Allegheny-Erie
Regional Chapter–SOT | Est.1988

38th Annual Meeting of the Allegheny-Erie Society of Toxicology Regional Chapter

Pressing Environmental Toxicants of our Region

West Virginia University
Alumni Center
Morgantown, WV

October 29, 2025

University of Pittsburgh | Rust to Resilience Center

iTOX Center for Inhalation Toxicology

SOT | Society of Toxicology
Creating a Safer and Healthier World by Advancing the Science and Increasing the Impact of Toxicology

MEETING REGISTRATION

Please contact Alison Sanders, President (aps109@pitt.edu) if you plan to register late (on site) so we can plan accordingly for programs.

___ $110 - full/associate member
___ $150 - non-member
___ $60 - member: postdoctoral fellow or graduate student
___ $80 - non-member: postdoctoral fellow or graduate student
___ $50 - retired
___ $150 - late, on-site registration
___ $0 - high school or undergraduate student
___ $0 - high school or undergraduate chaperone

Credit Card Payment/Registration (SOT login required - member & non-member options exist):
https://www.toxicology.org/groups/rc/allegheny/events.asp

2025-2026 Executive Committee

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Amber Mills
Postdoctoral Representative

Vivien (Jiaqi) Lyu
Graduate Student Representative

Maeve Morris
Graduate Student Representative

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SCHEDULE (October 29, 2025)

8:30 – 9:30 Registration
9:30 – 9:45 Welcome and Announcements

SYMPOSIUM 1: Local, regional and global toxicants of concern

9:50 Introduction/Symposium Overview (Chair: Alison Sanders, PhD, A-E SOT President)
10:00 **Toxic Relationships: When Liver Meets Industrial Chemicals**
Dr. Juliane Beier, University of Pittsburgh, Department of Medicine, Division of Gastroenterology, Hepatology and Nutrition and School of Public Health, Department of Environmental and Occupational Health; Pittsburgh Liver Research Center, UPMC Hillman Cancer Center and Rust to Resilience Environmental Chemical Research Center
11:00 **Maeve Morris**, graduate student, West Virginia University
11:15 **Dr. Md Shahnur Alam**, postdoctoral fellow, University of Pittsburgh
11:30 **Dr. Venkat Ramakrishna**, postdoctoral fellow, Pennsylvania State College

11:50–12:50 **Lunch Break**
11:50–12:35 "Lunch with an Expert" & Networking (For Trainees)

SYMPOSIUM 2: Toxicity Across the Life Course

1:00 Introduction/Symposium Overview (Chair: Mark Olfert, PhD, A-E SOT Past President)
1:10 **END H^3 (Hidden Health Hazards)**
Dr. Sarah Commodore, Indiana University, Department of Environmental and Occupational Health, School of Public Health
2:10 **Haley Arbore**, graduate student, University of Pittsburgh
2:25 **Dr. Russel Hunter**, postdoctoral fellow, West Virginia University
2:40 **Dr. Natalie Price**, postdoctoral fellow, University of Pittsburgh

3:00–4:15 **POSTER SESSION – Networking**

SYMPOSIUM 3: Environmental and Public Health Impacts

4:15 Introduction/Symposium Overview (Juliane Beier, PhD, A-E SOT President-Elect)
4:25 **Toxicants in Western Pennsylvania: Denying, Omitting and Obscuring the Data**
Jane Scott Cleary, CEASRA member**,** Legal Liaison/Historian*, and* **Lisa Johnson,** Former Environmental Attorney
5:25 **Devon Collins**, graduate student, West Virginia University
5:40 **Dr. Evan DeVallance**, early-stage investigator, West Virginia University

6:00–6:20 Awards, Closing Comments and Adjourn

6:30–8:30 Group Social – Apothecary Ale house (scan QR code for directions)
227 Spruce St, Morgantown, WV 26505

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Keynote Speaker (Symposia #1)

Dr. Juliane I. Beier is an Assistant Professor at the University of Pittsburgh School of Medicine in the Department of Medicine with a secondary appointment in the School of Public Health. She is a member of both the Pittsburgh Liver Research Center and the UPMC Hillman Cancer Center. Dr. Beier's research focuses on the interaction between environmental toxicants and metabolic liver diseases. Her work on vinyl chloride has contributed significantly to our understanding of how environmental chemicals can modify liver disease risk, particularly in the context of fatty liver disease and cancer. Her laboratory has demonstrated that even low-level exposures to vinyl chloride can exacerbate underlying liver conditions and accelerate carcinogenesis. As principal investigator on her R01 grant "Vinyl chloride modifies the risk for nonalcoholic fatty liver disease," Dr. Beier also serves as MPI on an R21 focused on the East Palestine Community-Engaged Environmental Exposure, Health Data, and Biospecimen Bank. Most recently, Dr. Beier was awarded an OT2 grant from NIEHS, which enables her to continue research into the health impacts of the East Palestine train derailment on affected communities in both Ohio and Pennsylvania. Additionally, she participates in the Pitt Momentum Fund Scaling grant for the "Rust to Resilience" project, helping to build a stronger research program around environmental health in the region.

Dr. Beier has published over 60 peer-reviewed articles, including original research and invited reviews in high-impact journals. She has also authored multiple book chapters on hepatotoxicity and has been recognized with multiple President's Choice Awards from the American Association for the Study of Liver Diseases. Her expertise was nationally recognized following the East Palestine train derailment, where she provided insights on vinyl chloride's health effects in numerous media appearances.
She currently serves as President of the Society of Toxicology's Mechanisms Specialty Section and has been elected to serve as President of A-E SOT in the coming term. With her h-index of 30, Dr. Beier continues to advance the field in understanding how environmental exposures impact liver health. Her extensive research portfolio and leadership in environmental toxicology make her an ideal keynote speaker on the critical intersection of environmental health and human disease.

Title: Toxic Relationships: When Liver Meets Industrial Chemicals

Abstract: Environmental chemical exposures represent an underrecognized but critical component of liver health, serving as risk modifiers that influence disease development, severity, and complications. While traditional hepatology focuses on genetic, viral, and lifestyle factors, mounting evidence demonstrates that environmental toxicants significantly modify liver disease risk, particularly in metabolic dysfunction-associated steatotic liver disease (MASLD). The liver serves as a primary target organ for environmental chemicals, with major pollutants consistently associated with MASLD development and progression. These exposures exhibit substantial health disparities across populations, creating differential vulnerability patterns. Environmental chemicals function through diverse pathways including mitochondrial dysfunction, inflammatory activation, oxidative stress, and disruption of cellular metabolism.

Our research demonstrates that low-level vinyl chloride exposure, at concentrations previously considered safe, significantly enhances Western diet-induced liver injury. This interaction transforms manageable dietary stress into severe hepatotoxicity characterized by inflammation, necrosis, and accelerated tumorigenesis. Transcriptomic analyses reveal that Western diet backgrounds amplify toxicant responses 4.6-fold and uniquely enable carcinogenic pathway activation. Beyond single chemicals, environmental mixtures present complex challenges. Military burn pit exposures cause rapid-onset hepatic pathology within days, characterized by disrupted liver architecture and ultrastructural alterations. Chemical mixtures containing metals and emerging contaminants like PFAS synergistically enhance liver injury, promoting severe inflammation while activating cancer-related pathways. Human epidemiological studies consistently demonstrate associations between environmental exposures and liver dysfunction across diverse populations. Particulate matter (PM2.5) significantly associates with liver dysfunction and chronic liver diseases, with developing countries showing slightly higher MASLD risk levels than developed nations. Chemical disasters and industrial accidents provide natural experiments demonstrating how acute exposures can trigger long-term hepatic consequences. The mechanisms underlying these interactions involve complex cellular processes. Environmental chemicals disrupt mitochondrial function, alter gene expression patterns, activate inflammatory cascades, and impair cellular detoxification systems. These effects are particularly pronounced when combined with underlying metabolic stress, suggesting that environmental factors may explain inter-individual variability in MASLD progression.

Clinical translation requires incorporating environmental exposures into precision medicine approaches for liver health. This includes developing exposure reduction strategies, enhancing toxicant clearance, and understanding exposure sources. Future directions involve longitudinal studies to understand how environmental factors influence disease progression, therapy response, and patient outcomes, ultimately advancing environmental hepatology as a critical component of comprehensive liver care worldwide.

Keynote Speaker (Symposia #2)

Dr. Sarah Commodore is an Assistant Professor in the Department of Environmental and Occupational Health in the School of Public Health Bloomington at Indiana University. Her research interests include improving the current understanding of how exposures to environmental pollutants influence inflammatory and immune responses during critical developmental and disease windows. Her background in environmental health includes an undergraduate degree in biological science and a PhD in toxicology with a focus on environmental health, specifically air pollution exposures. She received additional training in environmental epidemiology during her postdoctoral studies and has also worked as a research contractor for the United States Environmental Protection Agency (US EPA). Her research program, combines environmental, preclinical, molecular, and clinical data to inform effective public health and regulatory interventions and protection from long-term adverse health effects. To this end, she focuses on exposomics – the study of the environmental exposures that occur throughout the lifetime of an individual and how such exposures influence the person's biology and health. Funding for her research comes from sources such as NHLBI, NIEHS, the School of Public Health Bloomington, and the Indiana Clinical and Translational Sciences Institute (CTSI). She also assists with interpretating air pollution data to the public and non-academic groups and has served on scientific grant review panels and facilitated scientific symposia. At the end of the day, she aims to translate environmental health and toxicology studies into real-world applications to improve public health.

Title: END H^3 (Hidden Health Hazards)

Abstract: The widespread adoption of Electronic Nicotine Delivery Systems (ENDS), including e-cigarettes, has been driven in part by perceptions of reduced harm relative to traditional, combustible tobacco products. Despite reductions in conventional smoking, the rise in ENDS use has introduced new challenges for public health. A growing body of evidence suggests that ENDS contain nicotine, aldehydes, volatile organic compounds, metals, and other constituents that can negatively impact the user's health. ENDS aerosols can even persist on surfaces long after active use has occurred, thereby contributing to passive exposures. And, if the user is pregnant, passive exposures can occur in utero. Both active and passive ENDS aerosols are hidden health hazards. While the health impacts of passive cigarette smoke have been documented, the toxicological and molecular impacts of ENDS-derived active and passive smoke remain understudied. Few studies have addressed whether residues from ENDS aerosols can meaningfully alter immune function, gene expression, and epigenetic regulation. Given the scale of ENDS adoption, identifying these risks is critical for shaping both scientific understanding and informing effective interventions.

This presentation will center on three main themes. The first theme will focus on what available tools can help link or even simulate environmental chemical concentrations and personal exposures. After establishing the fact that exposures may have occurred, a second related theme will address whether intrauterine smoke or vape exposure influences early lung development and respiratory disease through genetic and/or epigenetic mediation. Then, a final theme, will examine whether ENDS use is associated with adverse health impacts during a key developmental window such as adolescence. The goal is to lay the groundwork to build future studies which can lead to better diagnostics, personalized treatments, as well as identification (and elimination) of specific triggers associated with ENDS-related adverse health.

Keynote Speaker (Symposia #3)

Jane Scott Cleary received a degree in English from Miami University, a Masters in Library Science from Columbia University, and a Certificate of Advanced Study in Library and Information Science from the University of Pittsburgh. She taught in the public schools outside New York City, then joined the Library Faculty at Slippery Rock University as an associate professor for 25 years. In that capacity she served as Coordinator of Instruction, Health Sciences Librarian, and Reference Librarian. She has been a member of the Citizens' Environmental Association of the Slippery Rock Area (CEASRA, Inc.) since 1990. Successes that the 38-year-old non-profit helped realize included the defeat of a federally mandated low-level nuclear incinerator, monitoring of the Grove City Osborne Superfund Site, and most recently, the overturning of a municipal landfill permit for radioactive waste.

Lisa Johnson is a former environmental attorney based in Pittsburgh, PA, with 20 years of experience in environmental law. Lisa successfully managed a diverse range of legal challenges and her expertise included creating and maintaining a litigation and appellate practice, engaging in challenges to environmental permits, complex jurisdictional disputes, and representing vulnerable populations against the oil and gas industry and governmental entities. Lisa has a proven track record in environmental law and recently overturned a Department of Environmental Protection permit at the Commonwealth Court level that would have allowed a municipal landfill to accept oil and gas waste. Beyond her professional achievements, Lisa is committed to community service. She envisioned and established a pro bono legal clinic for the street homeless in Pittsburgh and has also provided pro-bono representation to people seeking safe harbor in the United States. Lisa holds a Juris Doctor, cum laude, from the University of Pittsburgh School of Law, where she also served as an editor for the Law Review, and a Bachelor of Science in Psychology, cum laude, also from the University of Pittsburgh.

Title: Toxicants in Western Pennsylvania: Denying, Omitting and Obscuring the Data

Abstract: The 2024 Integrated Water Quality Report by the Pennsylvania Department of Environmental Protection reveals that 34% of Pennsylvania's 85,568 miles of rivers and streams are polluted, affecting 28,820 miles. There is a strong connection between surface water pollution and groundwater pollution. Approximately 3.5 million Pennsylvanians depend on private water wells for their drinking water. The state also ranks poorly in air quality, with the Pittsburgh-Weirton-Steubenville metro area being 12th worst for year-round and 16th worst for short-term particle pollution. Despite the evident health risks, efforts by residents and environmental groups to identify local toxicants face resistance from the EPA, ATSDR, PA DEP, and PA DOH. Jane Cleary, from the Citizens' Environmental Association of the Slippery Rock Areas (CEASRA, Inc.), has spent over 30 years documenting pollution in Grove City, Pennsylvania, particularly from the Osborne Superfund Site and Tri-County Landfill. CEASRA and Liberty Township have been involved in litigation over the Tri-County Landfill's permit, with the Commonwealth Court recently siding with them to vacate the landfill's solid waste permit. Lisa Johnson, a former attorney, represented them and will also discuss the need for toxicology testing near polluted sites. Co-presenters will share further details and future recommendations.

LODGING

The closest hotel to the Alumni Center (walking distance) is:

Hampton Inn (click **HERE** for link to the website)
1053 Van Voorhis Rd, Morgantown, WV, 26505
Phone: 304-223-4098

Other hotels (within 2 miles of the Alumni Center) are:

Holiday Inn (Morgantown) (click **HERE** for link to the website)
1188 Pineview Dr., Morgantown, WV 26505
Phone: 304-241-6649

Hilton Garden Inn (click **HERE** for link to the website)
150 Suncrest Towne Centre, Morgantown, WV 26505
Phone: 304-225-9500

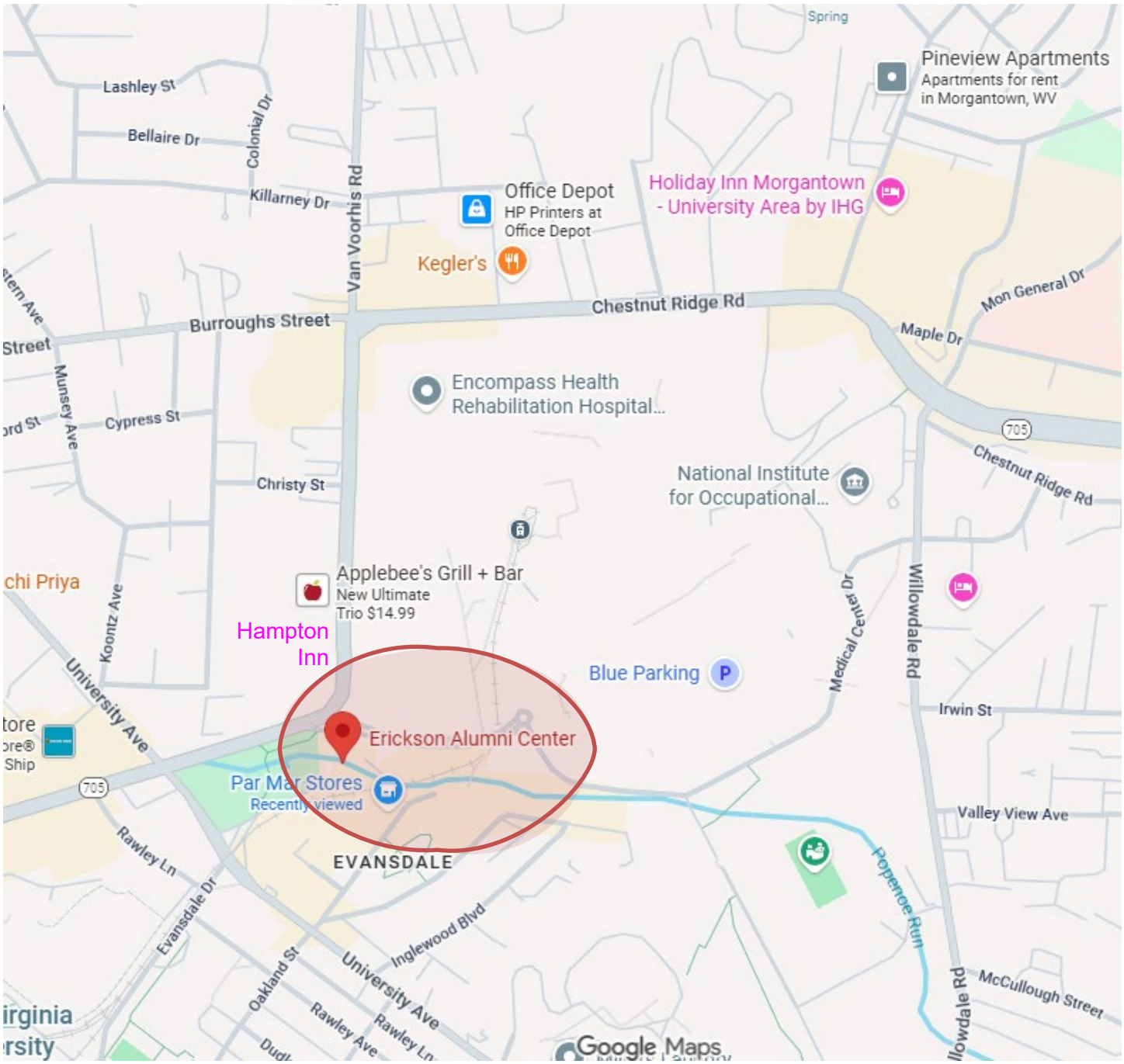
DIRECTIONS TO THE ERICKSON ALUMNI CENTER

From I-79 North or South

1. Take I-79 Exit 155 at Star City. At bottom of exit ramp, bear right if traveling north, left if traveling south.
2. Bear to the right at the traffic light at Sheetz on Route 7
3. Make a left onto Patteson Drive at the traffic light at the Coliseum and merge into the right lane
4. At third traffic light, turn right onto University Ave.
5. Turn left at the first traffic light onto Alumni Dr. (formerly Medical Center Dr.). Parking is available in the lot on the right.

From I-68 East

1. Take I-68 East to Exit 7 (Airport/Pierpont Road) and turn right (Merge into middle lane)
2. Go straight through first traffic light
3. At the second traffic light, turn left onto 119 South
4. Go through traffic light (the airport will be on your left)
5. At the next traffic light, turn right onto 705
6. Go through five traffic lights
7. At the fifth light, turn left onto Van Voorhis Road
8. Go through one traffic light and get in the left-hand lane. Turn left at the next traffic light onto University Ave.
9. Turn left at the first traffic light onto Alumni Dr. (formerly Medical Center Dr.). Parking is available in the lot on the righ


Spring
Pineview Apartments
Apartments for rent
in Morgantown, WV
Lashley St
Bellaire Dr
Colonial Dr
Killarney Dr
Van Voorhis Rd
Office Depot
HP Printers at
Office Depot
Holiday Inn Morgantown
- University Area by IHG
Kegler's
Chestnut Ridge Rd
Mon General Dr
Maple Dr
Burroughs Street
Encompass Health
Rehabilitation Hospital...
Cypress St
Munsey Ave
Christy St
705
Chestnut Ridge Rd
National Institute
for Occupational...
Applebee's Grill + Bar
New Ultimate
Trio $14.99
Hampton
Inn
Koontz Ave
University Ave
Blue Parking
Medical Center Dr
Willowdale Rd
Irwin St
Erickson Alumni Center
Par Mar Stores
Recently viewed
Valley View Ave
Rawley Ln
EVANSDALE
Evansdale Dr
Inglewood Blvd
Oakland St
Rawley Ave
Popenoe Run
McCullough Street
Google Maps

SOT 65TH ANNUAL MEETING & ToxExpo

SAN DIEGO, CA MARCH 22-25, 2026

WWW.TOXICOLOGY.ORG/2026

IMPORTANT DATES AND DEADLINES

MAY 15, 2025
Scientific Session and Continuing Education Course Proposal Submission Deadline

AUGUST 1, 2025
Registration and Housing Open

OCTOBER 9, 2025
SOT Awards Nomination and Application Deadline

NOVEMBER 13, 2025
Abstract Submission Deadline

SOT Provides Opportunities for Undergraduates

- SOT Undergraduate Student Affiliate status, providing access to toxicology news and resources
- Poster presentation and other award opportunities through SOT and its Regional Chapters, Special Interest Groups, and Specialty Sections
- Internships and research experiences in SOT members' labs
- Activities at the SOT Annual Meeting and Regional Chapter meetings, as well as professional development opportunities and resources

www.toxicology.org/undergraduate

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Graduate Student Awards

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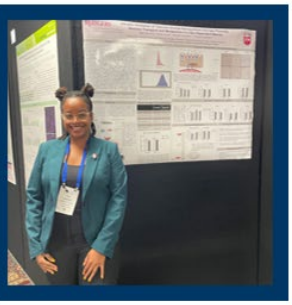
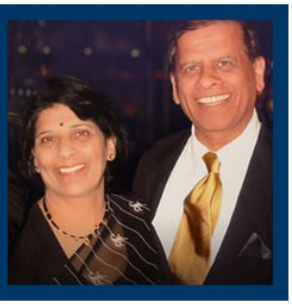
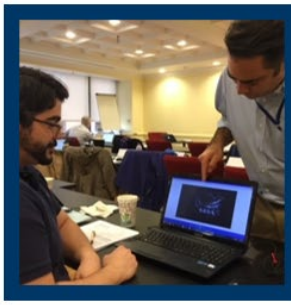
Career Development Award (launching September 1)



Graduate Intern Fellowship in Toxicology (GIFT)

Mehendale Welcome Award





Supplemental Training in Education Program (STEP)

Postdoctoral Awards

Best Postdoctoral Publication Award (BPPA)

New Experiences in Toxicology (NEXT) Program

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Abstract and Poster Presentations

Poster# 01

IMPACT OF BENZALDEHYDE AND VERATRYLALDEHYDE ON ACROLEIN-INDUCED CYTOTOXICITY

Y Twum[1], G Pagan[2], L Fox[1], A Rebok[1], V Ungarala[1], Z Bitzer[1], TE Spratt[1]

1- Penn State College of Medicine, Hershey, PA
2- Penn State University, University Park, PA

Artificial flavors have become widespread in e-cigarettes (e-cigs), with over 14,000 classified e-liquid products currently available on the market. These flavoring agents significantly contribute to the appeal and uptake of e-cigs, particularly among the youth, raising concerns about their potential pulmonary toxicity. Since many flavor compounds are aldehydes, and potentially reactive with proteins, there is a need to assess the impact of the flavoring agents with known e-cig toxicants, such as acrolein. Therefore, the objective of this study is to assess the potential synergistic interactions between benzaldehyde (BA) and veratrylaldehyde (VA) in enhancing acrolein-induced cytotoxicity. BEAS-2B and A549 cells were seeded into 96 mm cell culture plate inserts and treated with increasing concentrations of acrolein, either alone or in combination with BA or VA, for 24 and 48 h. Cell viability was evaluated through a MTT assay and colony-forming assay. Oxidative stress was assessed using the DCFDA assay.
A549 cells exhibited significant cytotoxicity to acrolein (IC_{50}: 60 µM at 24h and 58 µM at 48h), while the aldehydes were less cytotoxic, BA (IC_{50}: 2.5 mM at 24h and 2.0 mM at 48h) and VA (IC_{50}: 1.2 mM at 24h and 3.8 mM at 48h). Similarly, acrolein was toxic to BEAS-2B cells (IC_{50}: 34 µM at 24h and 30 µM at 48h), while the aldehydes were much less toxic, BA (IC_{50}: 2.0 mM at 24h and 1.1 mM at 48h) and VA (IC_{50}: 2.1 mM at 24h and 2.2 mM at 48h). The combination of BA or VA with acrolein, produced an additive cytotoxic effect. Our colony-forming assay supported the results obtained from the MTT assay. Acrolein, alone or in combination with BA or VA, induced a dose-dependent increase in oxidative stress in both A549 and BEAS-2B cell lines. Our findings indicate that neither BA or VA impact the toxicity nor oxidative stress caused by acrolein in cell culture. However, further studies are warranted to elucidate the combined effects of acrolein with BA or VA in inducing pulmonary oxidative damage following e-cig exposure in humans.

Poster# 02

CIGARETTE SMOKE EXPOSURE MASKS PATHOLOGICAL FEATURES OF *HELICOBACTER PYLORI* INFECTION WHILE PROMOTING CANCER INITIATION

MT Morris, BC Duncan, B Piazuelo, IM Olfert, X Xu, S Hussain, RM Peek, Jr., JT Busada

West Virginia University School of Medicine, Morgantown, WV

Gastric cancer is the fifth leading cause of cancer and cancer-related deaths worldwide. Chronic infection with the bacterium *Helicobacter pylori* is the best-known risk factor of gastric cancer, but only 1-3% of infected individuals will develop gastric cancer. Cigarette smoke is another leading risk factor of gastric cancer, with *H. pylori*-infected smokers being at a 2-11-fold increased risk of gastric cancer. The direct impact of cigarette smoke on *H. pylori* pathogenesis and cancer initiation remains unknown. In this study, male C57BL6 mice were infected with *H. pylori*, then exposed to 10 cigarettes daily, five days a week, for 8 weeks. Cigarette smoke on its own did not have any notable impacts on gross gastric morphology or inflammatory status compared to filtered air-exposed controls in mock-infected mice. However, cigarette smoke exposure significantly blunted *H. pylori*-induced gastric inflammatory responses, reducing gastric atrophy and pyloric metaplasia development. Despite blunting these classic pathological features of *H. pylori* infection, cigarette smoke exposure increased DNA damage within the gastric epithelial cells and accelerated *H. pylori*-induced dysplasia onset in the INS-GAS gastric cancer model. These data suggest that cigarette smoking may clinically silence classic clinical symptoms of *H. pylori* infection but enhance the accumulation of mutations and accelerate gastric cancer initiation.

Poster# 03

EFFECTS OF *IN UTERO* EXPOSURE TO NTIO$_2$ AND PRE-PUBERTAL HIGH-FAT DIET ON DEVELOPMENTAL MILESTONES, WEIGHT GAIN, AND METABOLIC OUTCOMES IN RATS

TD Gluth[1,2], RP Hunter[1,2], ML Nichols[1,2], CJ Kiddy[1,2], SL Thorn[1,2], RR Nett[1,2], KS Seman[1,2], EC Bowdridge[1,2]

[1]*Department of Physiology, Pharmacology, & Toxicology, West Virginia University School of Medicine, Morgantown, WV*
[2]*Center for Inhalation Toxicology, West Virginia University School of Medicine, Morgantown, WV*

Maternal inhalation of titanium dioxide nanoparticles ($nTiO_2$), through particle translocation and/or hostile uterine environment, negatively impacts F1 offspring health including reproductive, cardiac, glucose tolerance, redox balance, and immune profile. These outcomes were further altered by introducing a high-fat diet (HFD) post-pubertally. We then sought to determine the effects of *in utero* $nTiO_2$ exposure on F1 metabolic health when a HFD is introduced pre-pubertally. Pregnant rats were exposed to $nTiO_2$ (12mg/m^3) or HEPA-filtered air (25mL/min) for 6h for 6d from GD12-19. Dams delivered their pups naturally. Developmental milestones and pup mass were tracked daily until weaning. At weaning, rats received grain-based diet (18% kcal from fat) or HFD (60% kcal from fat). Calorie consumption and mass were recorded weekly. From 1-5wk, body fat and lean tissue composition were measured weekly by echoMRI. At 3-4wk, rats were placed in Comprehensive Lab Animal Monitoring System to measure caloric balance. At 10wk, we performed 6-hour fasted glucose tolerance test, followed by euthanasia. There was no difference in mass or body composition prior to weaning, but $nTiO_2$ offspring had earlier fur, upper incisor and eye development. Post-weaning mass and calorie intake differed only by diet, except $nTiO_2$ HFD females started to consume more calories at 8wk when compared to control HFD females (493±23 vs. 413±14 kcal/wk). $nTiO_2$ rats were significantly more glucose intolerant than controls, independent of diet. Altogether, these observations demonstrate that both *in utero* environmental exposure and perinatal diet can alter metabolic outcomes. When considered together with our post-pubertal diet studies, the data also indicate that timing of the diet challenge is an important factor in adult health outcomes.

Poster# 04

$PM_{2.5}$ EXPOSURE DURING PREGNANCY AND THE IMPACT ON PRETERM BIRTH IN A WEST VIRGINIA COHORT USING PROJECT WATCH DATA AND EPA'S AQI DATA.

Devon T. Collins, Amna Umer, Christa Lilly, Candice Lefeber, Collin John, Timothy R. Nurkiewicz, Caroline P. Groth.

West Virginia University School of Medicine, Morgantown, WV

Background and Purpose: $PM_{2.5}$ inhalation has been associated with poor health outcomes in humans and can harm the reproductive system. Local and systemic inflammation, oxidative stress, genotoxicity, and cellular dysfunctions all can contribute to organ malfunction. Gestational age (GA) related to the $PM_{2.5}$ component of the Air Quality Index (AQI) has been explored but has not been assessed directly in the WV Project WATCH birth cohort. Appalachia is known for higher rates of adverse health outcomes including reproductive health outcomes. The entire state of WV is uniquely located in Appalachia. Researchers hypothesized a potential relationship between maternal inhalable $PM_{2.5}$ exposure and GA in WV.
Methods: WATCH data from 2018-2021 were combined with AQI databases for 2017-2021 of daily PM exposure readings. Primary outcome was GA of ≥37 weeks (full-term) or <37 weeks (preterm). Descriptive and inferential statistics assessed the relationship between GA and exposure to $PM_{2.5}$ during pregnancy. Univariate assessment of $PM_{2.5}$ values were used to create the primary exposure variable. Proportions, means, medians, and quartiles were used to determine the exposure of 30% of total pregnancy time exposed or not to 'moderate' and/or 'unhealthy' $PM_{2.5}$ levels. Final logistic regression model was adjusted for the mother's education level, prenatal care visits, race, maternal diabetes, smoking status, and other substance use. Statistical tests were performed in SAS 9.4 and the alpha level was 0.05 to indicate statistical significance.
Results: 27,176 live birth records were included in the total study sample, where 79.2% of the study sample spent less than 30% of their entire time pregnant at a 'moderate' and/or 'unhealthy' level of AQI measured by $PM_{2.5}$; and 20.8% spent 30% or more of their time pregnant at a 'moderate' and/or 'unhealthy' level (p=0.9946). A majority of the study sample were infant males (51.6%, p=0.355), with a birthweight of ≥2,500g (normal/overweight) (90.8%, p<0.0001), full-term birth (87.4%, p=0.0002), no congenital abnormality (99.4%, p=0.2014), an APGAR Score of ≥7 (95.5%, p=0.0088). Mothers in majority were white (89.3%, p<.0001), ≤12^{th} grade education level (53.2%, p<0.0001), ≥1 previous pregnancy (69.3%, p=0.0367), ≥10 prenatal care visits (88.9%, p=0.0003), did not have diabetes present during pregnancy (90.1%, p=0.0005), and did not smoke during pregnancy (79.8%, p=0.2917), and no substance use during pregnancy (85.8%, p<0.0001). Results showed a 15% increased odds (95% CI: 1.053-1.257, p=0.0019) of having a preterm infant by mothers exposed to moderate/unhealthy $PM_{2.5}$ levels for 30% or more time of total pregnancy in the adjusted model. Model was adjusted for the mother's education level, number of prenatal care visits, race, maternal diabetes status, smoking, and substance use. In the adjusted model, <10 prenatal care visits had 2.64 times (95% CI: 2.388-2.923, p<0.0001) the odds of preterm birth. Those who smoked during pregnancy had 1.33 times (95% CI: 1.203-1.469, p<0.0001) the odds of preterm birth in the adjusted model.
Conclusions: Crude and adjusted models demonstrated a statistically significant relationship among those exposed for ≥30% of pregnancy duration to a moderate/unhealthy $PM_{2.5}$ level of AQI and preterm birth, indicating a relationship for preterm birth. Prenatal care and smoker status are demonstrating a significant role on preterm birth predictors in tandem with the exposure of interest. Researchers need to push for studies across toxicology and epidemiology and use findings to inform policy, regulations, and healthcare professionals.

Poster# 05

EMISSIONS CHARACTERIZATION OF SIMULATED WILDLAND-URBAN INTERFACE FIRES

William T Goldsmith[1,2], Anand Ranpara[1,2], Thomas P Batchelor[1,2], David Kalafut[4], Mark Wilson[4], Cynthia Choo[4], Robert Burns[3,], Salik Hussain[1,2], David P Harper[5], Timothy R Nurkiewicz[1,2]

1 Department of Physiology, Pharmacology & Toxicology, West Virginia University (WVU), Morgantown, WV
2 Center for Inhalation Toxicology (iTOX), WVU, Morgantown, WV
3 Division of Forestry and Natural Resources, WVU, Morgantown, WV
4 Chemical Insights Research Institute of Underwriters Laboratories Research Institutes, Marietta, GA
5 Center for Renewable Carbon, University of Tennessee, Knoxville, TN

As modern building approaches regularly situate structures adjacent to (and in) wildlands, the frequency of wildland-urban interface (WUI) fires has risen. Novel building materials are consumed in WUI fires, but our understanding of these complex emissions is poor. The purpose of this study was to develop pellets made from mixtures of wood and building materials and to characterize the emissions. Mixtures of sawdust and building materials: 1) oriented strand board (OSB), 2) foam board insulation (FB), 3) vinyl flooring (VF)], and 4) mix of all building materials (MIX) were ground into suitable sizes and processed into pellets. These pellets were fed into a combustion generator and the emissions were sampled to measure: 1) environmental conditions, 2) aerosol characteristics, and 3) gas levels. Wood only and OSB pellets tended to produce more particles that were smaller. Additionally, they produced higher CO_2 and lower CO levels. Conversely, the VF MIX pellets exhibited lower particle counts, larger mass concentrations, and less efficient combustion. Volatile organic concentration levels tended to increase as synthetics were added with the highest levels being seen in the MIX pellets. Additionally, individual gases with known adverse health effects were identified and measured for each pellet type. The results of this study may be used to identify potential risks encountered by the public and first responders in proximity to WUI fires.

Support: NIH U54 GM104942 (TRN), R01 ES031253 (SH), R21 ES034942 (TRN), P20GM103434, funded in part by Chemical Insights Research Institute of Underwriters Laboratories Research Institutes

Poster# 06

EVALUATING MICROVASCULAR FUNCTION AFTER EXPOSURE TO SIMULATED MILITARY BURN PIT EMISSIONS

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Over one million of US Veterans have presented with “Chronic Multisymptom Illness” associated with inhalation exposures to open-air waste combustion from military burn pits (BP). These emissions are complex mixtures of particles and gases. The mechanisms of underlying health effects are poorly understood. The purpose of the study was to: 1) simulate BP combustion emissions using a surrogate generator, 2) characterize emissions, and 3) perform whole body inhalation exposure in rats. Pellets (~6 g/min) composed of 80% wood, 10% plastic, and 10% rubber were combusted with jet fuel with additives (0.25 mL/min) in a modified pellet stove. BP emissions were characterized in real-time and off-line for particles (size distribution, concentrations) and gases (total and speciation of volatiles). Sprague Dawley rats (sham control or BP emission) were exposed to ~10 mg/m^3 aerosols for 2-6 days. 24 hrs post exposure, arteriolar function was assessed via intravital microscopy. BP emissions contained: total particle 7.3e+6±9.5e+5 #/cc, mass 10.5±1.82 mg/m^3, and volatile chemicals 1.4±0.8 PPM. Particles had a median size range of 78-228 nm with diverse morphology. Gas speciation revealed formaldehyde (94.6 µg/m^3), ethylbenzene (68.5 µg/m^3), and acrolein (53.7 µg/m^3). Inhalation exposure to BP emissions significantly impaired endothelium dependent arteriolar dilation (20±14% change from control) as compared to sham-controls (113±24%). BP emissions contained a mixture of respirable particles and toxicants that may explain illnesses after inhalation exposures. This is the first report to document microvascular dysfunction after BP inhalation exposures. Future studies will incorporate more diverse combustion materials and extensive microvascular assessments.

Funding: NIH-U54-GM104942, P20-GM103434, and R21-ES034942 (TRN), R01-ES031253 (SH)

Poster# 07

CHARACTERIZATION OF EMISSION FROM THE NEWEST VS PREVIOUS ECIG GENERATIONS AND MODELLED DOSIMETRY ESTIMATES

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Since 2007, e-cigarette (Ecig) that vaporize liquid (e-liquid) has been undergoing advancements to attract users. Surge, a modern device, ultrasonicates to aerosolize e-liquid for emissions. IQOS devices heat tobacco-laced material without vaporizing e-liquid. The purpose of the study is to: 1) characterize and compare particles and chemicals emitted from Ecig (i.e., JoyTech), IQOS, and Surge at two puff topologies, and 2) evaluate dosimetric estimates for lung depositions among users. Emissions were generated by an automated syringe set up at 55- and 100-mL puff volumes within 5 sec duration and 30 sec intervals from JoyTech at 9W, IQOS, and Surge. Total particle mass and median aerodynamic diameters (MMAD: μm) were determined off-line using MiniMOUDI™ to estimates deposits in head, tracheobronchial (TB), and alveolar regions. Real-time concentrations (maximum: parts per million (PPM)) of 49 speciated chemicals was considered using FTIR. Results showed that higher aerosol mass (mg/puff) and smaller size of particles were emitted for 100- vs 55-mL puff volumes: JoyTech (10.19 vs 8.39), IQOS (0.79 vs 0.59), and Surge (4.73 vs 4.38). MMAD of IQOS (0.53 μm vs 0.60 μm) was significantly different ($p<0.05$) than JoyTech (1.25 μm vs 1.55 μm) and Surge (0.96 μm vs 1.25 μm) at 100- vs 55-mL. However, dosimetry estimated similar lung deposition in head (~39%), TB (~21%), and alveolar (~40%) for all the emissions. IQOS and Surge emitted harmful chemicals Pentenal (52.11-69.87 PPM) and possible human carcinogens: Acetaldehyde (132.31-171.87 PPM) and Glycerol (200.71-1780.49 PPM). JoyTech also emitted toxicants such as Isobutyraldehyde (71.89 PPM) and Nitrobenzene (2197.71 PPM) at 100 mL. Outcomes of the study highlight that: 1) statistical difference in MMADs do not imply practical implications in lung deposits, 2) real-time speciation of chemicals reveals previously unreported chemicals, 3) maximum concentrations of chemicals outweigh traditionally reported averages that undervalue exposure assessment and thereby biological impacts, and 4) though quantitatively lesser, newer devices *do not* pose safer emission profile than previous Ecig devices. Future study will include animal exposure to better address inferences of such emissions.

Poster# 08

UNIQUE EXTRACELLULAR VESICLE DERIVED SMALL NON-CODING RNA SIGNATURES ASSOCIATED WITH EARLY-LIFE LOW LEVEL ARSENIC EXPOSURE

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Arsenic (As) is a naturally occurring metalloid that crosses the blood-brain barrier, accumulates in the brain, and is linked to cognitive deficits in children. There is growing interest in the role of extracellular vesicles (EVs) in mediating intercellular communication and disease processes. EVs encapsulate proteins, nucleic acids, lipids, and metabolites within a lipid bilayer, protecting their contents and enabling long-distance molecular transfer. Developmental exposure to environmental toxicants like arsenic poses long-term risks to neural health, but the molecular mechanisms underlying such effects remain poorly understood. To address this, C57BL/6 wild-type mice were exposed to 100 ppb sodium arsenite in drinking water from preconception through weaning. Controls were exposure to normal drinking water. EVs were isolated from brain and plasma to assess alterations in small non-coding RNA (ncRNAs) cargo. Characterization confirmed stable EV morphology, size, and concentration across exposure groups. Small RNA sequencing revealed broad changes in EV-associated ncRNA profiles following arsenic exposure, especially in brain-derived EVs. These included differential expression of miRNAs, circRNA, snoRNA, snRNA, and tRNA. Brain EVs showed reduced abundance of brain-enriched miRNA and tRNAs involved in synaptic function. CircRNA profiling identified arsenic-responsive species predicted to regulate neurodevelopmental gene networks. In parallel, plasma EVs also exhibited altered ncRNA content, including decreased levels of brain-specific miRNA and overlapping circRNA profiles with brain EVs. Comparative analysis revealed both shared and compartment-specific responses, with some transcripts inversely regulated across brain and plasma. GO enrichment showed stronger neurodevelopmental associations in brain EVs, while plasma EVs reflected broader cellular responses. Together, these results identify EV-associated ncRNAs as accessible markers of neurodevelopmental toxicity and demonstrate compartment-specific molecular responses to early-life arsenic exposure.

Poster# 09

INITIAL ASSESSMENTS ON THE INFLUENCE OF WILDLAND URBAN INTERFACE FIRES ON SYSTEMIC MICROVASCULAR FUNCTION

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Air pollution is the second greatest global mortality risk. A major contributor to air pollution are forest fire emissions. In 2025, at least 49,462 wildfires have burned 4,377,661 acres in the United States. Wildland urban interface (WUI) fires occur where urban and residential areas are built alongside or integrate with the natural land. WUI fires are increasingly prevalent as communities grow. WUI emission exposures have been linked to adverse cardiovascular health. To date, the systemic microcirculation has not been studied after WUI emission exposures. This project's purpose is to assess systemic microvascular function after WUI emission inhalation exposures.

The initial phase assessed the potential of stress to affect microvascular reactivity. Male Sprague-Dawley rats were put into one of two control groups: naïve (N=11) or sham (N=9). Naïve rat characteristics: age (57±3 days), weight (281±16 g), mean arterial pressure (116±6 mmHg), and heart rate (365±21 bpm). Sham rat characteristics: age (58±2 days), weight (291±11 g), mean arterial pressure (123±6 mmHg), and heart rate (366±22 bpm). Naïve rats had no exposure or handling prior to surgery. Sham rats were placed into a chamber with HEPA-filtered air for a minimum of 4 hours. 24 hours later, the spinotrapezius muscle was prepared for intravital microscopy. The spinotrapezius muscle was superfused with acetylcholine (ACh, 10^{-6}–10^{-4} M) and angiotensin II (ANG II, 10^{-6}–10^{-4} M) to assess endothelium-dependent arteriolar dilation and vasoconstriction (respectively). Naïve arteriolar characteristics: n=43, ACh vasodilation (29 – 123±13%, change from control), and ANG II vasoconstriction (-11 – -39±5%). Sham arteriolar characteristics: n=31, ACh vasodilation (20 – 114±10%), and ANG II vasoconstriction (-9 – -38±4%).

A linear regression analysis was used to determine no significant differences between the two control groups. Handling and stress do not impact microvascular function. Future experiments will expose rats to WUI fire emissions by burning "WUI" pellets in a combustion generator.

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Poster# 10

CADMIUM EXPOSURE IMPAIRS CALCIUM HANDLING IN FEMALE MICE

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Cadmium is an environmental toxicant known to induce multi-organ damage, with widespread exposure common among U.S. and international populations. Interestingly, women are more likely to accumulate cadmium and may be more vulnerable to cadmium-induced cardiac toxicity. We set out to characterize the effects of acute cadmium exposure on female cardiac electrophysiological and metabolic changes. Female mice at 3-months-old (n=5/group) were intraperitoneally injected with 1.25mg/kg of cadmium on two consecutive days before euthanizing the mice and optically mapping their hearts. Simultaneous recordings of metabolic (NADH, FAD), calcium (Ca), and voltage (V_m) parameters were obtained using a quadruple parametric optical mapping system. Hearts were stained with RH237 and RHOD-2AM, voltage and calcium dyes, respectively, and dyes were excited by 520 nm excitation high power LED light. A second excitation light at 365 nm was used to induce autofluorescence of NADH and FAD. Female mice exposed to cadmium had significantly increased Ca-rise time (CaRT, 9.24 ± 1.30 ms) compared to controls (7.19 ± 0.51 ms, p=0.0112). Ca-transient duration (CaTD) was also significantly prolonged in cadmium mice compared to controls (81.15 ± 7.25 ms, vs 71.31 ± 4.23 ms, respectively, p=0.0306). Voltage and metabolic parameters were not significantly different except for action potential duration (APD) which was significantly shortened in cadmium-exposed mice (53.59 ± 4.20 ms) compared to controls (59.71 ± 3.40 ms, p=0.0350). Additionally, the number of arrhythmias was significantly increased in cadmium-exposed mice compared to controls (p=0.0055). Cadmium-exposed mice lost on average 1.78 grams over the exposure timeframe compared to controls (p=0.0002). This change in body weight resulted in elevated heart weight to body weight ratio (p=0.0495) among the cadmium-exposed mice compared to controls. Taken together, these data indicate that cadmium exposure in females, even acutely has negative impacts on calcium handling in the heart, leading to increased risk for arrhythmia and poorer health outcomes.

Funding: Cardiology T32 and Department of Pharmacology and Chemical Biology Start-up funds, University of Pittsburgh

Poster# 11

DERMAL & IMMUNE PROTEOME CHANGES WITH DERMAL PFPeS OR PFBS EXPOSURE

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Purpose: Despite regular detection of short chain Perfluoroalkyl substances (PFAS) in human samples and dermally encountered products, the dermal and immune molecular changes associated with exposure are under-characterized. Identification of exposure-associated early molecular changes in dermal and immune tissues is an important step in identifying molecular initiating events that may contribute to toxicity. To address this gap, changes in immune and dermal proteomes of mice dermally exposed to Perfluoropentanesulfonic acid) PFPeS or Perfluorobutanesulfonic acid (PFBS) were quantified.
Methods: Mice were dermally exposed, 25ul to each ear, for 10 days to 5% PFPeS or PFBS in acetone; control mice received vehicle. Endpoint body and spleen weights were collected, and ear, spleen, and bone marrow proteomes were analyzed via LC-MS/MS. Proteome Discoverer identified and quantitated peptides. Proteins with significantly altered expression were analyzed by overrepresentation analysis using the DAVID bioinformatics tool. Gene Set enrichment analysis (GSEA) was used to additionally identify sets of genes with altered expression.
Results: Dermal inflammation at the application site was not grossly evident and exposure did not largely alter spleen weight. Proteomic analysis of the ear, spleen, and bone marrow identified 1375, 1083, and 140 differentially expressed (DE) proteins in PFPeS exposed mice relative to vehicle controls. In PFBS exposed mice 1402, 404, and 146 proteins were DE in the ear, spleen, and bone marrow relative to control mice. Overrepresentation analysis of the DE genes in the PFPeS exposed mouse spleens identified enrichment of proteins with a role in ‘negative regulation of signaling’ and ‘regulation of cell differentiation.’ GSEA of splenic proteins of PFBS exposed mice identified negative enrichment of the ‘TNFα signaling via NFKβ’ gene set. In the ear, the biological process ontology ‘macromolecule glycosylation’ was significantly enriched in the PFBA exposure group. Three proteins contributing to this enrichment for PFBS exposed skin, ST3GAL1, MGAT4D, and B4GALT5, are also DE in the ears of PFPeS exposed mice. In bone marrow of PFBS exposed mice, GTPase NRAS is significantly upregulated and was 20X more abundant compared to control mice’s bone marrow. Although NRAS was not significantly upregulated in PFPeS exposed mouse bone marrow, 13 other genes were significantly DE in the same direction in both the PFBS and the PFPeS exposed mice. These include proteins with various functions.
Conclusion: Following future validation by secondary methods, these results guide the focus of follow-up studies into the molecular consequences of dermal PFBS and PFPeS exposure. As structurally similar longer chain PFAS are immunotoxic, this data also supports the need to consider the potential immunotoxicity of shorter chain PFAS including PFPeS and PFBS.

Poster# 12

THE ASSOCIATION OF INORGANIC ARSENIC EXPOSURE WITH HYPERTENSION AND HIGH BLOOD PRESSURE AMONG AFRICAN CARIBBEAN ADULTS IN TOBAGO

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Arsenic is a leading environmental toxicant contributing to the global burden of hypertension and cardiovascular disease. Although the mechanisms remain unclear, peoples of African ancestry, including those in the Caribbean, have an elevated risk of hypertension. To investigate whether environmental factors, such arsenic, increase hypertension in this population, we examined 965 middle aged and older Afro-Caribbean men and women from the Tobago Health Study for arsenic exposure and incidence of hypertension (defined as systolic BP >=140, diastolic BP >= 90, or use of antihypertensive medication) and high blood pressures. Arsenic exposure was measured as the sum of urinary arsenicals (ΣAs = inorganic As + dimethylarsinic acid + monomethylarsonic acid). Linear regression analyses were done to examine cross-sectional associations of urinary arsenicals with systolic, diastolic, pulse pressure and mean arterial pressure. We did logistic regression to examine odds of hypertension, and we also examined potential effect modification by sex. Each unit increase in ΣAs was associated with 2% higher odds of hypertension in the total cohort and 4% higher odds among women. Sex-stratified analyses indicated that arsenic exposure was related to higher systolic and pulse pressure in women, and to higher diastolic and mean arterial pressure in men. Evidence of sex-based effect modification was observed, with ΣAs exerting a greater influence on pulse pressure in women and on mean arterial pressure in men. These findings suggest that exposure to inorganic arsenic contributes to sex-specific patterns of greater odds of hypertension and high blood pressure among Afro-Caribbean adults in Tobago.

Poster# 13

DETERMINANTS OF TOXICANT FORMATION IN E-CIGARETTES: IMPACT OF WICK MATERIAL, TEMPERATURE AND E-LIQUID COMPOSITION

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Aldehydes and polycyclic aromatic hydrocarbons (PAHs), byproducts of cigarette smoke linked to toxicological risks and adverse health outcomes, are also formed during e-cigarette use, raising health concerns. Device temperature and e-liquid composition influence emissions, but wick material's role is unclear. This study investigates how temperature, solvent, and wick type jointly affect toxicant emissions, providing insights into material-dependent mechanisms relevant to exposure risk. E-cigarette devices with cotton or silica wicks were tested using e-liquids with varying propylene glycol (PG) to glycerol (G) ratios (100:0, 70:30, 50:50, 30:70, 0:100) at two power settings (lower: 0.2Ω, 15W; higher: 1.0Ω, 60W). Aldehydes and PAHs in the aerosols were quantified via HPLC and GC-MS/MS, respectively.

At lower temperatures, aldehyde and PAH levels were minimal across all conditions. Higher temperatures significantly increased aldehydes, with the highest levels observed in silica wicks using 100% glycerol. Silica wicks produced elevated aldehydes with both neat and mixed solvents (30:70, 70:30), while cotton wicks peaked at a 50:50 PG:G ratio. PAHs increased at higher temperatures, with 100% PG yielding the highest levels in cotton wicks and glycerol-rich mixtures driving PAH formation in silica.

Silica's low porosity and thermal stability may tend to concentrate aldehydes in glycerol-rich e-liquids, through limited airflow and heat dissipation promoting glycerol degradation at high temperatures. Conversely, porous cotton wicks with better heat dissipation appear to favor PAH formation, especially in PG-rich mixtures, as increased porosity may enhance e-liquid penetration and localized heating, facilitating near-pyrolysis of PG into PAHs. These findings underscore the critical role of wick material, solvent composition, and temperature in modulating emissions and identify wick porosity and formulation as key safety considerations to minimize toxicant formation.

Poster# 14

THE EFFECTS OF WESTERN DIET AND ENVIRONMENTAL CHEMICAL MIXTURES ON CARDIAC GENE EXPRESSION

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Introduction: A fatty, processed Western diet is associated with an increased prevalence of obesity, diabetes, and other conditions. Environmental chemical mixtures may be a significant risk factor in the change of nutritional stress into heart damage. The “Rust to Resilience” (R2R) environmental chemical mixtures used in this study contain the toxicants lead, cadmium, arsenic, and per-/polyfluoroalkyl substances (PFAS) which are prevalent environmental chemicals globally and in Pennsylvania populations.
Methods: R2R mixture was defined using data from a population of U.S. women of reproductive age. Adult mice were fed Western (WD) or control (CD) diets for 12 weeks. Subgroups received R2R doses at 0, 1x, or 100x concentrations. Heart tissue was isolated, and RNA was extracted for sequencing and qPCR. Differentially expressed genes were identified with Benjamini-Hochberg adjusted p-values <0.05 and a fold-change limit of ±0.5. We used ingenuity pathway analysis (IPA) to identify and compare pathways altered by R2R mixture in the WD or CD settings.
Results: We mapped 107 cardiac genes differentially expressed with R2R mixture and CD vs 2110 genes exposed to both R2R mixture and WD using IPA. In the CD analysis, R2R associated biological pathways included cardiac arrhythmia, dilation, and tachycardia, along with mitochondrial dysfunction. In contrast, WD with R2R mixture showed changes in heart signaling pathways including cardiac enlargement, dilation, and cell death. The WD group showed more extensive mitochondrial pathway disruption, including altered mitochondrial translation, dysfunction, and protein degradation.
Conclusions: These findings highlight chemical mixtures as an important risk-modifying factor in the setting of WD, indicating that dietary context influences the cardiac toxicity of environmental chemical exposure with potential implications for long-term cardiac health.

Poster# 15

PLACENTAL GROWTH FACTOR AS A TARGET OF ARSENIC TOXICITY: IMPLICATIONS FOR TROPHOBLAST FUNCTION

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Chronic exposure to inorganic arsenic (iAs) in drinking water above the EPA standard of 10 ppb remains a major public health concern and has been associated with pregnancy complications and adverse birth outcomes. The placenta, serving as the vital interface that delivers nutrients and oxygen and removes waste, is essential for fetal development. Placental Growth Factor (PGF), a member of the VEGF family, is a key regulator of angiogenesis, vascular remodeling and placental development. Our preliminary data showed that early-life exposure to iAs impaired placenta function, increased placental inflammation, and altered placental transcriptome. In particular, PGF expression was downregulated in mouse placenta tissues of both male and female fetus whose mother exposed to 10 parts per billion (ppb) in drinking water, suggesting a role for PGF in mediating arsenic-induced placental dysfunction.

To investigate the role of PGF in iAs-induced trophoblast dysfunction, we first used siRNA to knockdown PGF in human trophoblast BeWo cells and observed decreased trophoblast proliferation, impaired fusion, and diminished angiogenic capacity. Moreover, iAs exposure significantly downregulated PGF expression at the promoter activity, mRNA and protein levels in trophoblast cells, as well as its extracellular secretion. These changes were concordant with altered expression of genes involved in trophoblast dysfunction. Strikingly, we found that epigenetic modulation of PGF promoter methylation restored the iAs-induced PGF downregulation and alleviated placental dysfunction.

Together, these findings suggest that PGF could serve as a biomarker for identifying pregnant women at risk from iAs exposure, and that epigenetic interventions (such as modulation of PGF promoter methylation) helps to mitigate iAs-induced placental dysfunction and adverse fetal outcomes.

Poster# 16

PAINTING A PICTURE OF PREGNANCY: COMPARATIVE ASSESSMENT OF NONINVASIVE IMAGING MODALITIES IN A GESTATIONAL NANOTITANIUM DIOXIDE EXPOSURE MODEL

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Pregnancy is relatively brief timespan that produces profound physiological remodeling and adaptation for the mother. Toxicological insults during pregnancy may have direct deleterious effects on the growing feto-placental unit, or indirect effects on maternal somatic processes that may perturb physiological mechanisms needed for proper growth and development. Several non-invasive imaging modalities exist that allow for tracking of fetal growth and development across gestation without requiring euthanasia at predefined timepoints. The current study explores the use of echocardiographic and magnetic resonance imaging (MRI) in a titanium dioxide nanoparticulate (nano-TiO_2) gestational exposure to provide a comparison of benefits and drawbacks of respective applications. Concurrent with mid-to-late nano-TiO_2 exposure, Sprague Dawley rats underwent serial echocardiographic and MRI assessments on gestational days 13,15,17, and 20. Motion mode acquisition was used to assess fetal and maternal cardiac output, while brightness mode acquisition was used to measure cardiac strain across pregnancy. T2 MRI imaging was used to measure fetal and placental size. Both imaging modalities have clinical applications for assessing maternal and fetal health during healthy and potentially pathological complications of pregnancy. The continued development of early detection of fetomaternal maladaptation to external toxicants is crucial for providing the best therapeutic and/or surgical responses to sustain the health of both the mother and child.

Poster# 17

INHALATION OF ULTRAFINE CARBON BLACK INDUCED MITOCHONDRIAL DYSFUNCTION IN MOUSE HEART THROUGH CHANGES IN ACETYLATION

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Air pollution, particularly from fine and ultrafine particulate matter (PM) has been increasingly associated with cardiovascular diseases. Ultrafine carbon, a component of ultrafine PM widely used in industrial settings, is both an environmental and occupational hazard. But the cardiac toxicity of repeated inhalation exposure to ultrafine carbon black (CB) remains unclear. In this study, we investigated how repeated inhalation of CB affects cardiac mitochondrial function, focusing on metabolic pathways and regulatory mechanisms involved in energy production. Male C57BL/6J mice were exposed to either filtered air or CB aerosols (10 mg/m³) for four consecutive days. Cardiac tissues were collected and analyzed to assess changes in metabolic enzyme activity, protein expression, and mitochondrial function using western blotting, enzymatic assays, and immunoprecipitation. Despite few changes in overall protein expression levels, we observed significant impairments in fatty acid oxidation, increased glucose oxidation, and disrupted electron transport chain (ETC) supercomplex assembly, particularly in Complexes III and IV. These changes were accompanied by increased hyperacetylation of mitochondrial proteins and elevated levels of GCN5L1, a mitochondrial acetyltransferase. We also found increased lipid peroxidation and hyperacetylation of antioxidant enzyme SOD2 at the K-122 site which reflects reduced enzymatic activity contributing to oxidative stress. Our findings suggest that repeated CB inhalation leads to mitochondrial dysfunction in the heart by dysregulating substrate utilization, impairing ETC activities, and weakening antioxidant defenses primarily through lysine acetylation. These findings reveal a potential role of key post-translational mechanism in environmental particulate exposure to mitochondrial impairment and provide a potential therapeutic target for CB induced cardiotoxicity.

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Poster# 18

ARSENIC-INDUCED MITOCHONDRIAL DYSFUNCTION IN HUMAN PLACENTAL TROPHOBLAST CELLS

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Chronic exposure to inorganic arsenic (iAs) through drinking water is a major public health concern linked to pregnancy complications and adverse birth outcomes. The placenta serves as the essential interface for nutrient exchange between mother and fetus, so its proper function relies on mitochondrial activity, which supports normal trophoblast growth and function. Preliminary data show that gestational exposure to 10 parts per billion (ppb) iAs in drinking water results in placenta dysfunction and alterations in placental transcriptome. Gene Set Enrichment Analysis (GSEA) revealed differentially expressed genes enriched in mitochondrial pathways in male placentae.

We exposed BeWo cells (human trophoblast cells derived from male placentae) to sodium arsenite at concentrations between 0.02 to 1 μM for 14 days. iAs increased mRNA levels of several mitochondrial-encoded genes including MT-ND1, MT-ND2, MT-ND3, MT-ND4L, and MT-ND6, but downregulated the mRNA levels of NDUFS8, a nuclear-encoded Complex I gene. The observed alterations in gene expression, particularly within Complex I, suggest that iAs disrupts Complex I activity, impairing electron transport and mitochondrial efficiency.

To determine whether iAs-induced changes in mitochondrial gene expression could be reversed, we treated BeWo cells with iAs in combination with SS-31 (Elamipretide) and Erlotinib for 72 hours. SS-31 partially restored the expression of nuclear encoded complex I genes (e.g. NDUFS8) but had no effect on mitochondria-encoded counterparts; Erlotinib showed no restorative effect. Together, these findings suggest that iAs impairs Complex I function by modulating gene expression. SS-31 appears to counteract this imbalance by restoring nuclear gene expression essential for Complex I activity. These findings suggest SS-31 may help counteract iAs-induced mitochondrial dysfunction in trophoblasts, which could support placental health.

Poster# 19

DOES ALZHEIMER'S DISEASE AND OBESITY ALTER LYSINE ACETYLATION IN THE BRAIN?

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One of the largest modifiable risk factors for Alzheimer's disease (AD) is obesity. AD, typically associated with cognitive decline, is also commonly referred to as type III diabetes due to the severe metabolic dysregulation that occurs. Lysine acetylation, a post translation modification, has been seen to regulate metabolism in obese states within other organs, but has not clearly been investigated within the brain. We hypothesized that lysine acetylation plays a role in AD induced metabolic dysregulation by altering metabolism within key regions of the brain. To test this, we used 3xTg (AD) and wild type control (WT) mice (M/F) and placed them on a 60% high fat diet (HFD) or a 10% low fat diet (LFD) upon weaning. The diet lasted until 9 months of age. Before terminal procedures body composition measurements and glucose tolerance testing were performed. The cortex and hippocampus were isolated and homogenized from these animals for western blotting. Both male and female 3xtg HFD groups saw increased adiposity and decreased glucose metabolism. We saw that total acetylation was significantly altered amongst our groups within the hippocampus. However, within the cortex only males show significant alterations in total acetylation. This suggests both a region and sex specific role of lysine acetylation in the metabolic disruption seen in AD.

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Poster# 20

REDOX-EPIGENETIC REGULATION OF MATERNAL-FETAL IRON FOLLOWING PARTICLE EXPOSURE

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Inhalation of ultrafine particles (UFP) can lead to detrimental health effects during pregnancy, a critical period in the development of the fetus. During this time, maternal iron availability is essential for adequate fetal development. We hypothesized that UFP-induced oxidant production decreases iron regulation and availability for the fetus, stunting growth. Pregnant SD rats were exposed to titanium dioxide nanoparticle (nTiO2) aerosols or filtered air from GD (gestational day) 10-19, with terminal procedures at GD20. As before, maternal nTiO2 exposure increased H2O2 production leading to stunted growth in offspring. Iron concentration was increased in maternal liver and decreased in maternal plasma and fetal liver, indicating maternal anemia and decreased fetal iron delivery. Furthermore, reduced estrogen receptor α (ERα) DNA binding and increased levels of hepcidin were found in the liver and circulation, respectively. When hepatocytes were presented with nTiO2 or glucose oxidase with and without estradiol (E2), it was found that E2 decreased hepcidin levels and iron uptake, but nTiO2 and Gox increased hepcidin and iron cellular uptake beyond control levels, even in the presence of E2. Mechanistically, nTiO2 exposure leads to oxidation of ERα, which decreases interaction with histone methyltransferase (HMT) G9a. HMT G9a is crucial for the methylation and suppression of the hepcidin promoter. Thus, nTiO2 exposure leads to decreased repression of hepcidin, even in the presence of E2. Altogether, this work highlights a novel mechanism for ERα/G9a/Hepcidin-mediated disruption of iron homeostasis leading to intrauterine growth restriction in UFP exposed Sprague Dawley dams.

Poster# 21

LIVER HEALTH CONSIDERATIONS FOR ASTRONAUTS AND LUNAR HABITATION

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NASA's Artemis program envisions building lunar infrastructure for long-term human habitation. One problem to overcome is how to design filtration systems to keep lunar regolith dust (LR) from accumulating and determine permissive exposure limits (PELs) for long-term missions on the lunar surface and dwellings. The potential health burden of long-term exposure to LR following return to earth is potentially a relevant consideration. Particulate matter that moves past the lungs has a propensity to accumulate in the liver. With this in mind we asked the question does low concentration LR exposure induce cellular dysfunction in hepatocytes? To model this we used a mouse hepatocyte cell line AML-12 and exposed them to 100ng/ml of LR. We found that LR exposure in hepatocytes significantly reduced cell viability measured by ~30% reduction in Cell Glo ATP detection and an 80% reduction in scratch closure ($p<0.005$). This was accompanied by a 30% increase in hydrogen peroxide production, which could be reversed by NADPH oxidase inhibition with APX. We found that pretreating AML-12 cells with APX partially prevented LR-induced reductions in viability and scratch closure ($p<0.001$). Increased expression of BAX and the BAX/ BCL-2 ratio indicated that LR induced apoptosis in AML-12 cells supported by increased cleaved caspase 9 and caspase 3/7 activity, which were all mitigated by APX treatment. LR exposure also significantly induced senescence in AML-12 cell which was again prevented by APX. In conclusion LR has potential to stimulate long-term liver dysfunction in humans, and thus rigorous testing and evaluation of PELs related to cardiovascular outcomes from moon dust exposure are needed.

Poster# 22

BENCHMARK DOSE MODELING OF PROTEINURIA INDUCED BY A POPULATION-BASED METAL MIXTURE OF ARSENIC, CADMIUM AND LEAD: RESULTS FROM A ZEBRAFISH MODEL

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OBJECTIVE: Early exposure to metal mixtures can impair kidney development and function across the life course. Real-world exposures occur as complex mixtures, yet the toxicological evidence that informs risk assessment is traditionally derived from single-metal studies. To address this gap, we integrated human-relevant metal mixture exposure data with experimentally derived kidney outcomes in a kidney toxicology in vivo model, zebrafish.
METHODS: Using NHANES 2017-2020 data from women aged 20-44, we derived urinary mixing ratios of arsenite (As[3]), cadmium (Cd), and lead (Pb): 35%, 36%, and 28% of total molar concentration, respectively. Tg(NL-D3) zebrafish larvae were exposed to mixture doses ranging from 1x to 1000x nM (excluding controls) with 1x defined using the geometric mean of human exposure. At 6-7 days post fertilization, urinary nanoluciferase was quantified as an indicator of proximal tubule impairment, reflecting low-molecular weight proteinuria. Luminescence values were expressed as fold change relative to the control mean and modeled using a log-log linear regression without an intercept: ln(fold change)=β × log10(dose+1). The benchmark response (BMR) was defined as 2 SD above the control mean, and the corresponding benchmark dose (BMD) was then estimated.
RESULTS: The log-log linear model provided an adequate fit to the dose-response data, with a slope parameter of β=1.09 ± 0.04. A BMR set at 2 SD above the control mean corresponded to a 2.04-fold change in response and a BMD of 3.48x the mixture.
CONCLUSION: We established benchmark dose-response values for a population relevant mixtures of As(3), Cd, and Pb using a zebrafish model with BMD in the range of human exposures. Our next step will identify which subpopulations may be at risk of reduced kidney function from real-world exposures.

Poster# 23

EMPOWERING THE NEXT GENERATION OF PUBLIC HEALTH LEADERS: SLIPPERY ROCK UNIVERSITY'S ONLINE MASTER OF PUBLIC HEALTH IN ENVIRONMENTAL AND OCCUPATIONAL HEALTH

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Slippery Rock University offers a **Council on Education for Public Health (CEPH)-accredited** Master of Public Health (MPH) program in a fully online asynchronous format, designed for working professionals. The program includes two practitioner-focused concentrations: **Environmental and Occupational Health (EOH)** and **Health Promotion and Wellness (HPW)**.

The EOH concentration is a 42-credit curriculum completed in 21 months full-time, with up to 12 graduate credits transferable. It prepares students to address complex public health challenges through interdisciplinary competencies in leadership, communication, and systematic thinking. Specialized training includes toxicology, industrial hygiene, regulatory policy, risk assessment, and management.

Practicum and capstone courses are structured to embed CEPH core and concentration competencies, offering students hands-on experience in real-world public health settings. The program's flexible format allows students to maintain full-time employment and participate from any location, removing geographical barriers to graduate education.

Graduates emerge as critical thinkers, effective communicators, and collaborative problem solvers, equipped to address public health issues at the community, institutional, and population levels. In conclusion, we highlight the program structure, applied learning model, and workforce relevance, demonstrating how online graduate education can expand capacity in environmental and occupational health.

Poster# 24

RUST BELT ENVIRONMENTAL CONTAMINANTS AMPLIFY HEPATOTOXICITY IN MICE

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Background: Metabolic dysfunction-associated steatotic liver disease (MASLD) affects over 30% of Western populations with disproportionate impact on lower socioeconomic communities. While early-stage MASLD prevalence approaches 100% in at-risk individuals, progression to severe forms is not inevitable, suggesting additional risk factors drive disease severity. Environmental chemical mixtures may be such a risk factor and transform manageable dietary stress into severe liver injury. "Rust to Resilience" (R2R) chemical mixtures contain legacy toxicants (lead, cadmium, arsenic) and emerging PFAS relevant to industrialized countries and of high priority concern in southwestern Pennsylvania. This study investigated whether R2R-mixture exposure transforms Western diet-induced metabolic stress into severe hepatotoxicity. **Methods:** C57Bl/6J mice were fed Western or control diets for 12 weeks, with subgroups receiving R2R mixtures at 1× and 100× concentrations. Analysis included plasma biochemistry, histopathological assessment, and RNA-sequencing with integrated pathway analysis to determine molecular mechanisms of toxicant-diet interactions. **Results:** R2R-mixture exposure synergistically enhanced Western diet-induced liver injury, causing severe inflammation, coagulative necrosis, and portal expansion. Toxicant exposure promoted pathological lipid accumulation and hepatocyte ballooning - indicative of mitochondrial dysfunction. RNA-sequencing revealed that Western diet background amplified toxicant transcriptional responses 4.6-fold (137 vs 30 significant GO pathways) and uniquely enabled carcinogenic pathway activation absent under control diet conditions (15 vs 0 significant KEGG pathways). Western diet transformed manageable environmental exposure into severe hepatotoxicity characterized by metabolic dysregulation and activated carcinogenesis pathways. **Conclusion:** This study reveals a critical paradigm shift: environmental toxicant exposure doesn't merely add to Western diet-induced liver injury - it fundamentally transforms the hepatic response from metabolic adaptation to pathological crisis. Western diet creates a permissive environment where otherwise manageable environmental exposures trigger severe hepatotoxicity and activate carcinogenic pathways. These findings highlight complex environmental chemical exposure as a crucial risk-modifying factor explaining interindividual variability in MASLD progression.

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Poster# 25

HFD-INDUCED METABOLIC AND HEPATIC DYSFUNCTION IN A 3xTg-AD MODEL

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Obesity is now one of the most prevalent health issues threatening society. 21st-century estimates state that approximately one billion people are overweight or obese, with the occurrence of this pathology largely driven by nutritional imbalances. Particularly, high-fat diets (HFDs) are strongly linked with metabolic dysfunction. This nutritional excess is specifically associated with hepatic fatty acid oxidation enzyme acetylation, which can decrease the liver's capacity to properly regulate metabolism, thereby driving metabolic pathology. Moreover, the consequences of this diet extend to threaten the brain and cognition as well. This relationship has become especially important given the high prevalence of HFDs and cognitive disorders such as Alzheimer's Disease (AD). Here, male and female wild type (WT) and triple transgenic (3xTg, carrying three mutations commonly seen in familial AD) mice were fed either a 10%-fat or 60%-fat diet from weaning until 9 months of age. Thereafter, body weight, organ weight, and hepatic lipid accumulation were assessed. Hepatic mitochondrial protein levels, as well as acetylation of hepatic proteins, were quantified via Western blotting. On HFD, both male and female mice showed increased body weight compared to LFD, regardless of genotype. Further, WT HFD males showed hepatomegaly compared to their LFD counterparts. HFD males also showed increased total acetylation of hepatic mitochondrial proteins compared to LFD males, particularly among WT animals. Finally, hepatic lipid levels were significantly increased in response to HFD only in 3xTg males. These results emphasize the harmful metabolic effects of an HFD independent of sex or genetic differences. However, they highlight that males may be particularly affected by this dietary pattern, as both WT and 3xTg male mice experienced diverse manifestations of hepatic dysfunction in response to HFD. As a whole, this study confirms the toxic consequences of an HFD on overall metabolism and opens the door for further investigation into the sex- and genotype-specific pathologies seen in response to injurious dietary patterns.

Poster# 26

ROLE OF XANTHINE OXIDASE IN ULTRAFINE PARTICLE AND OZONE INHALATION INDUCED PULMONARY DYSFUNCTION IN OBESE MICE

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Rationale: Epidemiological and experimental evidence indicate that the lungs of obese individuals are among the most susceptible organs to air pollution-induced adverse outcomes. However, mechanisms implicated in this phenomenon, especially the role played by xanthine oxidoreductase (XOR) in the lungs of obese individuals in the context of air pollution exposures is largely unknown. We aimed at evaluating the role of xanthine oxidase (XO) by genetic and pharmacological manipulation hypothesizing that its inhibition would be beneficial.
Methods: Obesity/metabolic syndrome was induced in C57BL/6 mice by feeding high-fat (60% calories from fat) or control diets for 18 weeks. Ultrafine carbon black (CB) and ozone (O_3) aerosols were generated by mixing 2.5 mg/m^3 CB and 1 ppm O_3 and animals were exposed by whole-body inhalation for 3 hours per day for four days and euthanized 24 hours after last exposure. Lung inflammation was quantified by broncho-alveolar lavage and real-time PCR while lung function was assessed by FlexiVent. Oxidant production was evaluated by electron paramagnetic resonance spectroscopy. XO enzyme activity was assessed by an HPLC based assay with electrochemical detection.
Results: Aerosol characterization by scanning and transmission electron microscopy demonstrated ultrafine size agglomerates. Real-time exposure chamber aerosol concentration monitoring confirmed stable aerosol exposures. Obese mice demonstrated a decrease in lung function that worsened after exposure to co-exposure aerosols. Similarly, inhalation exposure resulted in augmented neutrophils ($p>0.01$) in the lavage of obese mice compared to lean mice. A significantly greater gene and protein expression of multiple inflammatory cytokines/chemokines IL-6, KC, IL-33, TNF-α, TSLP and IL1-β were observed in exposed obese mice compared to lean exposed mice. EPR an immuno spin-trapping demonstrated significantly greater lavage, lung tissue, plasma and liver XO activity in obese mice compared to lean mice. Administration of XO -specific inhibitor febuxostat (50 mg/L in drinking water) significantly prevented inhalation exposure-induced exacerbation phenotype.
Conclusions: In conclusion, we demonstrate that XO contributes to the exacerbated lung and systemic inflammatory phenotype in diet-induced obesity and its inhibition can be used as an intervention to counter air pollution-induced adverse outcomes in obese subjects.

Funding: Supported by NIH grants R01ES031253 (SH), R01ES03125304S1 (SH)

Poster# 27

IMPACT OF OXYGEN SOURCE AND PURITY ON THE FINE-TUNING OF OZONE-INDUCED PULMONARY INFLAMMATION AND INJURY

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Background and Purpose: Ground-level ozone (O_3) is a criteria pollutant with significant adverse health impacts, both acute and chronic. Due to increased unforeseen climate events O_3 levels are anticipated to rise over the next decade. Ground-level O_3 is generated in the environment through a reaction between the volatile organic compounds and nitrogen oxides (NOx) in the presence of sunlight. During experimental O_3 generation varying amounts of NOx are produced as a by-product of the reaction depending upon the method and purity of the oxygen source. These NOx are usually not measured and their relative contribution to the biological outcomes after O_3 and ultrafine particle and O_3 mixed inhalation exposure is unknown. In this study, we aimed to evaluate O_3 generation from room air containing 21% Oxygen vs pure medical grade (100% pure) oxygen and studied lung injury, redox imbalance, and inflammation.
Methods: Eight-to 10-week-old male C57BL/6J mice (purchased from Jackson Laboratories) were exposed to air or a mixture of 2 ppm O_3 and 10 mg/m^3 CB using O_3 generated by either room air-CB+O_3 (RA) or pure oxygen-CB+O_3(Oxy). In a second set of experiments, mice were exposed to filtered room air, O_3 generated using room air-O_3(RA) or O_3 generated using pure oxygen-O_3(Oxy). Filtered room air was used as a control. We studied lung inflammation and injury by evaluating broncho-alveolar lavage cellularity, differential cell counts, cytokine secretion by multiplex assay, inflammatory gene expression, histology, and lactate dehydrogenase release in lavage. Oxidant generation was studied using electron paramagnetic resonance spectroscopy and western blot for 3-nitrotyrosine (3-NT).
Results: The use of RA to generate O_3 leads to significant NO_2 formation. We demonstrate that O_3 generated using RA when mixed with ultrafine CB leads to eosinophil recruitment in the lungs while O_3 generated using pure oxygen only causes neutrophil recruitment. Similarly, greater lung injury, oxidant generation and antioxidant depletion were observed in RA O_3 and RA CB+O_3 compared to Oxy O_3 and Oxy CB+O_3. Lung tissue 3-NT levels were only significantly elevated in the case of RA O_3 generation.
Conclusions: In sum, we demonstrate that the O_3-induced magnitude and nature of lung damage are impacted by the method used for its generation. We recommend consistent monitoring and reporting of the NOx levels in the experiment exposure studies with O_3.

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Poster# 28

THE IMPACT OF IN UTERO AND EARLY LIFE ARSENIC EXPOSURE ON SKELETAL MUSCLE METABOLIC HEALTH: EVIDENCE OF GLYCOGEN DEPLETION AND METABOLIC SHIFT.

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Background: Arsenic, a widespread environmental contaminant, is linked to various metabolic disorders, yet its effect on skeletal muscle metabolism remains underexplored. Our previous studies demonstrated that arsenic exposures disrupt muscle energy balance, impairing muscle maintenance, function, and regenerative capacity. Such disruptions in muscle metabolism are known to contribute to systemic metabolic dysfunction. This study investigates metabolic shifts in skeletal muscles of mice exposed to arsenic in utero and early life.
Methods: C57BL6 were exposed to 0 or 100 µg/L of arsenite in drinking water in utero and continued for 12 weeks post-weaning. Male offspring were analyzed for fasting plasma glucose, insulin, and lipid levels. Tibialis anterior and quadriceps muscles were collected for histologic, biochemical, and metabolomic analyses. Glycogen content was measured by periodic acid-Schiff (PAS) staining, immunofluorescent imaging and enzymatic assay. Multi-omics LC-MS analysis was used to assess metabolic pathway disruptions.
Results: Arsenic exposure did not result in differences in fasting plasma glucose, insulin, or lipid levels, although there was a trend towards elevated non-esterified fatty acids. In contrast, skeletal muscle glycogen was significantly decreased. GLUT4 translocation was enhanced, despite no systemic glucose impairment. Metabolomic analysis revealed disrupted glycolysis, with reduced phosphocreatine, 6-phosphogluconic acid, 2-phosphoglyceric acid, and 3-phosphoglyceric acid, alongside an increased lactate, suggesting a Warburg-like metabolic shift.
Conclusion: Low to moderate arsenic exposure in utero and early life disrupts skeletal muscle metabolism, leading to glycogen depletion and altered energy metabolism. The Warburg-like metabolic aligns with impaired mitochondrial function and increased muscle fatigue, providing insight into arsenic-related metabolic dysfunction.

Funding: *Supported by NIEHS grant R01ES033519*

Poster# 29

INVESTIGATING THE EFFECTS OF GLYPHOSATE-BASED HERBICIDES (GBHs) ON YEAST METABOLISM

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The steady and rapid rise of the global population underscores the need to ensure food security around the world. An important part of efficient agricultural practices is pest control, with RoundUp and its active ingredient glyphosate representing the most widely used herbicide. Glyphosate inhibits the shikimate pathway, essential for biosynthesizing chorismate and aromatic amino acids. Although animals lack the pathway, increasing reports of glyphosate toxicity in various model organisms highlight the need for a deeper understanding of its molecular mechanisms. The budding yeast *Saccharomyces cerevisiae* serves as a versatile eukaryotic model organism to investigate non-target-site effects of glyphosate. Previous work from our group identified *DIP5*, a glutamate/aspartate permease, as a key player in glyphosate uptake, with *DIP5* deletion mutants exhibiting resistance—likely because Dip5 facilitates glyphosate transport into the cell due to its structural similarity to its canonical substrates. In this study we show that cells lacking *DIP5* have significantly lower levels of glyphosate compared to wild-type, confirming that Dip5 is essential for the import of the pesticide. We further conducted a whole metabolome liquid-chromatography and mass-spectrometry analysis on yeast treated with glyphosate, as well as isolated organelle fractions and purified mitochondria. Our findings reveal that glyphosate disrupts amino acid balance compared to the control group, including molecules outside the shikimate pathway. Additionally, glyphosate disrupted urea and carbohydrate metabolism, as well as mitochondrial function as shown by key molecules of mitochondrial function and direct oxygen consumption rate measurements. These results contribute to recent evidence supporting off-target glyphosate toxicity, underscore the importance of studying glyphosate's effects beyond the shikimate pathway, and enhance our understanding of its potential impact on more complex eukaryotes.

Poster# 30

REAL-TIME HEPATIC SURVEILLANCE IN RESIDENTS FOLLOWING THE EAST PALESTINE, OH CHEMICAL DISASTER

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Background: The February 2023 train derailment in East Palestine, Ohio, released vinyl chloride and other hepatotoxic chemicals, creating urgent need for health surveillance. This study represents the first systematic liver function assessment in residents potentially exposed to these environmental toxicants, establishing critical baseline data for long-term health monitoring. **Methods:** Adults ≥18 years within 8 miles of the derailment site have been recruited since June 2024. Participants provide informed consent for blood sampling and complete questionnaires on demographics, alcohol consumption, medical history, and health status. Liver function is assessed via serum ALT and AST levels. Body mass index (BMI) is calculated from measured anthropometric data. **Results:** To date, 47 participants enrolled (mean age 65.9 years, range 32-81), representing robust community response. All participants self-identified as White. Mean BMI was 29.0 kg/m² with 25% overweight (BMI 25-29.9 kg/m²) and 56% obese (BMI ≥30 kg/m²). Alcohol consumption: 75% drank <4 times weekly, 19% abstained, and 6% consumed alcohol ≥4 times weekly. Mean liver enzyme levels remained within normal ranges: ALT 18.25 U/L and AST 20.13 U/L. Only one participant demonstrated elevated ALT (48 U/L); this individual had BMI of 30 and abstained from alcohol, while all others exhibited normal values. No correlation was observed between enzyme levels and alcohol consumption or BMI. As recruitment remains active, these preliminary findings may evolve. **Conclusions:** This pioneering surveillance study reveals preliminary findings: despite potential vinyl chloride exposure, the vast majority demonstrate normal liver enzyme levels, though traditional biomarkers ALT and AST may not detect early hepatotoxicity. Continued vigilance remains essential, as one participant showed elevation warranting monitoring. Future analyses will include CK-18, which has demonstrated superior predictive value for vinyl chloride-related liver damage. These baseline data enable longitudinal tracking of hepatic health in this uniquely exposed population. This study represents a critical model for environmental health response with implications extending beyond East Palestine to communities worldwide facing similar toxicant exposure threats.

Poster# 31

REGIONAL BRAIN VOLUME CHANGES IN ADULT OFFSPRING WITH IN UTERO ELECTRONIC CIGARETTE EXPOSURE

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Electronic cigarette (ECig) use has increased rapidly and even promoted as a safer alternative to smoking to pregnant women. Yet ECig use is known increase oxidative stress and the long-term neurobiological effects to maternal-fetal dyad remain poorly understood. We used magnetic resonance imaging (MRI) to examine brain volumes in adult offspring with history of in utero exposure from maternal exposure to either either Air or ECig aerosol. Time-mated C57BL/6J female mice were exposed from gestational day 7-21 to either Air (n=14 dams) or ECig aerosol using 50:50 VG:PG, no flavor or nicotine (n=13/dams). Nine-month-old male offspring had MRI performed (1T-Brukar; T_2-weighted, 160µm sagittal view) to assess regional brain volumes (forebrain, hindbrain, olfactory and ventricles) normalized to total brain volume (e.g. region/total volume). Regional brain volumes were assess for forebrain, hindbrain, olfactory and ventricles regions and accounted for ~65%, ~27%, ~6% and ~2% of whole brain volume (WBV), respectively. WBV was 2.3% smaller in Ecig compared to Air offspring ($p<0.05$). ANOVA analysis revealed statistically significant decrease in normalized forebrain volume (Air 65.3±0.008% vs ECig 64.2±0.011%, mean±SD, p=0.008) and increase in normalized hindbrain volume (Air 26.3±0.006% vs ECig 26.9±0.007%, mean±SD, p=0.026), but no significant difference in olfactory (Air 6.1±0.004% vs ECig 6.5±0.007%, p=0.157) or ventricle volumes (Air 2.1±0.003% vs ECig 2.3±0.005%, p=0.151). These findings are consistent with emerging evidence of adverse neurobiological health in offspring which experience in utero exposure to harmful or potentially harmful constituents (HPHCs) from ECigs. Future studies need to provide longitudinal MRI assessment and behavior testing in offspring throughout its life course.

Funding: Support by NIH R56 ES035719-01 and WV-INBRE NIH Grant P20GM103434

Poster# 32

ALPHA DIVERSITY OF HEPATIC GENE EXPRESSION PATTERNS: A NOVEL DIAGNOSTIC TOOL FOR ALCOHOL-RELATED LIVER DISEASE

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Background: Alpha diversity analysis of transcriptomes represents an underutilized yet powerful diagnostic tool for detecting disease-related changes in gene expression patterns. While traditional approaches like differential gene expression (DEG) and beta-diversity analyses are commonly used to study transcriptional changes, measuring within-population diversity (alpha diversity) offers unique diagnostic insights into how diseases affect global gene expression patterns. Environmental stressors and disease conditions often impact the entire transcriptional landscape, making alpha diversity metrics valuable tools for understanding pathological changes. In our investigation of alcohol-related liver disease (ALD), we examined global hepatic gene expression patterns using novel Differential Shannon Diversity (DSD) analysis and transcriptome heterogeneity measurements (α-diversity) to better understand disease-induced changes in gene expression patterns. **Methods:** We evaluated alpha diversity's diagnostic potential in alcohol-related liver disease (ALD) using RNA sequencing data from healthy controls (n=10), early silent ALD (ASH, n=11), and severe AH (n=18) patients. Alpha diversity indices were calculated using PAST software, complemented by Differential Shannon Diversity (DSD) analysis to measure individual genes' contributions to total transcriptome heterogeneity. **Results:** ALD significantly decreased the α-diversity of the hepatic transcriptome versus healthy controls and correlated with an increase in the relative contribution of select genes to overall expression. These changes were driven by a net loss of expression of lower abundance genes. IPA analysis of significantly changed genes determined by DEG and DSD showed overlapping genes and canonical pathways by both analyses. However, DSD analysis also identified novel genes and pathways not highlighted by DEG approach. Importantly, novel pathways identified differences between preclinical ALD (ASH), as well as between severe and non-severe AH more effectively than DEG analysis. Moreover, some of these pathways have been established to potentially contribute to ALD. **Conclusion:** Alpha diversity analysis demonstrates significant potential as a diagnostic tool in liver disease. By measuring transcriptome heterogeneity, it can effectively differentiate disease stages and identify novel pathways involved in ALD progression. The complementary use of DSD analysis enhances diagnostic capabilities by revealing disease mechanisms and potential biomarkers that conventional analyses might overlook.

Poster# 33

MZB1 ORCHESTRATES HEPATIC REGENERATION: ESSENTIAL ROLE IN CELL CYCLE PROGRESSION FOLLOWING LIVER INJURY

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Background: Marginal Zone B and B1 Cell-Specific Protein (MZB1) is a B-cell-specific protein in the endoplasmic reticulum involved in B cell function, cellular proliferation, and inflammation. Deep proteome profiling shows MZB1-positive plasma B cells in human lung and skin fibrosis, with MZB1 knockout (KO) mice protected from bleomycin-induced fibrosis in these organs. This study investigated MZB1's role in liver fibrosis and regeneration, a function previously unexplored.
Methods: Human fibrotic liver specimens from alcohol-related hepatitis, alcohol-related liver disease, MASLD, and primary biliary cholangitis were immunostained for MZB1. For mechanistic studies, two MZB1 knockout mouse models (whole-body and inducible conditional) were utilized. Mice were administered CCl_4 for acute (1 day) or chronic (28 days) exposure to induce liver injury and fibrosis. To assess regenerative capacity, mice underwent 70% partial hepatectomy with 24-hour recovery. Liver tissues were analyzed through histology, biochemical analyses, and gene expression profiling.
Results: Immunofluorescence analysis revealed elevated MZB1 expression in all examined fibrotic liver diseases, with MZB1 signal colocalizing with fibrotic septae. MZB1 KO mice developed more severe liver injury and fibrosis following CCl_4 treatment compared to controls. Importantly, these mice exhibited impaired regenerative capacity in the CCl_4 model, prompting further investigation using partial hepatectomy. Following hepatectomy, MZB1 deficiency dramatically impaired liver regeneration, with hepatocytes blocked at the G0-G1 cell cycle transition due to downregulation of CDK6 and cyclin D1. Transcriptomic analysis revealed fundamental alterations in gene expression profiles governing cell cycle progression and growth factor signaling, with dysregulation of HGF/c-Met signaling, STAT3 activation, and mTOR pathway components.
Conclusions: MZB1 plays a critical role in hepatocyte proliferation and liver regeneration, despite its presence in fibrotic areas of human liver disease. The exacerbated liver injury in MZB1 KO mice reflects its role in supporting hepatocyte proliferation rather than a direct antifibrotic effect, contrasting with its apparent profibrotic function in lung and skin. Mechanistically, MZB1 loss disrupts the crosstalk between cell cycle proteins and growth factor signaling. These findings identify MZB1 as a potential target for enhancing liver regeneration in clinical settings.

Poster# 34

CALPAIN-4 KNOCKDOWN MODULATES CHOLESTEROL METABOLISM AND LXRA NUCLEAR LOCALIZATION IN ALCOHOL-RELATED LIVER DISEASE

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Background: Alcohol-related liver disease (ALD) has a high prevalence worldwide, yet effective treatments remain unavailable. Ethanol affects lipid metabolism through multiple pathways, leading to fatty liver development in most ALD patients. Recent studies have highlighted the role of calpain, a calcium-dependent protease, in liver inflammation and fibrosis. Calpain activity is regulated by its essential subunit, Capns1, (calpain-4, Capn4), which stabilizes and modulates the activity of its catalytic isoforms, calpain-1 and calpain-2. This study investigated calpain's impact on lipid metabolism in ALD.
Method: Six-week-old C57Bl6/J mice were injected with rAAV8 vectors encoding Capn4 shRNA or control vectors. After four weeks, mice underwent a 10-day period of ad libitum ethanol consumption, followed by a single gavaged ethanol administration on day 11.
Result: Following Capn4 knockdown, microvesicular steatosis was attenuated. While triglycerides and free fatty acids levels showed no significant changes, cholesterol levels were significantly reduced in the ethanol (EtOH) group with Capn4 knockdown. *Cpt1a* expression increased significantly in the EtOH group with Capn4 knockdown. Western blot analysis revealed increased Cleaved-HMGCR to Pro-HMGCR ratio in Capn4 knockdown mice, suggesting reduced HMGCR activity and suppressed cholesterol biosynthesis. LXRα expression was mainly increased in the cytoplasm in the EtOH group, and following Capn4 knockdown, it was relocalized to the nucleus via its activation. In addition, RNA sequencing analysis suggests that Capn4 knockdown contributes to the reprogramming of ethanol-induced disruptions in metabolic and homeostatic pathways, primarily those involving cholesterol metabolism.
Conclusions: Further investigation into the relationship between Capn4 and cholesterol biosynthesis proteins may provide insights into using calpain inhibitors as a therapeutic approach for alcohol-related hepatitis.

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Poster# 35

SILENCING HEPATIC CAPN4 PROTECTS AGAINST DIET-INDUCED MASH IN MICE

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Background: Metabolic dysfunction-associated steatohepatitis (MASH) is a severe liver disease characterized by hepatocellular inflammation and fibrosis that affects a significant portion of the population. Plasma proteomic profiling reveals a distinctive pattern of protein degradation in MASH compared to healthy liver, with computational analysis implicating elevated calpain- mediated proteolysis. Calpains (particularly Calpain 1/2 isoforms) are Ca2+-dependent proteases activated under cellular stress that regulate tissue remodeling and inflammation, yet their specific role in MASH pathogenesis remains poorly understood. This study investigated whether hepatic Calpain 1/2 activity is necessary for MASH development. **Methods:** C57Bl/6J mice received rAAV8 vectors encoding shRNA targeting Capn4 or scrambled control sequences under hepatocyte-specific (albumin) promoter control. After 4 weeks of vector integration, mice were fed either a low-fat control diet (13% saturated fat) or a Western-style high-fat, high-fructose diet (42% saturated fat) for 12 weeks. Hepatic Capn4 expression was quantified by qPCR. Analysis included plasma biochemistry, histopathological assessment of liver injury and steatosis, and quantitative PCR analysis of inflammatory gene expression to determine the contribution of calpain activity to MASH pathogenesis. **Results:** rAAVB-mediated knockdown achieved robust suppression of hepatic Capn4 expression. As expected, Western diet induced obesity, insulin resistance, and severe SteatoHepatitis. Despite minimal systemic differences in obesity and adiposity metrics, Capn4 knockdown substantially attenuated liver injury and fibrosis as well as suppressed key inflammatory genes associated with MASH progression. **Conclusion:** This study reveals that Capn4-mediated hepatic calpain activity is a critical driver of MASH development, specifically affecting disease initiation rather than advanced fibrosis progression. Blocking hepatic calpain proteolysis disrupts early pathogenic mechanisms while having minimal impact on systemic metabolic parameters. These findings establish Capn4 targeting as a potential therapeutic strategy for early intervention in MASH and highlight the critical role of hepatic Calpain 1/2 in disease development.

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