
# PROGRAM

## South Central Chapter 2025 Fall Meeting

***"Contemporary Studies in Toxicology"***

## Friday, November 14th, 2025

**Hosted by Mississippi State University in Starkville, Mississippi**

**Location:** College of Veterinary Medicine
Mississippi State University
Starkville, MS

**Address:** 240 Wise Center Drive, Mississippi State, MS 39759

**8:30 – 9:00** **Registration and poster set up & On site registration – CVM Bull Ring**

**9:00 – 9:10** **Welcome remarks – Nicholas Frank, DVM, PhD, DACVIM (Dean, MSU CVM) – Tait Butler Classroom**

**Graduate Student Podium Presentations**

**9:10** **LS-100 and LS-200: Novel nanoparticles with strong hemocompatibility and unexpected pharmacological properties,** Nicole Akers, Louisiana State University School of Veterinary Medicine

**9:30** **IL-10 Deficiency Improves Lung Function in 14-16-day-old Mouse Offspring Exposed *In Utero* to E-cigarette Aerosols,** Caiden Ingram, Louisiana State University School of Veterinary Medicine

**9:50** **Pregnane X Receptor (PXR) Activation as a Modulator of Fibroblast Behavior Using *In Vitro* Wound Healing Models,** Aliaa Ismail, Mississippi State University College of Veterinary Medicine

**10:10** **Uncovering the Role of Glucocorticoid Signaling in Arsenic-mediated Stress Behavioral Alterations,** Demetrius McAtee, Louisiana State University School of Veterinary Medicine

**10:30** **Coffee Break – CVM Bull Ring**

**10:40** **Organophosphate-Induced Neurotoxicity and Oxime 20's Intervention on Neurodegeneration Markers in Rats,** Lydia Ogebule, Mississippi State University College of Veterinary Medicine

**11:00** **Developmental Lead (Pb) Exposure Disrupts Noradrenergic Regulation of Stress-Related Behaviors in Zebrafish (*Danio rerio*),** Melanie Wilson, Louisiana State University School of Veterinary Medicine

**Non-Faculty Non-Student Podium Presentations**

**11:20** **The Association Between PM2.5, Black Carbon and Respiratory and Cardiovascular-related Admissions in Mississippi, USA,** Hang Nguyen, University of Mississippi

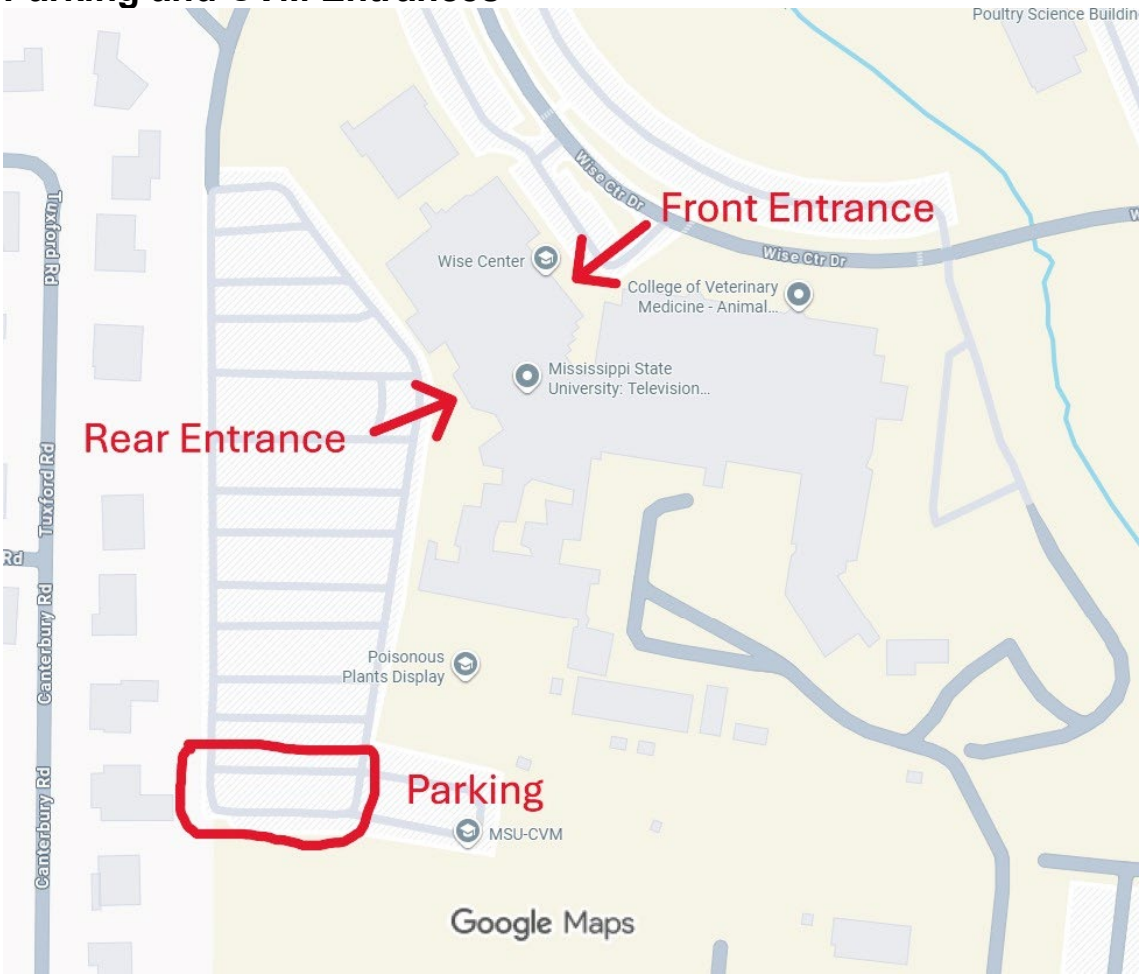
**11:40** **Multiple doses of elesclomol-copper are beneficial and does not trigger cuproptosis in a mouse model of Menkes disease,** Krishna Maremanda, Oklahoma University Health Sciences Center

**12:00** **Lunch Break – Poster Session – CVM Bull Ring**

**1:00** **"From Idea to Experiment"** – An interactive exercise in critical thinking and adverse outcome pathway applications with an emphasis on student involvement

**2:00** **Awards and Closing Remarks**

## Parking and CVM Entrances




**Parking:** SCCSOT participants must park in the parking spots indicated on the map above. All vehicles must be registered with MSU parking services. SCCSOT will be paying for the parking fee. A parking permit code and instructions must be obtained from the registration table.

**CVM Entrance and Meeting Location within the CVM:** After parking, the most direct route into the CVM is to enter via the rear entrance marked above. Both front and rear entrances will be open. Our meeting will utilize the "Bull Ring" area of the CVM. After entering via the rear entrance, the Bull Ring is a circular bricked bench area straight ahead. If entering from the front entrance, go up the stairs, take a left, and the Bull Ring will be straight ahead. The Tait Butler Classroom is immediately adjacent to the Bull Ring. Posters will be set up in the Bull Ring foyer.

## Poster assignments

| Poster # | First Name | Last Name | Classification |
|---|---|---|---|
| 1 | Oluwabori | Adekanye | Graduate student |
| 2 | Olawale | Ajisafe | Graduate student |
| 3 | Arpita | Deb | Graduate student |
| 4 | Brooklyn | Johnson | Graduate student |
| 5 | Kendall | McKinnon | Graduate student |
| 6 | Valentina | Medina | Graduate student |
| 7 | Zechariah | Myles | Graduate student |
| 8 | Anusha | Zaman | Graduate student |
| 9 | Eliana | Carter | Non-student Non-faculty |
| 10 | Russell | Morales | Non-student Non-faculty |
| 11 | Shilpa | Thota | Non-student Non-faculty |
| 12 | Hayden | Anderson | Undergraduate student |
| 13 | Maggie | Burnett | Undergraduate student |
| 14 | Lexi | Holdiness | Undergraduate student |
| 15 | Payton | Kelly-Van Domelen | Undergraduate student |

## Questions

- Dr. George (Trey) Howell (President) at geh3@msstate.edu
- Dr. Gunnar Boysen (Vice President) at gboysen@uams.edu
- Dr. Barb Kaplan (Treasurer) at BKaplan@cvm.msstate.edu
- Dr. Eddie Meek (Councilor) at EMeek@cvm.msstate.edu

# ABSTRACTS

## Undergraduate Students

### Development of a Preclinical Model that can be used to Test Novel Therapeutics for the Treatment of Mild and Moderate Traumatic Brain Injury

Hayden M. Anderson[1], Lexi Holdiness[1], Hannah Mask[1], Kendall N. McKinnon[1], Shirley X. Guo- Ross[1], Anna Marie Clay[2], and Russell L. Carr[1]

[1]Department of Comparative Biomedical Sciences, College of Veterinary Medicine
[2]Department of Agricultural and Biomedical Engineering, Mississippi State University, Mississippi State, MS

Traumatic Brain Injury (TBI) occurs when a foreign object induces damage to the skull and brain through a forceful blow. It is well known that severe TBIs can result in persistent physical, cognitive, and socioeconomic consequences and the timing of treatment following this injury plays critical role in the outcome. It would be beneficial to develop a safe therapeutic that could be administered rapidly after impact that could greatly improve the recovery of the patient. However, the vast majority of TBI cases are mild so while the consequences of mild TBI are less distinct, persistent effects are still commonly reported. Unfortunately, negative morphological changes following mild TBI in preclinical models are absent, greatly reducing their use as improvement indicators. The goal of this project is to establish a mild to moderate TBI model that could be used to test therapeutics using subtle behavioral changes. To model mild TBI, a weight drop device was used to deliver a 2.25J impact in adult male rats. Behavioral performance on a ledged balance beam and in an open field was determined. On the beam, the TBI Rats had a higher number of foot slips than the control rats, and the controls traveled a greater distance before they had to use the ledge for support than the TBI rats. In the open field, TBI rats showed greater signs of anxiety-induced behavior. These subtle behavioral changes may therefore be useful endpoints that can help determine if a therapeutic intervention exerts a positive effect following mild TBI.

**Behavioral and Morphological Effects of Minor Phytocannabinoids in Zebrafish Development**

Maggie Burnett[1], Taylor Shamblin[1], Lisa Seid[2], Eliana Carter[1], Sadie McCoy[1], Katherine Martin[2], Cammi Thornton[2], Kristine Willett[2], Nicole Ashpole[1]

[1]Department of Comparative Biomedical Sciences, Mississippi State University
[2]Department of BioMolecular Sciences, University of Mississippi

The consumer market has increased access to cannabis and cannabinoid-containing products significantly over the past decade. Prior literature has shown that exposure to ∆9-tetrahydrocannabidiol (THC) during embryonic development causes sex-dependent brain development deficits and persistent behavioral disorders, in humans and animal models. However, less is known about the other cannabis constituents, particularly minor cannabinoids like cannabigerol (CBG) and tetrahydcrocannabivarin (THCV). We hypothesize that minor cannabinoids will also impact behavioral and morphological development, and these effects are likely mediated by the canonical endogenous cannabinoid receptors- CB1 and CB2. Utilizing zebrafish models for early development (6-96 hpf), photolocomotor and morphological responses were assessed following exposure to varying concentrations of minor cannabinoids. In wild-type zebrafish, ∆8-THC, THCV, CBD, CBG, and HHC all significantly reduce photolocomotor response, in a dose-dependent fashion. Alterations in morphology were observed with these minor cannabinoids as well with significantly increased rates of pericardial edema and yolk sac edema as well as reduced body length and reduced eye diameter at the highest doses. Interestingly, these cannabinoids induced similar behavioral and morphological responses in cnr2-/- fish, suggesting limited CB2 involvement in the observed toxicities. Studies with cnr1-/- fish are ongoing to evaluate the involvement of CB1. Overall, these studies highlight that several cannabinoids available on the consumer market have increased risk of toxicity in early development.

**Behavioral Performance and Neurobiological Effects from Repeated Exposure to the Prophylactic Peripheral Drug Pyridostigmine Bromide in Adult Rats**

Lexi Holdiness, Noah Martin, Hayden Anderson, Sarah Broadaway, Caroline Carroll, Janice Chambers, Katrina Jackman, Kendall McKinnon, Edward Meek, Angela Ross, Cameron Whitmore, Shirley Guo-Ross, and Russell Carr

Center for Environmental Health Sciences, Department of Comparative Biomedical Sciences, College of Veterinary Medicine, Mississippi State University

Pyridostigmine bromide (PB) is an organophosphate (OP) nerve agent prophylactic commonly used during the U.S. Gulf Wars as a protectant against OP nerve agent attacks. As part of its protective mechanism, therapeutic doses of PB inhibit ~30% of the peripheral cholinesterase (ChE) but PB does not cross the blood-brain barrier. Even so, this persistent low-level cholinergic hyperactivity induced in the periphery could result in inappropriate signals to the brain through the vagal nerve. That signaling could lead to altered function. This study investigated whether repeated PB treatment could induce neural excitation in the brain and affect behavior. Male and female adult rats were treated daily with either PB or vehicle for 21 days. Behavioral tests included the elevated plus maze (EPM, anxiety), open field test (OF, locomotor activity and anxiety), sucrose preference test (SPT, anhedonia), and novel object test (NO, learning and memory). qPCR analysis was performed on the amygdala and thalamus to determine the expression levels of c-Fos and brain-derived neurotrophic factor (BDNF) as measures of neural excitation. PB treatment did not affect behavioral performance in the EPM, SPT, or NO but a sex-specific anxiolytic effect (females but not males) was observed during the OF test with treated females exhibiting increased entries into the center area. PB treatment significantly altered BDNF expression in both regions regardless of sex. The expression of c-Fos exhibited some sex-specific differences in both regions. The behavioral and biochemical results suggest that PB can influence neural excitation despite its inability to cross the blood-brain barrier.

**Investigation of the Role of Aryl Hydrocarbon Receptor (AHR) in Antibody-Triggered Signaling in Innate Cells**

Payton Kelly-Van Domelen, Arpita Deb, Barbara L. Kaplan

Center for Environmental Health Sciences and Department of Comparative Biomedical Sciences, College of Veterinary Medicine, Mississippi State University

Multiple Sclerosis (MS) is a neurodegenerative autoimmune disease for which there is no cure. Currently available therapies have variable efficacy, so novel treatments are needed. Chemicals that bind to the aryl hydrocarbon receptor (AHR) are immune-suppressive and can attenuate MS-like disease in mice. However, some of these chemicals are also toxic, so ligands that bind AHR but do not exhibit toxicity are needed. Previously, I3C, derived from cruciferous vegetables, suppressed antibody production from B cells in a mouse MS model. Thus, we wanted to determine if I3C would also suppress antibody-triggered signaling in innate cells through a mechanism involving AHR. We hypothesized that I3C would suppress antibody-triggered signaling and that effects would be lost in Ahr-/- mice or in the presence of an AHR antagonist. We obtained splenocytes from untreated female mice, treated them with I3C, then stimulated with a streptavidin-biotin IgG2b (SBIgG2b) immune complex to activate innate cells. I3C suppressed the cytokines IL-6 and TNF-a. Next, we used splenocytes derived from Ahr-/- mice and found that I3C-mediated suppression of TNF-a was AHR- dependent but IL-6 was not. To confirm these results, we initiated studies using an AHR antagonist, but results were not consistent. These studies have provided clarification on the effects of I3C, but future studies are needed using lower concentrations of the antagonist and its vehicle to further clarify the role of AHR. Regardless of the role of AHR, the studies provide initial evidence that I3C is immune-suppressive, suggesting it might have efficacy in autoimmune diseases such as MS.

## Graduate Students

### Lipid peroxidation triggers IL-1b release from CES1-deficient macrophages

Oluwabori Adekangye, Abdolsamad Borazjani, Matthew Ross

College of Veterinary Medicine, Mississippi State University

Macrophages are immune cells derived from hematopoietic precursors. They are important cells of innate immunity that maintain host defense and tissue homeostasis. They patrol tissues to identify damage-associated molecular patterns (DAMPs) and pathogen associated molecular pattern (PAMPs) from micro-organisms. When macrophage pattern recognition receptors detect these signals, the cells respond by secreting lipid mediators, cytokines, and chemokines to initiate inflammation. Lipid peroxidation is a chemical reaction that occurs when oxygen molecules (free radicals) damage lipids (fats) in the body generating DAMPs that trigger cytokine release. Polyunsaturated fatty acids (PUFA) are highly susceptible to lipid peroxidation.
Carboxylesterases belong to the α/β-hydrolase fold family of proteins and catalyze the hydrolysis of ester containing substrates into alcohols and carboxylic acids. We previously reported that human CES1 hydrolyzes triacylglycerols (TAGs), including PUFA-TAGs and oxidized TAGs in macrophages. Also, we reported that CES1-deficient (CES1KD) macrophages express and secrete more IL-1b than control macrophages. Here, we show a significant accumulation of select oxidized TAG species in CES1KD macrophages that were treated with exogenous PUFA (linoleic acid), while there was an upward trend in IL-1b released from THP-1 cells treated with arachidonic acid and menadione, a redox cycling agent. Furthermore, CES1KD cells treated with ascorbic acid and alpha tocopherol secreted lower amounts of IL-1b than CES1KD cells that were not treated with these antioxidants. Our results suggest that lipid peroxidation within CES1- deficient macrophages can induce IL-1b secretion and indicate that CES1 could be a potential target in managing and regulating hyper-inflammation.

**Drug-Drug Interaction Potential of Novel Oxime-20: a Promising Compound for Organophosphate Poisoning Treatment**

Olawale Ajisafe, Mary E. Dail, Janice E. Chambers

Center for Environmental Health Sciences (CEHS), College of Veterinary Medicine,
Mississippi State University, Mississippi State, MS

Organophosphate (OP) anticholinesterase poisoning remains a major global health problem, demanding safer and more effective antidotes. Oxime-20, a novel acetylcholinesterase reactivator, shows promise for improved OP treatment. Since polypharmacy is common in OP management, this study evaluated the drug-drug interaction (DDI) potential of Oxime-20 by assessing its effects on key cytochrome P450 (CYP) enzymes using two in vitro models. P450 enzymes using two in vitro models. First, a fluorescence-based P450 Glo assay (Promega) was employed to evaluate inhibitory effects of Oxime-20 on CYP1A2, CYP2B6, and CYP3A4 activities. Oxime-20 was tested across a concentration range of 1–500 μM, with appropriate selective inhibitors as positive controls. In parallel, CYP3A4-mediated testosterone 6β-hydroxylation was examined in liver microsomes from Aroclor 1254-induced rats, and metabolite formation was quantified by UPLC-MS. Oxime-20 caused minimal inhibition of CYP1A2 and CYP3A4 below 200 μM, with notable inhibition only at higher concentrations. CYP2B6 showed more pronounced inhibition, suggesting potential interaction at therapeutic levels. In the testosterone hydroxylation assay, Oxime-20 did not significantly reduce 6β-hydroxylation formation at therapeutically relevant concentrations, supporting the fluorescence assay findings for CYP3A4. These findings suggest that Oxime-20 poses a low DDI risk via CYP1A2 and CYP3A4 inhibition and hence support the continued development of Oxime-20 as a promising therapeutic for OP poisoning management with a favorable metabolic interaction profile.
(Supported by NIH U01 NS123255).

**LS-100 and LS-200: Novel nanoparticles with strong hemocompatibility and unexpected pharmacological properties**

*Nicole Akers[1], Ashlyn Harmon[1], M. Ryan Smith[2], Carlos E. Astete[3], Cristina Sabliov[3], and Tammy Dugas[1]

[1]Department of Comparative Biomedical Sciences
[2]Department of Veterinary Clinical Sciences, Louisiana State University School of Veterinary Medicine
[3]Department of Biological and Agricultural Engineering, Louisiana State University Agricultural Center, Baton Rouge, Louisiana

Peripheral artery disease (PAD) is a vascular disease associated with atherosclerotic and thromboembolic obstruction in the lower extremities. While obstructed arteries can be cleared using angioplasty and stenting, blockages can recur. Two common mechanisms for reocclusion include neointimal hyperplasia (NIH) and thrombogenesis. Novel nanoparticle (pNP) formulations LS-100 and LS-200 are designed to deliver drugs that address these mechanisms. Neither formulation induces significant hemolysis and LS-200 prolongs activated partial thromboplastin time, but their hemocompatibility is unknown. Canine blood was obtained with an IACUC-approved protocol. Porcine blood was obtained commercially. Platelet activation in pNP exposed canine blood was measured using PDGF-BB and thromboxane B2 ELISA. Endothelial viability and function were assessed using endothelial ATP and NO assays. A novel physiologic flow study measured thrombus formation on materials of differing thrombogenic potential inserted into loops containing pNP exposed porcine blood. Platelet activation markers were unchanged with LS-200. ATP production was unaffected below 0.36 mg/mL of LS-200 pNP and below 1.5 mg/mL with LS-100. NO production did not significantly decrease with either formulation. Material thrombus coverage was significantly decreased in LS-200 exposed blood under flow. Overall, LS-200 decreased thrombus formation on thrombogenic materials and maintained hemocompatibility. Measurements of immunogenicity, mutagenicity, and other key aspects of biocompatibility are required. Given the bioactivity of LS-200 absent drug cargo, future studies will assess LS-200 as a hydrophilic coating for cardiovascular medical devices. Early LS-100 data suggests inert behavior in the blood compartment, but additional analysis of hemocompatibility including platelet activation and thrombus development assays are required.

**INVESTIGATING THE EFFICACY OF ARYL HYDROCARBON LIGAND I3C IN A COMBINATION THERAPY WITH APROBIOTIC AND AN ANTIDEPRESSANT FOR TREATING MULTIPLE SCLEROSIS IN VIVO**

*Arpita Deb, Barbara L. F. Kaplan

Center for Environmental Health Sciences, Department of Comparative Biomedical Sciences, College of Veterinary Medicine, Mississippi State University

Multiple sclerosis (MS) is a neurodegenerative autoimmune disorder characterized by the demyelination of neurons in the central nervous system. Despite therapeutic advances, MS remains difficult to treat, and no curative therapies currently exist. Experimental autoimmune encephalomyelitis (EAE) is an MS mouse model that can be induced by injecting mice with myelin oligodendrocyte glycoprotein (MOG). In EAE, MOG-specific IgG antibodies are thought to contribute to pathology by recruiting cytolytic immune cells to attack myelin-expressing cells. Our pilot studies demonstrated that the aryl hydrocarbon receptor (AHR) ligand, indole-3-carbinol (I3C), suppressed disease-specific IgG1, IgG2a, and IgG2b antibodies in EAE serum and reduced expression of proinflammatory genes (Il6, Tnf, and Ifng) in the cerebellum of the disease mice. Considering the growing interest in therapies such as probiotics and antidepressants in addition to anti-inflammatory and immunosuppressive therapies for MS, we were interested to study whether combining I3C with the probiotic Lactobacillus and the antidepressant duloxetine would enhance disease attenuation in EAE. For experimental purposes, female C57BL/6 mice were induced with EAE and orally gavaged with different treatment groups for six days. At day 15, serum was collected from all the mice. The cerebellum of the mice was collected in RNA Later solution for RT-PCR analysis, and the rest of the brain was preserved in -80°C. We found that I3C alone modestly reduced disease-specific IgG1, while both I3C and the combination treatment (I3C + duloxetine + Lactobacillus) suppressed disease-specific IgG2a and IgG2b antibody production in serum. The combination treatment also modestly reduced expression of proinflammatory cytokine genes in the cerebellum of the disease mice (Ifng, Il17a, Tnf, and Il6) and corresponding protein levels (IFN-γ, IL-6, TNF-α) in the central nervous system. Together, all these studies provide evidence that I3C in combination with antidepressant and a probiotic exhibits modest immunosuppressive and anti-inflammatory effects that may attenuate disease severity in EAE.

**IL-10 Deficiency Improves Lung Function in 14-16-day-old Mouse Offspring Exposed *In Utero* to E-cigarette Aerosols**

Caiden Ingram[1], Torrie Cook[1], Matthew Schexnayder[2] and Alexandra Noël[1]

[1]Department of Comparative Biomedical Sciences, Louisiana State University School of Veterinary Medicine, Baton Rouge, LA
[2]IDEXX Laboratories, Inc., Westbrook, ME

**Rationale**: Electronic-cigarette (e-cig) devices are commonly used by the U.S. population, including pregnant women, as recent studies report that 2.2–7.0% of individuals use e-cigs during pregnancy. Our previous studies showed in utero exposure to e-cig aerosols up-regulated interleukin-10 (IL-10), a crucial immunoregulatory cytokine in lung homeostasis. This study aims to investigate both the impact of gestational e-cig exposure and the role of IL-10 on mouse offspring lung function.
**Methods**: C57BL/6 wildtype (WT) and IL-10 knockout (KO) dams were exposed to either air or e-cig aerosol. Exposure consisted of 1.5-hour/day for 14 days prior to conception plus 20 days during gestation. Lung function in 14 - 16-day-old offspring was evaluated using the flexiVent.
**Results**: Compared to the air exposure, in utero e-cig exposure significantly reduced both the birth weight and length in WT pups, an effect driven by shorter female WT pups. In neonates, in utero e-cig exposure significantly affected the lung pressure-volume loops in WT offspring, reflecting a restrictive pulmonary phenotype, primarily driven by the WT females. In utero e-cig exposure significantly increased the respiratory system elastance, lung tissue damping and tissue elastance compared to the air group in WT mice. Removal of IL-10 in the e-cig group preserved these parameters in the range of the IL-10 KO air-exposed offspring. Sex-specific effects of IL-10 deficiency were identified.
**Conclusion**: In utero e-cig exposure has significant effects on lung function in early-life in WT offspring, with lungs exhibiting reduced ability to stretch and expand, whereas IL-10 deficiency shielded from these impairments.

**Pregnane X Receptor (PXR) Activation as a Modulator of Fibroblast Behavior Using *In Vitro* Wound Healing Models**

Aliaa Ismail and George Howell III

Department of Comparative Biomedical Sciences, College of Veterinary Medicine, Mississippi State University

Delayed wound healing in diabetic foot ulcers (DFUs) is driven by impaired fibroblast migration, excessive collagen deposition and persistent inflammation. PXR, a xenobiotic nuclear receptor, has recently emerged as a potential modulator of fibrotic and inflammatory signaling. However, its impact on fibroblast behavior in the context of DFU remains poorly understood. Our objective is to investigate the effects of PXR activation via pregnenolone 16α-carbonitrile (PCN) on fibroblast migration, proliferation, collagen production, and myofibroblast gene expression in 3T3-L1 and NIH3T3 cells. Scratch wound, Boyden chamber migration, and MTT proliferation assays were performed on NIH3T3 and 3T3-L1 cells treated with DMSO (0.025%) or PCN (20 μM) in serum-free and serum-supplemented conditions. Real time PCR was used to quantify myofibroblast markers including α-smooth muscle actin (αSma), collagen I and collagen III expression following treatment with DMSO, PCN, TGF-β1 (10 ng/mL), or PCN + TGF-β1. Sirius Red assay was used to assess intracellular and extracellular collagen levels under the same treatment conditions. PCN enhanced wound closure in both cell lines under both serum conditions. Boyden chamber migration and MTT assays showed increased motility and proliferation following PCN treatment, particularly in serum-rich media. Real time PCR revealed that PCN suppresses αSma and Col1a1 expression while upregulating Col3a1, suggesting a shift toward regenerative ECM remodeling. Sirius Red staining confirmed reduced collagen deposition in PCN + TGF-β1 group compared to TGF-β1 alone. These findings demonstrate that PXR activation promotes fibroblast migration and attenuates TGF-β1–driven fibrotic signaling, offering mechanistic insight into its translational relevance for chronic wound repair.

**$PM_{2.5}$ and Black Carbon Concentrations during Prescribed Burn and Burn-Ban Season in Georgia**

Brooklyn Johnson, Logan Harden, Khloe Osborne, Courtney Roper

Department of BioMolecular Sciences, University of Mississippi School of Pharmacy

Prescribed burns manage wildfires by weakening fuel loads which lowers intensity and fire duration. The burning of trees is a significant contributor to air pollution, releasing fine particulate matter (PM2.5) composed of harmful chemicals including black carbon and other hazardous air pollutants. Prescribed burns are common in the southeastern United States mainly for wildfire prevention and ecosystem management purposes with Georgia burning 1.4 million acres annually. This study aims to investigate PM2.5 and black carbon concentrations in Georgia during 2015, specifically comparing concentrations during the prescribed burn (October 1- April 30) and burn-ban (May 1-September 30) seasons. PM2.5 was collected on Teflon filters by the Environmental Protection Division of the Georgia Department of Natural Resources (GDNR) throughout 2015 at 4 locations in Georgia every 3 days. PM2.5 concentrations were determined through gravimetric analysis by the GDNR. All collected filters were then analyzed for black carbon at 800nm. Site locations were compared between seasons (burn vs. burn ban). Preliminary data shows average PM2.5 concentrations were 10.15 ± 3.57 μg/m³ during Georgia's prescribed burn season and 12.29 ± 3.83 μg/m³ during burn-ban season; Black carbon concentrations were 3.4 ± 2.21 μg/m³ and 0.01 ± 1.32 μg/m³, respectively. Future directions include using prescribed burn records to compare PM2.5 and black carbon data from specific sites during prescribed burn days and non-burn days. PM2.5 and black carbon analysis can also be expanded to more sites in the state while considering possible temporal variations in concentrations.

**Uncovering the Role of Glucocorticoid Signaling in Arsenic-mediated Stress Behavioral Alterations**

Demetrius McAtee, Melanie Wilson, Ahmed Abdelmoneim

Department of Comparative Biomedical Sciences, Louisiana State University School of Veterinary Medicine, Baton Rouge, Louisiana

Arsenic (As) is a widespread environmental contaminant linked to numerous adverse health outcomes. Growing epidemiological and experimental evidence suggest its role as a risk factor for stress-related disorders such as anxiety and depression. However, the neuroendocrine mechanisms driving these stress behavioral alterations remain poorly understood. Our previous work demonstrated As-induced hyperactive stress behavioral phenotypes in larval zebrafish. Glucocorticoid (GC) signaling plays a key role in regulating behavioral stress responses and As has been shown to dysregulate it; therefore, in this study, we investigated the role of GC signaling in mediating physiological and As-induced stress behavioral phenotypes in larval zebrafish. To study this link, we used wild- type and transgenic zebrafish lines along with a combination of approaches, including pharmacologic GC modulations, co-exposures with As, high throughput stress behavioral assessments, and in vivo imaging of corticotropin-releasing hormone (CRH) neuronal structure and activity—key regulator of GC signaling. Pharmacological modulation of GC signaling (dexamethasone, mifepristone, and metyrapone) produced behavioral phenotypes that mirrored As exposure; while coexposure studies supported a mechanistic link. Structural imaging of CRH neurons revealed As-dependent changes in the neuronal count. In vivo calcium imaging of CRH neurons demonstrated changes in neuronal activity in response to GC pharmacological modulations and As-induced alterations that can be closely linked to previously observed stress behavioral phenotypes. Our findings provide deeper insights into the neuroendocrine mechanisms underlying As-mediated stress behavioral disorders and identify GC signaling as a possible driver of effects, highlighting GC-targeting strategies as potential avenues for mitigation and therapeutic interventions.

**Dose-Dependent Effects of the Organophosphorus Insecticide Metabolite Chlorpyrifos-oxon on Cholinesterase Activity in Juvenile Rats Following Acute Exposure.**

Kendall N. McKinnon, Lexi J. Holdiness, Hayden M. Anderson, Ellianna J. Uldrich, Shirley X. Guo-Ross, and Russell L. Carr

Center for Environmental Health Sciences, Department of Comparative Biomedical Sciences College of Veterinary Medicine, Mississippi State University

Chlorpyrifos (CPF), an organophosphorus insecticide hypothesized to cause developmental neurotoxicity, targets the nervous system. At higher levels, CPF is converted to chlorpyrifos-oxon (CPO), which irreversibly binds acetylcholinesterase (AChE) and causes acetylcholine accumulation. This induces hyperactivity in cholinergic system, which may cause death. Typically, environmental CPF exposure occurs at lower levels. One target of CPF inhibition is fatty acid amide hydrolase (FAAH). This prevents endocannabinoid degradation, disrupting normal development/function. This project's purpose was to establish a dose-response relationship between CPO exposure and cholinesterase inhibition to study its impact on enzyme activity at varying exposure levels. At 21 days old, rat pups were subcutaneously administered vehicle or CPO (0.5, 0.75, 1.0, 1.25, 1.5, 1.75, 2.0, 2.5, 3.0mg/kg). Pups were sacrificed 3 hours post-exposure with tissue collected to determine ChE activity. For brainstem AChE activity, no inhibition was observed at 0.5mg/kg. At 0.75, 1.0, and 1.25mg/kg, AChE activity decreased approximately 17%, 27%, and 34%, respectively. Dosages 1.5 (40%), 1.75 (43%), and 2.5mg/kg (59%) showed moderate inhibition of AChE. The most severe inhibition was 3.0mg/kg with reduction of 75% brain AChE activity. In serum, ChE activity was suppressed at 0.5mg/kg by 25%. A slight plateau in serum ChE activity was demonstrated with increasing CPO levels: 0.75 (33%), 1.0 (35%), 1.25 (38%), 1.5 (49%), 1.75 (43%), and 2.0 (48%). At 2.5 and 3.0mg/kg, activity was inhibited by 54% and 63%. These findings provide preliminary data for future studies to investigate CPO effects on FAAH activity and determine impact on gene expression.

**Adverse behavioral and morphological outcomes resulting from developmental exposure to cannabidiol depend on the timing of exposure**

Valentina Medina-Ardila[1], Caitlyn M. Callahan[1], Taylor S. Shamblin[2], Jonathan Y. Lott[1], Mirielle E.W. Clayton[1], Katherine A. Martin[1], Courtney Roper[1], Nicole M. Ashpole[2], Kristine L. Willett[1]

[1]University of Mississippi, School of Pharmacy, Department of Biomolecular Sciences, Oxford, MS
[2]Mississippi State University, College of Veterinary Medicine, Starkville, MS

Cannabidiol (CBD) is becoming increasingly available and is often marketed to pregnant women to mitigate pregnancy symptoms commonly present during the first trimester such as nausea, insomnia, and pain. The goal of this study is to consider windows of developmental susceptibility using the zebrafish (Danio rerio) model. Wildtype (5D) embryos were exposed to control (0.05% DMSO) from 6-102 hours post fertilization (hpf) or 2 μM CBD from 6-102 hpf, 6-30 hpf, 30-54 hpf, 54-78 hpf, or 78-102 hpf, with mortality and hatching monitored daily. After each exposure period, embryos were collected for gas chromatography-mass spectrometry to assess CBD bioaccumulation or transferred to clean egg water until 120 hpf. At 120 hpf, behavior (larval photomotor response assay) and morphology, including eye diameter and body length, were evaluated. Larvae exposed to CBD from 6–102 hpf showed reduced body length, smaller eyes, and decreased locomotor activity, indicating developmental impairment from continuous exposure. Shorter exposure windows caused less pronounced effects. The 54–78 hpf group showed the greatest morphological and behavioral deficits among exposure windows, while the 30–54 and 78–102 hpf groups exhibited moderate decreases. Chi-square analysis revealed increased yolk sac and pericardial edema, along with more uninflated swim bladders and body axis defects, particularly in the 54–78 and 6–102 hpf groups. Identifying critical periods of susceptibility will provide insight into how the timing of exposure influences adverse developmental outcomes and can contribute to a better understanding of potential risks associated with CBD use during pregnancy.

This research was supported by grant R01DA057317 from the National Institute of Drug Abuse and National Institute of General Medical Sciences.

**Vascular endothelial dysfunction induced after exposure to environmentally persistent free radicals is mediated by the release of miRNA from the air-blood interface model**

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Background and Purpose: Particulate matter containing environmentally persistent free radicals (EPFRs) is produced when Superfund wastes are thermally remediated. EFPRs form when organic pollutants are incompletely combusted and adsorb onto the surface of particles containing redox-active metals. redox-active metals. Previous studies with mice showed that EPFRs reduced vascular function downstream of the lung. However, this effect was abolished in mice lacking the aryl hydrocarbon receptor (AhR) in alveolar type II (ATII) cells, and it also promoted the systemic release of miRNAs. We hypothesize that at the air-blood interface, EPFRs alter the miRNA profile released into the plasma, which, in turn, alters the expression of genes essential for controlling blood vessel function in peripheral lung vessels. Methods: To test our hypothesis, we isolated and cultured mouse alveolar type-II (AT-II) cells at the air-liquid interface (ALI) and exposed them to aerosolized EPFRs (~30 μg/cm²) in a Vitrocell exposure system. At 24 h after ALI exposures, the basal medium was collected, filtered, and exposed to commercially sourced murine lung microvascular endothelial cells (mLMVEC). Results: Compared with control, activation of the AhR was observed in AT-II cells exposed to EPFRs, evidenced by increased Ahrr, Cyp1a1, and CYP1b1 mRNA levels. Activation of AT-II-AhR resulted in a decrease in the release of miR-1906 and miR-542-3p into the basal medium. In mLMVEC exposed to the conditioned medium, we observed reduced nitric oxide levels, reduced Nos3 and Pik3r2 mRNA expression, and increased End1. Conclusions: Our findings suggest that miRNAs released into basal medium after treatment of AT-II cells with ALI regulate endothelial cell expression required for maintaining vascular homeostasis, including genes that regulate eNOS expression/function.

**Organophosphate-Induced Neurotoxicity and Oxime 20's Intervention on Neurodegeneration Markers in Rats**

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Organophosphates (OPs), such as the nerve agent sarin and its surrogate nitrophenyl isopropyl methylphosphonate (NIMP), are potent neurotoxicants that inhibit acetylcholinesterase (AChE), causing acetylcholine (ACh) accumulation and excessive cholinergic signaling, which leads to seizures, respiratory failure, and death. Beyond acute toxicity, OP exposure causes long-term effects, including neuroinflammation, neurodegeneration, blood brain barrier (BBB) disruption, and cognitive impairments. Current treatments like 2-PAM offer limited protection across the BBB, highlighting the need for new therapeutics with better CNS penetration. The novel reactivator Oxime 20 (US patent 9,277,937), developed in our lab, penetrates the BBB, and reactivates OP-inhibited AChE. This study investigates Oxime 20's neuroprotective effects against NIMP-induced neurotoxicity by examining neurodegeneration (Cln5, Fos), BBB integrity (Ocln), cholinergic signaling (Chrna7), and cannabinoid receptor (Cnr1) expression in adult male Sprague Dawley rats across Control, NIMP, Oxime 20, and Therapy groups. Tissue from the piriform cortex and hippocampus was collected post-treatment. RTqPCR and western blotting were used to assess gene and protein levels, then, normalized to Rplp1 and β-ACTIN, respectively. NIMP significantly elevated Cln5, Chrna7, and Fos gene expression, and decreased CHRNA7 protein expressions while Oxime 20 therapy reduced Cln5 and normalized Chrna7 levels in the hippocampus. In the piriform cortex, NIMP increased Cln5 and Cnr1 while decreasing Chrna7 and Ocln gene expression; Oxime 20 therapy restored Cln5 and Chrna7 to control levels and elevated Ocln gene expression, suggesting its great potential as a neuroprotective agent against OP-induced neurotoxicity. (Supported by NIH U01 NS123255).

**Developmental Lead (Pb) Exposure Disrupts Noradrenergic Regulation of Stress-Related Behaviors in Zebrafish (Danio rerio)**

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Lead (Pb) remains a prevalent neurotoxicant affecting millions of children worldwide, yet the mechanisms linking early-life exposure to stress-related disorders remain poorly understood. Our previous work demonstrated significant alterations in behavioral stress responses and noradrenergic (NA) signaling of larval zebrafish beginning at 75 µg/L. This study investigates how developmental Pb exposure disrupts NA regulation of stress responses using the same translational model. Zebrafish embryos were exposed to environmentally relevant Pb concentrations (15 – 750 µg/L) from 6 – 120 hours post fertilization. Confocal fluorescence and calcium imaging were utilized to characterize structural and functional changes in the locus coeruleus (LC) and dorsal telencephalon (DT), key regions governing noradrenergic signaling and stress regulation. Neuroimaging revealed dose-dependent increase in LC/NA neuronal number with disrupted spatial organization and suppressed spontaneous neuronal activity as measured by calcium imaging. Reductions were recorded in DT volume and NA axonal complexity, with rostral regions showing greatest vulnerability. This suggests enhanced neuronal survival coupled with diminished functional integration. Transcriptomic profiling of heads of larvae expressing altered stress behavioral phenotype confirmed upregulation of oxidative phosphorylation genes alongside downregulation of ion-channel and proteolytic functions, indicating compensatory metabolic activation and impaired calcium signaling. Pharmacological manipulations with alpha 1- and 2-adrenergic receptor antagonists differentially modulated stress behaviors, with yohimbine (alpha 2 antagonist) producing biphasic responses dependent on exposure duration. These findings demonstrate that developmental Pb exposure disrupts NA stress circuits through coordinated structural, functional, and transcriptomic alterations. This work establishes mechanistic links between early-life Pb exposure and stress-related disorder risk

**Effects of electronic nicotine delivery systems (ENDS) vehicle solution and copper nanoparticles on mouse T-cells**

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**Rationale:** Electronic nicotine delivery systems (ENDS) heat an e-liquid composed of nicotine, propylene glycol (PG), vegetable glycerin (VG), and flavors, using a coil/atomizer with metal parts to generate an aerosol containing the initial e-liquid ingredients, plus aldehydes and metals, generated from the thermal degradation of the e-liquid ingredients and the wearing of the device's metal parts, respectively. Our lab previously shown that ENDS aerosols contained copper (Cu) (15 ng/puff). Given that metals are recognized by the immune system and can activate humoral and cellular immunity, in this study we investigated *in vitro* the effects of ENDS vehicle solution and Cu nanoparticles (NPs) on T cells, playing key roles in immuno-inflammatory diseases.
**Methods:** Mouse T-cells (3A9) were grown at the air-liquid interface (ALI) and exposed to filtered-air, ENDS aerosols containing 30/70 PG/VG, phosphate-buffered saline (PBS), or CuNPs for 1-hour. Twenty-four hours post-exposure, we assessed cell viability and gene expression.
**Results:** Cells were exposed to deposited doses of 28.5 μg/cm$^2$ (PG/VG), 1.2 μg/cm$^2$ (PBS) and 1.7 μg/cm$^2$ (CuNPs), equivalent to Cu levels found after 1h of ENDS use. Compared to air, exposure to PG/VG did not significantly alter cell viability; however, compared to PBS, exposure to CuNPs significantly increased cell proliferation. Copper-induced cell proliferation is well-documented. We are currently evaluating oxidative stress, cytotoxic responses, and gene expression associated with Cu metabolism, biotransformation, and inflammation.
**Conclusions:** Thus far, our data suggest that Cu induce an increased proliferation of T cells and, in the context of vaping, this could worsen immuno-inflammatory diseases, including asthma.
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## Non-student and Non-faculty

### Exploring the Psychoactive Effects of Individual Impurities Found in Δ8 -THC Products

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The rapid surge in commercially available delta-8-tetrahydrocannabinol (Δ 8 -THC) products has raised concerns regarding safety and regulations. Manufacturers typically synthesize Δ8-THC to meet product demand, as only trace amounts are found in cannabis plant material. During synthesis, numerous impurities form that may impact the safety of consumption. Our collaborative team synthesized Δ8-THC and identified 15 cannabinoid impurities, including 9α-hydroxy-HHC, Δ4(8)-iso-THC, 9β-hydroxy-HHC, and Δ4(5)-iso-THC. We hypothesize that these impurities will activate CB1 signaling cascades and lead to psychoactive responses, thereby contributing to the responses consumers report with Δ8-THC consumption. To assess potential biological impacts of these impurities, 6–8-week-old male C57BL/6 mice received intraperitoneal injections of 1-30 mg/kg of each cannabinoid, since biphasic dose-response curves are well-documented in cannabinoids. Classic psychoactive effects present in the tetrad assay, which is comprised of evaluations of core body temperature, locomotion, catalepsy (rigidity), and thermal nociception. Our preliminary results indicate Δ8-THC, 9β-hydroxy-HHC, and Δ4(5)-iso-THC had no statistical effect at 10mg/kg. At 30mg/kg, Δ8-THC had a reduction in locomotion, an average -2°C drop in temperature, and an increase in % maximal possible effect for tail flick as expected. Interestingly, the 10mg/kg dose for 9α-hydroxyHHC and Δ4(8)-iso-THC acted as a stimulant, demonstrated by an increase in locomotion. Future work will examine the remaining cannabinoid contaminants and assess the effects of each when coadministered with Δ8-THC, mimicking products on the market. Individual cannabinoids displaying psychoactive effects will also need to analyze abuse liability and the potential development of tolerance to better understand their safety profile.

**Multiple doses of elesclomol-copper are beneficial and does not trigger cuproptosis in a mouse model of Menkes disease**

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Menkes disease is an X-linked disorder of copper (Cu) deficiency, caused by loss-of-function mutations in the Cu transporter ATP7A. The disease is characterized by progressive neurodegeneration and connective tissue defects, with death occurring at three years of age. Currently, no FDA-approved drug is available for the treatment of this fatal pediatric disease. We recently discovered that an investigational chemotherapy drug, elesclomol (ES), when complexed with Cu (ES-Cu), rescues Cu deficiency, activates cuproenzymes, and prevents perinatal lethality in a mottled-brindled (mo-br) mouse model of Menkes disease. We showed that a mere two doses of ES-Cu can rescue mo-br mice from early mortality; however, within a few months of life, the Cu deficiency remains visible, as reflected by the decrease in Cu- dependent proteins, such as COX1, in the mitochondria. The current study was conducted to evaluate the feasibility of administering extra doses of ES-Cu at later stages of life to correct Cu deficiency without causing unwanted toxic effects. Here, we report that multiple ES-Cu doses in mo-br mice, at various stages of growth, are beneficial in preserving the mitochondrial COX1 without triggering cuproptosis. Our results support the concept of repurposing ES for the treatment of Cu deficiency disorders.

**Co-Exposure of Geek Bar E-Cigarette and Particulate Matter Containing Environmentally Persistent Free Radicals Enhances Lung Detoxification Pathways in Male Mice**

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**Rationale:** Geek Bar Pulse X (GB) is an e-cigarette containing synthetic nicotine salt, potentially presenting distinct respiratory hazards due to its formulation. While GB raises concerns, environmental airborne toxicants also contribute to pulmonary disease risk. Particulate matter containing environmentally persistent free radicals (EPFR(PM)), formed during thermal remediation of hazardous waste at Superfund sites, induce oxidative stress and pulmonary dysfunction. We hypothesized that co-exposure to GB aerosol and EPFR (PM) will synergistically exacerbate lung inflammation and oxidative stress.
**Methods:** Male C57BL/6J mice were exposed to either air, GB aerosol (~0.32 mg/puff), EPFR(PM) (~317 μg/m³), alone or in combination over a 7-week period. Lung function was assessed and tissues collected for biotransformation, inflammation, and oxidative stress gene expression analysis.
**Results:** GB significantly impaired lung function at two weeks, with reduced minute volume and breathing frequency, followed by recovery and an upward shift in the pressure-volume loop. While no pulmonary inflammation was detected (macrophages >99%) in all groups, at the molecular level GB+EPFR(PM) induced a synergistic Cyp1a1 up-regulation (58.9-fold) compared to 23.8-fold for EPFR(PM) and 2.9-fold for GB. This suggests amplified detoxification caused by co-exposure. In total, GB+EPFR(PM) up-regulated 5 genes (Cxcl5, Aldh3a1, Cyp1a1, Cyp1b1, Nqo1), whereas GB up-regulated 11 genes, including Mmp12, Col4a1, Hmox1, and Tnf, showing effects on pathways associated with airway remodeling, oxidative stress and inflammation. EPFR up-regulated 7 genes, including Mmp9, Cyp1a1, Cyp1b1, Nqo1, Il-1β. Overall, GB exposures induced more robust pulmonary responses.
**Conclusion:** These findings reveal distinct molecular profiles and underscore the importance of assessing co-exposures in inhalation toxicology.

**The Association between PM2.5, Black Carbon and Respiratory and Cardiovascular-related Admissions in Mississippi, USA**

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Exposure to fine particulate matter (PM2.5) and its major component, black carbon (BC), poses significant risk to global public health. Mississippi faces distinct air pollution issues, demographic characteristics, and a high prevalence of diseases. However, research on PM2.5 and BC health effects in this region is still limited. In this study we investigated the associations between PM2.5 and BC exposure and respiratory and cardiovascular emergency department visits and hospitalizations, referred to as related admissions, across three regions of Mississippi. Time-series analyses using quasi-Poisson generalized additive models combined with a distributed lag non-linear model were conducted to investigate exposure-response and lagged effects between pollutant exposure and respiratory and cardiovascular-related admissions among Medicare beneficiaries. During the study period, PM2.5 and BC levels were highest in Jackson (11.2 and 1.87 μg m-3). Exposure - response relationships between PM2.5, BC and respiratory and cardiovascular-related admissions at the inter-quartile range with 0-3 day lags exhibited no significant associations between PM2.5 exposure and admissions at any location. BC exposure was significantly associated with increased the risks of respiratory (Relative Risk (RR) = 1.012, 95% CI: 1.003 – 1.021) and cardiovascular-related admissions (RR = 1.006, 95% CI: 1.000 – 1.012) at lag 0 in Jackson, with no significant associations observed elsewhere. Adverse health effects of BC were more pronounced in the high polluted urban area of Jackson compared to the Grenada region. These findings emphasize the need for further research on environmental health disparities in Mississippi.

## *In Utero* E-Cigarette Exposure and IL-10 Deficiency Modulate Epigenetic Regulation Associated with T Regulatory(Treg) Cells During Lung Development

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**Rationale:** The increasing use of e-cigarettes (e-cigs) during pregnancy has raised growing concerns about their developmental toxicity, particularly in the fetal lungs where epigenetic regulation shapes immune tolerance. Interleukin-10 (IL-10) is a pleiotropic cytokine essential for maintaining immune homeostasis and is involved with TGF-β, STAT5a, and Foxp3, which are core T-regulatory (Treg) cell signaling components. Disruption of this pathway may alter DNA-methylation-dependent control of immune balance, predisposing offspring to pulmonary immune-inflammatory disorders.

**Methods:** Pregnant IL-10 knockout (IL-10KO) and wild-type (WT) mice were exposed to e-cig aerosols or filtered air throughout gestation. Lungs from one-day-old pups were collected to assess global DNA methylation (%5-mC) and gene-specific promoter methylation by bisulfite conversion followed by methylation-specific PCR. Methylation changes were correlated with RNA sequencing.

**Results:** Our findings revealed a 2.0-fold reduction ($p<0.01$) in global methylation (%5-mC) in IL-10KO e-cig pups compared to WT e-cig pups. This correlated with increased dysregulation of lung genes in IL-10KO male pups. Within the Treg axis, TGF-β and Foxp3 promoters were significantly hypermethylated (1.3-fold and 1.6-fold, respectively; $p<0.01$) in IL-10KO e-cig lungs. This hypermethylation pattern corresponded with reduced IL-10 expression and impaired transcriptional coordination within the TGF-β–STAT5a–Foxp3 network. STAT5a was hypomethylated in IL10-KO e-cig group (1.2-fold; $p<0.01$), consistent with active Treg signaling, suggesting a compensatory mechanism.

**Conclusion:** Overall, *in utero* e-cig exposures associated epigenetic modulation of the TGF-β–STAT5a–Foxp3 axis, is influenced by IL-10 deficiency, underscoring IL-10's critical role in maintaining immune homeostasis in the developing lung exposed to e-cig aerosols.