results/Findings: We found significant preservation of HCs ($p<0.001$) in double mutant mice with reduced EP compared to *Tmprss3*-mutant mice.

Conclusions/Discussion: HC degeneration in *Tmprss3*-deficient mice is due to endocochlear potential driven K+ toxicity. *Tmprss3*-deficient mice likely have faulty apical TJs that result in leakage of K+ ions from the endolymph to the basolateral side of HCs, leading to HC degeneration. Future research should work to elucidate TMPRSS3's proteolytic target and its mechanism of TJ-related regulation.

Translational/Human Health Impact: These findings have large implications for potential therapeutic approaches in patients with Tmprss3 mutations. For instance, this implies that clinicians can reduce endocochlear potential in humans using a drug like furosemide to buy time before hair cells degenerate. Patients with a partially functional TMPRSS3 have hearing loss at higher frequencies at cochlea's base, thus implicating Tmprss3 gene modulation as a potential gene therapy approach.

 # 18

Poster Title: Intraoperative Cognitive Load in Surgical Training: Eye-Tracking Insights on Trainees and Attending Surgeons

Poster Presenter: Nelson, Alex
Poster Presenter Institution: Indiana University School of Medicine

Poster Authors: Alex Nelson, Indiana University School of Medicine; Nicholas Anton, Indiana University School of Medicine, Department of Surgery; Mohammed Kalantar, Indiana University School of Medicine, Department of Surgery; Ryan Toy, Purdue University, School of Industrial Engineering; Denny Yu, PhD, CPE, Purdue University, School of Industrial Engineering; Dimitrios Stefanidis, Indiana University School of Medicine, Department of Surgery

Abstract:
Background/Significance/Rationale: Cognitive load (CL) is the amount of mental resources required to complete a task and process information in working memory. In a surgical setting, high CL increases errors, decreases attention to critical details, and slows down decision-making, which compromise patient safety. Few studies, however, have measured surgeon CL in the clinical environment using objective measures. The purpose of this study was to use objective eye-tracking methods to measure surgeons' and trainees' intraoperative CL.

Methods: In this pilot, general surgery attendings and residents performed gastrointestinal procedures on the Da Vinci Robot while wearing a mobile eye tracker. The quantitative eye-tracking metrics of average fixation duration (AFD), fixation to saccade (F:S) ratio, and mean pupil size between attending and trainee experimental groups were compared to determine differences in intraoperative CL. Second-by-second eye-tracking metrics were compared between attendings and trainees from two distinct procedures, case 1 and case 2.

Results/Findings: A total of six attending (n = 3) and trainee (n = 3) general surgeons participated. While operating, trainees had a lower AFD (M=0.775, SD= 0.093) compared to attendings (M=0.842, SD=0.152) and lower F:S (M=0.497, SD=0.102) than attendings (M=0.592, SD=0.243). During case 1, trainees had a significantly higher ($p< 0.001$) mean pupil size (M=4.594, SD=0.47) compared to attendings (M=3.584, SD=0.35), and a significantly lower ($p< 0.001$) AFD (Mdn=210) compared to attendings (Mdn=281). During case 2, trainees had a significantly higher ($p< 0.001$) mean pupil size (M=3.615, SD=0.37) and a significantly lower ($p< 0.001$) AFD (Mdn=130) compared to attendings (M=3.576, SD=0.27, AFD: Mdn=130).

Conclusions/Discussion: In this pilot study, we determined eye tracking metrics can be used to objectively detect higher intraoperative CL in trainees compared to attending surgeons.

Translational/Human Health Impact: By measuring CL objectively in the OR, educators can create more effective learning environments for aspiring surgeons and improve patient outcomes.

 # 19

Poster Title: The Potential Tripartite Connection: Alzheimer's Disease, Fracture Healing, and the Gut Microbiome

Poster Presenter: Parker, Reginald
Poster Presenter Institution: Indiana University School of Medicine

Poster Authors: Reginald S. Parker, Department of Orthopaedic Surgery, Indiana University School of Medicine; Will A. Verner, Department of Orthopaedic Surgery, Indiana University School of Medicine;; Murad K. Nazzal, Department of Orthopaedic Surgery, Indiana University School of Medicine; Amy Creecy, Department of Orthopaedic Surgery, Indiana University School of Medicine; Sonali J. Karnik, Department of Orthopaedic Surgery, Indiana University School of Medicine; Rachel J. Blosser, Department of Orthopaedic Surgery, Indiana University School of Medicine; Elizabeth Schott, Department of Orthopaedic Surgery, Indiana University School of Medicine; Alexander C. Harris, Department of Orthopaedic Surgery, Indiana University School of Medicine; Ashlyn J. Morris, Department of Orthopaedic Surgery, Indiana University School of Medicine; Hannah S. Wang, Department of Orthopaedic Surgery, Indiana University School of Medicine; Tyler J. Margetts, Department of Orthopaedic Surgery, Indiana University School of Medicine; Marko Dragisic, Department of Orthopaedic Surgery, Indiana University School of Medicine; Upasana Ganguly, Department of Orthopaedic Surgery, Indiana University School of Medicine; Jill C. Fehrenbacher, Pharmacology and Toxicology, Indiana University School of Medicine; Kathryn D. Fischer, Pharmacology and Toxicology Indiana University School of Medicine; Alexandru Movila, Biomedical Sciences and Comprehensive Care, Indiana University School of Medicine; Adrian L. Oblak, Radiology and Imaging Sciences, Indiana University School of Medicine; Jessica Hathaway-Schrader, Division of Periodontics, Medical University of South Carolina; Melissa A. Kacena, Department of Orthopaedic Surgery, Indiana University School of Medicine, Richard L. Roudebush VA Medical Center,

Abstract:
Background/Significance/Rationale: Alzheimer's disease (AD), fracture healing, and the gut microbiome are interconnected aspects of health that have gained significant research interest. Recent studies suggest gut dysbiosis may play a role in AD pathogenesis, potentially through the gut-brain axis, a bidirectional communication system. Moreover, the gut microbiome's role in bone health could link dysbiosis and fracture risk. Furthermore, research reports have revealed that the brain communicates with bone, termed the bone-brain axis. Despite these insights, the effect of the gut microbiome on fracture healing in AD remains largely unexplored.

Methods: To uncover these connections, our study uses the AD mouse model, 5xFAD. We conducted osteotomies on these mice and analyzed fecal samples that were collected at different timepoints. Fecal samples are being examined via qPCR 16s RNA analysis and 16s rRNA genome sequencing to identify and quantify bacterial phyla. These findings will be linked to both AD progression, gauged through behavior and histological analyses, and fracture healing, quantified using X-ray, mRUST scoring, microCT, and histology.

Results/Findings: Preliminary qPCR data shows differences in the bacterial phylae Bacteroidota and Actinomycetota one-week post-surgery. We will soon analyze other time points to determine if these differences remain significant. Ongoing research will gather endpoint data from other analyses and correlate it to microbiome changes to identify potential connections.

Conclusions/Discussion: We hypothesize that the progression of AD could alter the gut microbiome, potentially affecting fracture healing. This might occur through inflammation pathways triggered by specific gut bacteria. We may identify specific gut bacteria that play critical roles in both fracture healing and AD. We anticipate finding a shift towards pro-inflammatory bacterial phyla in the context of AD progression and during the fracture healing process.

Translational/Human Health Impact: This study could eventually unlock new therapeutic strategies aimed at targeting the gut microbiome to improve bone health, fracture healing, and AD progression in patients.

 # 20

Poster Title: The Detection and Characterization of R-loops on the HPV Genome

Poster Presenter: Sran, Ishanpreet
Poster Presenter Institution: Indiana University School of Medicine

Poster Authors: Ishanpreet Sran, Indiana University School of Medicine; Leny Jose, Indiana University School of Medicine; Marsha DeSmet, Indiana University School of Medicine; Elliot Androphy, Indiana University School of Medicine

Abstract:
Background/Significance/Rationale: Papillomaviruses (PVs) are double-stranded 8 kb DNA viruses that infect mucosal and cutaneous epithelia. The HPV E2 protein is responsible for viral transcription and replication on viral episomes. We hypothesize that viral replication forks collide with nascent viral RNA formed during transcription of viral genes. We predict that these DNA-RNA hybrids (R-loops) composed of three stranded structures occur on replicating and transcriptionally active viral genomes. Our goal is to determine if R-loops occur on viral genomes and to identify the host machinery necessary to resolve these conflicts.

Methods: DNA from CIN612 keratinocyte cell lines (HPV-31) harboring episomal and integrated genomes was isolated, and R-loops were immunoprecipitated and detected with the S9.6 antibody. Next, we tested if HPV E2 interacts with host R-loop resolving proteins such as ZPR1, SMN, and a fragment of SETX 1-667 amino acids using co-immunoprecipitation.

Results/Findings: We detected R-loops on the viral p97 promoter in CIN612 episomal cells, but not integrated cells. We observed that HPV-16 E2 co-immunoprecipitated with ZPR1 and SMN, but not SETX 1-667.

Conclusions/Discussion: During replication, we observed a significant increase of R-loops in episomal cell lines when compared to integrated HPV cell lines. The viral protein E2 may be recruiting host cell factors such as ZPR1 and SMN to resolve viral R-loops.

Translational/Human Health Impact: These preliminary experiments indicate that HPV could be using cellular machinery to resolve R-loops, aiding viral propagation as observed in other viruses such as Cytomegalovirus and Herpes Simplex Virus. This finding can revolutionize our understanding of viral replication and potentially alter the approach of treatment research.

SEED/STEM

 # 21

Poster Title: Observing Morphological Changes in Microglia Cells Treated with LPS and a Potent TAK1 Inhibitor

Poster Presenter: Flores Gonzalez, Daniela
Poster Presenter Institution: Indiana University-Purdue University Indianapolis

Poster Authors: Daniela Flores Gonzalez, North Central High School, Indianapolis, IN; Leander Quiroz, Carleton College, Northfield, MN; Casandra Carrillo, Teri Belecky-Adams, Carleton College, Northfield, MN, Department of Biology, Indiana University-Purdue University Indianapolis

Abstract:
Background/Significance/Rationale: Diabetic retinopathy (DR) is a complication of diabetes mellitus and the leading cause of blindness in working-age adults. Microglia are immune cells present in the CNS that when activated for long periods of time can cause damage to the cell and blindness in patients. TAK1 is a downstream signaling pathway that if inhibited, could become a treatment for DR.

Methods: Microglia cultures were grown on 6-well plates and then treated with 100pM of TAKinib or Vehicle for 24 hours before being treated with 10ng LPS or Vehicle for 1 hour. Cells were fixed with 4% paraformaldehyde. Cells were stained with cell mask orange cytoplasm stain and a nuclear label, Hoechst and imaged on a fluorescent microscope at 40X magnification. Cell morphology in all treatment groups were analyzed to conclude perimeter using ImageJ software.

Results/Findings: Untreated microglia, when compared across all treatment groups, produced a higher degree of significance compared to microglia treatments compared across all groups. LPS-treated microglia combined with another treatment resulted in a higher perimeter compared to untreated, Vehicle, and LPS-treated alone.

Conclusions/Discussion: Since a higher perimeter was observed in DMSO+10ng LPS treatment compared to 100pM TAKinib+10ng LPS treatment, this could indicate that there is a more prominent activation effect on microglia given LPS treatment than when given a TAK1 specific inhibitor. A more thorough quantification of cell morphology is necessary to conclude that cell activation occurs in cells.

Translational/Human Health Impact: The inhibition of TAK1 as a possible treatment for DR is becoming increasingly studied for its ability to control microglia activation. There is also a growing need for more accurate and effective methods for detecting cell activation not only for research but also for diagnosing DR in its earlier stages and preventing a patient's further vision loss.

#22

Poster Title: Neuromuscular Junction Degenerate in Mouse Models of Amyotrophic Lateral Scierosis

Poster Presenter: Aderinwale, Lois Adetutu
Poster Presenter Institution: Brownsburg High School, Class of 2024

Poster Authors: Lois Adetutu Aderinwale, Brownsburg High School; Brian Pierchala, Indiana University School of Medicine

INDIANA CTSI AFFILIATED RESEARCH

 # 23

Poster Title: Unraveling Retinal Phenotypic Changes in a Hyperglycemic Late-Onset Alzheimer's Disease Mouse Model

Poster Presenter: Abhyankar, Surabhi
Poster Presenter Institution: Department of Biochemistry and Molecular Biology, Indiana University School of Medicine

Poster Authors: Abhyankar, Surabhi D., Department of Biochemistry and Molecular Biology, Indiana University School of Medicine, Department of Ophthalmology, Eugene and Marilyn Glick Eye Institute; Luo, Qianyi, Department of Ophthalmology, Eugene and Marilyn Glick Eye Institute; Department of Ophthalmology, Eugene and Marilyn Glick Eye Institute, Stark Neurosciences Research Institute; Hartman, Gabriella D., Department of Ophthalmology, Eugene and Marilyn Glick Eye Institute; Stark Neurosciences Research Institute; Corson, Timothy W, Indiana University, Department of Biochemistry and Molecular Biology, Department of Ophthalmology, Eugene and Marilyn Glick Eye Institute, Stark Neurosciences Research Institute, Department of Pharmacology and Toxicology; Oblak, Adrian L., Stark Neurosciences Research Institute, Department of Pharmacology and Toxicology; Lamb, Bruce T., Stark Neurosciences Research Institute, Department of Pharmacology and Toxicology; Bhatwadekar, Ashay, Department of Biochemistry and Molecular Biology, Indiana University School of Medicine, Department of Ophthalmology, Eugene and Marilyn Glick Eye Institute, Department of Pharmacology and Toxicology

Abstract:
Background/Significance/Rationale: At least 33 million people worldwide have Alzheimer's disease (AD). Apolipoprotein *E4* (*APOE4*) is a key predisposing gene variant in late-onset AD (LOAD) pathophysiology, the most common form of AD. Dementia and cognitive decline are more prevalent in people with diabetes. Diabetes and the *APOE4* variant may interact to exacerbate retinal dysfunction and promote the onset and progression of diabetic retinopathy (DR). We examined visual impairment in *APOE4*-knock-in (LOAD-risk) and *APOE3*-KI (LOAD-neutral) mice, and whether the treatment with a western diet (WD) accelerates the development of DR phenotype.

Methods: *APOE4*-KI and *APOE3*-KI mice were fed either WD or control diet (CD) for six-months. The effect of WD on body weight (BW) and fasting blood glucose was monitored. Retinal structure was assessed using optical coherence tomography (OCT) and fundus photography. Vasculature was visualized by fluorescein angiography (FA). Neural function of retinas was assessed using an electroretinogram (ERG).

Results/Findings: Both WD-treated *APOE4* and *APOE3* mice exhibited increased BW and fasting blood glucose compared to CD-treated *APOE4* and *APOE3* mice. *APOE4* mice showed evidence of reduction of retinal thickness by OCT, largest vein width, and vasculature by FA. *APOE4* CD and WD-treated mice showed increased avascular area and arterial tortuosity compared to *APOE3* mice. Retinal functional testing by ERG demonstrated significant reduction in a-wave and b-wave amplitudes for *APOE4* CD and WD-treated mice.

Conclusions/Discussion: *APOE4* alleles are associated with retinal vascular dysfunction, functional deficits in the retinas, and increased susceptibility to retinal degeneration as compared to *APOE3*

alleles. Vascular changes and neural functional deficits are the earliest indicators of damage in the retina of LOAD-risk mice.

Translational/Human Health Impact: These discoveries shed light on the mechanisms behind retinal dysfunction in a mouse model with a heightened risk of LOAD combined with diabetes and identify potential non-invasive novel biomarkers for AD for diagnosing and monitoring the disease progression.

 # 24

Poster Title: Up and Down Regulation of Aldehyde Expression by External and Internal Mechanisms and their Therapeutic Value in EAE Mice

Poster Presenter: Alford, Anna
Poster Presenter Institution: Purdue University

Poster Authors: Anna Alford, Weldon School of Biomedical Engineering, Center for Paralysis Research, Purdue University; Jonathan Tang, Department of Basic Medical Sciences, College of Veterinary Medicine, Weldon School of Biomedical Engineering, Center for Paralysis Research, Purdue University; Gary Leung, Department of Basic Medical Sciences, College of Veterinary Medicine, Center for Paralysis Research, Purdue University; Melissa Tully, Weldon School of Biomedical Engineering, Center for Paralysis Research, Purdue University, MSTP Program, Indiana University School of Medicine; Riyi Shi, Department of Basic Medical Sciences, College of Veterinary Medicine, Weldon School of Biomedical Engineering, Center for Paralysis Research, Purdue University

Abstract:
Background/Significance/Rationale: Acrolein, a pro-inflammatory aldehyde, has been shown as a critical factor in MS pathology. It has been demonstrated that the acrolein scavenger hydralazine (HZ) can suppress acrolein as well as alleviate motor deficits in a mouse model of MS, experimental autoimmune encephalomyelitis (EAE). We therefore hypothesize that the up and down regulation of aldehyde dehydrogenase 2 (ALDH2), an enzyme capable of metabolizing aldehydes, could instigate behavioral changes in EAE.

Methods: We used three acrolein scavengers to mitigate behavioral deficits in EAE mice. The levels of acrolein and myeloperoxidase (MPO) were measured by immunohistochemistry. The mRNA of TRPA1 was assessed using RT-PCR. Motor function was determined using a 5-point system; mechanical hyperreflexia was evaluated using von Frey filaments. ALDH2 was down-regulated through a genetically modified mouse model, and activated using Alda-1, an ALDH2-activator.

Results/Findings: Application of acrolein scavengers decreased motor and sensory deficits in EAE mice when applied post-induction. Particularly, HZ could alleviate motor deficits when applied following symptom emergence. This additionally corresponded to a reduction in both acrolein and inflammatory markers in EAE mice.

Furthermore, we observed that ALDH2*2 mice not only display more severe behavioral deficits, but also heightened levels of acrolein, inflammation, and demyelination markers in EAE compared to wild-type mice. In addition, treatment with Alda-1, an activator of ALDH2, can lower acrolein and inflammation in EAE.

Conclusions/Discussion: We have shown that three structurally distinct acrolein scavengers can behavioral and immunohistochemical deficits in EAE mice. Additionally, up- and down-regulation of ALDH2 corresponded to marked behavioral and biological changes in EAE, underscoring the critical involvement of acrolein in EAE pathogenesis.

Translational/Human Health Impact: These findings further consolidate the critical role of aldehydes in the pathology of EAE and its mechanisms of regulation. This is expected to reinforce and expand the possible therapeutic targets of anti-aldehyde treatment to achieve neuroprotection through both endogenous and exogenous manners.

 # 25

Poster Title: Using an end-to-end deep learning model in older adults with MCI to identify AD risk factors on chromosome 19 that exacerbate cognitive decline

Poster Presenter: Bae, Jinhyeong
Poster Presenter Institution: Indiana University – Purdue University, Indianapolis

Poster Authors: Jinhyeong Bae, Indiana University School of Medicine; Kwangsik Nho, Indiana University School of Medicine; Andrew J. Saykin, Indiana University School of Medicine; Angelina Polsinelli, Indiana University School of Medicine; Dustin Hammers, Indiana University School of Medicine; Kelly Nudelman, Indiana University School of Medicine; Valentin T. Pentchev, Indiana University Network Sciences Institute; Liana G. Apostolova, Indiana University School of Medicine

Abstract:
Background/Significance/Rationale: Research into genetic mapping possesses strong potential to inform the conversion from mild cognitive impairment (MCI) to Alzheimer's disease (AD). We extended our previously developed novel deep learning framework to analyze MCI participants. The top 35 strongest AD-risk factors and their chromosomal risk impact score (CRIS), which indicates each SNP's contribution in AD occurrence, determined by the model were utilized to characterize participants with MCI who were likely to convert to AD dementia (MCI-C) vs not (MCI-NC) over 3 years.

Methods: The highest CRIS-ranked 35 AD-risk SNPs were utilized to differentiate MCI-C (n=203) and MCI-NC (n=213) participants enrolled in the Alzheimer's Disease Neuroimaging Initiative. We predicted the rate of cognitive decline (memory, language, executive, and visuospatial function) in MCI using multiple regression with 5 SNPs' CRIS as predictors. Lastly, we performed computational CRISPR to demonstrate the impact of SNP rs56131196 (APOC1), the strongest AD-risk SNP, in MCI-C participants.

Results/Findings: SNPs in APOC1, TOMM40, and NECTIN2 showed significantly stronger CRIS for MCI-C than MCI-NC participants ($p<0.001$). All regression models predicting the rate of cognitive decline were significant ($p<0.001$). The r2-adjusted values were 0.279, 0.163, 0.098, and 0.178, for the memory, language, executive, and visuospatial models, respectively. MCI-C participants with the substitution of AA or AG genotype with GG were predicted to have a significantly lower likelihood of AD occurrence than those without substitution ($p<0.001$).

Conclusions/Discussion: Our deep learning model trained on AD and CU participants successfully determined SNPs that predict conversion from MCI to AD dementia.

Translational/Human Health Impact: Genetic screening based on regression models could be useful for patient selection in clinical trials with disease-modifying therapies. Furthermore, our computational CRISPR simulations in MCI-C confirm the significant promise of CRISPR for precision medicine. In vitro and in vivo animal and human studies exploring nucleotide-level substitutions are warranted to fully appreciate their role in translational neuroscience.

 # 26

Poster Title: The profibrotic phenotype in *COL4A3* mouse model of Alport Syndrome

Poster Presenter: Belamkar, Ameya
Poster Presenter Institution: Indiana University Bloomington

Poster Authors: Ameya Belamakar, Indiana University, Bloomington; Qianyi Luo, Department of Ophthalmology, Eugene and Marilyn Glick Eye Institute, Indiana University School of Medicine; Neha Mahajan, Department of Ophthalmology, Eugene and Marilyn Glick Eye Institute, Indiana University School of Medicine; Surabhi Abhyankar, Department of Ophthalmology, Eugene and Marilyn Glick Eye Institute, Indiana University School of Medicine; Bryce Jones, Department of Biochemistry and Molecular & Cellular Biology, Georgetown University Medical Center; Padmanabhan Pattabiraman, Department of Ophthalmology, Eugene and Marilyn Glick Eye Institute, Indiana University School of Medicine; Moshe Levi, Department of Biochemistry and Molecular & Cellular Biology, Georgetown University Medical Center; Ashay D. Bhatwadekar, Department of Ophthalmology, Eugene and Marilyn Glick Eye Institute, Indiana University School of Medicine

Abstract:
Background/Significance/Rationale: The mechanism of ocular pathology in Alport Syndrome (AS) is poorly understood. This study characterizes inflammatory and fibrotic changes between the eyes of wild-type (WT) and *COL4A3* knockout (KO) mice.

Methods: Col4a3^{tm1Dec} mice were euthanized at 25 weeks, and eyes were processed for paraffin sectioning. Sections were stained with 1:200 anti-α3 (IV) antibody with 1:2000 secondary antibody to evaluate the localization of the α3 (IV) in WT eyes. Staining for inflammatory markers included 1:200 anti-TGF-ß2 with 1:500 secondary antibody, 1:100 anti-CTGF with 1:800 secondary antibody, and 1:100 anti-ß-catenin with 1:800 secondary antibody. All sections were also stained with DAPI. Photomicrographs visualizing protein distribution were taken under a confocal microscope. mRNA levels of pro-fibrotic genes were assessed using real-time quantitative PCR (qPCR).

Results/Findings: Retinal staining of the α3 (IV) protein revealed no positive staining, while corneal staining showed positive staining in Descemet's membrane. An upregulation of TGF-ß2 was observed in both the retina and cornea. While there was an increase in CTGF and ß-catenin in the cornea, there was no observable difference in the retina.
qPCR showed a significant increase in the levels of FSP1, αSMA, Col1a1, SNAIL, and SLUG in KO retinas. There was a moderate increase in FSP1 and SLUG in the corneas of KO mice.

Conclusions/Discussion: The observed increase in inflammatory cytokines in the corneas of KO mice may be due to degradation of corneal endothelium integrity in KO mice caused by an absence of the α3 (IV) protein. However, a similar increase in the transcription of pro-fibrotic genes was not clearly observed in KO corneas. Surprisingly, there was a clear trend in increasing levels of pro-fibrotic mRNA in the retina despite finding no α3 (IV) protein in WT retinas.

Translational/Human Health Impact: Ocular abnormalities are often observed in patients with AS. Yet, the pathology causing these abnormalities is not currently well understood. This study aims to evaluate the role of inflammation and fibrosis in the ocular pathogenesis of AS.

 # 27

Poster Title: Age-associated inflammatory response changes after repeated closed-head traumatic brain injury

Poster Presenter: Brumett, Andrew
Poster Presenter Institution: Indiana University Purdue University Indianapolis

Poster Authors: Andrew Brumett, Indiana University Purdue University Indianapolis; Tyler Nguyen, Stark Neuroscience Research Institute, Department of Anesthesia, Indiana University School of Medicine, Richard L. Roudebush VA Medical Center; Natalie Nguyen, Department of Anesthesia, Indiana University School of Medicine, Richard L. Roudebush VA Medical Center; Fletcher A. White, Stark Neuroscience Research Institute, Department of Anesthesia, Indiana University School of Medicine, Richard L. Roudebush VA Medical Center

Abstract:
Background/Significance/Rationale: Mild traumatic brain injury (mTBI) is a common neurological injury and is associated with central and peripheral inflammation. A principal mechanism of this inflammation is the NLRP3 inflammasome cascade. This activated caspase-1 dependent neuroinflammation is often associated with chronic nociplastic pain states. Aging may be a major contributor to the worsening of clinical outcomes.

Methods: To model the effect of aging, a luciferase-based caspase-1 reporter mouse line was used to assess inflammation post-repeated mTBI in vivo. Two groups young (4-6 month) (n=4) and aged (18-20 months) (n=4) animals underwent a skull-thinning procedure and repetitive closed-head control impact (CCI). In vivo bioluminescence imaging was utilized to monitor caspase-1 mediated inflammation. Three injuries, each separated by 1 week, were performed and each followed by IVIS imaging, von Frey, and Grimace behavioral assays. Three timepoints were also observed after the third injury to assess the chronic nature of the inflammation.

Results/Findings: The aged animals showed a significant increase in caspase-1 activation at the 3 days after 3rd injury timepoint in both the brain and paw regions compared to young animals. There were no significant differences in either behavioral assay between the young and aged animals and any timepoint.

Conclusions/Discussion: This study will be repeated with increased group sizes to increase predictive effect and decrease standard errors.

Translational/Human Health Impact: Understanding the role of inflammasome-caspase 1 in TBI pathophysiology will enable more effective therapeutic strategies in treating post-traumatic pain.

 # 28

Poster Title: Elucidating Abnormal Myeloid-Mechanical Interactions in Glioblastoma

Poster Presenter: Burchett, Alice
Poster Presenter Institution: University of Notre Dame

Poster Authors: Alice Burchett, University of Notre Dame; Meenal Datta, University of Notre Dame

Abstract:
Background/Significance/Rationale: The glioblastoma microenvironment is highly immunosuppressive and features growth-induced compressive solid stress. Macrophages can make up nearly half of the tumor bulk and contribute to immunosuppression, making them an attractive therapeutic target. This work aims to understand how solid stress affects macrophage phenotype, and how macrophages in turn contribute to solid stress.

Methods: To assess the macrophage response to compression, a weight is applied to the cells to apply 0.15 kPa of solid stress, within the range found in brain tumors. To determine their contribution to solid stress, macrophages are embedded in a 1% agarose gel, where they proliferate to form spheroids, displacing the surrounding gel. The magnitude of stress generated from this displacement can be quantified either by imaging the displacement of embedded fluorescent microbeads, or by importing a 3D model of the spheroid to COMSOL to obtain a simulated stress field.

Results/Findings: Preliminary results suggest that compression of macrophages alters the expression of canonical polarization markers. Macrophages embedded in agarose proliferate and generate solid stress. Further investigation is required to determine the functional macrophage response to solid stress, and to quantify macrophages' ability to generate stress in different conditions.

Conclusions/Discussion: This work suggests that macrophages can sense and respond to the magnitude of solid stress that is found in brain tumors, and also that macrophages may themselves be responsible for some of this stress. Further understanding of the reciprocal regulation of macrophages and solid stress may highlight new therapeutic approaches for glioblastoma.

Translational/Human Health Impact: Understanding and overcoming immunosuppression could tip the balance towards a successful anti-tumor immune response and improved patient outcomes for glioblastoma as well as other solid tumors. These in vitro models of solid stress can also be tuned for other tumor and disease types and used to screen drugs for their impact on the mechanical tumor microenvironment.

 # 29

Poster Title: Sex-dependent Effects of Alcohol and Oxycodone Polysubstance Use

Poster Presenter: Chen, Yueyi
Poster Presenter Institution: Purdue University

Poster Authors: Yueyi Chen, Department of Basic Medical Sciences, Purdue University; Salvador Huitron Resendiz, The Scripps Research Institute, Animal Models Core, La Jolla, CA; Amanda Roberts, The Scripps Research Institute, Animal Models Core, La Jolla, CA; Adam Kimbrough, Department of Basic Medical Sciences, Purdue University

Abstract:
Background/Significance/Rationale: This study aimed to investigate concurrent polysubstance use disorder (PUD) by designing two preclinical models involving alcohol and oxycodone. We hypothesized that withdrawal from one substance would lead to increased intake of the other.

Methods: To study alcohol withdrawal on oxycodone self-administration, mice were exposed to chronic intermittent ethanol vapor to induce alcohol dependence, while a control group remained alcohol naïve. Both groups experienced two weeks of intravenous oxycodone self-administration sessions during alcohol withdrawal of mice experienced CIE.
To study oxycodone withdrawal on alcohol intakes, mice were made oxycodone-dependent through i.p. injections, while a control group received saline injections. During oxycodone withdrawal, the mice had access to alcohol and water for 2-hour drinking sessions.

Results/Findings: The results from the first study showed a significant increase in oxycodone self-administration during the last three sessions in male mice from the alcohol withdrawal group compared to control group. However, female mice did not exhibit the same increase. In the second study, female mice injected with oxycodone showed a significant increase in alcohol intake compared to the control group. However, male mice did not demonstrate the same effect.

Conclusions/Discussion: These findings establish preclinical models of concurrent alcohol and oxycodone use in mice. Interestingly, the effects of withdrawal and substance modulation differed between males and females. Males appeared to be more sensitive to alcohol withdrawal's influence on oxycodone intake, while females showed greater sensitivity to oxycodone withdrawal's impact on alcohol consumption.

 # 30

Poster Title: Gene Co-Expression Network Analyses in Mild Cognitive Impairment

Poster Presenter: Dorsant-Ardon, Valerie
Poster Presenter Institution: Indiana University Purdue University Indianapolis

Poster Authors: Valerie Dorsant-Ardon, Indiana University School of Medicine; Apoorva Bharthur Sanjay, Indiana University School of Medicine; Rion Brattig Correia, Indiana University Network Sciences Institute; Luis M Rocha, Indiana University Network Science Institute; Liana G Apostolova, Department of Neurology, Indiana University School of Medicine

Abstract:

Background/Significance/Rationale: Multiomic data analysis has been extensively developed in recent years. Particularly, microarray data can be used as biomarkers of disease of progression specially in pathologies as cancer, autoimmunity and others. This modality of data analysis can also be employed in other multifactorial diseases as Alzheimer's disease specially the progression from normal cognition to mild cognitive impairment and finally to dementia. These genes work in intricate relationship with each other. Thus, the establishment of computational gene interaction networks shows the complexity of the biological systems but increases the complexity of the analysis, for this reason, the removal of redundant edges leaves a network backbone revealing important driver nodes that are essential for the observed interactions, reducing the number of genes of interest and narrowing potential diagnostic or therapeutic targets.

Methods: We used data from the ImaGENE study and the Weighted gene co-expression network analysis (WGCNA) pipeline to analyze complex gene-gene interactions of mRNA transcripts obtaining hierarchical clustering of genes and eigengenes in a sample of 160 individuals. The backbones were obtained using the shortest path computation and Gene ontology was used to classify processes associated with these genes.

Results/Findings: We identified 42 hubs of differentially expressed genes and we analyzed the group with the strongest association with amnestic MCI phenotype ($r=0.45$, $pfdr<0.0001$). This cluster consisting of 46 genes was further classified according to function and interactions with other nodes in the backbone identifying processes like Calcium signaling, Nucleotide excision repair, Fatty acid metabolism among others.

Conclusions/Discussion: There is an identifiable difference in gene expression in individuals with MCI compared to normal controls, the analysis of the backbone of the gene hubs allowed to reduce the number of genes of interest.

Translational/Human Health Impact: This approach can help to elucidate important biological interactions, potential therapeutic targets and could eventually be used as risk factors markers for the development of MCI and AD.

 # 31

Poster Title: Out of Sight, Out of Mind: Using visual perception to probe subtle effects of mild traumatic brain injury on cortical physiology

Poster Presenter: Frazier, Elizabeth
Poster Presenter Institution: Purdue University

Poster Authors: Elizabeth Frazier, Purdue University; Anne Sereno, Purdue University; Maria Dadarlat, Purdue University

Abstract:
Background/Significance/Rationale: Approximately 75% of traumatic brain injuries are mild (mTBI). mTBIs often cause protracted cognitive and behavioral symptoms without discernible cortical damage, posing diagnostic and monitoring challenges. Previous work has shown that mTBIs frequently lead to visual deficits and changes in cortical physiology but has failed to relate the two. Our objective is to use a murine mTBI model to study how post-mTBI changes in visual perception relate to physiological dysfunction and long-term deficits.

Methods: We trained head-fixed C57BL/6 mice on a two-alternative forced choice (2AFC) task involving wheel-turn responses to indicate global motion perception in random dot kinematograms (RDK). We modulated task difficulty by varying RDK coherence. Once mice achieve proficiency, we will acutely record cortical activity using microelectrode arrays during 2AFC task performance. Finally, we validated parameters for inducing mTBI via a controlled cortical impact (CCI). We assessed injury severity through observations of skull cracking and cortical hematoma. Future steps will administer mTBI to trained mice and subsequently replicate the electrophysiology protocol.

Results/Findings: A pilot group of mice (n = 3) demonstrated rapid learning in the 2AFC task, exceeding chance within five sessions. Mice achieved greater accuracy on higher global motion coherence trials but showed no significant reaction time differences. Selected CCI parameters (3 m/s speed, 0.5 mm depth, and 180 ms dwell time) produced the desired mild injury without anatomical damage. Further behavior testing will validate injury severity.

Conclusions/Discussion: Preliminary psychometric data suggests mice can quickly and accurately learn to report their global motion perception. Further, upon integration of this task with electrophysiology, we can obtain concurrent evaluations of behavior and cortical physiology.

Translational/Human Health Impact: Linking neural circuit dysfunction and visual acuity after mTBI allows estimation of human physiological damage via simple behavioral tasks. Success would provide an accessible, cost-effective tool to improve diagnosis and rehabilitation of patients with conventionally undetectable cortical injuries.

 # 32

Poster Title: Diffusion magnetic resonance imaging and gene expression profiles during postnatal mouse brain development

Poster Presenter: Han, Xinyue
Poster Presenter Institution: Indiana University

Poster Authors: Xinyue Han, Department of Radiology and Imaging Sciences, Indiana University; Nian Wang, Department of Radiology and Imaging Sciences, Indiana University, Stark Neurosciences Research Institute, Indiana University

Abstract:
Background/Significance/Rationale: The development of brain is a highly complex process that are orchestrated by the expression of numerous genes. Each distinct region of the brain exhibits unique

transcriptome patterns that undergo dynamic changes throughout development, reflecting the progressive specialization of structures and functions. These spatio-temporal patterns coordinate the microstructural transformations occurring in the brain. Diffusion tensor imaging (DTI) is the most common approach for investigating brain microstructures based on the water diffusion properties.

Methods: In this study, we aimed to explore the correlation between DTI metrics and the spatio-temporal profiles of gene expression. We first conducted diffusion magnetic resonance imaging (dMRI) on wild-type mice at postnatal P4 and P14. Next, we extracted DTI metrics— axial diffusivity (AD), fractional anisotropy (FA), mean diffusivity (MD), and radial diffusivity (RD)—from each mouse using the diffusion tensor model. We selected 11 distinct regions-of-interest (ROIs) from DTI analysis. Subsequently, we analyzed spatio-temporal gene expression profiles by using expression density data of 2002 genes of interest at P4 and P14 from these 11 brain regions. Lastly, we statistically examined the correlation of DTI metrics with the gene expression density data.

Results/Findings: We found that AD, FA, and MD exhibited decreasing values only in the "telencephalic vesicle" region from P4 to P14, while the other regions showed increasing values. As for RD, the "rostral secondary prosencephalon" and "prepontine hindbrain" regions had constant values while the others had increasing values. By using partial least squares (PLS) regression, we identified the first two PLS components that are negatively correlated to DTI.

Conclusions/Discussion: We concluded that the brain tissue diffusion changes captured by DTI during postnatal development are associated with unique spatio-temporal gene expression profiles.

Translational/Human Health Impact: This research contributes to our understanding of brain development and provides potential avenues for investigating neurodevelopmental disorders and neurodegenerative diseases using non-invasive imaging techniques.

 # 33

Poster Title: A Proteomics Based Approach for Material Selection in a Model of the Pre-Metastatic Niche

Poster Presenter: Howard, Madison
Poster Presenter Institution: Purdue University

Poster Authors: Madison Howard, Weldon School of Biomedical Engineering, Purdue University; Evelyn Nonamaker, Weldon School of Biomedical Engineering, Purdue University; Luis Solorio, Weldon School of Biomedical Engineering, Purdue University, Purdue Center for Cancer Research, Purdue University

Abstract:
Background/Significance/Rationale: Fibronectin (FN) is an essential extracellular matrix protein commonly used in tissue engineered models due to its attractive cell attachment properties. FN has been found to increase during pre-metastatic niche formation, making it of particular interest for use in *in vitro* models. Our lab has developed various breast cancer pre-metastatic niche models but found varying levels of fibrillar formation across different commercial brands of FN, thereby potentially altering the efficacy of the model.

Methods: Here, we compared five commercially available human-derived FN products used for cell culture. We evaluated fibrillar FN formation and coating efficiency on 3D SU-8 scaffolds using confocal microscopy. Proteomic analysis was performed on each product to determine the overall protein composition and peptide expression levels for the FN1 gene.

Results/Findings: We found only two of the commercial brands analyzed (Corning and Sigma Aldrich) formed FN fibrils on the scaffolds and our proteomic analysis revealed all the brands had unique compositional signatures. EMD showed high levels of blood clotting proteins, while Advanced Biomatrix had upregulated levels of immune response proteins. Examination of amino acid sequence domains demonstrated domains associated with fibrillogenesis were significantly upregulated in Sigma and Corning.

Conclusions/Discussion: These data indicate the choice of commercial FN products could affect how well *in vitro* models mimic the pre-metastatic niche. Future work will compare FN secreted by human lung fibroblasts and Ca1h breast cancer cells to the commercial products to determine which product most accurately represents the pre-metastatic niche.

Translational/Human Health Impact: Metastasis is the single greatest driver of breast cancer related mortalities, where the five-year survival rate drops almost 75% when the disease progresses into a metastatic state. There is a critical need to model the breast cancer pre-metastatic niche to probe how cancer cells remodel their environment and how the extracellular matrix (ECM) affects cancer cell growth and drug sensitivity. To develop this model, we must first determine which materials, including FN, are most representative of the pre-metastatic niche. Our work will aid researchers in their material selection process and help ensure the models being produced are as physiologically relevant as possible and can be used to help create better treatments for patients.

 # 34

Poster Title: Associations of GFAP, NfL, Aβ42/40, and pTau231 with global cognition in LEADS

Poster Presenter: Kostadinova, Ralitsa
Poster Presenter Institution: Indiana University School of Medicine

Poster Authors: Ralitsa Kostadinova, Indiana University School of Medicine; Dustin B. Hammers, Indiana University School of Medicine; Paige E. Logan, Indiana University School of Medicine; Mohit K. Manchella, Indiana University School of Medicine, University of Southern Indiana; Sára Nemes, Indiana University School of Medicine; Anne M. Fagan, Washington University in St. Louis School of Medicine; Tatiana M. Foroud, Indiana University School of Medicine; Kaj Blennow, The Sahlgrenska Academy, University of Gothenburg; Henrik Zetterberg, The Sahlgrenska Academy, University of Gothenburg; Joel H. Kramer, University of California, San Francisco; Paul S. Aisen, University of Southern California; Maria C. Carillo, Alzheimer's Association; Gil D. Rabinovici, The Sahlgrenska Academy, University of Gothenburg; Bradford C. Dickerson, Massachusetts General Hospital, Harvard Medical School; Liana G. Apostolova, Indiana University School of Medicine; Jeffrey L. Dage, Indiana University School of Medicine

Abstract:

Background/Significance/Rationale: Alzheimer's disease (AD) biomarkers have been used to identify the presence of pathology. While previous research has evaluated plasma pTau231 and its associations with cognition, little to none of this research has focused on early-onset AD (EOAD) populations. Here we investigate how select plasma biomarkers are associated with global cognitive measures in early-onset cognitive impairment.

Methods: The current sample included 367 Longitudinal Early-Onset AD Study (LEADS) participants (aged 41 to 65) categorized as amyloid PET-positive EOAD, amyloid PET-negative EOnonAD, or cognitively normal (CN). Each participant had baseline global cognitive (Mini-Mental State Examination [MMSE], Montreal Cognitive Assessment [MoCA], Clinical Dementia Rating Scale sum of boxes [CDR-SB], and ADAS-Cog13) and plasma biomarker assessments (Simoa-HDx N4PE kit: Aβ42/40, phosphorylated Tau [pTau231], Neurofilament light protein [NfL], and glial fibrillary acidic protein [GFAP]). Partial correlations were used to check for associations with cognitive performance controlling for age, sex, and years of education. Fisher r-to-z transformations were conducted to compare the performance across diagnostic groups.

Results/Findings: Partial correlations in the pooled sample showed moderate associations between cognition and plasma pTau231, GFAP and NfL (r=.42-.50, p<.001) and weaker associations with Aβ42/40 (r=.25-.33, p<.001). When split into diagnostic groups, the NfL and GFAP correlations were significant in EOAD and EOnonAD only. The pTau231 correlations were significant only in EOAD. Aβ42/40 correlations were non-significant within specific diagnostic groups. No differences were observed in the magnitude of the cognitive and biomarker associations between EOAD and EOnonAD samples (ps>.05).

Conclusions/Discussion: As expected, the neurodegenerative biomarkers pTau231 and NfL showed stronger association with cognition compared to the marker for brain amyloidosis (Aβ42/40). The nonspecific markers for neurodegeneration (NfL) and brain astrogliosis (GFAP) showed associations in both EOAD and EOnonAD while the markers specific to AD were only significant in EOAD.

Translational/Human Health Impact: Plasma biomarkers show great promise for future AD diagnosis and monitoring.

 # 35

Poster Title: Community drug checking in a restrictive regulatory environment: recovery of drugs from used fentanyl test strips

Poster Presenter: Lieberman, Marya
Poster Presenter Institution: University of Notre Dame

Poster Authors: Heather Whitehead, Department of Chemistry and Biochemistry, University of Notre Dame; Warnakulasuriya Thilini Hirudini Fernando, Department of Chemistry and Biochemistry, University of Notre Dame; Joanne Cogdell, Naxos Neighbors LLC; Marya Lieberman, Department of Chemistry and Biochemistry, University of Notre Dame

Abstract:

Background/Significance/Rationale: The rise in opioid overdose deaths across Indiana highlights the importance of monitoring the drug supply at the community level. There are significant barriers, such as regulations that prevent people from bringing illicit drugs to clinics for drug checking. SAMHSA and CDC have both recommended wider use of immunoassay test strips for drug checking, and in 2022, over 8 million fentanyl test strips were sold to harm reduction organizations.

Methods: This poster describes detection of drugs from used fentanyl test strips. The strips were used to test a solution containing twenty-one drugs (including fentanyl) at 5000 ng/mL levels. All strips gave positive results for fentanyl. The used strips were dried, stored at room temperature for a week to simulate normal delays in getting samples to the lab, and soaked in a water/methanol solution to recover residual drugs from the strips. The solutions were then analyzed by tandem mass spectroscopy using a validated protocol.

Results/Findings: All 21 drugs were recovered in quantifiable amounts from three different batches of test strips. Several drugs showed partial degradation during storage (eg, heroin to 6-monoacetylmorphine).

Conclusions/Discussion: Used fentanyl test strips contain a tremendous amount of information about the drug supply that is literally being thrown away in the trash. This method of drug checking could be implemented in restrictive regulatory environments.

Translational/Human Health Impact: This project was funded through the CTSI Trailblazer program in August of 2023. Naxos Neighbors will collaborate with harm reduction and substance use treatment centers to train people who use drugs and people recently in recovery to use fentanyl, benzodiazepine, and xylazine test strips at home. We will evaluate knowledge, attitudes, and practices related to the test strips to see if our training process is effective. Participants will be asked to return their used FTS for mass spec analysis, with anonymous results from the test strips and the LCMS analysis shared with stakeholders. We would ultimately like to expand this program to cover the other 83 counties in Indiana that restrict drug checking at clinical sites.

 # 36

Poster Title: Associations of plasma GFAP, NfL, and p-tau231 with early-onset Alzheimer's Disease pathology

Poster Presenter: Logan, Paige
Poster Presenter Institution: Indiana University School of Medicine

Poster Authors: Paige E. Logan, Indiana University School of Medicine; Jeffrey L. Dage, Indiana University School of Medicine; Dustin B. Hammers, Indiana University School of Medicine; Mohit K. Manchella, Indiana University School of Medicine; Ani Eloyan, Brown University, Providence; Nidhi S. Mundada, University of California, San Francisco; Renaud La Joie, University of California, San Francisco; Leonardo Iaccarino, University of California, San Francisco; Anne M. Fagan, Washington University School of Medicine; Tatiana M. Foroud, Indiana University School of Medicine; Henrik Zetterberg, The Sahlgrenska Academy at the University of Gothenburg; Kaj Blennow, The Sahlgrenska Academy at the University of Gothenburg; Robert A. Koeppe, University of Michigan; Paul Aisen,

University of Southern California, San Diego; Maria C. Carrillo, Alzheimer's Association; Gil D. Rabinovici, University of California, San Francisco; Bradford C. Dickerson, Harvard Medical School Massachusetts General Hospital; Liana G. Apostolova, Indiana University School of Medicine

Abstract:

Background/Significance/Rationale: Increased levels of glial fibrillary acidic protein (GFAP), neurofilament light (NfL), and phosphorylated tau 231 (p-tau231) in plasma have been associated with late-onset Alzheimer's Disease (AD). The impact of these biomarkers in early-onset AD (EOAD) is unclear and the novel plasma biomarker, p-tau231, has not been studied in this population. We aimed to demonstrate the effect of each biomarker on EOAD pathology by investigating their associations with amyloid burden, tau burden, and gray matter density (GMD).

Methods: 183 EOAD participants from the Longitudinal EOAD study were included. Voxel-wise multiple linear regression models of amyloid PET, tau PET, and T1-weighted MRI images yielded statistical maps with GFAP, NfL, or p-tau231 as predictors. Covariates were hierarchically added: Model 1: age, sex; Model 2: age, sex and APOE-ε4; Model 3: age, sex, APOE-ε4 and MMSE.

Results/Findings: Higher levels of GFAP, NfL, and p-tau231 were significantly associated with greater amyloid burden and tau burden. Higher levels of GFAP and NfL were also significantly associated with lower GMD. No significant associations were found for p-tau231 and GMD (Figures 1, 2 & 3). When controlling for APOE-ε4 carrier status, the effect of GFAP on amyloid burden was no longer significant (Figure 1). After additionally controlling for MMSE, the effects of NfL and p-tau231 on amyloid burden were no longer significant, while the effects of all three biomarkers on tau burden were reduced but remained significant. In terms in of GMD, the effect of NfL survived correction for dementia severity, while the effect of GFAP did not.

Conclusions/Discussion: These results suggest that all three plasma biomarkers show stronger associations with neurodegeneration (cortical atrophy and/or tau burden) than with amyloid burden. Future work should investigate longitudinal associations and the mediational role of APOE-ε4 and dementia severity.

Translational/Human Health Impact: This study highlights the importance of plasma biomarkers for AD diagnosis and disease monitoring.

 # 37

Poster Title: Multi-omics approach to study novel genes and pathways affected in Miller-Dieker Syndrome

Poster Presenter: Mahendran, Gowthami
Poster Presenter Institution: University of Notre Dame

Poster Authors: Gowthami Mahendran, University of Notre Dame; Kurtis Breger, University of Notre Dame; Philip J. McCown, University of Notre Dame; Jacob P. Hulewicz, University of Notre Dame; Jessica A. Brown, University of Notre Dame

Abstract:

Background/Significance/Rationale: Miller-Dieker Syndrome (MDS) is a neurogenetic condition resulting from a heterozygous deletion of MDS locus genes. Often MDS patients die in utero, but children who are born display lissencephaly, neurological disorders, epilepsy etc. Generally, the life expectancy is related to the severity of the lissencephaly. Hence, understanding the MDS pathogenesis linked to various pathways could be useful in therapeutics.

Methods: To better understand MDS at the molecular level, we utilized BJ (healthy) and GM06097 (MDS patient) cells. RNA-seq (transcriptomics) and tandem mass spectrometry (proteomics) were performed to analyze gene expression alterations in MDS.

Results/Findings: At the RNA level, significant up (1286) and downregulated (1515) genes in GM06097 cells were analyzed using Ingenuity Pathway Analysis (IPA), which suggested suppressed synaptogenesis and enhanced cardiac hypertrophy. At the protein level, significant up (213) and downregulated (237) genes in GM06097 cells have roles in synaptogenesis, skeletal system, and organ development. Among the differentially expressed RNAs and proteins, several genes (mettl16, camk2b, bex1, nrxn3, gabbr2, stx1a) are linked to nervous system development and phenotypic features reported in MDS patients. Specifically, mettl16 (methyltransferase like protein-16) is a gene located within the MDS locus that functions as an m6A writer protein. It showed reduced RNA and protein level expression at ~50% in MDS cells. Western blots validated significantly altered proteins in our proteomics results.

Conclusions/Discussion: Our multi-omics study proposes a significant overlap between the altered pathways identified in MDS and other metabolic and cellular pathways at the RNA and protein levels with associated genes and proteins. This observation implied that MDS patients have higher susceptibility to cancer and different organismal injuries.

Translational/Human Health Impact: Hence, our study will pave the way for understanding the implication of genes related to MDS, to help identify therapeutic biomarkers against MDS.

 # 38

Poster Title: Sex-associated differences in plasma and cerebrospinal fluid biomarkers in Early-onset Alzheimer's disease

Poster Presenter: Nemes, Sára
Poster Presenter Institution: Indiana University School of Medicine

Poster Authors: Sára Nemes, Neurology, Indiana University School of Medicine; Paige E. Logan, Neurology, Indiana University School of Medicine; Jeffrey L. Dage, Neurology, Indiana University School of Medicine; Anne M. Fagan, Neurology, Washington University School of Medicine; Dustin B. Hammers, Neurology, Indiana University School of Medicine; Mohit K. Manchella, Harvard School of Medicine; Ani Eloyan, Biostatistics, School of Public Health at Brown University; Ralista V. Kostadinova, Neurology, Indiana University School of Medicine; Tatiana M. Foroud, Medical & Molecular Genetics, Indiana University School of Medicine; Henrik Zetterberg, Psychiatry and Neurochemistry, University of Gothenburg; Robert A. Koeppe, Radiology, University of Michigan; Paul S. Aisen, Neurology, Keck School of Medicine USC; Maria C. Carrillo, Alzheimer's Association; Gil D. Rabinovici, Neurology, UCSF

School of Medicine; Bradford C. Dickerson, Neurology, Harvard School of Medicine; Liana G. Apostolova, Neurology, Indiana University School of Medicine

Abstract:
Background/Significance/Rationale: Female-sex is associated with greater atrophy, amyloid and tau burden in Early-onset Alzheimer's Disease (EOAD) in the Longitudinal EOAD Study (LEADS). *APOE-ε4*-non-carrier-status was found to be a further predictor of EOAD pathology. We expanded the analyses by examining the impact of sex and *APOE-ε4* on plasma and cerebrospinal fluid (CSF) biomarkers of AD. Plasma markers included: neurofilament light chain (NfL), plasma glial fibrillary acidic protein (GFAP), Aβ 42/40, and pTau231. CSF markers included: Aβ 42/40, neurogranin, tTau, pTau181, SNAP25, YKL-40, and VILIP1.

Methods: We included 201 amyloid-positive EOAD, 64 amyloid-negative EO cognitively impaired (EOnonAD), and 86 Cognitively-normal (CN) LEADS participants with plasma biomarker data. Of these 100 EOAD, 35 EOnonAD, and 38 CN participants also had CSF data. Participants were stratified by sex and APOE-ε4-genotype. Demographics (age, education, APOE-ε4, MMSE) and biomarker differences were compared using ANOVA within each diagnostic group. ANCOVAs were run to control for effects of age and education on biomarkers.

Results/Findings: Compared to men, EOAD women showed greater levels of plasma NfL (p=.03), and GFAP (p<.001) while Aβ 42/40, and pTau231 were comparable. In CSF, EOAD women showed higher levels of neurogranin (p=.01), tTau (p=.01), pTau181 (p=.01) and VILIP1 (p=.02). EOnonAD women showed significantly greater plasma GFAP levels (p=.02). In the CN cohort, women had greater CSF SNAP25 levels (p=.03) while men showed a trend for higher plasma pTau231 levels (p=.05).
APOE-ε4-carrier-status was not associated with differences in levels of plasma or CSF biomarkers in either sex.

Conclusions/Discussion: As new AD fluid biomarkers and treatments emerge, understanding sex-based differences in CSF and plasma is imperative. Female sex is associated with higher levels of neurodegeneration in EOAD and astrogliosis in both EOAD and EOnonAD.

Translational/Human Health Impact: This paves the way for further examination of sex and *APOE-ε4*-genotype-based differences in imaging and fluid biomarkers, their associations, and utility in early diagnosis and treatment.

 # 39

Poster Title: Yeast RNAi-based Attractive Targeted Sugar Baits (ATSBs) for Mosquito Control

Poster Presenter: Njoroge, Teresia
Poster Presenter Institution: Indiana University School of Medicine-South Bend

Poster Authors: Teresia Njoroge, Department of Medical and Molecular Genetics, Indiana University School of Medicine, South Bend; David Severson, Department of Biological Sciences, University of Notre Dame; Keshava Mysore, Department of Medical and Molecular Genetics, Indiana University

School of Medicine, South Bend; Molly Duman Scheel, Department of Medical and Molecular Genetics, Indiana University School of Medicine, South Bend

Abstract:

Background/Significance/Rationale: Attractive targeted sugar baits (ATSBs) exploit the intrinsic sugar feeding behavior of female and male mosquitoes, which can be lured to feed on a sugar source laced with an insecticide. In recent years, we have identified hundreds of RNAi-based pesticides, several which target genes required during both the developing and adult stages of the mosquito life cycle. A subset of the RNAi pesticides has target sites that are conserved in different species of disease vector mosquitoes, but which are not found in humans or other non-target organisms. These interfering RNA pesticides (IRPs), designed to be mosquito-specific, have the potential to enhance existing ATSB technology, combat pesticide resistance, and reduce the burden of mosquito-borne illnesses.

Methods: Short hairpin 463 matching the S*haker* gene with a conserved target site in *An. gambiae, Ae. aegypti*, ae. *albopictus*, *Culex pipiens* and Cx. *quinquefasciatus* was expressed in *Saccharomyces cerevisiae* (baker's yeast), propagated, heat inactivated and fed to larvae, and adult *An. gambiae, Ae. aegypti*, A*e*. *albopictus*, *Culex pipiens* and Cx. *quinquefasciatus* mosquitoes. For the adult mosquitoes, the RNAi yeast (active ingredient) was mixed with an attractive sugar bait and presented to the adults orally on petri plates.

Results/Findings: Consumption of 463 yeast IRP resulted in significant *An. gambiae, Ae. aegypti*, ae. *albopictus*, *Culex pipiens* and Cx. *quinquefasciatus* larvae and adult mosquito deaths (90-100% mortality). Additionally, the sh.463-yeast insecticide was not toxic to non-target arthropods (honeybees, milkweed bugs and red flour beetle).

Conclusions/Discussion: Although the yeast based ATSBs are toxic to *Aedes*, *Anopheles*, and *Culex* mosquitoes, in which they disrupt neural function, the insecticides have not been found to be toxic to non-target arthropods.

Translational/Human Health Impact: Yeast based- RNA interference RNA pesticides are novel mosquito-specific insecticides for disease vector control. They are excellent candidates for biorational mosquito control and are a perfect addition to the mosquito control toolbox. They can be used alone or in combination with other mosquito control methods to combat mosquito-borne diseases.

 # 40

Poster Title: Validation of a citizen screening kit for environmental lead (Pb)

Poster Presenter: Sisk, Matthew
Poster Presenter Institution: University of Notre Dame

Poster Authors: Matthew Sisk, University of Notre Dame; Alyssa Wicks, University of Notre Dame; Ornell Joseph, University of Notre Dame; Jocelyn Keranen, Hoosier Environmental Council; Angela Herrmann, Indiana University Purdue University Indianapolis; Gabriel Filippelli, Indiana University Purdue University Indianapolis; Marya Lieberman, University of Notre Dame; Graham Peaslee, University of Notre Dame; Heidi Beidinger, University of Notre Dame

Abstract:
Background/Significance/Rationale: Lead is a pernicious human health hazard with major lifelong implications for childhood brain development. The main source of lead exposure to children is the home environment. However, there are currently few methods for analysis that are cost effective and accurate. A full lead inspection is time consuming and expensive (~$600) and is usually done in response to a child's elevated blood lead level test.

Methods: The Lead Screening Kit is an inexpensive alternative (~$20) to allow families assess lead risk within their home. Residents provide three soil samples (dripline, yard, near street), two paint samples (interior, exterior), and three dust samples (threshold, windowsill, old dust). Samples are returned to a lab for analysis using x-ray fluorescence spectroscopy (XRF)

Results/Findings: Here we report on an implementation study and statistical analysis. First, we compared the results of LIRAs and screening kits in Indiana homes. Traditional inspections and screening kits were performed by different operators who analyzed different samples and locations within the homes. The lead screening kit and inspection agreed on the presence of lead in 79 of the 107 homes tested (74%). We analyzed results from an additional 400 screening kits for correlations among sampling locations. Correlations were strongest between the yard soil and dripline soil, between exterior paint and dripline soil, and between the two types of non-window dust samples.

Conclusions/Discussion: This analysis provides evidence that exterior paint is a major source of lead hazards both outside and inside the home. Additionally, the screening kit is an effective way to screen many locations for lead risk.

Translational/Human Health Impact: The kit is a scalable, translational, solution for the problem of how to protect the next generation of children from lead in their home. The use of the kit engages the community to be proactive and is a vehicle for education and outreach.

 # 41

Poster Title: Compounding Disparities: Patients Presenting to the Emergency Department for Acute Heart Failure with Medication Non-adherence Are Less Likely to be Prescribed Guideline-Appropriate Medical Therapies

Poster Presenter: Waugh, Karlee
Poster Presenter Institution: University of Notre Dame

Poster Authors: Karlee Waugh, University of Notre Dame; Nicholas E. Harrison, Department of Emergency Medicine, Indiana University School of Medicine; Matthew Durthaler, Indiana University School of Medicine; Madeline Woodson, Decatur Central High School

Abstract:
Background/Significance/Rationale: Acute decompensated heart failure (ADHF) accounts for over 1 million emergency department (ED) visits and hospitalizations in the US annually. Adherence to guideline-directed medical therapies (GDMT) for chronic heart failure (HF) is a common precipitant of

ADHF. Our objective was to characterize the relationship between medication non-adherence and pre-hospital prescribing patterns for GDMT among ED presentations for ADHF.

Methods: We reviewed 2807 ED encounters screened by diagnostic codes, of which 344 had a diagnosis of ADHF after two-rater adjudication. AHA/ACC guidelines for GDMT were used to determine appropriate medication 1) prescription, and 2) adherence ≤14 days prior to the ED encounter, based on the patients' pre-ED classification of HF with preserved ejection fraction (HFpEF) vs. HF with reduced EF (HFrEF). Adherence was further subclassified by specific medication and stratified before/after the 2022 AHA HF guideline update. Logistic regression compared adherence status to predictors including rates of GDMT prescription, other clinical factors, and demographics.

Results/Findings: Medication non-adherence was a factor in 53 (18%) patients. Non-adherent patients were less than half as likely as adherent patients to be prescribed appropriate GDMT (26% vs. 57%, $p<0.001$). After multivariable adjustment for age, sex, HFrEF vs. HFpEF, Get-With-The-Guidelines HF risk score, severity of edema on ED examination, and Charlson Comorbidity Index, non-adherent patients with HFrEF were over 3 times less likely to have been prescribed the appropriate GDMT prior to the ED visit, and patients with HFpEF >10 times less likely (both $p<0.01$). Medication non-adherence was also associated with worse edema, but lower risk scores, at ED presentation ($p<0.05$).

Conclusions/Discussion: Patient medication non-adherence and prescriber non-adherence to GDMT are highly prevalent among ED presentations for ADHF, and strongly associated with one another.

Translational/Human Health Impact: Increased efforts to facilitate GDMT and assist patients with medication adherence are needed to improve HF quality of care.

 # 42

Poster Title: Cannabinoid Receptor Type II Agonist LY2828360 Reverses Two Distinct Forms of Neuropathic Pain Without Producing Reward

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

Poster Authors: Jonah Wirt, Psychological and Brain Sciences, Indiana University, Bloomington; Program in Neuroscience, Indiana University, Bloomington; Gill Center for Biomolecular Science, Indiana University, Bloomington; Kelsey Guenther, Psychological and Brain Sciences, Indiana University, Bloomington; Program in Neuroscience, Indiana University, Bloomington; Gill Center for Biomolecular Science, Indiana University, Bloomington; Shahin Saberi, Psychological and Brain Sciences, Indiana University, Bloomington; Program in Neuroscience, Indiana University, Bloomington; Gill Center for Biomolecular Science, Indiana University, Bloomington; Andrea Hohmann, Psychological and Brain Sciences, Indiana University, Bloomington; Program in Neuroscience, Indiana University, Bloomington; Gill Center for Biomolecular Science, Indiana University, Bloomington

Abstract:
Background/Significance/Rationale: Chronic pain remains one of the top reasons to seek medical care, and finding non-addictive therapeutic interventions remains a clinical imperative during an ongoing opioid epidemic. The endogenous cannabinoid system has shown promise in treating various types of pain, and the cannabinoid type II (CB2) receptor when agonized shows minimal central nervous system mediated side effects. We asked whether CB2 agonist LY2828360 would be efficacious in treating neuropathic pain.

Methods: Two distinct rodent models of neuropathic pain were used to assess CB2 receptor agonist LY2828360's efficacy in rats. Sciatic nerve pain was induced by ligation of the common peroneal and sural branches. Chemotherapy-induced peripheral neuropathy was induced by administration of paclitaxel, a chemotherapeutic agent known to treat breast cancer, ovarian cancer, and lung cancer in humans. Conditioned place preference was used to assess addictive potential of LY2828360, and if LY2828360 could block the rewarding effects of morphine when combined.

Results/Findings: LY2828360 reversed sciatic nerve injury-induced neuropathic pain. LY2828360 reversed ongoing neuropathic pain induced by chemotherapy and *prevented* the development of neuropathic pain while onboard when administered prophylactically when administered before and alongside chemotherapeutic treatment. LY2828360 did not produce rewarding effects on its own and blocked the rewarding effects of morphine in conditioned place preference testing.

Conclusions/Discussion: LY2828360 shows promise in its ability to treat multiple neuropathic pain subtypes, without risk of abuse liability. In addition to this, LY2828360 also shows promise in reducing abuse liability of morphine itself and could be considered for combinatorial treatment to attenuate addictive potential of morphine given to pain patients.

Translational/Human Health Impact: CB2 agonist LY2828360 could help reduce pain in chronic neuropathic pain patients without risk of abuse. LY2828360 could also be used in cancer treatment centers to prevent the development of neuropathic pain induced by chemotherapeutic treatment. Lastly, LY2828360 could be used to help reverse or prevent opioid abuse.

 # 43

Poster Title: Changes in Protein Signaling Profiles of Brain Regions Involved in Drinking after a History of Chronic Binge-Like Drinking

Poster Presenter: Xiao, Tiange
Poster Presenter Institution: Purdue University

Poster Authors: Tiange Xiao, Basic Medical Sciences, Purdue University; Yueyi Chen, Basic Medical Sciences, Purdue University; Alyssa Boisvert, Basic Medical Sciences, Purdue University; Emily Knorr, Basic Medical Sciences, Purdue University; Hanna Hui, Basic Medical Sciences, Purdue University; Adam Kimbrough, Basic Medical Sciences, Purdue University

Abstract:
Background/Significance/Rationale: Binge drinking is a significant societal problem that is defined as a pattern of drinking that brings blood alcohol levels (BALs) to 80 mg/dL or above. A history of chronic

binge drinking may produce long term changes in the brain that result in increased susceptibility to alcohol and drug dependence. Many brain regions have been identified as critically involved in alcohol drinking behavior. **Recently the posterior cortical amygdala (pCOA), the ventrolateral periaqueductal gray (vlPAG), and the lateral habenula (Lh) have been identified as important in alcohol drinking behavior**. However, we do not adequately understand the long-term protein signaling changes that occur binge-drinking after chronic binge-like drinking in the pCOA, vlPAG, and Lh.

Methods: Thus, we sought to examine protein signaling changes in the pCOA, vlPAG, and Lh after 12 weeks of chronic binge-like drinking, using the 'Drinking in the Dark' (DID) mouse model, followed by Liquid Chromatography (LC)/Mass Spectrometry (MS) analysis of brain tissue. C57BL/6J mice (n=20; 10 male, 10 female) underwent 12 weeks of DID behavior. Each week consisted of drinking sessions beginning 3 hours into the dark cycle, with 3 days of 2-hour single-bottle access to 20% w/v alcohol, followed by 1 day of 4-hour single-bottle access to 20% w/v alcohol. The average amount of alcohol consumed on the final binge-like drinking day was 10.6±0.76 g/kg alcohol and the average BAL achieved each week was 104.87±10.24 mg/dL. After 12 weeks of chronic binge-like alcohol drinking, brains from the DID mice and age-matched alcohol naive control mice (n=16; 8 male, 8 female) were collected and snap frozen. Brain tissue from each target brain region (pCOA, vlPAG, and Lh) was then punched in order to process with LC/MS. Punches were stored at -80 degrees Celsius until processed by LC/MS for proteomic analysis.

Results/Findings: Brain tissue is currently being analyzed through Maxquant software to identify significant changes in protein signaling caused by chronic binge-like alcohol drinking.

Conclusions/Discussion: We expect to identify several proteins of interest that have had protein signaling significantly altered by binge-like drinking. The identified proteins of interest will be ideal targets for future binge-like drinking studies.

 # 44

Poster Title: Cancer-Associated Fibroblast-Like Cells Predict Response to Immunotherapy in Glioblastoma

Poster Presenter: Zarodniuk, Maksym
Poster Presenter Institution: University of Notre Dame

Poster Authors: Maksym, Zarodniuk, Department of Aerospace and Mechanical Engineering, University of Notre Dame; Alexander, Steele, Department of Electrical Engineering, University of Notre Dame; Xin, Lu, Department of Biological Sciences, University of Notre Dame; Jun, Li, Department of Applied and Computational Mathematics and Statistics, University of Notre Dame

Abstract:
Background/Significance/Rationale: Excessive deposition of extracellular matrix (ECM) is a hallmark of solid tumors; however, it remains poorly understood which cellular and molecular components contribute to the formation of ECM stroma in central nervous system (CNS) tumors.

Methods: Here, we undertook a pan-CNS analysis of retrospective gene expression datasets to characterize inter- and intra-tumoral heterogeneity of ECM remodeling signatures in both adult and pediatric CNS disease.

Results/Findings: We found that CNS lesions – glioblastoma in particular – can be divided into two ECM-based subtypes (ECM^{hi} and ECM^{lo}) that are influenced by the presence of perivascular cells resembling cancer-associated fibroblasts (CAFs). Ligand-receptor network analysis predicted perivascular fibroblasts activate signaling pathways that may be responsible for recruitment of tumor-associated macrophages and may promote cancer stemness enrichment. Our analysis reveals that perivascular fibroblasts are correlated with unfavorable response to immune checkpoint blockade in glioblastoma and poor patient survival across a subset of CNS tumors.

Conclusions/Discussion: Our study provides insights into novel stroma-driven mechanisms underlying immune evasion and immunotherapy resistance in CNS tumors like glioblastoma.

Translational/Human Health Impact: CAF-mediated immune suppression mechanisms proposed in this study may reveal unique therapeutic vulnerabilities that can be targeted in future preclinical studies.

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Biospecimen Management Core (CTSL/SSF)
IU - Indianapolis
https://indianactsi.org/servicecores/core/30/

Biostatistics and Health Data Science Core
IU - Indianapolis
https://indianactsi.org/servicecores/core/6/

Biostatistics Consulting Center
IU - Bloomington
https://indianactsi.org/servicecores/core/68/

Cellular Response Technologies Core
IU - Indianapolis
https://indianactsi.org/servicecores/core/31/

Center for Genomics and Bioinformatics (CGB)
IU - Bloomington
https://indianactsi.org/servicecores/core/20/

Center for Medical Genomics (CMG)
IU - Indianapolis
https://indianactsi.org/servicecores/core/10/

Center for Proteome Analysis
IU - Indianapolis
https://indianactsi.org/servicecores/core/12/

Center for Survey Research (CSR)

IU - Bloomington
https://indianactsi.org/servicecores/core/76/

Chemical Genomics Core Facility
IU - Indianapolis
https://indianactsi.org/servicecores/core/11/

Chemical Genomics Facility (CGF)
PurdueUniversity
https://indianactsi.org/servicecores/core/88/

CISAB Mechanisms of Behavior Laboratory
IU - Bloomington
https://indianactsi.org/servicecores/core/78/

Clinical Pharmacology Analytical Core (CPAC)
IU - Indianapolis
https://indianactsi.org/servicecores/core/7/

Cryo-EM Facility
PurdueUniversity
https://indianactsi.org/servicecores/core/63/

Electron Microscopy Center (IUB-EMC)
IU - Bloomington
https://indianactsi.org/servicecores/core/67/

Flow Cytometry and Cell Sorting Facility
PurdueUniversity
https://indianactsi.org/servicecores/core/37/

Flow Cytometry Core Facility (FCCF)
IU - Bloomington
https://indianactsi.org/servicecores/core/64/

Flow Cytometry Resource Facility (FCRF)
IU - Indianapolis
https://indianactsi.org/servicecores/core/17/

Freimann Life Sciences Center (FLSC)
University of Notre Dame
https://indianactsi.org/servicecores/core/26/

Genome Editing Center
IU - Indianapolis
https://indianactsi.org/servicecores/core/104/

Genomics and Bioinformatics Core Facility (GBCF)
University of Notre Dame
https://indianactsi.org/servicecores/core/29/

Genomics Facility
PurdueUniversity
https://indianactsi.org/servicecores/core/72/

Histology and Histomorphometry Core (HHC)
IU - Indianapolis
https://indianactsi.org/servicecores/core/93/

Histology Research Laboratory (HRL)
PurdueUniversity
https://indianactsi.org/servicecores/core/33/

Imaging and Flow Cytometry Core Facility
IU - South Bend
https://indianactsi.org/servicecores/core/56/

Imaging Facility
PurdueUniversity
https://indianactsi.org/servicecores/core/53/

Imaging Research Facility (IRF)
IU - Bloomington
https://indianactsi.org/servicecores/core/61/

In Vivo Therapeutics Core (IVT)
IU - Indianapolis
https://indianactsi.org/servicecores/core/108/

In-Vivo Imaging Core
IU - Indianapolis
https://indianactsi.org/servicecores/core/97/

Indiana Center for Biological Microscopy (ICBM)
IU - Indianapolis
https://indianactsi.org/servicecores/core/18/

Infectious Diseases Laboratory (IDL)
IU - Indianapolis
https://indianactsi.org/servicecores/core/66/

Integrated Imaging Facility (NDIIF)
University of Notre Dame
https://indianactsi.org/servicecores/core/28/

Integrated Imaging Facility – Histology Core (NDHC)
University of Notre Dame
https://indianactsi.org/servicecores/core/69/

Islet and Physiology Core
IU - Indianapolis
https://indianactsi.org/servicecores/core/62/

IUSM Center for Electron Microscopy (iCEM)
IU - Indianapolis
https://indianactsi.org/servicecores/core/16/

Laboratory Animal Resources (LAR)
IU - Bloomington
https://indianactsi.org/servicecores/core/89/

Laboratory for Biological Mass Spectrometry (LBMS)
IU - Bloomington
https://indianactsi.org/servicecores/core/50/

Light Microscopy Imaging Center (LMIC)
IU - Bloomington
https://indianactsi.org/servicecores/core/57/

Macromolecular Crystallography Facility Integrated with the Crystallization Automation Facility (MCF/CAF)
IU - Bloomington
https://indianactsi.org/servicecores/core/70/

Magnetic Resonance Research Center
University of Notre Dame
https://indianactsi.org/servicecores/core/24/

Mass Spectrometry and Proteomics Facility
University of Notre Dame
https://indianactsi.org/servicecores/core/23/

Metabolite Profiling Facility (MPF)
Purdue University
https://indianactsi.org/servicecores/core/42/

Multiplex Analysis Core (MAC)
IU - Indianapolis
https://indianactsi.org/servicecores/core/48/

NMR Facility
IU - Bloomington
https://indianactsi.org/servicecores/core/90/

Pre-Clinical Research Laboratory (PCL)
PurdueUniversity
https://indianactsi.org/servicecores/core/41/

Preclinical Modeling and Therapeutics Core (PMTC)
IU - Indianapolis
https://indianactsi.org/servicecores/core/111/

Proteomics Facility
PurdueUniversity
https://indianactsi.org/servicecores/core/43/

Purdue MRI Facility
Purdue University
https://indianactsi.org/servicecores/core/4/

Regenstrief Data Services
IU - Indianapolis
https://indianactsi.org/servicecores/core/75/

Transgenic and Genome Editing Facility (TGEF)
Purdue
https://indianactsi.org/servicecores/core/51/

Translation Core
IU - Indianapolis
https://indianactsi.org/servicecores/core/73/

Translational Pharmacology Facility
PurdueUniversity
https://indianactsi.org/servicecores/core/52/