

2026 Annual Meeting

Bridging Discovery and Regulation: NAMs Across the Toxicology Continuum

October 22nd and 23rd, 2026

University of Iowa College of Public Health, Iowa City, IA

Central States Chapter of the Society of Toxicology (CS-SOT): 2026 Meeting Agenda

“Bridging Discovery and Regulation: NAMs Across the Toxicology Continuum”

Thursday, October 22, 2026, College of Public Health Building (CPHB)

5:00 PM	Registration and Networking – 1 st Floor Atrium
6:30 PM	Dinner at CPHB – C217A,B (overflow seating in 5 th Floor Atrium)
7:30 PM	Welcome and Synopsis of the CS-SOT President – C217A,B Hans-Joachim Lehmler
7:45 PM	John Doull Award Presentation and Lecture – C217A,B
9:00 PM	UI Human Toxicology Program Student-Planned Event

Friday, October 23, 2026, College of Public Health Building (CPHB)

8:00 AM	Breakfast, Networking, and Poster Setup – 1 st Floor Atrium
8:45 AM	Opening words – Ellig Auditorium (N120) Dr. Hans-Joachim Lehmler, Director, Environmental Health Sciences Research Center Dr. David Schwebel, Vice President for Research, University of Iowa
9:00 AM	Keynote Presentation – Ellig Auditorium (N120) (Moderator: Khue Nguyen) From Molecules to Mechanisms to Regulation: Using Zebrafish NAMs to Decode Chemical Bioactivity Dr. Robyn Leigh Tanguay, Oregon State University
10:00 AM	Coffee/Tea Break
10:15 AM	4 Oral Presentations – Ellig Auditorium (Moderators: Mahbube Jafari, Kshitij Deshmukh) Caleigh Grote, Iowa State University: <i>Impact of perfluorooctanoic acid exposure on maturation and abundance of superoxide dismutase 1, Bcl2 associated X protein, and apoptosis inducing factor in the porcine oocyte</i> Diego Kevin Chavez, University of Kansas Medical Center: <i>Establishment of liver zonation is required for APAP induced liver injury in young mice</i> Sarah Preston, University of Iowa: <i>NRF2 signaling as a mechanism of protection against organophosphate toxicity</i> Changyong Lee, University of Nebraska Medical Center: <i>Kaempferol attenuates PFDA-induced disruption of estrous cyclicity and ovarian steroidogenic regulation in female mice</i>
11:15 AM	Poster Session I – Atrium (Even numbers)
12:15 PM	Lunch – CPHB-C217A,B (overflow seating in 5 th Floor Atrium)
12:45 PM	Poster Session II – Atrium (Odd numbers)
1:45 PM	4 Oral Presentations – Ellig Auditorium (Moderators: Shri Vishalini Rajaram, Edozie Okpara) Cassidy Kline, University of Iowa: <i>Chlorpromazine reveals GPNMB-mediated protection against toxicant-induced oxidative stress in cardiomyocytes</i> Khue Nguyen, University of Kansas Medical Center: <i>Per- and polyfluoroalkyl substances exposure disrupts fatty acid metabolism and exacerbates hepatocellular lipid accumulation in alcohol-associated liver disease</i>

Rasha Ghorab, University of Nebraska Medical Center: *Reproductive age influences ovarian physiological and transcriptomic patterns following short-term PFAS mixture exposure*

Md Abu Ebrahim Siddique, University of Iowa: *Repeated inhalation exposures shift nanoparticle-induced pulmonary inflammation from a transient response to persistent immune remodeling with distinct extracellular vesicles-microRNA signatures*

3:10 PM

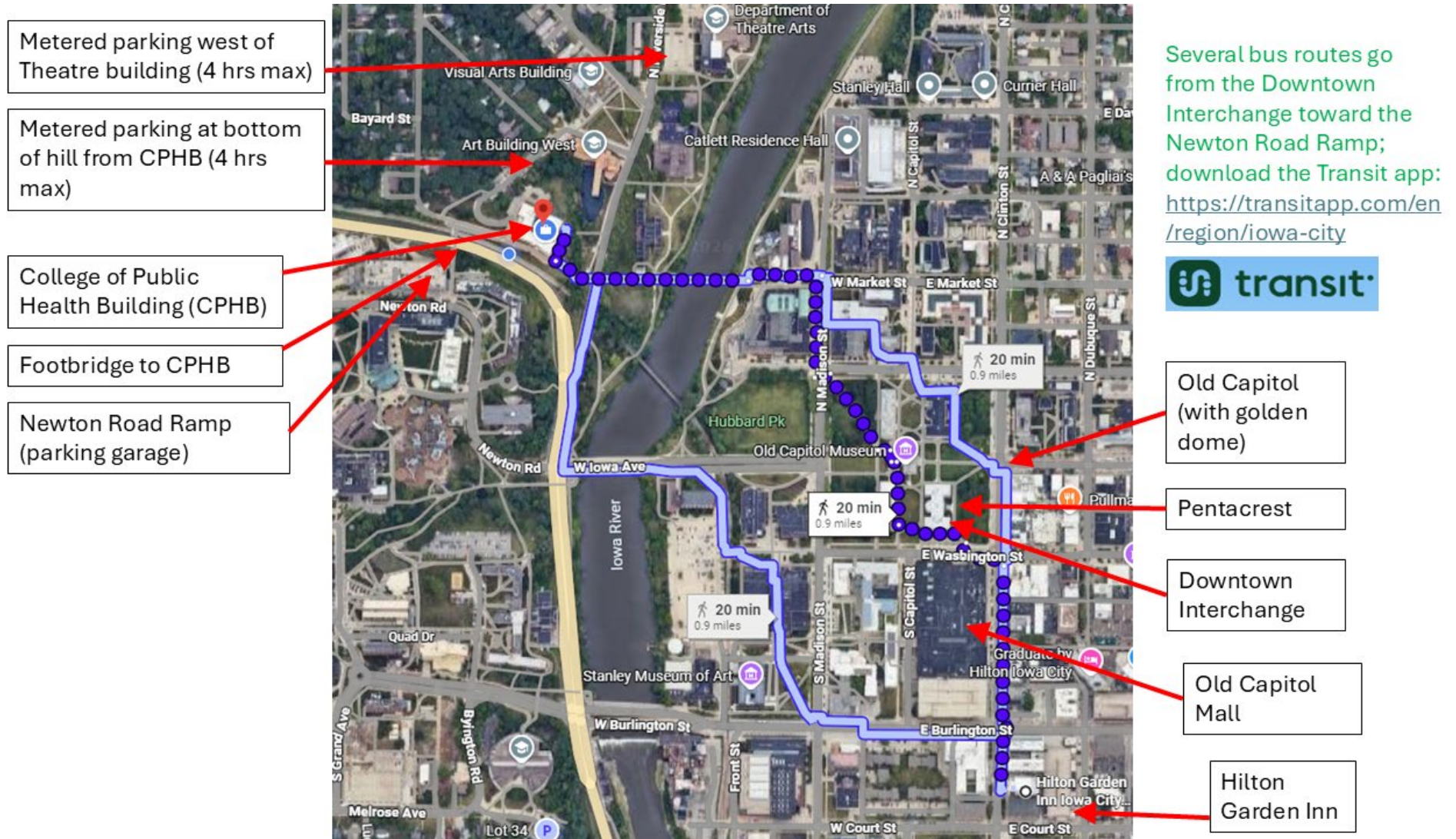
Presentation of Awards – Ellig Auditorium

(Poster and Oral Presentation Awards)

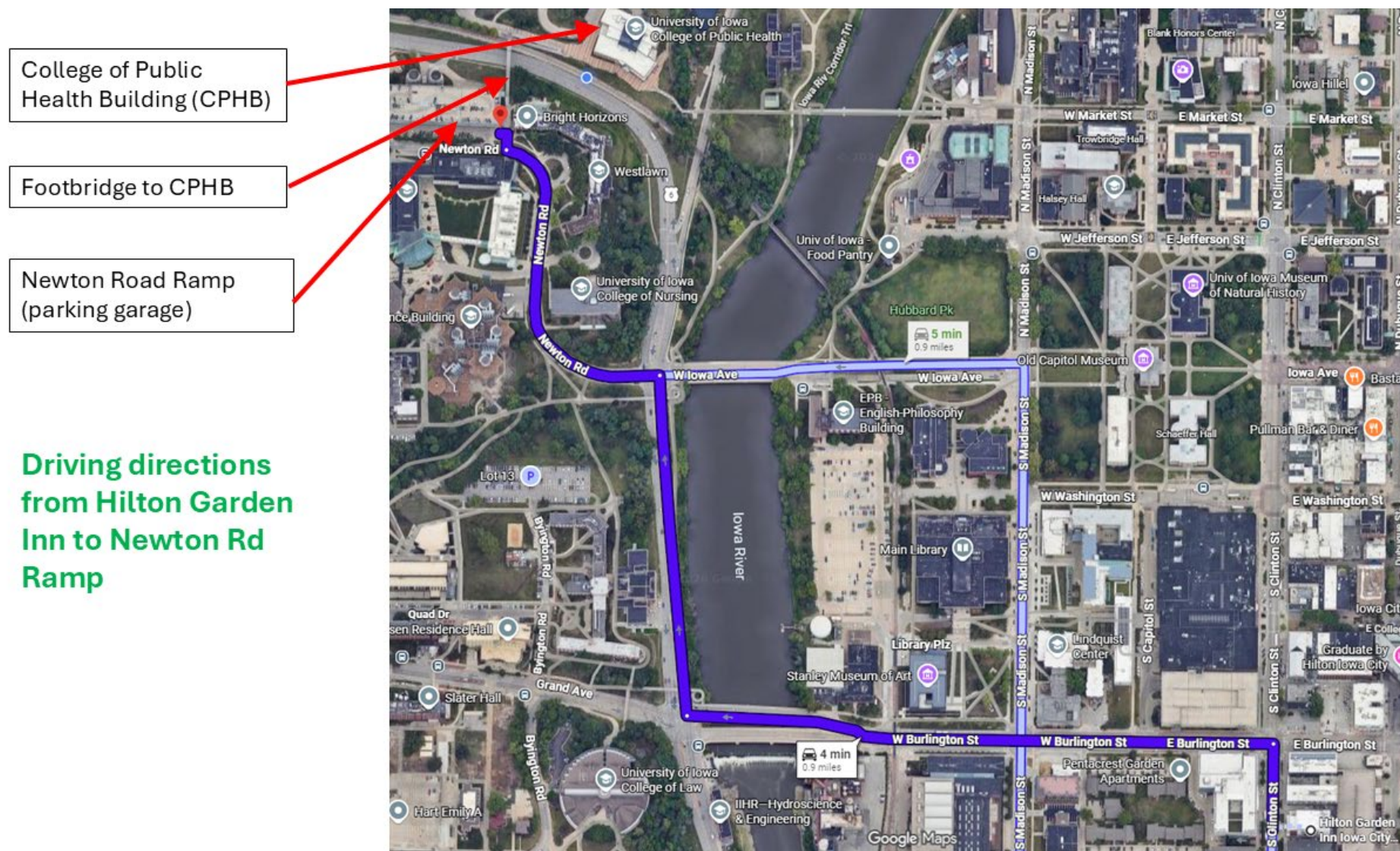
3:30 PM

Close of meeting

Walking and Driving Directions to the College of Public Health Building



Walking and Driving Directions to the College of Public Health Building



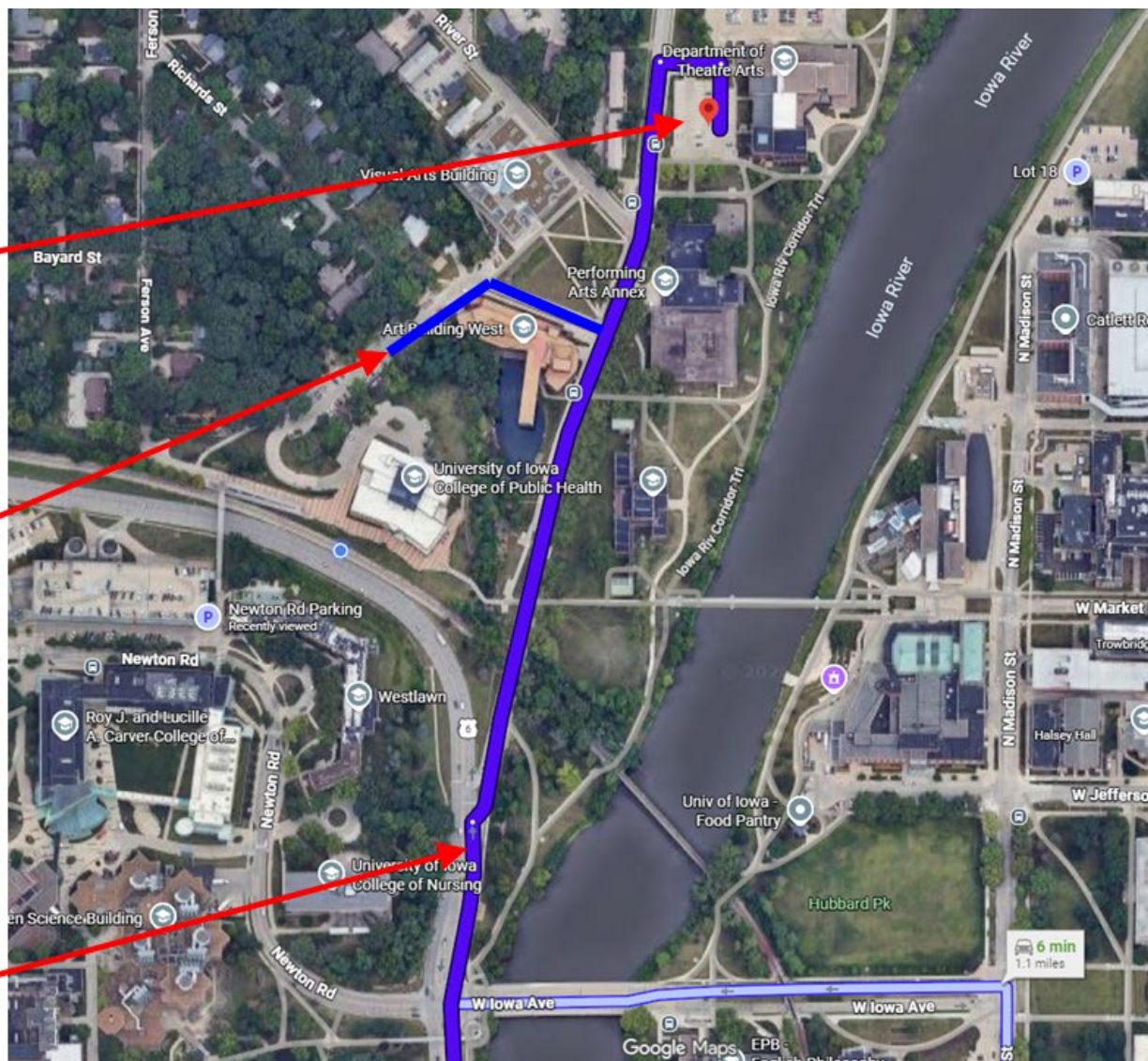
Walking and Driving Directions to the College of Public Health Building

Driving directions to Theatre lot or CPHB parking (coming N on Riverside Dr)

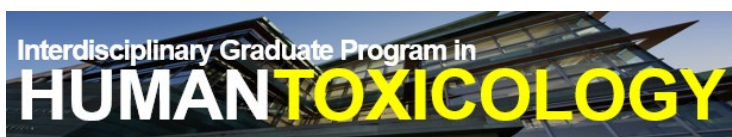
Metered parking west of Theatre building (4 hrs max during business hours) – turn R from Riverside Dr at Theatre building

Metered parking at bottom of hill from CPHB (4 hrs max during business hours) – turn L from Riverside Dr just after Art Building West

Stay in the right lane while going north on Riverside Dr



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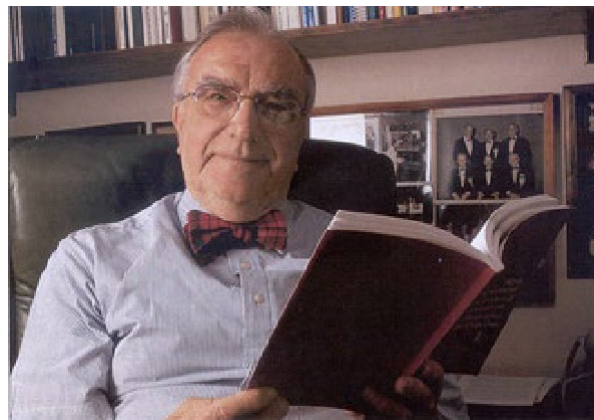


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THE JOHN DOULL AWARD

This prestigious award is presented each year by the Central States Chapter of the Society of Toxicology to honor the contributions of an outstanding member to the discipline of toxicology and the Chapter.

Dr. John Doull, PhD, MD, FAACT (1922-2017), was a Professor Emeritus of Toxicology at the University of Kansas Medical School. He received his BS in Chemistry from Montana State College in 1944 and his PhD (Pharmacology) and MD from the University of Chicago in 1950 and 1953 respectively.



Prior to coming to the University of Kansas in 1967 as a Professor of Pharmacology and Director of the Clinical Pharmacology/Toxicology Center, he was an Associate Professor of Pharmacology and the Assistant Director of the Toxicity Laboratory at the University of Chicago. He was certified in toxicology by the Academy of Toxicological Sciences and the American Academy of Clinical Toxicology. He was a Past President of the Society of Toxicology and the American Board of Toxicology and served on the Toxicology Study Section of NIH and the council of NIEHS. He was a member of the Presidential/Congressional Risk Assessment and Management Commission, the Mrak commission and the White House Woolridge Report Committee. He served as a trustee for the International Life Sciences Institute, the American Academy of Clinical Toxicology and the Toxicology Forum. He chaired the Value committee of ACGIH as well as serving on advisory panels for US EPA, US FDA, DHHS, FEMA, FIFRA, WRAIR, NCTR, DISCUS, and NIOSH. He consulted for local and international governments, industrial and private organizations, was the founding co- editor of *Casarett and Doull's Toxicology: The Basic Science of Poisons* and was a member of Sigma Xi and AOA.

Dr. Doull received the Kenneth DuBois Award from the Midwest Chapter of SOT in 1985 and the Kuna award from Rutgers University in 1989. In 1990 he received the Commander's Award for Public Service from the Armed Forces Epidemiological Board and the International Achievement Award from the International Society of Regulatory Toxicology. In 1991 he received a Distinguished Medical Alumnus Award from the University of Chicago and the Ambassador of Toxicology Award from the Mid-Atlantic chapter of SOT. He received the Stokinger Award from ACGIH and the first John Doull Award from the Central States Regional Chapter of SOT in 1992. He received the Merit Award from SOT in 1993 and the Snider Award from the University of Arkansas in 1994. In 1996 he received the Distinguished Service Award from the American College of Toxicology, the CIIT Founders Award, the ACGIH Meritorious Service Award and an honorary Doctor of Pharmacy from the University of Kuopio (Finland). Dr. Doull received the Shubik Award from the Toxicology Forum and became a National Academy of Sciences Associate in 2002. He received the first Founders Award given by SOT in 2008, the Mildred S. Christian Career Achievement Award from the Academy of Toxicological Sciences in 2013, and the American Academy of Clinical Toxicology Career Achievement Award in 2014.

KEYNOTE SPEAKER

Dr. Robyn Leigh Tanguay, PhD

“From Molecules to Mechanisms to Regulation: Using Zebrafish NAMs to Decode Chemical Bioactivity”

Robyn Leigh Tanguay is a University Distinguished Professor in the Department of Environmental and Molecular Toxicology, the Director of the Oregon State University Superfund Research Program, Director of the Sinnhuber Aquatic Research Laboratory, and the Director of an Environmental Health Sciences Center. She received her BA in Biology from California State University-San Bernardino, her PhD in Biochemistry from the University of California-Riverside, and postdoctoral training in Developmental Toxicology from the University of Wisconsin-Madison. She serves on a number of academic, commercial, and federal advisory boards and is on the editorial board for several scientific journals. Over the past several years she has pioneered the use of zebrafish as a toxicology model and recently developed automated high throughput instrumentation to accelerate phenotype discovery in zebrafish. A major focus is on identifying chemicals and mixtures that produce neurotoxicity. Phenotypic anchoring coupled with the inherent molecular and genetic advantages of zebrafish is used to define the mechanisms by which chemicals, drugs, and nanoparticles interact with and adversely affect vertebrate development and function.



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1. Impact of perfluorooctanoic acid exposure on maturation and abundance of superoxide dismutase 1, Bcl2 associated X protein, and apoptosis inducing factor in the porcine oocyte (Grote – Graduate Student)

Authors: Caleigh E. Grote, Isabel C. Rodriguez, Madison E. Brockman, Emily R. Nold-Schoelerman, Christine Mendez, Karl C. Kerns, Aileen F. Keating

Affiliation: Department of Animal Science, Iowa State University, Ames, IA

Understanding factors contributing to pre-ovulatory oocyte health is important to assisted reproduction technologies for humans and animals. The antral follicle is highly vascular, permitting toxicants to partition and accumulate within the follicular fluid. Perfluorooctanoic acid (PFOA) is detectable in follicular fluid of humans and animals and implicated in endocrine disruption, infertility, ovarian senescence, and impaired embryonic development. The objective of this study was to evaluate the effects of PFOA on oocyte maturation and abundance of superoxide dismutase 1 (SOD1), Bcl2 associated X protein (BAX), and apoptosis inducing factor (AIF). Oocytes (n=100 per replicate; 3 replicates) were exposed to either 0 ppt, 0.4 ppt (low), 4 ppt (medium), or 40 ppt (high) PFOA for 41h maturation period before being fixed and evaluated using fluorescent confocal microscopy. The maturation rate of oocytes exposed to low, medium, or high PFOA level did not differ from the control ($P = 0.92$, $P = 0.71$, $P = 0.60$). In MII oocytes, SOD1 was reduced in low and high PFOA groups ($P < 0.0001$, $P < 0.0001$), while there was a tendency for lower SOD1 in the medium PFOA group ($P = 0.10$). Decreased total BAX was noted in MII oocytes exposed to low PFOA compared to the control ($P = 0.02$) and there was a tendency for reduced BAX in in medium PFOA exposed oocytes ($P = 0.06$), but no impact on BAX in high PFOA exposed oocytes ($P=0.68$). In polar bodies of MII oocytes, BAX was noticeably present at all PFOA levels without an impact of any PFOA level (low: $P = 0.40$, medium: $P = 0.99$, high: $P > 0.99$). Decreased total AIF was observed in MII oocytes exposed to low and medium levels of PFOA compared to the control ($P < 0.0001$, $P = 0.0002$), while there was no impact on AIF in high PFOA exposed oocytes ($P = 0.14$). These polar bodies were also positive for AIF, but no difference was observed at any PFOA level (low: $P = 0.78$, medium: $P = 0.97$, high: $P = 0.99$). These findings suggest that PFOA does not directly impact oocyte maturation rate, but reduces SOD1 and apoptotic proteins in the oocyte. In addition, BAX, AIF, and SOD1 are localized to the polar bodies of mature oocytes. Thus, PFOA may be detrimental for oocyte viability and may influence the degradation of the first polar body.

2. Establishment of liver zonation is required for APAP induced liver injury in young mice (Chavez – Graduate Student)

Authors: Diego Chavez¹, Hartmut Jaeschke¹, Aparna Venkatraman^{1, 2} & Anup Ramachandran¹

Affiliations:

¹Department of Pharmacology, Toxicology & Therapeutics, University of Kansas Medical Center, Kansas City, KS

²Division of Neonatology, Department of Pediatrics, Children's Mercy Kansas City, Kansas City, MO

Acetaminophen (APAP) overdose is the most common identifiable cause of pediatric acute liver failure (PALF). However, unlike adults, mechanisms underlying APAP-induced acute liver failure (ALF) in children are not well characterized. In adults, APAP induces centrilobular necrosis due to established liver zonation; in contrast, hepatic zonation is immature at birth. To examine the role of hepatic zonation on APAP-induced liver injury, we examined hepatic zonation, liver injury and APAP metabolism, 6h after an APAP overdose (300mg/kg) in C57BL/6J mice at postnatal day (P) 5, 10, 14 and adults.

Analysis of publicly available scRNAseq data and immunostaining for CYP2E1 and CYP2F2 as markers of pericentral and periportal hepatocytes respectively, confirmed that hepatic zonation was not established at birth. Most hepatocytes expressed the pericentral marker during early post-natal period irrespective of spatial location. Thus, pericentral identity is established before periportal characteristics. We show that metabolism of APAP is significantly slower in young mice after an overdose, with significant upregulation of glucuronidation when compared to sulfation. While mice at P5 show minimal evidence of injury, those at P10 and P14 show generation of oxidative metabolites accompanied by glutathione depletion; indicating production of the reactive metabolite. Though mice at P14 show ALT elevation similar to adults, characteristic centrilobular necrosis is missing, indicative of alternate pathways of injury.

In conclusion, these findings suggest that the lack of hepatic zonation could contribute to alternate mechanisms of APAP-induced liver injury, which could be targeted to develop therapeutics to complement current antidotes and prevent development of PALF.

3. NRF2 Signaling as a Mechanism of Protection against Organophosphate Toxicity (Preston – Graduate Student)

Authors: Sarah E. Preston¹, Michael A. Garcia-Mares¹, Anna E. Bartman¹, David B.C. Martin², Jonathan A. Doorn¹

Affiliations:

¹Department of Pharmaceutical Sciences & Experimental Therapeutics, College of Pharmacy, University of Iowa, Iowa City, IA

²Department of Chemistry, College of Liberal Arts and Sciences, University of Iowa, Iowa City, IA

Human exposure to organophosphate (OP) pesticides such as chlorpyrifos (CPF) occurs in agricultural, occupational and military settings worldwide. OP pesticides can lead to cholinergic crisis via acetylcholinesterase (AChE) inhibition. OP exposure correlates with additional adverse outcomes, including depression and neurodegenerative diseases. Metabolism of CPF is critical to cholinergic toxicity as it can yield either bioactivation to the toxic chlorpyrifos-oxon (CPO), detoxication via glutathione or hydrolysis of CPO via the esterases, paraoxonase 1 (PON1) and carboxylesterase 1 and 2 (CES). Many enzymes critical to the metabolism of CPF are under the control of the transcription factor NRF2, including: GSH/GST, PON1 and CES. Our goal is to explore the role of NRF2 modulation in mitigating risk of toxicity and adverse effects to CPF/OP agents. Our central hypothesis is that NRF2 activation protects against OPs via altering OP disposition and potential for toxicity via induction of enzymes that modulate OP metabolism and cellular damage. We have found that pretreatment of PC12 cells with potent activators of NRF2 provides protection against acute CPF and CPO treatment. We have shown that NRF2 activators induce the expression of both CES and PON1 in HepG2 cells (liver) as well as increasing general intracellular esterase activity. NRF2 activation appears to protect HepG2 hepatic cells and SH-SY5Y neuronal cells from AChE inhibition and ROS production. Finally, we found that treatment of SH-SY5Y cells with NRF2 activated HepG2 media significantly protected against CPF insult. These data indicate the potential for NRF2 as a target to mitigate OP/CPF toxicity.

4. Kaempferol Attenuates PFDA-Induced Disruption of Estrous Cyclicity and Ovarian Steroidogenic Regulation in Female Mice (Lee – Postdoctoral Fellow)

Authors: Changyong Lee¹, Rasha Ghorab^{1,2}, Kendra L. Clark^{1,3,4}

Affiliations:

¹Department of Obstetrics and Gynecology, University of Nebraska Medical Center, Omaha, NE

²Department of Cellular and Integrative Physiology, University of Nebraska Medical Center, Omaha, NE

³Department of Environmental, Agricultural, and Occupational Health, University of Nebraska Medical Center, Omaha, NE

Background and Objective: Perfluorodecanoic acid (PFDA) is a persistent long-chain PFAS detected in human serum and follicular fluid and may disrupt ovarian endocrine function. However, its effects on ovarian steroidogenesis and potential protective interventions remain poorly defined. This study evaluated whether kaempferol attenuates PFDA-associated changes in estrous cyclicity, reproductive hormones, and ovarian steroidogenic and antioxidant markers.

Methods: Eleven-week-old female CD-1 mice received vehicle, kaempferol (25 or 50 mg/kg/day), PFDA (2.5 mg/kg/day), or their combinations. Kaempferol was administered by gavage for 17 days, including three days of pretreatment. PFDA was administered orally by pipette for 14 days. Estrous stages were monitored by daily vaginal cytology. Samples were collected during metestrus or diestrus for hormone analysis, ovarian quantitative PCR and Western blotting, and serum PFDA measurement.

Results: PFDA increased metestrus/diestrus occupancy, serum progesterone and follicle-stimulating hormone, and liver weight, while body weight remained stable. Kaempferol co-treatment reduced metestrus/diestrus occupancy and progesterone and increased estradiol relative to PFDA alone. PFDA decreased ovarian *Cyp19a1* and increased *Hsd3b1* transcripts, and reduced CYP19A1, HSD17B1, and heme oxygenase-1 (HO-1) proteins. Co-treatment with kaempferol at 50 mg/kg increased *Cyp19a1* and *Hsd17b1* transcripts and CYP19A1, HSD17B1, and HO-1 proteins relative to PFDA alone. Terminal serum PFDA was higher in the 50 mg/kg kaempferol co-treatment group than in the PFDA-only group ($p = 0.0100$).

Conclusion: Kaempferol partially attenuated PFDA-associated reproductive endocrine alterations. These improvements occurred despite higher terminal serum PFDA, warranting further investigation of ovarian antioxidant regulation and PFDA tissue distribution.

5. Chlorpromazine Reveals GPNMB-Mediated Protection Against Toxicant-induced Oxidative Stress in Cardiomyocytes (Kline – Graduate Student)

Authors: Cassidy Kline^{1,2}, Hammerlindl H³, Brambila D³, Borrman BB², Rao L³, Li Li³, Kim JS^{1,4}, Altschuler SJ³, Wu LF³, Shen SQ^{1,2,5}

Affiliations:

¹Interdisciplinary Graduate Program in Human Toxicology, Graduate College, University of Iowa, Iowa City, IA

²Department of Psychiatry, Carver College of Medicine, University of Iowa, Iowa City, IA

³Department of Pharmaceutical Chemistry, School of Pharmacy, University of California San Francisco, San Francisco, CA

⁴Department of Occupational and Environmental Health, College of Public Health, University of Iowa, Iowa City, IA

Cardiomyocytes are particularly susceptible to toxicant-induced oxidative damage given their high metabolic demands and limited capacity for renewal, yet protective therapeutic strategies remain limited. Because chlorpromazine (CPZ), a first-generation antipsychotic, has been reported to have antioxidant effects, we hypothesized that CPZ would protect cardiomyocytes through activation of cytoprotective pathways. Immortalized human cardiomyocytes (AC16 cells) were exposed to hydrogen peroxide (H₂O₂) with or without CPZ for 24 hours. CPZ significantly reduced H₂O₂-induced ROS accumulation and cell death, whereas another antipsychotic, quetiapine (QUE), did not. RNA sequencing identified glycoprotein nonmetastatic melanoma protein B (GPNMB) as the top differentially expressed gene following CPZ treatment, and protein-level increase was confirmed.

Genetic knockdown and recombinant protein experiments provided evidence that GPNMB is necessary and sufficient for CPZ-mediated protection against H₂O₂. To determine whether this protection extends to a more physiologically relevant human model, human induced pluripotent stem cell (iPSC)-derived cardiomyocytes were exposed to cadmium, a toxic heavy metal contaminant. CPZ restored cadmium-induced deficits in cardiomyocyte contractility. While prior studies have shown that macrophage-derived GPNMB protects the heart from oxidative stress, our findings demonstrate that cardiomyocytes themselves can be pharmacologically induced to produce GPNMB, identifying a potential strategy to protect cardiomyocytes from toxicant-induced oxidative stress. Future studies will investigate the mechanism of CPZ induction of GPNMB and whether pharmacologic GPNMB induction protects against oxidative damage *in vivo*.

6. Per- and Polyfluoroalkyl Substances Exposure Disrupts Fatty Acid Metabolism and Exacerbates Hepatocellular Lipid Accumulation in Alcohol-Associated Liver Disease (Nguyen – Graduate Student)

Authors: Nguyen, Khue, Apte, Udayan, Ni, Hong-Min

Affiliation: Department of Pharmacology, Toxicology, and Therapeutics, University of Kansas Medical Center, Kansas City, KS

Background: Per- and polyfluoroalkyl substances (PFAS) are persistent environmental pollutants that accumulate in the liver and disrupt hepatic metabolism. Emerging evidence suggests PFAS may contribute to alcohol-associated liver disease (ALD); however, the effects of PFAS/alcohol co-exposure on hepatic steatosis and lipid metabolism remain poorly characterized.

Methods: Wild-type C57BL/6J mice were exposed to an occupationally relevant PFAS mixture containing PFOA (1 mg/L), PFOS (1 mg/L), and GenX (2 mg/L) in drinking water for 28 days, followed by chronic-plus-binge alcohol exposure with continued PFAS treatment. Serum and liver tissues were analyzed for PFAS accumulation, liver injury, histopathology, and lipid metabolism. Bulk liver RNA sequencing was performed to characterize transcriptional changes.

Results: PFOA, PFOS, and GenX accumulated in serum and liver, with PFOA showing the greatest accumulation. PFAS exposure induced hepatomegaly and exacerbated alcohol-induced hepatic triglyceride and cholesterol accumulation. Heatmap analysis showed that PFAS increased expression of genes involved in fatty acid uptake and β -oxidation, with additional increases in subsets of genes associated with *de novo* lipogenesis (DNL) and very-low-density lipoprotein (VLDL) secretion. Alcohol decreased β -oxidation-associated genes and modestly increased subsets of DNL- and VLDL-related genes. The co-exposure further increased DNL-associated genes and decreased β -oxidation-associated genes, while enhanced selected VLDL secretion genes. Gene Ontology analysis revealed enrichment of fatty acid and lipid metabolic processes in co-exposed versus alcohol-exposed mice.

Conclusion: PFAS exposure exacerbated alcohol-induced hepatic steatosis and dysregulated multiple lipid metabolic pathways, providing insight into potential mechanisms underlying PFAS/alcohol co-exposure-induced liver toxicity.

7. Reproductive Age Influences Ovarian Physiological and Transcriptomic Patterns Following Short-Term PFAS Mixture Exposure (Ghorab – Graduate Student)

Authors: Rasha Ghorab¹, Changyong Lee¹, Kendra L. Clark^{1,2,3}

Affiliations:

¹Department of Obstetrics and Gynecology, Olson Center for Women's Health, University of Nebraska Medical Center, Omaha, NE

²Department of Environmental, Agricultural, and Occupational Health, University of Nebraska Medical Center, Omaha, NE

³Veterans Affairs Nebraska-Western Iowa Health Care System, Omaha, NE

Background and Objective: Per- and polyfluoroalkyl substances (PFAS) are persistent environmental contaminants associated with reproductive and endocrine disruption. Aging is accompanied by substantial changes in ovarian function and molecular signaling that may influence susceptibility to environmental exposures; however, how PFAS exposure interacts with ovarian aging remains poorly understood. This study examined how age influences ovarian physiological and transcriptomic patterns associated with short-term PFAS exposure.

Methods: Female CD-1 mice aged 4 months (young) or 16 months (aged) received vehicle or a PFAS mixture containing perfluorooctanoic acid (PFOA), perfluorooctanesulfonic acid (PFOS), perfluorononanoic acid (PFNA), and perfluorohexanesulfonic acid (PFHxS) (0.1 mg/kg each) for 15 days. Estrous cyclicity and body/organ weights assessed, and whole-ovary bulk RNA sequencing performed (n=4-5/group). DESeq2 identified differentially expressed genes (DEGs), and Ingenuity Pathway Analysis evaluated associated biological pathways.

Results: Age increased body weight, whereas PFAS had no effect. Relative ovarian weight showed significant effects of age (P=0.01) and PFAS (P=0.02). Aged mice spent less time in proestrus. PFAS was associated with 102 DEGs in young ovaries but 14 in aged ovaries, while aging was associated with 447 DEGs in controls and 1,096 following PFAS exposure. Aging increased immune signaling while reducing cell-cycle and oocyte-associated programs. In young ovaries, PFAS altered RXR, lipid-metabolism, and oxidative-stress pathways, whereas aging under PFAS exposure was associated with interferon and redox/NADPH-oxidase signaling.

Conclusion: Age dominated ovarian transcriptomic variation, while PFAS-associated patterns differed between young and aged ovaries. Formal interaction analysis and targeted validation are needed to determine whether PFAS modifies ovarian aging.

8. Repeated Inhalation Exposures Shift Nanoparticle-Induced Pulmonary Inflammation from a Transient Response to Persistent Immune Remodeling with Distinct Extracellular Vesicles-microRNA Signatures (Siddique – Graduate Student)

Authors: ¹Abu Ebrahim Siddique, ¹Shri Vishalini Rajaram, ²Xuefang Jing, ³Zachary Hutchins, ^{1,2}Peter S. Thorne, ³Yinsheng Wang, ⁴Josalyn L. Cho, ²Andrea Adamcakova-Dodd

Affiliations:

¹Human Toxicology Program, University of Iowa, Iowa City, IA

²Department of Occupational and Environmental Health, University of Iowa, Iowa City, IA

³Department of Chemistry, University of California, Riverside, Riverside, CA; ⁴Internal Medicine, University of Iowa, Iowa City, IA

Background and Purpose: Short-term inhalation of engineered nanoparticles (NPs) causes pulmonary inflammation, but how repeated exposure affects its resolution and immune persistence and which extracellular vesicles (EV)-miRNAs are associated with these processes, remains unclear. Our single-exposure studies showed that copper oxide (CuO) NPs produce neutrophilic inflammation that resolves by day 7, whereas cadmium sulfide (CdS) NPs cause persistent inflammation.

Methods: Female C57Bl/6J mice were exposed by nose-only inhalation to CuO (40 nm) or CdS (60 nm) NPs at 3 mg/m³, 2 h/day, 5 days/week for 2 weeks. Bronchoalveolar lavage fluid (BALF) and lungs were collected on days 1, 7, 14, and 21 post-exposure, with an additional day 28 time point for CdS. Lung cells were analyzed by flow cytometry, and BALF extracellular vesicle miRNAs were profiled.

Results: Repeated exposure produced sustained inflammation. CdS-exposed mice had elevated BALF total cell counts and neutrophilia through day 28, whereas CuO-exposed mice showed early inflammation followed by partial resolution. CdS caused sustained lung neutrophilia, whereas CuO induced only early neutrophil influx. EV-microRNA responses also diverged: CuO caused broad early suppression of let-7 and miR-29 family members that recovered by day 7 before a later resurgence, whereas CdS caused early induction alone, with progressive loss of let-7 and miR-29 family members and of miR-205 emerging only at a later time points, alongside sustained miR-146a induction.

Conclusions: Repeated inhalation exposure to CuO and CdS NPs produced distinct trajectories of pulmonary inflammation and identified specific EV-miRNAs associated with inflammatory resolution or persistence. Our findings support potential utility of EV-miRNAs as biomarkers of pulmonary inflammatory status and candidates for further investigation as regulators of inflammatory resolution.

Graduate Student Posters

9. Perfluorobutane Sulfonic Acid Exposure Increases Ovarian Follicular Atresia and Disrupts Steroidogenic, Inflammatory, and Metabolic Protein Signaling in the Ovary and Uterus (Adeyanju)

Authors: Omotoyosi Z. Adeyanju, Estefanía M. González-Álvarez, Aileen F. Keating

Affiliation: Department of Animal Science, Iowa State University, Ames, IA

Perfluorobutane sulfonic acid (PFBS) is increasingly used as a purportedly safer alternative to perfluorooctane sulfonate (PFOS), yet its reproductive toxicity remains poorly defined. The hypothesis that PFBS disrupts ovarian and uterine function by altering key steroidogenic, metabolic, and inflammatory signaling pathways was thus tested. Seven-week-old female C57BL/6J mice were exposed to saline or PFBS (2.5 mg/Kg BW) per os for 15 d. The ovarian and uterine protein abundance of cytochrome P450 (CYP) family 1, subfamily A, polypeptide 1 (CYP1A1), CYP family 1, subfamily B polypeptide 1 (CYP1B1), CYP family 11, subfamily A, polypeptide 1 (CYP11A1), CYP family 19, subfamily A, polypeptide 1 (CYP19A1), peroxisome proliferator-activated receptor (PPAR) α (PPAR α), δ (PPAR δ), γ (PPAR γ), and Toll-like receptor 4 (TLR4) were quantified by western blotting and unadjusted unpaired t-test. In the ovary, PFBS exposure tended to increase ($P \leq 0.1$) ovary weight and the abundance of CYP1A1 and CYP19A1 but tended to decrease ($P \leq 0.1$) the abundance of TLR4 protein. PFBS also increased ($P \leq 0.05$) the number of atretic follicles, indicating impaired follicular health. In the uterus, PFBS decreased ($P \leq 0.05$) PPAR γ and CYP11A protein abundance, without altering uterine weight ($P \geq 0.1$). Collectively, these findings demonstrate that PFBS is not biologically inert and may disrupt reproductive function by modulating steroidogenic enzymes and signaling pathways in both the ovary and uterus. This study raises important concerns about the reproductive safety of PFBS and highlights the need to re-evaluate short-chain PFAS as “safer” alternatives.

10. Establishing a PCB Metabolite Profile for Future Studies of Human Microbiome-Mediated Neurotoxicity (Brobston)

Authors: Sean Brobston¹, Xueshu Li², Sujitha Ravulapalli², Nicole Breese^{1,2}, Sal Lombardi³, Stacy E. Beyer^{3,4}, Snehajyoti Chatterjee^{3,4}, Hans-Joachim Lehmler^{1,2}

Affiliations:

¹ Interdisciplinary Graduate Program in Human Toxicology, University of Iowa, Iowa City, IA

² Department of Occupational and Environmental Health, College of Public Health, University of Iowa, Iowa City, IA

³ Department of Neuroscience and Pharmacology, Carver College of Medicine, University of Iowa, Iowa City, IA, USA

⁴ Iowa Neuroscience Institute, University of Iowa, Iowa City, IA

Polychlorinated biphenyls (PCBs) are persistent environmental contaminants with known neurotoxic effects. Environmental exposure to PCBs is rarely limited to a single congener, and the resulting toxic effects can vary depending on the mixture of PCB congeners an individual is exposed to. While several environmentally relevant mixtures have been assessed for toxicity, these simulated PCB mixtures differ from the PCBs present in the human brain. To more accurately assess PCB neurotoxicity, we generated a Human-Relevant PCB (HR-PCB) mixture based on PCBs found in postmortem human brain tissue. Furthermore, the gut microbiome can act on PCBs, influencing metabolic outcomes. Individual variation in gut microbial composition and function could result in different neurological outcomes. Our larger scope is to evaluate how differences in the human gut microbiome alter the PCB metabolite profile and resulting memory deficits from exposure to the HR-PCB mixture. This study was an early look into the PCB metabolite profile in regular mice exposed to the HR-PCB mixture.

11. Pathways to Depression Risk: Neural Networks of Stress Vulnerability in Adolescent Chlorpyrifos Exposure (Chen)

Authors: Michelle X. Chen¹⁻³, Madelyn M. Grueter³, Himali Wickramasinghe⁴, Rainbo Hultman⁴, Hanna E. Stevens¹⁻³

Affiliations:

¹ Medical Scientist Training Program, University of Iowa, Iowa City, IA

² Interdisciplinary Graduate Program in Neuroscience, University of Iowa, Iowa City, IA

³ Department of Psychiatry, Carver College of Medicine, University of Iowa, Iowa City, IA

⁴ Department of Molecular Physiology and Biophysics, Carver College of Medicine, University of Iowa, Iowa City, IA

Background: Major depressive disorder (MDD) is a leading cause of disability in adolescents, a group undergoing neurodevelopment and therefore sensitive to environmental stressors. Chlorpyrifos, an organophosphate pesticide, has been linked to neuropsychiatric symptoms in adolescents, but whether it induces symptoms or increases vulnerability to other stressors remains unclear. We pair chlorpyrifos exposure with social stress to study brain network and behavioral effects.

Methods: Adolescent male C57BL/6 mice (implanted with electrodes targeting seven MDD-relevant regions) were dermally exposed to pesticide (vehicle or chlorpyrifos) and stress (control or social defeat) (n=7-8/group). Mice underwent *in vivo* neurophysiological recordings and MDD-relevant tasks. Neurophysiological data (local field potentials) were evaluated with machine learning models to calculate activity of stress-relevant brain networks. Two-way ANOVAs assessed for pesticide and stress main and interaction effects.

Results: There were significant interaction effects on exploratory behaviors [Y-Maze entries ($F(1,27)=15.18$, $p=0.0006$), social interaction ($F(1,27)=4.28$, $p=0.04$)], and main treatment effects on exploratory and anhedonia-relevant behaviors [open field locomotion ($F(1,27)=16.69$, $p=0.0004$) and corner time ($F(1, 27)=4.41$, $p=0.04$), grooming latency ($F(1,24)=5.38$, $p=0.02$)]. Surprisingly, chlorpyrifos exposure induced a smaller activity increase in a stress vulnerability network during a negative-affect social task than in vehicle animals ($F(1,27)=7.28$, $p=0.01$).

Conclusions: Adolescent chlorpyrifos exposure reveals changes in MDD-relevant behaviors, which sometimes interacted with or were exacerbated by social stress. Unexpectedly, chlorpyrifos exposure led to smaller activity increases in a vulnerability brain network, despite behavioral changes. These results suggest chlorpyrifos exposure changes brain electrical activity but the mechanism underlying behavioral changes may lie in a different network.

12. Cell Stress and Senescence State in Airway Stem Cells Following Lung Transplantation (Da-Silva)

Authors: Oluwatobiloba F. Da-Silva^{1,2}, Kusum Devi², Kalpaj R. Parekh²

Affiliations:

¹ Interdisciplinary Graduate Program in Human Toxicology, Graduate College, University of Iowa, Iowa City, IA

² Department of Cardiothoracic Surgery, Roy J. and Lucille A. Carver College of Medicine, University of Iowa, Iowa City, IA

Chronic lung allograft dysfunction (CLAD) remains a major limitation to long-term survival following lung transplantation. Its pathogenesis involves repeated airway epithelial injury, impaired regeneration, and progressive fibrosis, yet the basal-cell responses contributing to regenerative failure remain incompletely understood. This study investigated whether airway basal cells acquire a stress- and senescence-associated phenotype following lung transplantation. We examined native and allograft airway tissues from a ferret orthotopic lung transplant model and evaluated basal-cell identity, injury-associated keratin expression, cell-cycle stress, and DNA-damage responses using immunofluorescence. These findings were complemented by single-cell transcriptomic analysis of basal cells from native, recipient, donor, and allograft tissues. Representative allograft airways exhibited expression of the injury associated marker KRT17 and an altered KRT17/KRT15 expression pattern compared with native airways, while KRT5 and TP63 confirmed basal-cell localization. Immunofluorescence also detected p21/p53 and γH2AX signals associated with cell-cycle stress and DNA-damage responses. Consistent with these observations, transcriptomic analysis demonstrated altered expression of stress-, repair-, and cell-cycle-response genes in allograft basal cells, including increased average expression of CDKN1A, PCNA, and TP53 relative to native basal cells. Together, these preliminary findings suggest that airway basal cells following transplantation acquire an injury-associated state characterized by altered regenerative identity and activation of DNA-damage responses. This phenotype may represent an early senescence-associated state that contributes to defective epithelial regeneration and CLAD progression.

13. Regulation of De Novo Lipogenesis by the Mitochondrial Dicarboxylate Carrier (Deshmukh)

Authors: Kshitij Deshmukh^{1,2}; Adam Rauckhorst^{2,3}; Ronald Merrill²; Adnan Ahmed²; Eric B. Taylor²

Affiliations:

¹ Interdisciplinary Graduate Program in Human Toxicology, Graduate College, University of Iowa, Iowa City, IA

² Department of Molecular Physiology and Biophysics, University of Iowa, Iowa City, IA

³ Florida International University, Miami, FL

Background: Human exposure to toxins dysregulates hepatic de novo lipogenesis (DNL). Hepatic DNL utilizes carbon from cytosolic and mitochondrial sources. Among these, mitochondria supply major proportion of lipogenic carbon through the mitochondrial citrate export, catalyzed by the citrate carrier (CiC). Citrate in the cytosol generates acetyl-CoA that feeds DNL. CiC requires cytosolic malate counterport substrate to export citrate. Malate compartmentation between mitochondria and the cytosol is mediated by the mitochondrial dicarboxylate carrier (DiC). We investigate the role of the DiC in providing cytosolic malate counterport substrate for the CiC to export lipogenic citrate and supply DNL.

Methods: We performed metabolite transport assays in mouse liver mitochondria isolated from novel inducible liver-specific DiC knockout (DiC LivKO) mice. To investigate mechanistic details of DiC in mediating DNL carbon supply, we traced [U13C]-pyruvate in cultured intact DiC knockout HEK293 cells, and 6 different [U13C]-labeled DNL carbon substrates in DiC LivKO mice in vivo.

Results: We show that mitochondrial malate and citrate export is diminished in DiC LivKO isolated mouse liver mitochondria. In vitro stable isotope tracing demonstrates that intact DiC knockout HEK293 cells have diminished mitochondrial citrate export. Physiologically, we show that DiC LivKO mice have decreased hepatic carbon supply from mitochondrially routed DNL substrates to synthesize palmitate.

Conclusions: This work highlights the critical role of the DiC in supplying counterport malate substrate for mitochondrial lipogenic citrate export to supply carbon for hepatic DNL. This work advances the framework for therapeutic development to improve metabolic health in toxin exposures and chronic disease conditions.

14. GST Activity in Cat Liver Subcellular Fractions (Frank)

Authors: Alexander Frank^{*1,2}, Yeonju Lee¹, James Sacco¹

Affiliations:

¹ Drake University College of Pharmacy and Health Sciences, Des Moines, IA

² Vanadro Drug Development Consulting, West Des Moines, IA

* Dr. Frank is a PharmD postdoctoral fellow, which is equivalent to a graduate student

Background: Glutathione-S-transferases (GSTs) conjugate toxic electrophiles with glutathione (GSH). While high GST-activity versus the GST-M and GST-T substrate 1,2-dichloronitrobenzene (DCNB) is present in dog liver, this reaction has not been investigated in cats. This study provided preliminary comparative data on DCNB glutathionylation between dogs and cats.

Methods: GST activity versus DCNB was measured at various pH in pooled beagle liver (DLC) and kidney cytosolic fractions (DKC) as well as pooled male (MCLS9) and female cat liver S9 fractions (FCLS9). Kinetic parameters for DCNB and GSH, and IC₅₀ values for various GST inhibitors were calculated using GraphPad Prism.

Results: GST_{DCNB} activity reached a maximum at pH 7.5-8.0 for DLC and DKC and at pH 8.0 for MCLS9 and FCLS9. Glutathionylation efficiency (V_{max}/K_m) for DCNB was higher in DLC than DKC (0.19 vs 0.12 mL/min/mg protein) due to a higher V_{max}, and higher in FCLS9 than MCLS9 (0.14 vs 0.07 mL/min/mg protein) due to a lower K_m. Glutathionylation efficiency for the co-substrate GSH was 0.09 mL/min/mg protein in DLC and similar in FCLS9 and MCLS9 (0.04 mL/min/mg protein). Inhibitor sensitivity varied between the 4 sample types. Ethacrynic acid was the most potent in MCLS9 and FCLS9 (~8 μM), while bromosulfophthalein was the most potent in DLC and DKC (~15 μM).

Conclusion: DCNB glutathionylation efficiency is highest in DLC and higher in FCLS9 compared to MCLS9. Distinct kinetic parameters and inhibitor sensitivities imply differences in the relative contribution of GST-T and GST-M enzymes to DCNB glutathionylation in the dog and cat fractions studied.

15. Evaluating the Impact of Remediation Activities on PCB levels in Air and Water at Portland Harbor (Kalteh)

Authors: Safa Kalteh¹, Andres Martinez²

Affiliations:

¹ IIHR-Hydrosience & Engineering, University of Iowa, Iowa City, IA

² Department of Civil and Environmental Engineering, University of Iowa, Iowa City, IA

Polychlorinated biphenyls (PCBs) persist in contaminated sediments and can partition into water and volatilize into air. Although remediation plans are intended to reduce long-term contamination, sediment disturbance may temporarily increase PCB mobilization and atmospheric emissions. However, the extent to which dredging changes air-water PCB exchange and airborne concentrations remains insufficiently characterized. This study aims to quantify these changes before, during, and after sediment remediation at the Portland Harbor Superfund Site.

Baseline sampling began in June 2026, with deployment of Polyurethane foam passive air samplers and polyethylene passive water samplers at a dock, with additional air sampling at a nearby residence. Monitoring will continue during and after remediation. Meteorological conditions, water temperature, and remediation activity will support interpretation of the measurements. PCB congeners will be quantified using gas chromatography-tandem mass spectrometry (GC-MS/MS). Air concentrations will be calculated using congener-specific effective sampling volumes. Freely dissolved water concentrations will be estimated using polyethylene-water partition coefficients and performance reference compound losses. Paired concentrations will be used to estimate congener-specific exchange direction and net air–water fluxes.

Comparisons across remediation phases will evaluate changes in PCB concentrations, congener profiles, and exchange while considering meteorological variability. This study will improve understanding of PCB fate and transport during remediation activities, including dredging, and support monitoring of PCB levels in air and water near contaminated waterways.

16. Assessment of softwood-derived biochars' efficacy for the environmental remediation of dicamba herbicides (Muhr)

Author: Ben Muhr

Affiliations: University of Iowa, Iowa City, IA; University of Wisconsin-Madison Popova Lab, Madison, WI

Dicamba is a highly destructive and environmentally-mobile herbicide used throughout the continental United States. This mobility leads to prolific off-sight contamination of both commercial crop-land and natural ecosystems. A potential solution to this is the application of biochar, a carbon-rich material produced through pyrolysis of biomass. In recent decades of study, biochar has shown great potential to sorb herbicides and other organic contaminants, though the literature on its proficiency with dicamba is limited. This study evaluates the capacity of biochar derived from the Jack Pine (*Pinus banksiana*) pyrolyzed at three different temperatures (350 °C, 450 °C, and 550 °C) to sorb dicamba from soil environments. Batch sorption experiments were conducted using soils of controlled clay, sand and silt content to account for real world differences in soil composition, and were emulsified with each biochar, at various concentrations of dicamba. After a period of 24 hours of emulsification to ensure homogeneity and equilibrium has been reached, the concentrations that remained in the soil were quantified using high-performance liquid chromatography (HPLC). Preliminary results demonstrate that all biochars reduced dicamba concentrations relative to control solutions, with notable differences across pyrolysis temperatures. The biochar pyrolyzed at 550 °C exhibited significant sorption relative to the other biochars and controls, suggesting that biochars pyrolyzed at higher temperatures have a higher affinity to sorb dicamba. These results show promise in biochar's ability to sorb dicamba, though with noticeable fluctuations in efficiency with regards to pyrolysis conditions influencing the biochar's chemistry and surface absorbance capacity.

17. Investigating the Cell-Type-Specific Effects of miR29a-KLF4 and miR29a-ADAM12 signaling in Peripheral Arterial Disease (PAD) (Okpara)

Authors: Edozie Samuel Okpara^{1,2}, Pratibha Singh¹, Arul M. Mani¹, Ayotunde Dokun^{1,3}

Affiliations:

¹ University of Iowa, Iowa City, IA

² Interdisciplinary Graduate Program in Human Toxicology, University of Iowa, Iowa City, IA

³ Fraternal Order of Eagles Diabetes Research Center, University of Iowa, Iowa City, IA

Background and Purpose: Peripheral arterial disease (PAD) causes severe disability and limb loss, particularly in diabetes. Because impaired muscle regeneration and vascular recovery drive PAD progression, and microRNA-29a (miR-29a) regulates ischemic repair by targeting angiogenesis and remodeling genes (ADAM12, KLF4), this study investigates the cell-type-specific effects of ischemia on miR-29a, KLF4, and ADAM12 expression in endothelial cells versus myoblasts.

Objective: To investigate the cell-type-specific effects of ischemia on miR-29a, KLF4, and ADAM12 expression in skeletal muscle microvascular endothelial cells (ECs) and myoblasts (MBs).

Methods: Mouse skeletal muscle microvascular endothelial cells and myoblasts were exposed to simulated ischemia (2% O₂ with nutrient deprivation). Total RNA was isolated, and miR-29a, KLF4, and ADAM12 expression were quantified using TaqMan and SYBR Green qPCR.

Results: Ischemia significantly altered target expression in endothelial cells, decreasing miR-29a and ADAM12 while increasing KLF4 expression. Conversely, myoblasts exhibited minimal or no significant changes. Direct comparison demonstrated a substantially greater ischemic response in endothelial cells than in myoblasts, revealing distinct cell-specific regulation of the miR-29a-KLF4 and miR-29a-ADAM12 axes.

Conclusions: Although ischemia induces distinct, cell-dependent changes in miR-29a, KLF4, and ADAM12 expression within endothelial cells—supporting the therapeutic potential of targeting endothelial miR-29a for vascular recovery—the lack of similar changes in myoblasts suggests that the effects of ischemia should be further tested in mature myofibers.

18. Organophosphate Pesticide Study in Oregon Orchard Community (Perales)

Authors: Isa Perales^{1,3}, Khalid Khan², Amy Ryan³, Marie Gaine¹, Diane Rohlman⁴

Affiliations:

¹ Department of Pharmaceutical Sciences and Experimental Therapeutics (PSET), College of Pharmacy, University of Iowa, Iowa City, IA; Interdisciplinary Graduate Program in Human Toxicology, University of Iowa, Iowa City, IA

² Department of Public Health, College of Health Sciences, Sam Houston State University, Huntsville, TX

³ Department of Anatomy and Cell Biology, Carver College of Medicine, Iowa City, IA

⁴ Department of Occupational and Environmental Health, University of Iowa, Iowa City, IA

Background and Purpose: Children residing in agricultural communities may be exposed to organophosphate pesticides through multiple pathways, including spray drift, contaminated household environments, dietary intake, and take-home exposure from parents working in agricultural workplaces. Although urinary metabolites are commonly used biomarkers of organophosphate exposure, few studies have used intensive repeated sampling linked to documented spray events to characterize exposure dynamics in children. Metabolite persistence and variability are likely underestimated in studies relying on single spot urine samples.

Methods: Seventeen children aged 5-13 years residing in orchard communities were enrolled in this pilot repeated-measures study. Urine samples were collected at least two times during each pre-spray, spray, and post-spray period. Urine samples were analyzed for six metabolites. Survey data were collected to characterize demographic factors and potential exposure pathways including parental agricultural employment history, residential proximity, and household pesticide use.

Results: Urinary metabolite concentrations demonstrated substantial temporal variability across sampling periods. Mean metabolite concentrations increased during application periods and generally declined after application season. Most peak concentrations occurred during documented spray intervals. Children experiencing repeated or closely spaced spray events exhibited prolonged metabolite persistence compared with children with single spray events. Survey-derived indicators suggested strong associations between metabolite elevations and parental agricultural employment history and age.

Conclusions: Repeated biomonitoring identified short-term fluctuations in urinary organophosphate metabolites that would likely not have been captured using conventional single-sample approaches. These findings highlight the importance of sampling frequency, spray-event timing, and occupational factors in characterizing pesticide exposure among children living in orchard communities.

19. Mobile Genetic Elements and Adaptive Functional Potential in the Oral Microbiome Across Dental Caries States (Rajaram)

Authors: Shri Vishalini Rajaram, Erliang Zeng

Affiliation: Division of Biostatistics and Computational Biology, College of Dentistry, University of Iowa, Iowa City, IA

Background: Mobile genetic elements (MGEs), including bacteriophages, insertion sequences, and transposons, contribute to horizontal gene transfer and the dissemination of genes involved in antibiotic resistance, stress response, virulence, and microbial adaptation. These functions are relevant to understanding how microbiomes respond to biological and therapeutic perturbations. However, the distribution and functional composition of MGEs in the oral microbiome, particularly between caries-free and caries-active states, remain poorly characterized.

Methods: We analyzed nine publicly available shotgun metagenomic datasets representing multiple oral sites and clinical conditions, including caries-free and caries-active states and intervention-based cohorts. Our analytical framework integrates assembly-based and read-based approaches to detect diverse classes of MGEs. Sequence homology and genomic context were combined to improve MGE classification and reduce misclassification of shared orthologous regions. MGE-associated genes were functionally annotated using curated databases to identify antibiotic resistance, stress-response, virulence-associated, and other adaptive functions. Statistical models incorporate clinical condition, oral site, intervention status, and study-specific covariates to evaluate differences in MGE abundance and functional profiles.

Results: MGEs were detected across all analyzed metagenomic datasets, demonstrating a substantial mobile genetic reservoir within the oral microbiome. Preliminary analyses indicate that MGE abundance and functional composition vary across datasets and clinical covariates. Functional annotation identified MGE-associated genes related to antibiotic resistance, stress response, and virulence, suggesting that the oral mobile gene pool contains functions with potential relevance to microbial persistence and adaptation. Intervention-based cohorts also provide an opportunity to examine whether perturbation is associated with changes in MGE composition and associated functions.

Conclusions: This study provides a scalable metagenomic framework for characterizing MGEs and their functional cargo in the oral microbiome. Defining how mobile genes associated with resistance, stress response, and virulence vary across caries states and perturbations may improve our understanding of the mechanisms through which microbial communities acquire and redistribute adaptive traits. From a toxicological perspective, these mobile functional reservoirs represent an understudied component of microbiome responses to environmental and therapeutic perturbations.

20. Macrophage Mitochondrial Function in Response to PCB Exposure (Sahly)

Authors: Emma C. Sahly^{1,2}, Ryan J. Byrd^{1,2}, Aloysius J. Klingehutz^{2,3}, James A. Ankrum^{1,2}

Affiliations:

¹ Roy J. Carver Department of Biomedical Engineering, University of Iowa, IA

² Fraternal Order of Eagles Diabetes Research Center, University of Iowa, Iowa City, IA

³ Department of Microbiology and Immunology, University of Iowa, Iowa City, IA

Human exposure to polychlorinated biphenyls (PCBs) has been linked to an increased risk of diabetes, obesity, and other metabolic diseases. Macrophages are key regulators of immunometabolism, and previous work has demonstrated that PCB exposure can alter macrophage polarization and inflammatory signaling. However, the mechanisms underlying these effects remain poorly understood. Because oxidative stress is a known consequence of PCB exposure in other cell types, we hypothesized that macrophage inflammatory skewing was mediated by changes to mitochondrial function accompanied by ROS. We first assessed PCB-induced mitochondrial stress using a Seahorse Assay.

Exposure to PCB 126 led to reduced basal respiration and spare respiratory capacity and greater reliance on glycolysis for ATP production. To determine if altered mitochondrial function was connected to ROS, we exposed PCB-treated macrophages in the presence or absence of vitamin E. Inflammatory signaling was assessed by measuring IL-8 production and was elevated with vit.E only under PCB exposure conditions. We hypothesized that this was due to ROS scavenging by vit.E that resulted in downregulation of nuclear factor erythroid 2-related factor 2 (Nrf2), a ROS induced transcription factor with both antioxidant and anti-inflammatory effects. To test this hypothesis, cells were treated with CDDO-Im, a pharmacological Nrf2 activator, which reversed the inflammatory response observed with PCB exposure and vit.E treatment. Together, these findings suggest that the relationship between antioxidant signaling and PCB-induced inflammation is complex. Further investigation of the Nrf2 pathway may provide insights into therapeutic strategies for mitigating the inflammatory and metabolic effects of PCB exposure.

Postdoctoral Posters

21. Lipid Peroxidation and Ferroptosis in Acetaminophen-induced Liver Injury: Is There a Dose Effect? (Ahamed)

Authors: Forkan Ahamed, Alyssa Williams, Hartmut Jaeschke, Anup Ramachandran

Affiliation: Department of Pharmacology, Toxicology and Therapeutics, University of Kansas Medical Center, Kansas City, KS

Background: Acetaminophen (APAP) overdose is the leading causes of acute liver failure (ALF) in the United States. APAP overdose causes mitochondrial dysfunction due to oxidative stress, which consequently results in hepatocyte necrosis. A moderate APAP overdose (300mg/kg) typically shows significant liver injury but no relevant lipid peroxidation (LPO) at early time points (6 hours). In contrast, iron supplementation with the APAP overdose exacerbates liver injury and shifts the injury mechanism to LPO. We examined whether a severe APAP-overdose (500mg/kg) promotes LPO at early and late time points, and whether a mitochondria-targeted SOD mimetic (Mito-Tempo) maintains protection against liver injury even after severe overdose.

Methods: Male C57BL/6J mice were fasted overnight and given 300 or 500 mg/kg of APAP intraperitoneally. A subset of mice received 20 mg/kg of Mito-Tempo ninety minutes post-APAP. Mice were euthanized 6 and 24 hours post APAP injection, and blood and liver samples were collected for analysis of liver injury and LPO.

Results: Plasma ALT and liver H&E staining showed that both 300 and 500 mg/kg APAP overdoses induced significant liver injury at 6 and 24 hours. Mito-Tempo significantly inhibited liver injury in mice given moderate APAP overdose, but protection was less robust after a severe overdose. Hepatic JNK activation was an early event at both doses and was unaffected by Mito-Tempo. Liver malondialdehyde (MDA) levels indicated no significant differences in LPO among all the treatment groups.

Conclusions: These data indicate that LPO-induced ferroptosis is not a relevant mechanism of liver injury even after a severe APAP overdose.

22. Ramping up the Heat: Induction of Systemic and Pulmonary Immune Responses and Metabolic Adaptations in Mice (Dean)

Authors: Laura E. Dean, Andrea Adamcakova-Dodd, Hans-Joachim Lehmler

Affiliation: Department of Occupational and Environmental Health, College of Public Health, University of Iowa, Iowa City, IA

Heatwaves are an increasing public health concern, yet most animal studies use sudden extreme heat exposure that poorly reflects real-world conditions. This study examined the effects of gradual exposure to extreme heat on mice. Adult male and female C57Bl/6 mice were randomly assigned to heat-exposed, control, or pair-fed experimental groups. Heat-exposed mice underwent a single 8-hour temperature ramp from 20°C to 38°C; control and pair-fed mice remained at ambient temperature. Multi-omics analyses after heat exposure included cytokine profiling in serum and lung, cecal microbiome characterization, lung transcriptomics, and serum metabolomics. Heat exposure altered several serum and lung cytokines (IL-17α, MIP-1α, MIP-1β, IL-1α, IL-12(p40), and RANTES). Random forest analysis identified microbial taxa that distinguished experimental groups, with a reduction in *Lactobacillus* observed in males; however, these effects were not statistically significant. Lung transcriptomics revealed changes in immune-related gene expression, particularly in pathways associated with B-cell activation. Serum metabolomics indicated modest disruptions in amino acid and energy metabolism, with enrichment of the glycine, serine, and threonine metabolism pathway. Integrated analyses identified associations among cytokines, gene expression, and bile acid-related metabolites. These findings demonstrate that gradual exposure to extreme heat triggers systemic and pulmonary responses in mice.

23. Temporal activation of cell death pathways in a multicellular human skin equivalent exposed to Sulfur Mustard and Lewisite (Gaviria)

Authors: Catalina Gaviria, Sarfaraz Ahmad, Christel Anthony, Patrick McNutt

Affiliation: Wake Forest Institute for Regenerative Medicine, Wake Forest University School of Medicine, Winston Salem, NC

Background and Purpose: Sulfur mustard (SM) and Lewisite (LW) are highly toxic vesicant agents that cause severe cutaneous and systemic injury, yet no medical countermeasures (MCMs) exist that can mitigate injury from vesicants with distinct toxidromes. Because skin is a primary site of exposure, understanding cutaneous responses to SM and LW is essential for developing broad-spectrum MCMs. Vesicants activate multiple cell death pathways, including ferroptosis, pyroptosis and apoptosis, their temporal activation remains poorly defined. To address this, we characterized the temporal activation of key cell death markers following SM and LW exposure in our multicellular 3D human skin equivalent (HSE).

Methods: HSEs were exposed to a range of doses of SM or LW vapors. Injury was assessed by histopathology, cytotoxicity, genotoxicity (H2A.X), and F-actin loss. Doses that preserved ~50% viability were used for temporal analyses of apoptosis (caspase-8/9 cleavage, TUNEL), ferroptosis (GPX4 depletion), and pyroptosis (GSDMD cleavage) over 48 h.

Results: SM and LW produced dose-dependent vesication in HSEs, an outcome rarely observed in animal models, along with cytotoxicity and DNA damage. Time-course analyses revealed sequential activation/inhibition of apoptosis, pyroptosis, and ferroptosis markers, with distinct timing patterns for each vesicant. These findings were confirmed by western blot analysis.

Conclusions: These findings demonstrate that HSEs provide a physiologically relevant platform for studying vesicant-induced skin injury. The model reproduces human-like pathology and reveals involvement of diverse cell death pathways, offering potential targets for therapeutic development. Our results highlight HSEs as an innovative new approach methodology to reduce reliance on animal testing.

24. Cell-Type-Specific Toxicological Responses to 6PPD and 6PPD-quinone in Human Cellular Models (Lee)

Authors: Dongkeun Lee¹, Marcelo Melo², Cassidy Kline^{2,3}, Susan Shen^{2,3}, Jong Sung Kim^{1,3}

Affiliations:

¹ Department of Occupational and Environmental Health, College of Public Health, University of Iowa, Iowa City, IA

² Department of Psychiatry, Carver College of Medicine, University of Iowa, Iowa City, IA

³ Interdisciplinary Graduate Program in Human Toxicology, Graduate College, The University of Iowa, Iowa City, IA

6PPD and its transformation product, 6PPD-quinone (6PPD-Q), are emerging tire-derived contaminants detected in environmental and human biological samples. Reported species-specific differences in toxicity complicate extrapolation to human health. This study investigated cellular and functional responses to 6PPD and 6PPD-Q using human-relevant models.

We evaluated cytotoxicity and intracellular reactive oxygen species (ROS) generation in six human cell models: A549 (lung), HepG2 (liver), Caco-2 (intestine), AC16 (cardiac), HTR-8/SVneo (placenta), and differentiated THP-1 macrophage-like cells. Tested concentrations ranged from 10 nM to 100 μ M, including environmentally relevant levels (10–100 nM). Neither compound induced significant cytotoxicity or ROS generation below 30 μ M. Additionally, high-content live-cell imaging using the Operetta system revealed no detectable changes in cellular morphology, mitochondrial organization, or cytoskeletal structure.

To further investigate potential neurotoxic effects, human iNgn2-WTC11 neurons were differentiated into glutamatergic neurons and exposed to 6PPD or 6PPD-Q. In contrast to the absence of detectable cytotoxic and morphological changes in the other human cell models, serial multielectrode array (MEA) recordings at baseline and 25 hours post-exposure showed increased neuronal firing activity following exposure to 100 nM 6PPD-Q, but not 6PPD. This observation suggests that 6PPD-Q may alter neuronal function at concentrations substantially below those associated with overt cytotoxicity in other human cell models.

These findings suggest that functional neuronal alterations may represent a sensitive endpoint of 6PPD-Q exposure and identify increased neuronal excitability as a potential early indicator of neurotoxicity. Ongoing studies aim to characterize concentration- and time-dependent neuronal responses and elucidate the molecular mechanisms underlying these neurofunctional alterations.

25. Mice with Human-Like Bile Acid Composition Develop PFIC-2-Like Cholestasis (Nickel)

Authors: Anthony M. Nickel^{1,2}, Jay L. Vivian^{1,2}, Chengpeng Bi¹, Yazen Alnouti³, James F. Daniel², Iván L. Csanaky^{1,2}

Affiliations:

¹ University of Kansas Medical Center, Kansas City, KS

² Children's Mercy Hospital, Kansas City, MO

³ University of Nebraska Medical Center, Omaha, NE

Bile acids (BAs) are essential for lipid absorption, bile formation, and metabolic control. Humans produce two primary BAs, cholic acid (CA) and chenodeoxycholic acid (CDCA). In mice, Cyp2c70 hydroxylates CDCA at the 6 β -position, producing hydrophilic muricholates (MCAs), unlike humans with a hydrophobic BA pool. These differences complicate translational research. For example, bile salt export pump (Bsep)-null mice, a model of progressive familial intrahepatic cholestasis type 2 (PFIC-2), have milder disease because their BAs are more hydrophilic. To model human BA composition, we engineered Cyp2c70-null mice. BA concentrations in liver, bile, and plasma and hepatic gene expression were quantified in wild-type and Cyp2c70-null mice.

In Cyp2c70-null mice, total (Σ) BA concentrations increased, particularly in females (liver, +79%; plasma, 14-fold). MCA formation was nearly abolished, whereas CDCA and its metabolites increased markedly, producing a hydrophobic, human-like BA pool. Despite increased hepatic CDCA and LCA, hepatic FXR-SHP and intestinal FXR-Fgf15 pathways were minimally activated. Biliary Σ BA excretion decreased by 18% in males and 25% in females, despite 16- and 32-fold increases in CDCA and LCA excretion, respectively, reflecting reduced TCA excretion (–19% males; –46% females). The hepatic TCDCA/TCA ratio increased from 0.12 in WT mice to 1.6 and 2.9 in male and female Cyp2c70-null mice, respectively. Increased TCDCA may inhibit Bsep-mediated TCA transport in females. Reduced TCA excretion limits intestinal FXR-Fgf15 activation, whereas hepatic FXR activation suppresses Cyp8b1.

In summary, Cyp2c70-null mice have a human-like hydrophobic BA pool and exhibit PFIC-like cholestatic features, providing a model for investigating mechanisms underlying human liver diseases.

26. Adolescent 2,2',5,5'-Tetrachlorobiphenyl-4-ol (4-OH-PCB52) Exposure via Polymeric Implant Disrupts Pulmonary Molecular Pathways (Roach)

Authors: Crystal M. Roach¹, Hui Wang¹, Nate R. Koester¹, Joel D. Nott², Xueshu Li¹, and Hans-Joachim Lehmler¹

Affiliations:

¹ Department of Occupational and Environmental Health, College of Public Health, University of Iowa, Iowa City, IA

² Office of Biotechnology Protein Facility, Iowa State University, Ames, IA

Hydroxylated polychlorinated biphenyls (OH-PCBs) are biologically active metabolites implicated in respiratory toxicity, yet their developmental effects on the lung remain poorly defined. We examined the developmental effects of the human-relevant metabolite 4-OH-PCB52 in postnatal day (PND) 28 female rats using a multi-omics framework. Animals were exposed via a 28-day subcutaneous implant exposure (sham (0%); low (1%); medium (5%); high (10%); (w/w)) through PND 56. GC-MS/MS confirmed tissue accumulation of 4-OH-PCB52 in the medium and high dose groups. Proteomic analyses at these doses revealed widespread alterations in pathways regulating surfactant regulation, mucociliary function, xenobiotic metabolism, and immunity. These proteomic alterations, occurring in the absence of transcript-level changes, highlight a post-transcriptional mode of toxicity consistent with PCB-induced biochemical stress. Together, these findings underscore the potential for hydroxylated PCB metabolites to act as developmental toxicants capable of impairing lung maturation and increasing susceptibility to respiratory dysfunction.

27. Neonicotinoids and Maternal Outcomes (Rhodes)

Authors: Mary C. Rhodes¹, Diane Rohlman¹, Darrin Thompson², Jonathan Davis¹, Donna Santillan³, Peter Thorne¹

Affiliations:

¹ Department of Occupational and Environmental Health, College of Public Health, University of Iowa, Iowa City, IA

² Office of Biotechnology Protein Facility, Iowa State University, Ames, IA

Hydroxylated polychlorinated biphenyls (OH-PCBs) are biologically active metabolites implicated in respiratory toxicity, yet their developmental effects on the lung remain poorly defined. We examined the developmental effects of the human-relevant metabolite 4-OH-PCB52 in postnatal day (PND) 28 female rats using a multi-omics framework. Animals were exposed via a 28-day subcutaneous implant exposure (sham (0%); low (1%); medium (5%); high (10%); (w/w)) through PND 56. GC-MS/MS confirmed tissue accumulation of 4-OH-PCB52 in the medium and high dose groups. Proteomic analyses at these doses revealed widespread alterations in pathways regulating surfactant regulation, mucociliary function, xenobiotic metabolism, and immunity. These proteomic alterations, occurring in the absence of transcript-level changes, highlight a post-transcriptional mode of toxicity consistent with PCB-induced biochemical stress. Together, these findings underscore the potential for hydroxylated PCB metabolites to act as developmental toxicants capable of impairing lung maturation and increasing susceptibility to respiratory dysfunction.

28. Integrating *In Vitro* and *In Silico* Approaches for the Safety Assessment of a Nanodrug Candidate for Alzheimer's Disease (Simões)

Authors: Mariana Crivellari M. Simões, Maria Eduarda S. Leite, Nathalia O. Nascimento, Carlos A. Tagliati

Affiliation: Toxicology Laboratory (ToxLab), Faculty of Pharmacy, Graduate Program in Applied Sciences to Toxicology (PPGACT), Federal University of Minas Gerais (UFMG), Belo Horizonte, Brazil

Alzheimer's disease (AD) urgently requires innovative therapeutic strategies and predictive safety assessment approaches that can reduce reliance on animal testing. Nanotechnology-based therapies offer promising opportunities for AD treatment, but their complex physicochemical properties may result in biological interactions that are not fully captured by conventional toxicity approaches. New Approach Methodologies (NAMs), integrating complementary *in vitro* and *in silico* models, provide an opportunity to generate mechanistic and translationally relevant safety information while advancing alternatives to animal testing. This study aimed to characterize the preliminary safety profile of a nanodrug candidate for AD and establish an integrated NAM-based framework for its safety assessment. Initial cytotoxicity screening was performed after 24 h exposure using MTT in A549, HEK-293, HepG2, and Neuro-2A cells. Neutral Red Uptake was assessed in 3T3 cells according to OECD Guideline 129. Immunogenic potential was evaluated in THP-1 cells using multiplex Luminex cytokine analysis, and oxidative stress was assessed through reactive oxygen species (ROS). The nanodrug maintained viability above 70% in A549, HEK-293, and Neuro-2A cells, consistent with low cytotoxicity according to ISO 10993-5 criteria. HepG2 cells showed concentration-dependent cytotoxicity at 24 h, followed by recovery at 48 h. No evident inflammatory response was observed in THP-1 cells, while ROS levels decreased. Nano-QSAR modeling and the EV-PROTEOMICS software developed in our laboratory are being integrated to support mechanistic interpretation within an Integrated Approach to Testing and Assessment (IATA). Additional analyses, including human neural cell models, are ongoing.

Research Scientist Posters

29. Comprehensive Assessment of PCB Burden, Congener Profiles, and Toxic Potential in the Human Cerebellum: across Age, Geography, Race, and Sex (X. Li)

Authors: Xueshu Li¹ Jonathan A. Davis¹ Rachel F. Marek² Keri C. Hornbuckle² Hans-Joachim Lehmler¹

Affiliations:

¹ Department of Occupational and Environmental Health, College of Public Health, University of Iowa, Iowa City, IA

² IIHR-Hydrosience and Engineering, University of Iowa, Iowa City, IA

Polychlorinated biphenyls (PCBs) are persistent neurotoxicants that accumulate in human tissues; however, congener-specific data for the human brain remain scarce. We quantified 173 individual or co-eluting PCB congeners in 126 postmortem human cerebellum samples and examined differences in PCB burden, congener composition, and estimated toxic potential by age, geography, race, and sex. Twenty-three congeners, predominantly hexa- through deca-chlorinated, were detected in >60% of samples. Median Σ PCB concentrations ranged from 775 to 4,388 ng/kg and were dominated by non-dioxin-like congeners. Σ PCB increased with age (approximately 2.7% per year; $p = 2.3 \times 10^{-6}$) and was 1.7-fold higher in males than females, with no racial differences. Congener profiles were largely conserved across age, race, and sex ($\cos \theta = 0.890$ - 0.960), indicating differences primarily in burden rather than composition; the greatest compositional divergence occurred among tissue banks. Neurotoxic equivalents increased with age and were higher in males and in the California tissue bank, whereas toxic equivalents, which showed a bimodal distribution, varied only by geography and sex. These findings identify age, sex, and geographic origin as important correlates of PCB burden and estimated toxic potential in the human brain.

30. The bladder as a target for PCB toxicity: Evidence from PCB levels, phase I metabolite levels, and cytochrome P450 expression following developmental exposure to a human-relevant PCB mixture in mice (Wang)

Authors: Hui Wang¹, Elaine Schumacher², Audrey Spiegelhoff², Conner L. Kennedy², Monica M. Ridlon², Rachel F. Marek³, Kimberly P. Keil Stietz², Hans-Joachim Lehmler¹

Affiliations:

¹ Department of Occupational and Environmental Health, College of Public Health, University of Iowa, Iowa City, IA

² Department of Comparative Biosciences, University of Wisconsin-Madison, Madison, WI

³ Department of Civil and Environmental Engineering, University of Iowa, Iowa City, IA

Background and Purpose: Lower urinary tract dysfunction is multifactorial, yet the role of environmental exposures is not well understood. Developmental exposure to polychlorinated biphenyls (PCBs) has been linked to altered voiding in mice; however, the disposition of PCBs in the bladder, their bioactivation, and the effects on cytochrome P450 (CYP) expression remain unclear.

Methods: We exposed mice to an environmentally relevant PCB mixture via maternal diet during gestation and lactation (vehicle, 0.1, 1, or 6 mg/kg/day). Offspring were euthanized at 6 to 7 weeks of age. PCBs and hydroxylated PCBs (OH-PCBs) levels were quantified in bladder, liver, blood, and urine. CYP expression was measured in bladder and liver.

Results: PCBs and OH-PCBs accumulated in all tissues in a dose- and sex-dependent manner, with higher-chlorinated congeners (e.g., PCB118, PCB138, PCB153, and PCB180) preferentially retained. Females exhibited greater hepatic accumulation, reduced urinary elimination, and distinct CYP regulation, characterized by increased hepatic and decreased bladder expression.

Conclusions: These findings, for the first time, define the signature of PCBs and OH-PCBs in the bladder and reveal sex-specific PCB disposition and CYP responses. Our results provide new mechanistic insight into developmental PCB exposure and its potential contribution to voiding dysfunction relevant to wildlife, domestic animals, and humans.

Undergraduate Student Posters

31. Iron chelator-mediated protection against acetaminophen-induced liver injury in mice (Dang)

Authors: Ethan Dang, Hualong Zhu, Wen-Xing Ding**Affiliation:** Department of Pharmacology, Toxicology and Therapeutics, Liver Center, University of Kansas Medical Center, Kansas City, KS

Acetaminophen overdose is a leading cause of acute liver injury. Excessive APAP metabolism produces reactive metabolite N-acetyl-p-benzoquinone imine (NAPQI), which depletes glutathione, induces oxidative stress, and can lead to hepatocyte necrosis. Recent evidence suggests that excessive iron contributes to oxidative liver injury. Our objective was to evaluate whether N-acetylcysteine (NAC), deferiprone (DFP), or their combination can protect against APAP-induced liver injury in mice.

We evaluated liver injury in mice 24 hours after APAP was administered. To test the therapeutic values of NAC and DFP in a clinically relevant model, NAC, DFP, or NAC+DFP were administered 6 hours post APAP treatment. After treatments, liver sections were analyzed using hematoxylin and eosin (H&E) staining to quantify hepatic necrosis and immunohistochemistry (IHC) to mark proliferating cell nuclear antigen (PCNA) and assess hepatocyte proliferation.

Quantification of H&E-stained liver sections showed that both DFP and NAC treatments reduced necrotic liver tissue compared with APAP alone. The combined NAC+DFP treatment produced the greatest reduction in the percentage of liver injury among all treatment groups. PCNA immunohistochemistry data revealed an increased DAB-positive hepatocytes in both NAC- and DFP-treated mice compared with APAP alone. The NAC+DFP combination showed the highest level of hepatocyte proliferation.

Our findings suggest that both NAC and DFP can reduce APAP-induced liver injury by attenuating hepatic necrosis and promoting hepatocyte proliferation. The combination of NAC and DFP provided the greatest protective effect. Further studies are required to investigate the molecular mechanisms of DFP- and NAC-mediated protection as a potential against APAP-induced acute liver injury.

32. Quantification of PCB52 Metabolites in the Brain of Female Sprague-Dawley Rats Exposed to 4-Hydroxy-2,2',5,5'-Tetrachlorobiphenyl via Polymeric Implant (J. Li)

Authors: Jessie Li, Hui Wang, Hans-Joachim Lehmler

Affiliation: Department of Occupational and Environmental Health, University of Iowa, Iowa City, IA

Polychlorinated biphenyls (PCBs) are persistent organic pollutants (POPs) that are ubiquitous in the environment. PCB exposure has been linked to cancer and multisystem toxicity, including endocrine disruption, reproductive toxicity, and neurotoxicity. Among the 209 PCB congeners, 2,2',5,5'-tetrachlorobiphenyl (PCB52) is one of the most frequently detected congeners in both the environment and humans. 2,2',5,5'-Tetrachlorobiphenyl-4-ol (4-OH-PCB52) is a human-relevant PCB metabolite that has been shown to be more toxic than PCB52. To investigate the neurotoxicity of 4-OH-PCB52, female Sprague–Dawley rats were exposed to 4-OH-PCB52 via polymeric implants at total loading concentrations ranging from 0%, 1%, 5%, and 10% of the implant (w/w) for 28 days. Behavioral assessments, including the Y-maze, hole board test, open field test, and elevated plus maze, were performed to evaluate behavioral outcomes. After 28 days of exposure, the rats were sacrificed, and tissues were collected for analysis of PCB metabolites. In this subproject, 4-OH-PCB52 and its metabolites were extracted using a liquid–liquid extraction method and analyzed by gas chromatography–tandem mass spectrometry (GC-MS/MS) in multiple reaction monitoring (MRM) mode. Preliminary data indicate that 4-OH-PCB52 and its metabolite, 4,4'-diOH-PCB52, were detected in brain tissue. Further investigations into their association with behavioral outcomes are ongoing.

33. Sequencing of glutathione transferase transcripts in cats (Luong)

Authors: Ana Kirillov, Caitlin Luong*, James Sacco

Affiliation: Drake University College of Pharmacy and Health Sciences, Des Moines, IA

*Presenting author

Glutathione transferases (GSTs) are a superfamily of enzymes that eliminate reactive electrophilic molecules by conjugating them to glutathione. GSTs are further subdivided into classes (e.g. M and T), each encoded for by multiple genes. In the cat, 4 GSTA, 2 GSTM and 4 GSTT transcripts are predicted to be expressed. The objective of this study was to experimentally identify GSTA, GSTM and GSTT transcripts in cat brain and peripheral blood mononuclear cells (PBMCs) and screen the sequences for polymorphisms. cDNA was obtained from total RNA isolated from brain and PBMCs. To test for the presence of GST transcripts, PCR primer pairs were designed to target unique sequences within each GST cDNA. Amplified products of the expected size were observed in both tissue types for the GSTA2, GSTA4, GSTM3, GSTP, GSTT1, GSTT1-like, GSTT3-like and GSTT4-like genes but not for the GSTA4-like and GSTM4 genes. To ascertain the identity of these GST transcripts, new PCR primer pairs were designed to amplify the entire coding sequence of each of the transcripts. All samples sequenced successfully, except for GSTA2 and GSTT4-like. After PCR optimization, the amplicons were submitted for DNA sequencing following exonuclease cleanup. The experimental forward and reverse sequences aligned with the predicted sequences from GenBank (>88 % identity). Several synonymous and non-synonymous genetic polymorphisms were observed in the coding region of the GST1 and GSTT1-like genes. In conclusion, this study verified that the GSTA2, GSTA4, GSTM3, GSTT1, GSTT1-like, GSTT3-like, and GSTT4-like genes are expressed in PBMCs and the brain of cats.

34. Authentication and Characterization of Chlorobenzoic Acids (Shahid)

Authors: Haider Shahid¹, Dane M. Lew¹, Timonthy E. Mattes², Xueshu Li¹, Hans-Joachim Lehmler¹

Affiliations:

¹ Department of Occupational and Environmental Health, College of Public Health, University of Iowa, Iowa City, IA

² Department of Civil and Environmental Engineering, University of Iowa, Iowa City, IA

Chlorobenzoic acids (CBAs) are chlorinated aromatic carboxylic acids formed during the biotransformation of polychlorinated biphenyls (PCBs) and released from agricultural and industrial sources. As relatively stable degradation products, CBAs are important markers of both PCB metabolism and environmental transformation. CBAs are also environmental toxicants with documented biological activity, so accurate identification and characterization are essential. However, the 19 possible CBA congeners, spanning mono- through pentachlorinated isomers, have not been systematically characterized as a complete set. In this work, all 19 CBAs were obtained from commercial chemical and biotechnology suppliers. We authenticated each CBA by liquid chromatography-high-resolution mass spectrometry (LC-HRMS), proton nuclear magnetic resonance (¹H NMR), and carbon-13 nuclear magnetic resonance (¹³C NMR) spectroscopy. LC-HRMS confirmed molecular formulas from accurate mass and chlorine isotope patterns, and chromatographic retention times helped distinguish isomers. ¹H and ¹³C NMR spectra confirmed the chlorine substitution pattern of individual compounds. Together, these complementary techniques provide a verified authentication dataset for each CBA compound. The authenticated CBAs will be used in future toxicological and environmental studies, ensuring researchers use the correct analyte and produce accurate, reproducible results.