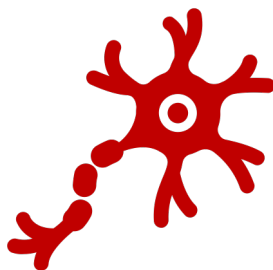
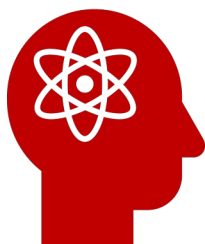




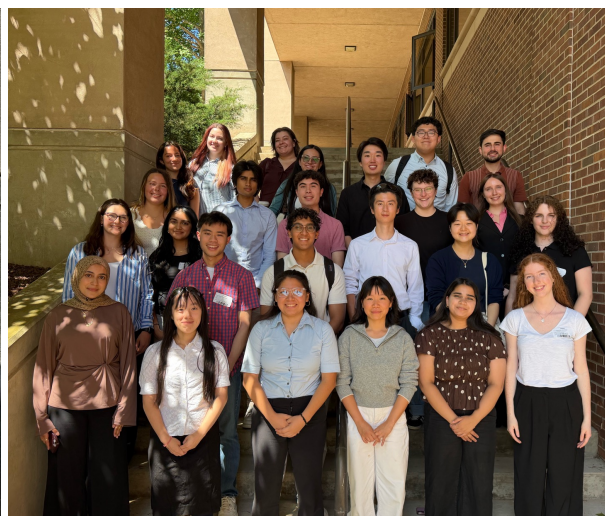
Summer Undergraduate Research Fellowship (SURF)

Final Presentations

July 30, 2026



Week	SURF Weekly Activities
1	Orientation (Lab Notebook keeping, Reading Manuscripts, & Safety Training)
	Advice from SURF Alumni
	Responsible Conduct of Research
2	Getting Noticed and Building Your Brand on LinkedIn
3	What's in My Personal Care Products? Are They Safe?
4	Getting Noticed and Building Your Brand on LinkedIn
5	Grover Symposium
	Plastics in Our Lives: From Nano to Macro
	Plastics Field Trip
6	Careers, Networking, and Painting
7	Written and Graphical Abstracts
8	Bristol Myers Squibb Field Trip
	Communicating Science
9	Pharmacy Honors Presentations
10	Closing Session
11	Final Symposium



Session I Presentations (11:00 a.m. – 12:00 p.m.)

Presenter	Mentor
Julia Sierzputowski	Drs. Andrew and Rachel Sun
Swati Bangalore	Drs. Mary Bridgeman and Daniel Abazia
Alexandra Brodska	Drs. Longqin Hu and Abdusemi Abduweli
Samuel Potenciano	Dr. Cheryl Dreyfus and Yangyang Huang
Audrey Chodkiewicz	Dr. Mi-Hyeon Jang
Jack Sicat	Drs. Lauren Aleksunes and Shams Shams
Sarah Dardir	Dr. Lauren Aleksunes and Brianna Ames
Radha Pandya	Drs. Phoebe Stapleton and Talia Seymore
Viktorina Leopold	Dr. Memo Laurent

Session II Presentations (12:15 p.m. – 1:15 p.m.)

Presenter	Mentor
Ramla Basharat	Drs. Luigi Brunetti and Jorge Ponce Zea
Thanh Du	Drs. Nav Narayanan and Sana Mohayya
Victoria Berger	Dr. Matthew McBride and Emily Hyde
Neev Siram	Dr. Igor Shmarakov
Maxwell Bouffard	Drs. Stevn An, Jordan Lee, and Shanzeh Rauf
Sara Calvo Londono	Dr. Lauren Poole and Gina Capece
Samantha Strickland	Drs. Grace Guo, Bo Kong, Anisha Bhattacharya
Joan Dischert	Drs. Brian Buckley and Rachel Buckley
Kevin Lu	Drs. Tom Lin and Changfeng Deng

Session III Presentations (1:30 p.m. – 2:30 p.m.)

Presenter	Mentor
Aarhan Chakraborty	Dr. Emmanuel Diccio-Bloom, Xiaofeng Zhou
King-Yang Simeon Wong	Drs. Laurie Joseph, Peihong Zhou, Kevin Ozkuyumcu
Natalia Kalinowska	Drs. Debra Laskin and Candace Longoria
Bridget Broncales	Drs. Debra Laskin and Candace Longoria
Jaein Chung	Dr. Debra Laskin and Jess Rodriguez
Jessica Wangsa	Dr. Sara Campbell and Andi Cheng
Emma Andrechek	Drs. Lauren Aleksunes and Chenghui Jiang
Jenny Chen	Drs. Shuo Xiao and Jiyang Zhang

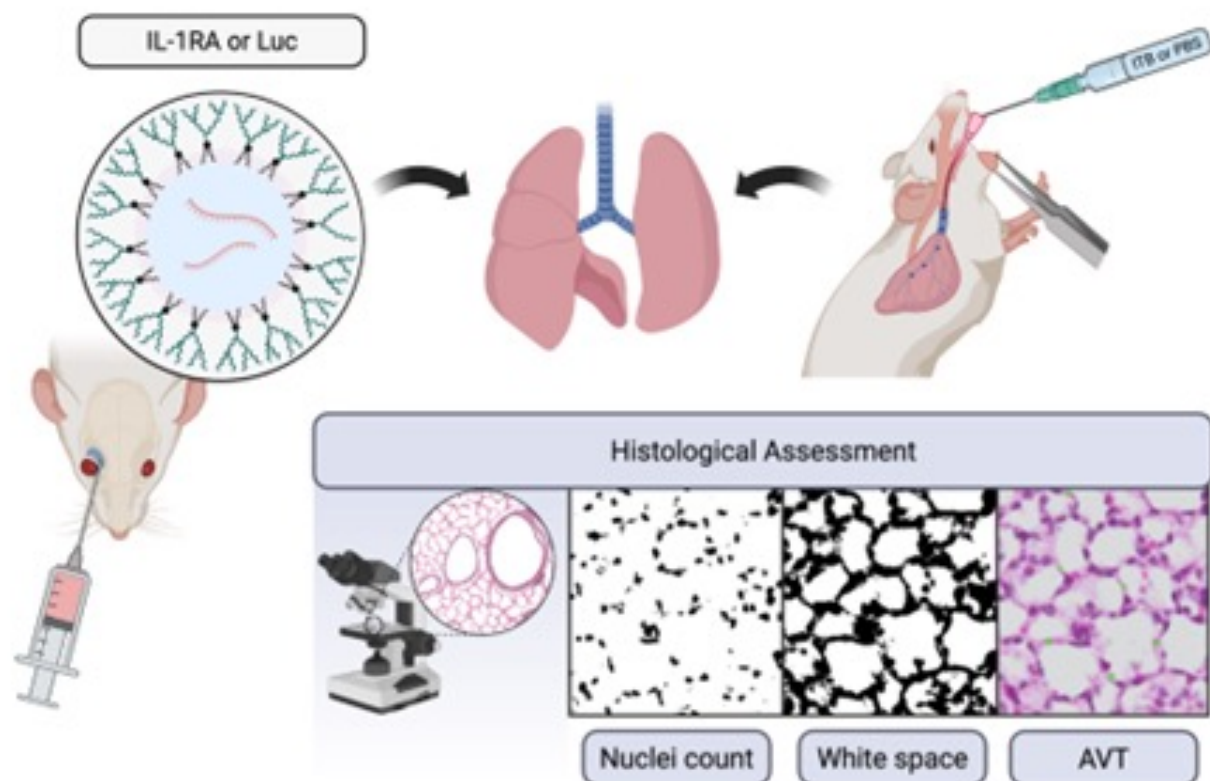


Histological Changes Subsequent Targeted Delivery of IL-1RA mRNA to ITB-Induced Acute Lung Injury Model

Julia Sierzputowski, Rachel Sun, Elena Abramova, Chang-Jiang Guo,
Elena Atochina-Vasserman, Andrew J. Gow

Ernest Mario School of Pharmacy, Rutgers University

Acute lung injury (ALI) occurs when there is damage to the lower lung portions from multiple insults, characterized by alveolar epithelial dysfunction and reduced gas exchange. Potential ALI treatments have limited bioavailability to lower lung regions and off-target effects in uninjured organs. A key component of ALI is inflammation mediated by pro-inflammatory interleukin-1 (IL-1). IL-1 binds to IL-1R on the surface of inflammatory cells. This activation results in epithelial injury in ALI. IL-1 signaling can be reduced by IL-1RA, which stops IL-1 from signaling inflammatory cells. We reasoned that increasing IL-1RA expression by delivering mRNA could reduce bleomycin-induced ALI. IL-1RA mRNA formulated with IAJD34 (known to target the lower lung) were administered i.v. to BALB/c mice exposed intratracheally to either PBS control or bleomycin (4 U/kg). Lung tissues were collected 3 days post-administration and stained with H&E. Morphological changes were imaged, using OlyVIA software (400x) and analyzed with Fiji. Nuclei count, white space, and alveolar wall thickness were measured to assess immune cell infiltration, tissue consolidation, and epithelial thickening respectively. Minimal morphological changes were observed between mice exposed with bleomycin treated with IL-1RA compared to control alone. IL-1RA treated mice displayed an increase in nuclei count, but no significant changes in white space and alveolar thickness. Notably, the bleomycin-induced injury was low in BALB/c mice. Our data show that IL-1RA appears to alter cell recruitment but further experiments are required to establish the effects on overall injury. Supported by NIH R25ES020721, T32-ES01984, and P30-ES005022.

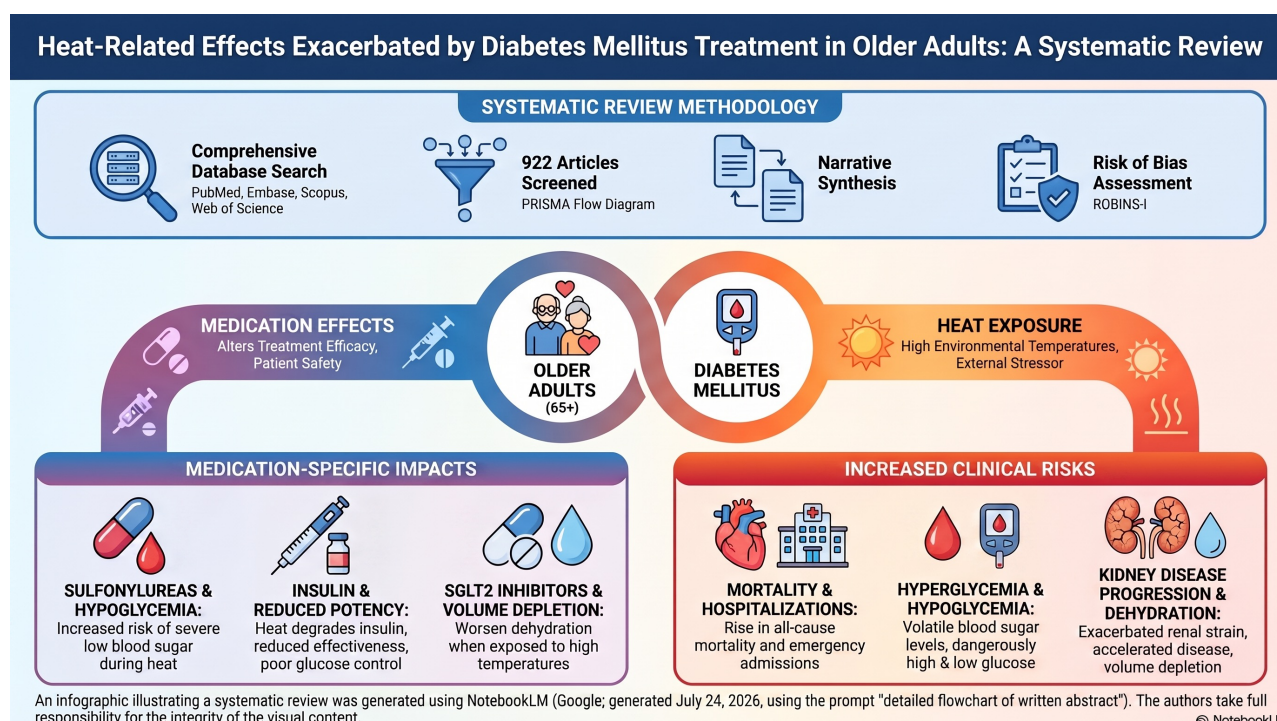


Systematic Review of Heat-Related Effects on Diabetes Mellitus Treatment in Older Adults

Swati Bangalore, PharmD¹; Mary Barna Bridgeman, PharmD¹; Catherine Chen, MD²; Sidrah Rafiq, MD²; Matthew C. Bridgeman, MLS³; Daniel T. Abazia, PharmD¹

¹Ernest Mario School of Pharmacy, Rutgers, The State University of New Jersey, Piscataway, New Jersey USA; ²Rutgers-Robert Wood Johnson Medical School, ³Rutgers Health Science Library

Heat-related illnesses are increasingly prevalent, particularly in the context of rising global temperatures. Older adults (aged 65 years and older) with diabetes mellitus are physiologically vulnerable to elevated temperatures due to impaired thermoregulatory mechanisms and increased heat sensitivity, which may be exacerbated by medications. The objective of this systematic review was to analyze heat-related medication effects in older adults with diabetes mellitus. The databases queried included PubMed, Embase, Scopus, and Web of Science. The Covidence systematic review software was used to manage screening, selection, and extraction of articles. A total of 922 articles were screened, and 50 were selected for analysis. The results of the search and study inclusion process are reported and presented visually in a Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 flow diagram. ROBINS-I was used to conduct risk-of-bias assessments. Due to substantial heterogeneity, results were summarized narratively without meta-analysis. Extreme heat increases the risk of diabetes-related mortality and hospitalization, while worsening chronic kidney disease and increasing the risk of dehydration. The risk of serious heat-induced hypoglycemia increases with sulfonylurea and insulin use; insulin potency is reduced in response to heat stress; and SGLT2 inhibitors may increase risks of volume depletion. Older adults with diabetes mellitus remain susceptible to heat-related health effects. Healthcare providers must take heat stress into account when making clinical decisions. This project is supported by the NJ ACTS CREST Program, funded by NIH R25TR00477.

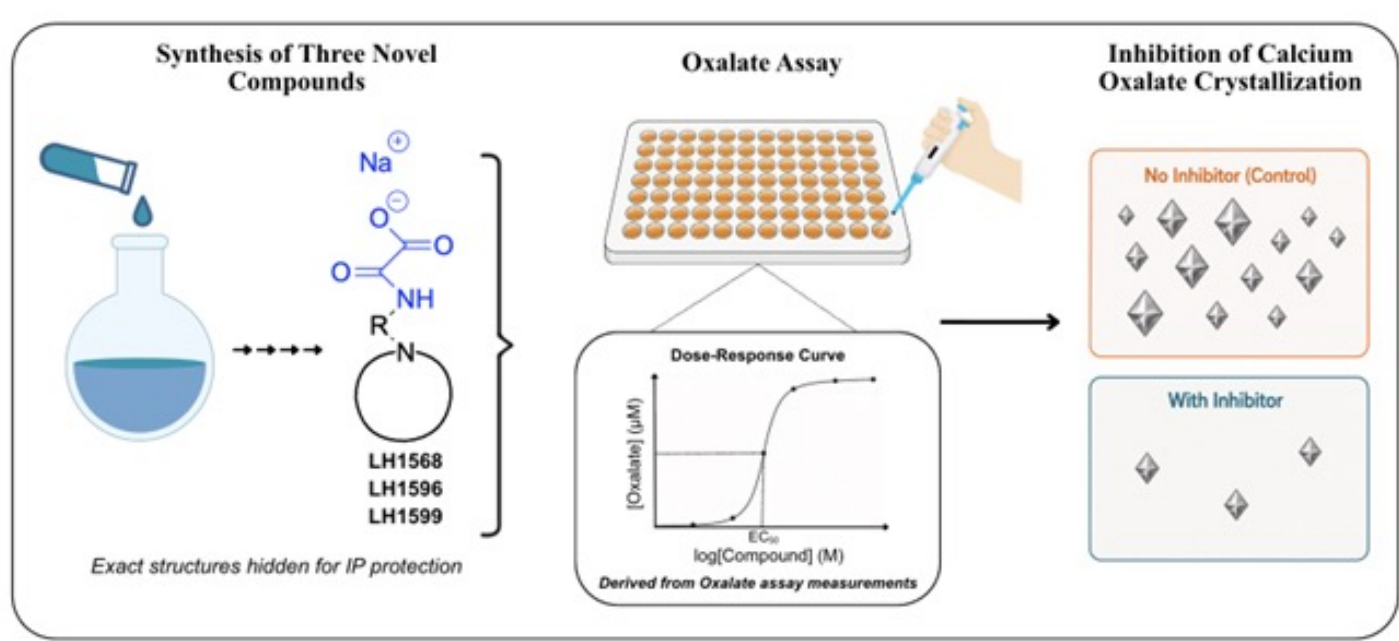


Synthesis and Evaluation of Three Small-Molecule Inhibitors of Calcium Oxalate Crystallization for Hyperoxaluria

Alexandra Brodska¹, Abdusemi Abduweli², Longqin Hu²

¹CUNY Hunter College, ²Department of Medicinal Chemistry, Ernest Mario School of Pharmacy, Rutgers, The State University of New Jersey

Calcium oxalate (CaOx) crystallization is the primary cause of urolithiasis, accounting for nearly 80% of all kidney stone cases. Potassium citrate remains the standard pharmacological therapy for recurrent kidney stones associated with hyperoxaluria. However, its low potency requires high doses to achieve some therapeutic efficacy, increasing the risk of adverse side effects and disruption of calcium homeostasis. To develop more effective therapeutics with fewer side effects, novel small molecules are being designed, synthesized, and evaluated as potent inhibitors of CaOx crystallization in our laboratory. In this SURF project, three compounds were synthesized in 4 steps, in 4–7% overall yields. Purification was performed using extraction, normal- and reversed-phase chromatography, and structures were confirmed by ¹H-NMR, ¹³C-NMR, and LC-MS. The ability of target compounds to inhibit CaOx crystallization was measured by incubating a supersaturated calcium oxalate solution in varying concentrations of test compounds for 72 h at 20 °C in HEPES buffer (pH 6.8). After incubation, oxalate concentrations in the supernatant after centrifugation were quantified using an oxalate assay kit. Dose-response curves generated by plotting free oxalate concentrations vs inhibitor concentrations were used to derive EC_{50} values. Two of the three compounds were tested and demonstrated concentration-dependent inhibition of CaOx crystallization with EC_{50} of 308 ± 24 nM for LH1568 and 27 ± 2 nM for LH1599, which are 690- and 7,900-fold more potent than potassium citrate ($EC_{50} = 212 \pm 23$ μ M), respectively. These results help identify leads for further optimization as potential therapeutics to prevent CaOx kidney stone formation in patients with hyperoxaluria. Supported by NIH R25ES020721.

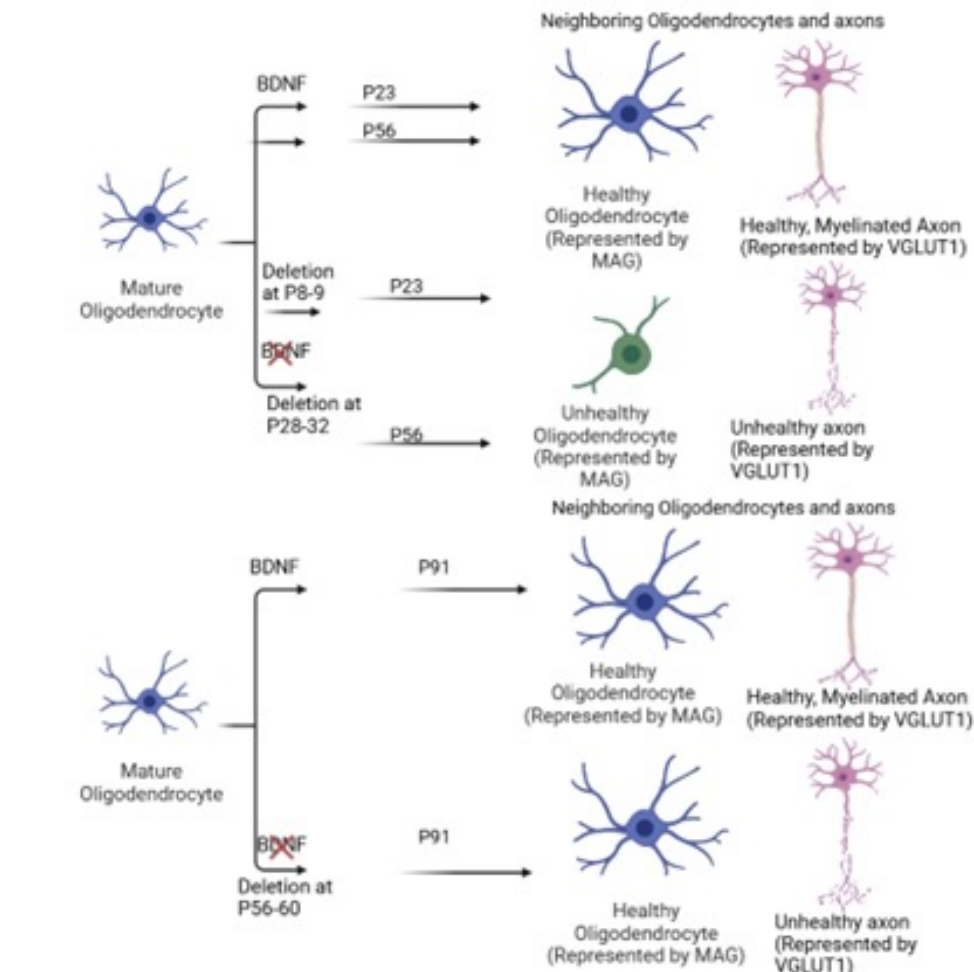


Effects of a Brain-Derived Neurotrophic Factor Deletion from Oligodendrocytes During Development

Samuel Potenciano¹, Amanda Pan¹, Yangyang Huang¹, Cheryl Dreyfus¹

¹Rutgers Robert Wood Johnson Medical School

In the past, the Dreyfus lab found that mature oligodendrocytes synthesize and secrete brain-derived neurotrophic factor (BDNF). The oligodendrocyte-derived growth factor was shown to increase the survival and maturation of neuronal cells in vitro. The purpose of this study was to investigate mature oligodendrocyte-derived BDNF's effect on neuronal axons and myelination during development in vivo using murine models. We hypothesized that BDNF deletion from mature oligodendrocytes would negatively affect the development of axons and mature oligodendrocytes. BDNF deletion from mature proteolipid protein-positive oligodendrocytes was induced using Cre-LoxP technology at Postnatal day (P) 8-9, or P28-32, or P56-60, and results were assessed at P23, or P56, or P91, respectively. Effects were determined using Western blots to detect myelin and axonal proteins in the corpus callosum. Preliminary results indicate that the BDNF deletion examined at P-23 and P-56 resulted in a decrease in myelin-associated glycoprotein (MAG). However, at P91, no effect on MAG was observed. In contrast, vesicular glutamate transporter 1 (VGLUT1), a neuronal axonal protein, was reduced at all time points examined. These data suggest that the mature oligodendrocyte-derived BDNF deletion negatively influences early oligodendrocyte development. This influence is lost between P56-P91. On the other hand, effects on proximate axons are evident throughout development and the latest ages investigated. Supported as a Grover Scholar by Dr. and Mrs. Gary Grover.



Secreted Frizzled-Related Protein 3 (sFRP3) Inhibition as a Target for Chemotherapy-induced Cognitive Impairment Treatment

Audrey Chodkiewicz¹, Euiyeon Lee^{2,3}, Sang Hoon Kim^{2,3}, Mi-Hyeon Jang^{2,3}

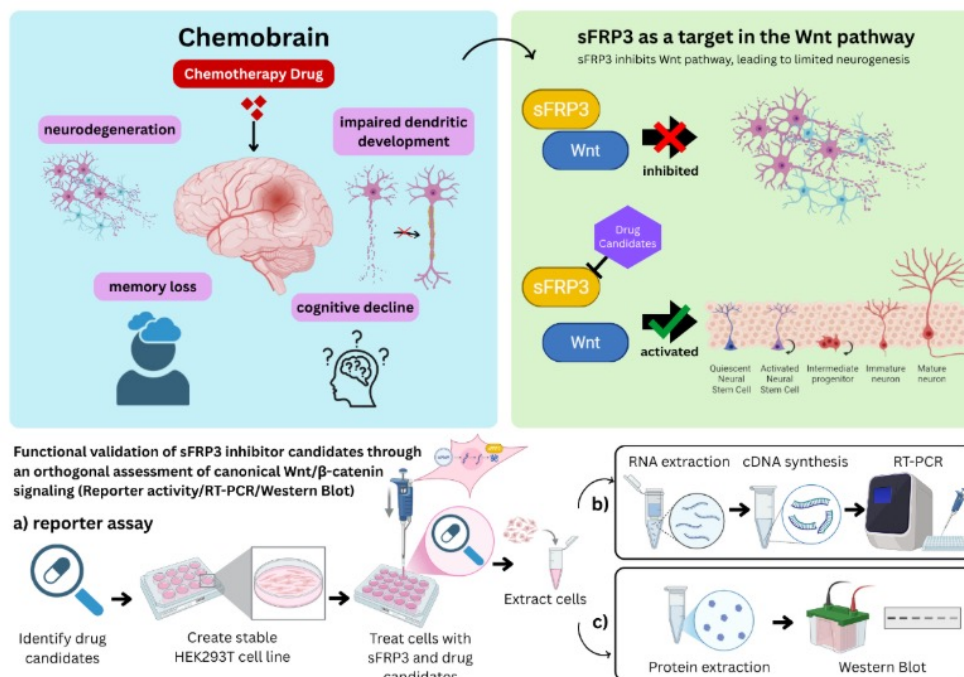
¹Department of Biomedical Sciences, Quinnipiac University, Hamden, Connecticut, United States; ²Department of Neurosurgery, Robert Wood Johnson Medical School, Rutgers University, Piscataway, New Jersey, United States; ³Brain Health Institute, Rutgers University, Piscataway, New Jersey, United States.

Background: Despite advances in cancer treatment, quality of life after chemotherapy is a major concern for both adult and pediatric survivors. Chemotherapy-induced cognitive impairment (CICI), or "chemobrain," is characterized by cognitive dysfunction caused by the neurotoxic effects of chemotherapy. Currently, no approved treatment addresses the underlying neuronal injury. Previous studies from the Jang Lab found that secreted frizzled-related protein 3 (sFRP3), a naturally secreted Wnt/ β -catenin inhibitor, showed increased expression after chemotherapy, which impaired neuronal development and cognitive function. AI-based modeling and bioinformatics identified blood-brain barrier-permeable candidate sFRP3 inhibitors. This study aimed to identify candidate compounds that reverse sFRP3-mediated suppression of Wnt/ β -catenin signaling as a potential therapy for CICI.

Methods: To test this, a stable HEK293T TCF/LEF reporter cell line was developed by lentiviral transduction for measuring canonical Wnt/ β -catenin activity. Six candidate compounds were screened with a TCF/LEF reporter assay. Wnt/ β -catenin pathway downstream activation was assessed through RT-qPCR analysis of *AXIN2* expression and Western blot analysis of active β -catenin.

Results: Four of the six screened compounds increased canonical Wnt/ β -catenin pathway activation, confirmed through RT-qPCR showing statistically significant increases in *AXIN2* expression. Western blot analysis showed increased active β -catenin levels following treatment with ABC99 and Yoda1.

Conclusion: Findings supported that ABC99 and Yoda1 may enhance Wnt/ β -catenin signaling, making them promising candidates. However, ABC99 may preserve Wnt activity through NOTUM inhibition, and Yoda1 may activate β -catenin through PIEZO1-mediated signaling. Further studies using an sFRP3-overexpression model are needed to determine whether these compounds specifically counteract sFRP3-mediated suppression of Wnt/ β -catenin signaling and to confirm their therapeutic potential for chemobrain. Supported by NIH R25ES020721.

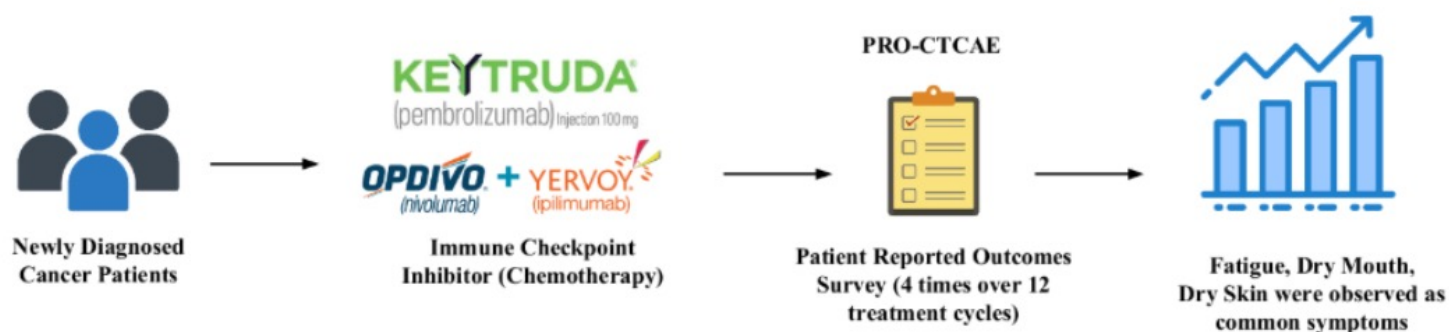


Patient-Reported Adverse Effects in Cancer Patients Undergoing Immune Checkpoint Inhibitor Therapy

Jack Sicat¹, Shams Shams¹, Sarah Asby², Xia Wen^{1,3}, Melanie Joy², Lauren Aleksunes^{1,3}

¹Department of Pharmacology & Toxicology, Ernest Mario School of Pharmacy, Rutgers University, Piscataway, NJ, ²University of Colorado, ³Environmental & Occupational Health Sciences Institute, Rutgers University, Piscataway, NJ

Immune checkpoint inhibitors (ICIs) have improved survival rates for patients with cancer but can also cause adverse events (AEs). These events may affect multiple organ systems and quality of life of a patient with varying severities. This study sought to evaluate patient-reported adverse effects over time in a prospective cohort study of adult oncology patients treated with ICIs at Rutgers University and University of Colorado Cancer Centers. Adult cancer patients initiating ICI treatment were given the Patient-Reported Outcomes Common Terminology Criteria for Adverse Events (PRO-CTCAE) electronic survey, consisting of 76 questions, on 1 to 4 visits over a 12-cycle treatment period to identify symptom patterns that develop. Forty-seven cancer patients completed the survey. The severity and frequency of symptoms reported were recorded at each treatment cycle. Scores were listed between a range of 0 to 4 to describe their experience of the symptoms. The most frequent symptoms reported were fatigue (76% reported), dry skin (60% reported), and dry mouth (58% reported) with an increase in frequency between cycles 2 and 3 of treatment. Despite high frequency reports of each symptom, fatigue (28%) had the greatest number of reports of either 3 or 4 when compared to dry mouth (18%) and dry skin (8%). Overall, the PRO-CTCAE survey is feasible and informative for longitudinal symptom monitoring among patients but does not have the ability to predict development of certain symptoms. A larger sample size is necessary to check if there is a stronger correlation between treatment and the symptoms. Supported by NJ ACTS CREST Program funded by NIH R25TR004777.

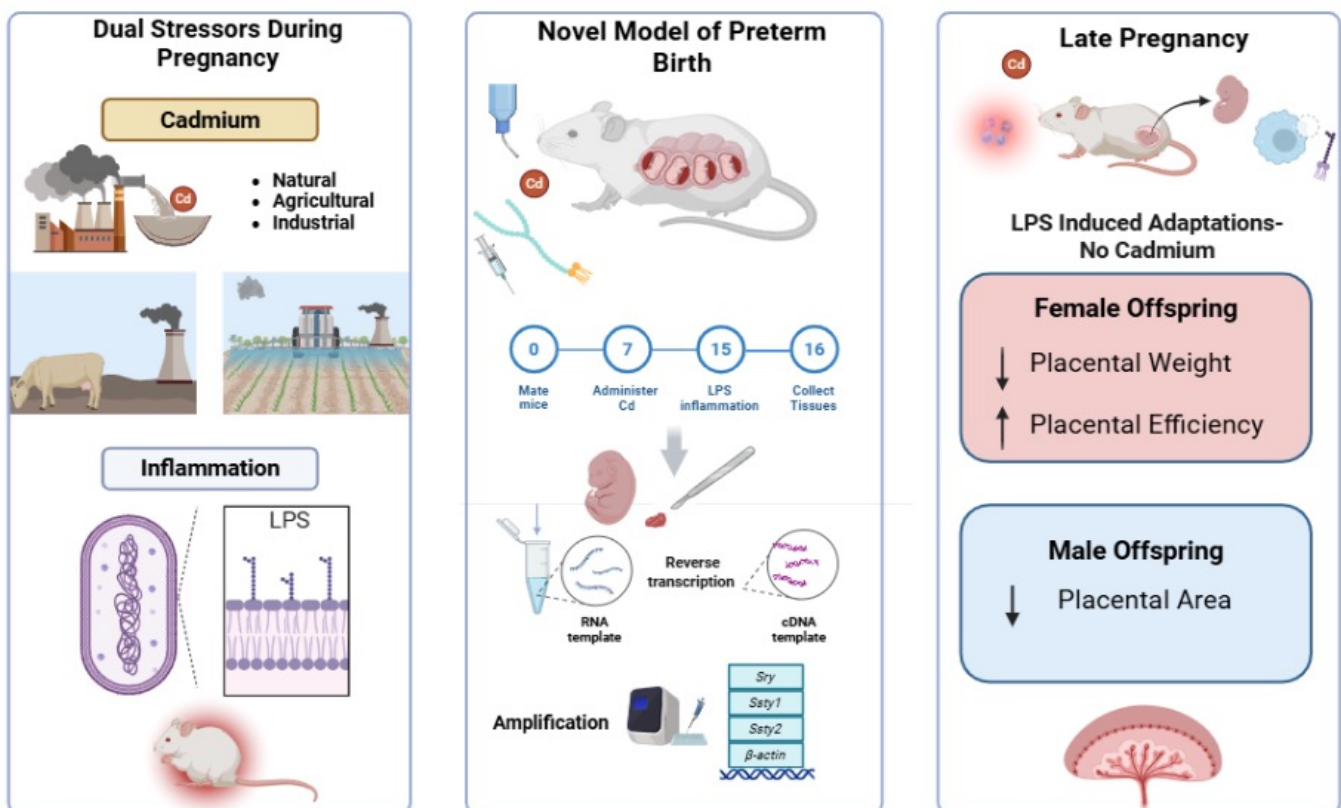


Cadmium Exposure Prevents Placental Adaptation to Inflammation During Pregnancy: Sex Differences in Fetal Responses

Sarah Dardir¹, Brianna Ames¹, Lauren Aleksunes¹

¹Rutgers University, the State University of New Jersey

The placenta facilitates nutrient delivery, waste removal, and fetal protection from xenobiotics. The placenta is not a complete barrier, and toxic substances can accumulate, including the environmental metal cadmium (Cd). Cd is ubiquitous in the environment and can move freely in water, soil, and air. Cd is detectable in maternal plasma and placentas, and exposure during pregnancy has been associated with poor pregnancy outcomes. Cd alters macrophage phenotypes in mouse placentas and has been linked to an increased susceptibility to infection in preterm infants. Therefore, we sought to determine whether prenatal Cd exposure alters susceptibility of mice to preterm birth caused by lipopolysaccharide (LPS) exposure in late gestation. C57BL/6J mice were mated overnight and separated in the morning, designated gestational day (GD) 0. On GD7, pregnant dams began to receive either distilled water (Ctrl), or 50 ppm cadmium chloride (CdCl₂) in drinking water. On GD15, dams received saline or LPS (100 µg/kg, ip) 16 or 24 hours prior to tissue collection. Enrichment of male-specific genes (*Sry*, *Ssty1*, *Ssty2*) and *β-actin* (housekeeping gene) was quantified in fetal tissues using RT-qPCR. Exposure to LPS caused sex-dependent adaptation in placenta morphometrics, with female offspring exhibiting lower placental weights and increased placental efficiency at 24 h. In male offspring, placental area was reduced by LPS at 16 and 24 h. Remarkably, cadmium pre-exposure prevented these adaptations and instead increased preterm birth to 70% compared to 17% in dams treated only with LPS. Future work will examine placental vasculature development using endothelial markers CD31 and CD34. Supported by NIH R25ES020721.

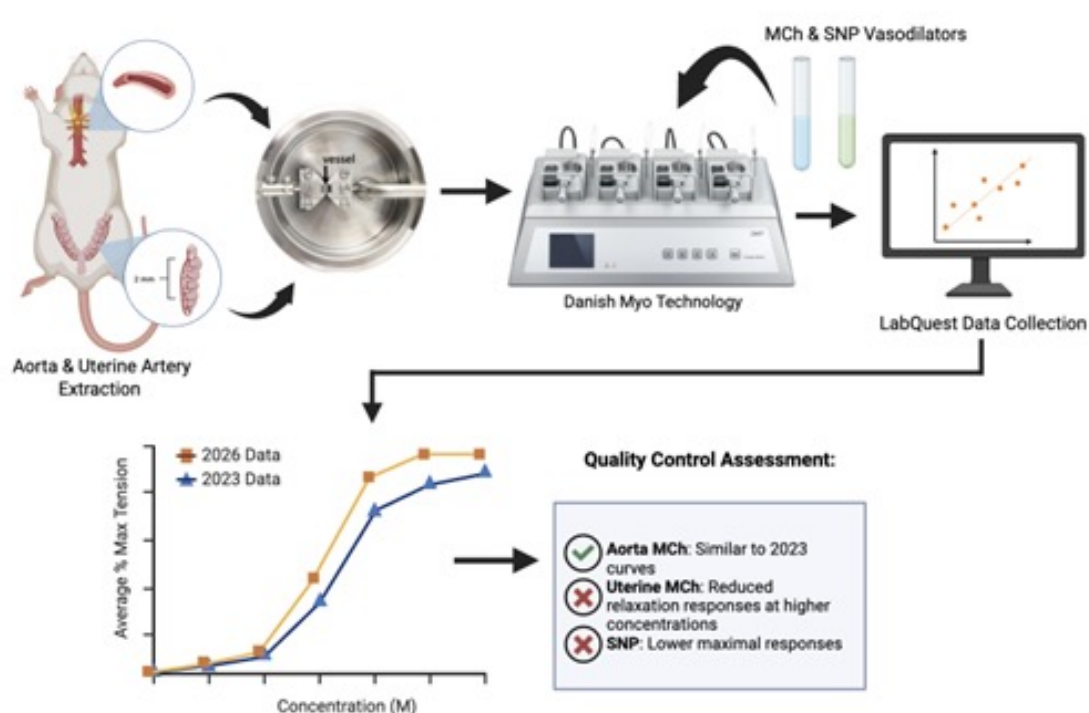


Quality Control Assessment of Vascular Reactivity in Aorta and Uterine Arteries Using Wire Myography

Radha Pandya¹, Talia Seymore², Phoebe Stapleton²

¹Ernest Mario School of Pharmacy; ² Environmental and Occupational Health Sciences Institute, Rutgers University, New Brunswick, NJ

During pregnancy, vascular adaptations are important to meet the oxygen and nutrient demands of a growing fetus. Maternal blood flow and cardiac output increase while systemic vascular resistance decreases. Nitric oxide (NO), an endothelium-derived vasodilator, promotes smooth muscle relaxation, reducing vascular resistance. However, recent studies suggest that particle exposure impairs NO signaling and disrupts vascular relaxation during pregnancy. The purpose of this study was to establish quality control methodology by ensuring vascular responses from 2026 Sprague-Dawley rats are consistent with established 2023 laboratory data. Uterine arteries and aortas were collected from virgin female Sprague-Dawley rats and placed in chilled physiological salt solution (PSS). Vessel segments (2 mm) were mounted on a wire myograph (Danish Myo Technology, Inc) and placed in warmed PSS to equilibrate for 20 minutes. Chemical agonists, methacholine (MCh), an endothelium-dependent agonist, and sodium nitroprusside (SNP), an endothelium-independent agonist, were added to the vessel bath in increased concentrations (10^{-9} – 10^{-4} M) following high-potassium physiological salt solution (KPSS)-induced contraction. Force measurements (mN; LabChart) were recorded and compared to historical data. Aortic MCh responses demonstrated similar maximal responses (99.69% vs. 95.72%) and slightly greater relaxation at the highest concentration (18.19% vs. 21.12%). In contrast, uterine artery MCh responses showed similar peaks (96.43% vs. 98.16%) but did not replicate the relaxation-curve slope or reach equivalent relaxation (60.04% vs. 22.54%). SNP responses were attenuated in both, with lower peak responses. This indicates that greater consistency with 2023 data is needed before evaluating particle exposure on vascular function and therapeutic interventions. Supported by: NIH R01-ES031285, R25-ES020721, T32-ES007148, and P30-ES005022

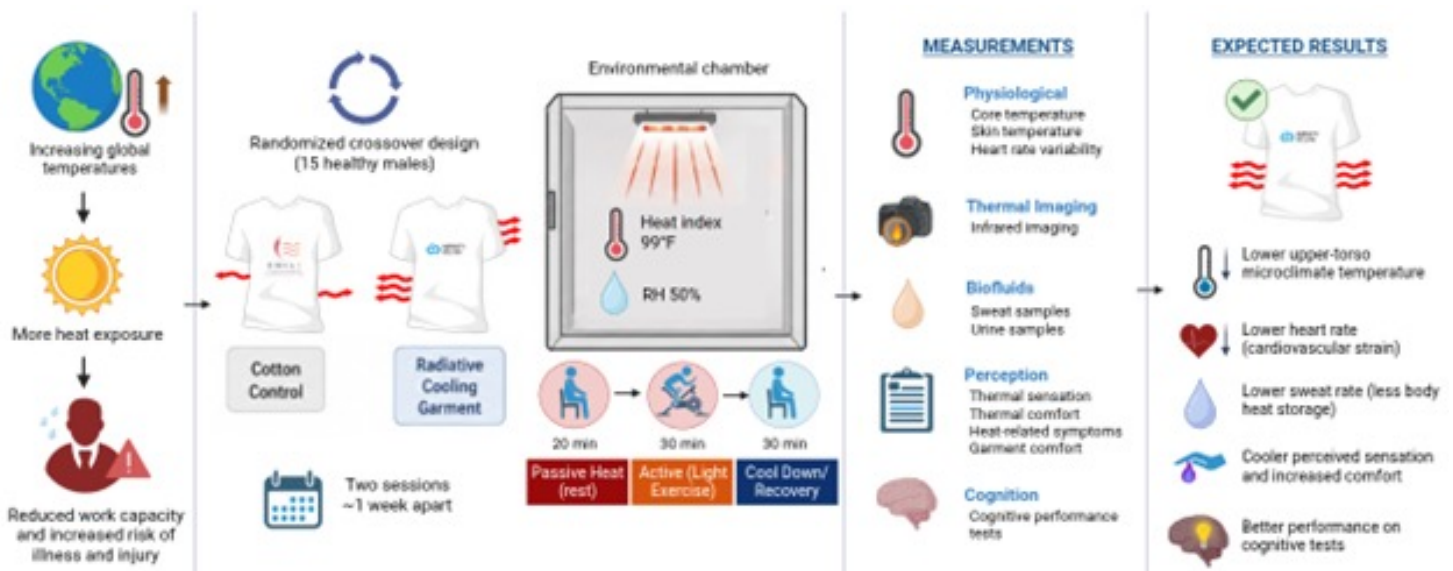


Clothing-Based Heat-Stress Intervention Using Lightweight Infrared-Transparent Apparel

Viktoria Leopold, Niki Tavallali, Huaigu Sun, Jose Guillermo Cedeño Laurent

Rutgers University, Environmental and Occupational Health Sciences Institute – Piscataway, NJ

Global temperatures continue to rise due to climate change, making heat stress a growing health and occupational risk as sustained high temperatures hurt work capacity and increase injuries and illness. While conventional cooling strategies such as air conditioning systems are widespread, they are also highly energy inefficient and inaccessible to vulnerable populations, which emphasizes the need for individualized garment-based cooling solutions. The purpose of this clinical study was to evaluate the efficacy of passive radiative cooling garments to reduce heat stress and perceived thermal discomfort compared with a cotton control during controlled radiant and humid heat exposure. Fifteen healthy male participants were enrolled in a randomized crossover study, with participants randomly assigned to wear either the experimental cooling garment or the cotton control during their first session and then the other garment approximately one week later. During each session, participants underwent a simulated heat stress protocol in an environmental chamber consisting of sedentary rest and exercise phases during which physiological measures were assessed. Sweat and urine samples were collected, infrared thermal imaging was performed, and participants completed questionnaires assessing heat-related symptoms, thermal sensation, and garment comfort. At this time, the study is underway with participants completing their two sessions a week apart. After completion of trials, physiological and survey data will be analyzed to assess whether the experimental garment reduces heat strain in comparison with the matched cotton control, providing insights into more feasible and sustainable methods of combatting extreme heat. This project is supported by NIH R25ES020721.

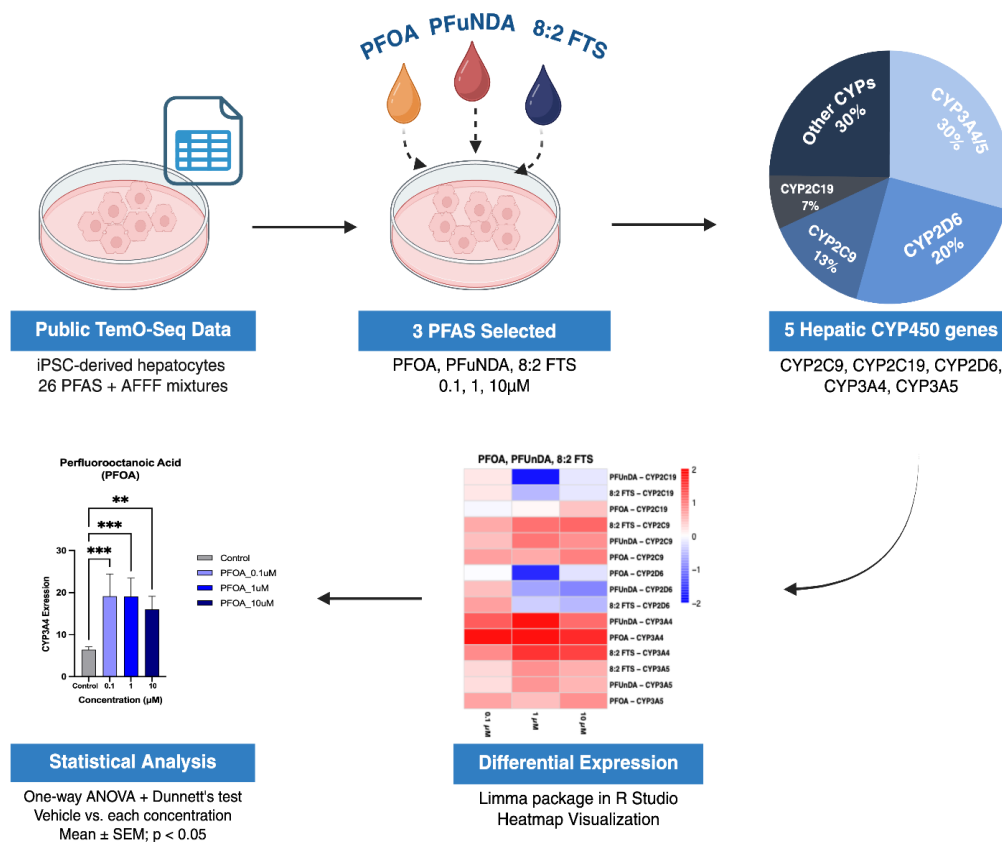


Investigating the Effects of PFAS Treated Cells on Key CYP450 Gene Regulation

Ramla Basharat, Jorge Ponce Zea, Luigi Brunetti

Ernest Mario School of Pharmacy, Rutgers University, Piscataway, NJ

Per- and polyfluoroalkyl substances (PFAS) are environmentally persistent synthetic chemicals with documented hepatotoxicity; however, their effect on the hepatic drug-metabolizing enzymes and transporters remain incompletely characterized. Previous studies suggest that individuals with elevated PFAS plasma concentrations have worse cancer treatment outcomes. Whether altered expression of drug metabolizing enzymes contributes to these outcomes remains unknown. This study investigated whether PFAS exposure alters the expression of key CYP450 drug metabolizing genes and whether these effects are dose dependent. We performed a focused transcriptomic reanalysis of publicly available TempO-Seq data (GEO: GSE244107) from human induced pluripotent stem cell-derived (hiPSC) hepatocytes exposed to 3 PFAS (PFOA, PFuNDA, 8:2 FTS) representing 2 structural classes at 0.1, 1, 10 μ M. Differential expressions of 5 key hepatic CYP450 drug metabolizing genes were assessed using the limma package in R, and expression patterns were visualized using heatmaps. For each CYP450 gene and PFAS, differences among vehicle control and the three exposure concentrations were evaluated in GraphPad Prism using one-way ANOVA and Dunnett's multiple comparison test. Statistical significance was defined as $p < 0.05$. PFAS exposure produced gene and concentration specific changes in CYP450 expression both within and across PFAS structural classes. CYP3A4 and CYP2C9 were significantly induced by all 3 PFAS, while CYP3A5 has shown significant induction under selected exposure conditions. These findings suggest that PFAS exposure may alter hepatic drug metabolism through changes in the expression of CYP450 enzymes. Functional assays are needed to determine whether these transcriptional changes alter CYP450 activity and drug disposition. Supported by NJ ACTS CREST Program funded by NIH R25TR004777.

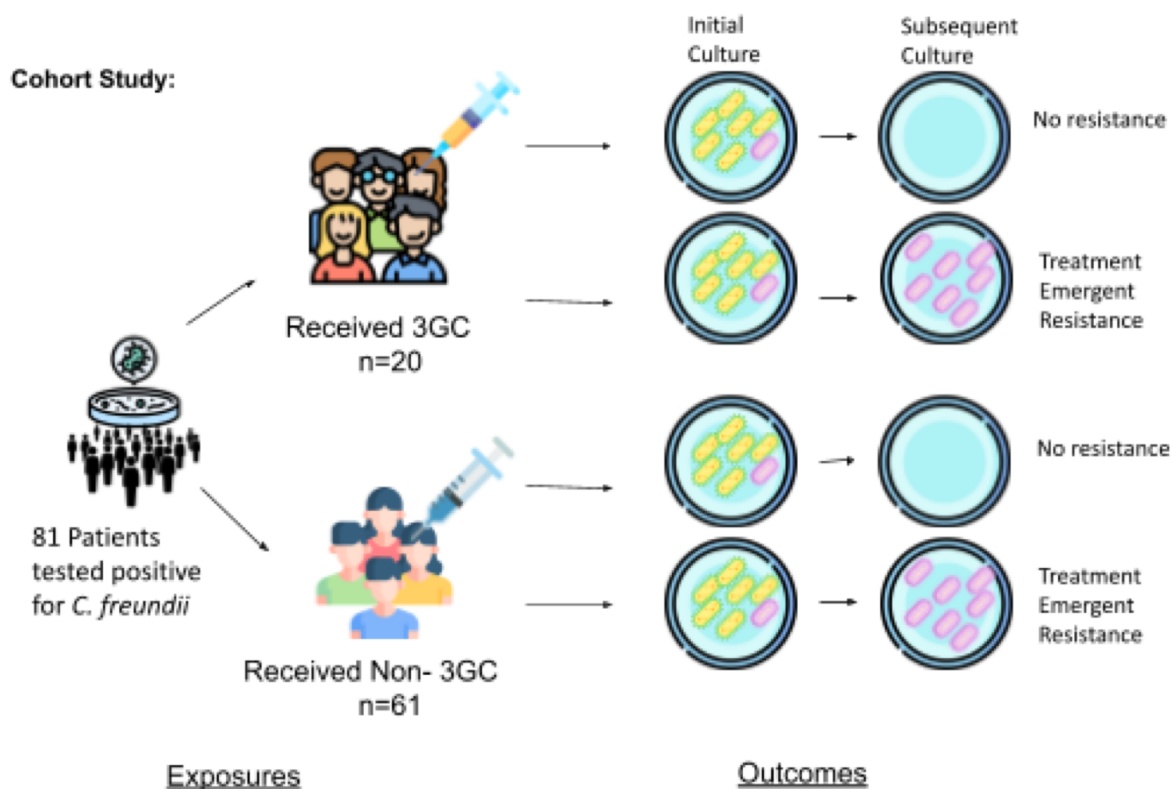


Risk of Treatment Emergent Resistance in *Citrobacter freundii* Infections Managed with Third Generation Cephalosporins

Thanh Du, Sana M. Mohayya, Navaneeth Narayanan

Rutgers, the State University of New Jersey

Treatment of *Citrobacter freundii* infections with third-generation cephalosporins (3GC) poses a challenge due to the presence of an inducible chromosomal AmpC- β lactamase gene that renders 3GCs and other β -lactams ineffective. The Infectious Diseases Society of America guidelines recommend against the use of 3GCs in moderate risk AmpC β -lactamase producing organisms due to the potential of inducible resistance. However, the majority of clinical evidence that advises the guidelines focus on *Enterobacter spp.* with a small number of *C. freundii* clinical cases informing these recommendations. The purpose of this study is to examine the difference between 3GC vs. non-3GC antibiotics on the emergence of resistance in *C. freundii* infections. This is a multicenter, retrospective cohort study that included patients ≥ 18 years old, had a positive clinical culture for *C. freundii* susceptible to 3GCs, and treated with ≥ 1 dose of an antibiotic. Patients were stratified into 3GC and non-3GC groups. The primary outcome was treatment emergent resistance. Data were analyzed using RStudio with descriptive and inferential statistics. Our study enrolled 81 patients with 20 in the 3GC group and 61 in the Non-3GC group. Two patients in the 3GC group had a subsequent culture that developed resistance to 3GC as compared to zero patients in the non-3GC group ($p > 0.05$). In our clinical cohort, we did not detect a statistically significant difference in the rate of treatment emergent resistance in patients who received 3GC vs other antibiotics. Further analyses will be performed to support our findings. Supported by NJ ACTS CREST Program funded by NIH R25TR004777.

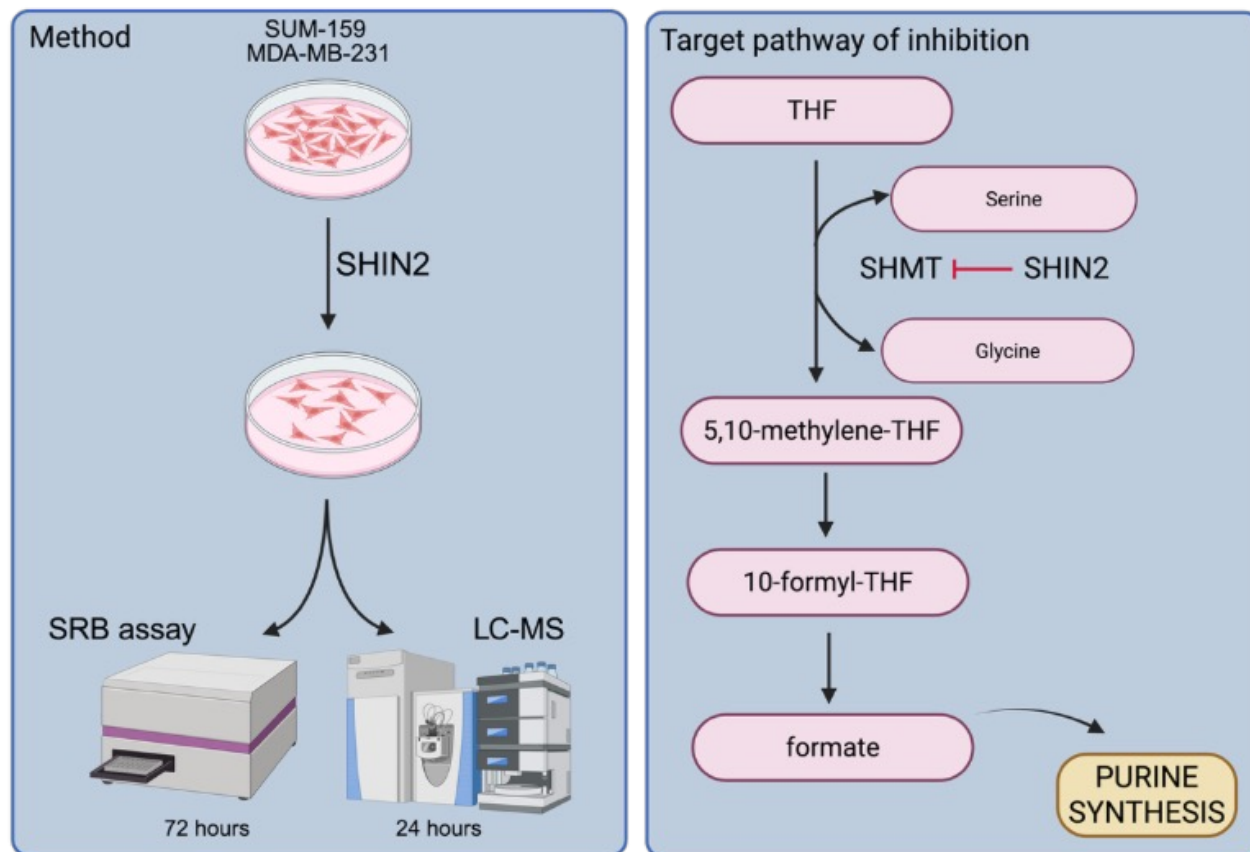


Targeting One-Carbon Metabolism in Triple Negative Breast Cancer Cells

Victoria Berger, Emily Hyde, Matthew J. McBride

Rutgers, The State University of New Jersey

Triple-negative breast cancer (TNBC) is the most aggressive breast cancer subtype and is characterized by its lack of estrogen, progesterone, and human epidermal growth factor (HER2) receptors, making hormonal and HER2-targeted therapies ineffective. One-carbon metabolism supports tumor proliferation by supplying carbon units for nucleotide synthesis. Tumors often rely heavily on specific one-carbon metabolism enzymes, such as serine hydroxymethyltransferase (SHMT) which correlate with increased tumor aggressiveness, higher metastatic potential, and poor overall patient survival. Based on this, we hypothesized that SHIN2, a small-molecule SHMT inhibitor, would reduce one-carbon unit production, leading to impaired nucleotide synthesis and reduced cell proliferation. SUM159 and MDA-MB-231 TNBC cell lines were treated with SHIN2 in the presence or absence of formate supplementation. Cell viability was quantified using sulforhodamine B (SRB) assays to evaluate SHMT dependence and the ability of formate to rescue SHIN2-induced growth inhibition. Liquid chromatography-mass spectroscopy (LC-MS) was additionally used to quantify metabolic changes with SHIN2 treatment and formate supplementation. Preliminary data shows that treating TNBC cell lines with SHIN2 causes a significant decrease in cell viability and formate supplementation rescues these effects, indicating an on-target drug response. LC-MS analysis further revealed significant glutathione depletion with SHIN2 treatment, suggesting future exploration of ferroptosis as promising therapeutic vulnerabilities in TNBC. Supported by NIH R25ES020721, NIH R35GM154956, and the New Jersey Health Foundation.

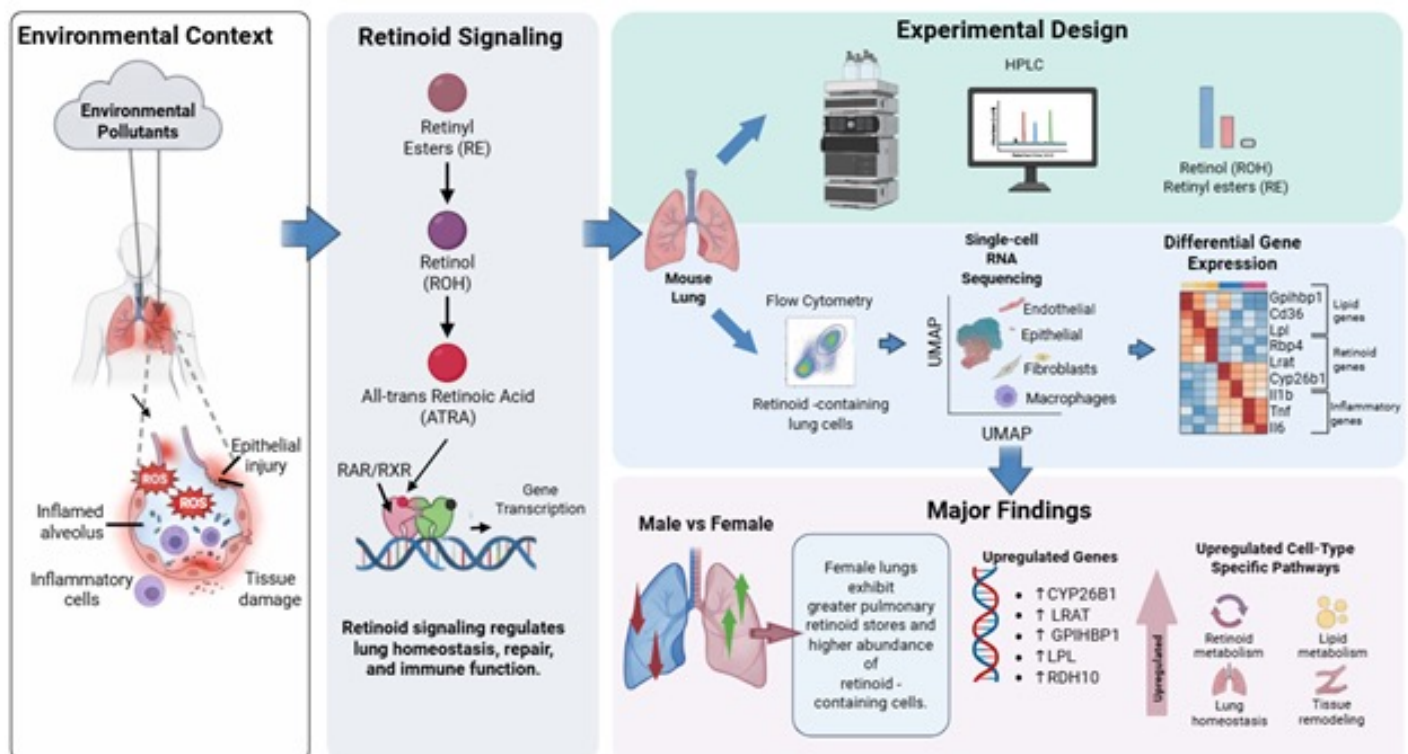


Lung Retinoid Metabolism in Sexually Dimorphic Susceptibility to Environmental Exposure

Neev Siram^{1,2}, Igor Shmarakov²

¹Undergraduate Program in Biological Sciences, ²Department of Animal Sciences at Rutgers, The State University of New Jersey

Biological sex influences susceptibility and responses to environmental pollutant-induced lung injury, however the molecular mechanisms underlying these sex-specific responses remain incompletely understood. Retinoids (vitamin A and its metabolites) are essential regulators of lung development, homeostasis, and repair following injury. We hypothesized that sex-specific differences in retinoid metabolism contribute to divergent responses to environmental pollutant exposure. High-performance liquid chromatography (HPLC) was used to assess lung retinoid metabolites, while flow cytometry was employed to sort retinoid-containing lung cell populations and characterize using single-cell RNA sequencing (scRNA-seq). scRNA-seq datasets from healthy male and female murine lungs were analyzed to identify cell type-specific transcriptional differences. Furthermore, publicly accessible scRNA-seq datasets of human lungs were analyzed to assess the translational relevance of our findings. Differential gene expression and pathway enrichment analyses were conducted on lipid and retinoid metabolic pathways. Integrated single-cell transcriptomic analyses identified robust sex-specific transcriptional programs across lung endothelial cells, epithelial cells, fibroblasts, and macrophages. When compared with males, female mouse and human lungs demonstrated pathway enrichment of the “Retinol metabolism”, “Response to retinoic acid”, and associated lipid metabolic pathways, including “PPAR signaling”, “Fatty acid metabolism”, and “Lipid transport”. These pathway-level differences were driven by increased expression of key retinoid metabolic genes, including *CYP26B1*, *LRAT*, *RDH10*, *ALDH1A2*, *ALDH1A3*, and *CRABP2*, alongside increased expression of lipid metabolism-associated genes, including *GPIHBP1*, *LPL*, and *CD36*. These findings provide a framework for understanding sex-specific differences in lung retinoid metabolism and establish a foundation for future investigations on how retinoid metabolism and associated lipid metabolic pathways contribute to sexually dimorphic susceptibility and responses to environmental pollutant exposure. Supported by NIH R25ES020721.

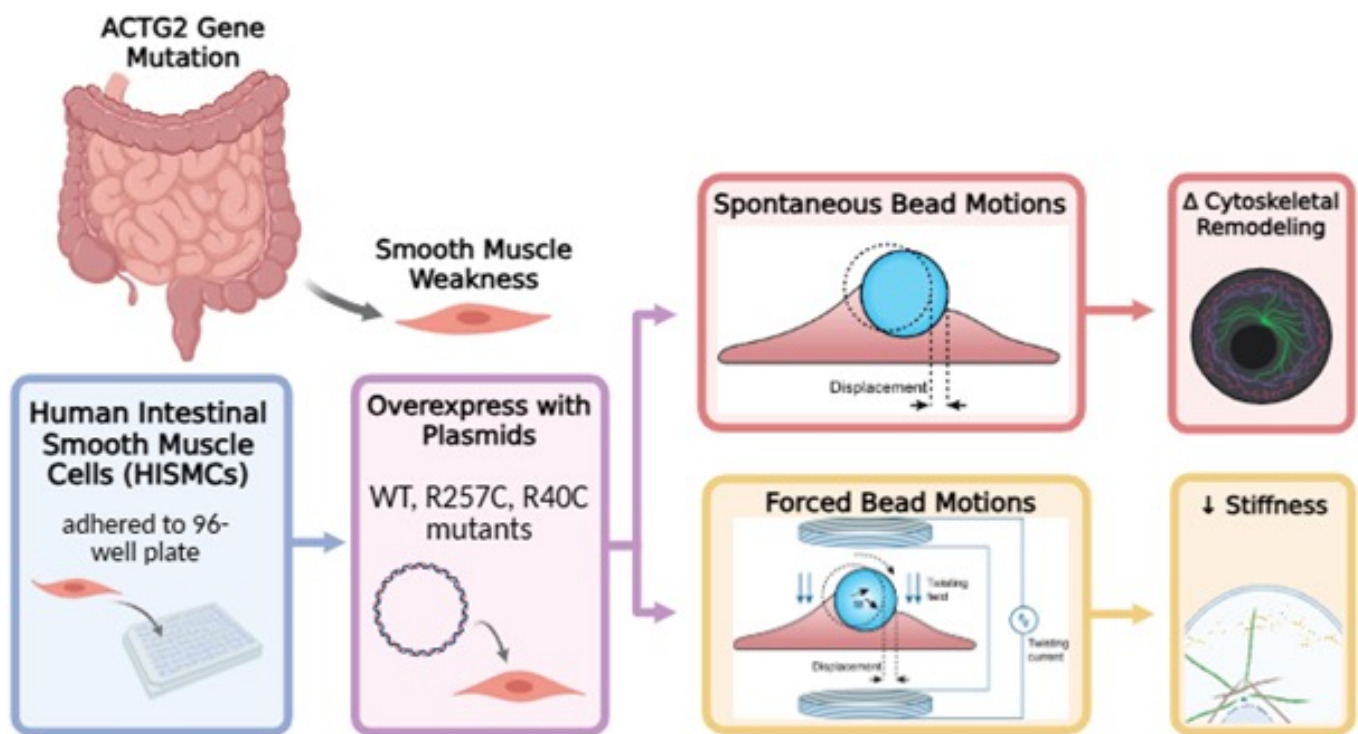


Visceral Myopathy-Associated ACTG2 Mutants Decrease Stiffness in Intestinal Smooth Muscle Cells

Maxwell Bouffard¹, Jordan Lee¹, Shanzeh Rauf¹, Robert O. Heuckeroth³, Steven An^{1,2}

¹Rutgers Institute for Translational Medicine and Science, New Brunswick, NJ; ²Department of Pharmacology, Rutgers-Robert Wood Johnson Medical School, Piscataway, NJ; ³Department of Pediatrics, Children's Hospital of Philadelphia Research Institute, and Perelman School of Medicine at the University of Pennsylvania, Abramson Research Center, Philadelphia, PA

Visceral myopathy is a life-threatening myopathic disorder primarily caused by heterozygous mutations in smooth muscle γ -actin (ACTG2). Individuals with ACTG2 mutations suffer from weakness of bowel, bladder, and uterine smooth muscle, which often culminates in childhood death. Currently, we do not know how disease-causing mutations impair visceral smooth muscle function. This study sought to investigate the effects of two prevailing ACTG2 mutations (R257C and R40C) on the mechanical properties of primary human intestinal smooth muscle cells. Adherent cells were overexpressed with wild-type (WT), R257C, and R40C plasmids for 48 hours, after which RGD-coated ferrimagnetic beads were functionalized to the cytoskeleton (CSK) through cell surface integrin receptors. We first visualized *spontaneous* bead motions and found no substantial differences in the rate of cytoskeletal remodeling (as computed by mean square displacements of beads over time) between ACTG2 mutants and WT overexpressing cells. Interestingly, after imposing large oscillatory mechanical force to the cells, R257C cells exhibited a markedly increased rate of CSK remodeling while R40C cells showed decreased CSK remodeling dynamics. Compared to WT cells, R257C and R40C cells produced notably reduced cellular stiffness as measured by *forced* bead motions with optical magnetic twisting cytometry. These findings characterize previously undefined genotype-specific mechanical properties of disease-causing ACTG2 mutants. Future studies include utilization of traction force microscopy and live-cell microscopy to evaluate the effects of ACTG2 mutants on the contractile stress and migratory behavior of intestinal smooth muscle cells. Supported as a Grover Scholar by Dr. and Mrs. Gary Grover, NIH R01HL164404, and NIH P01HL180318.

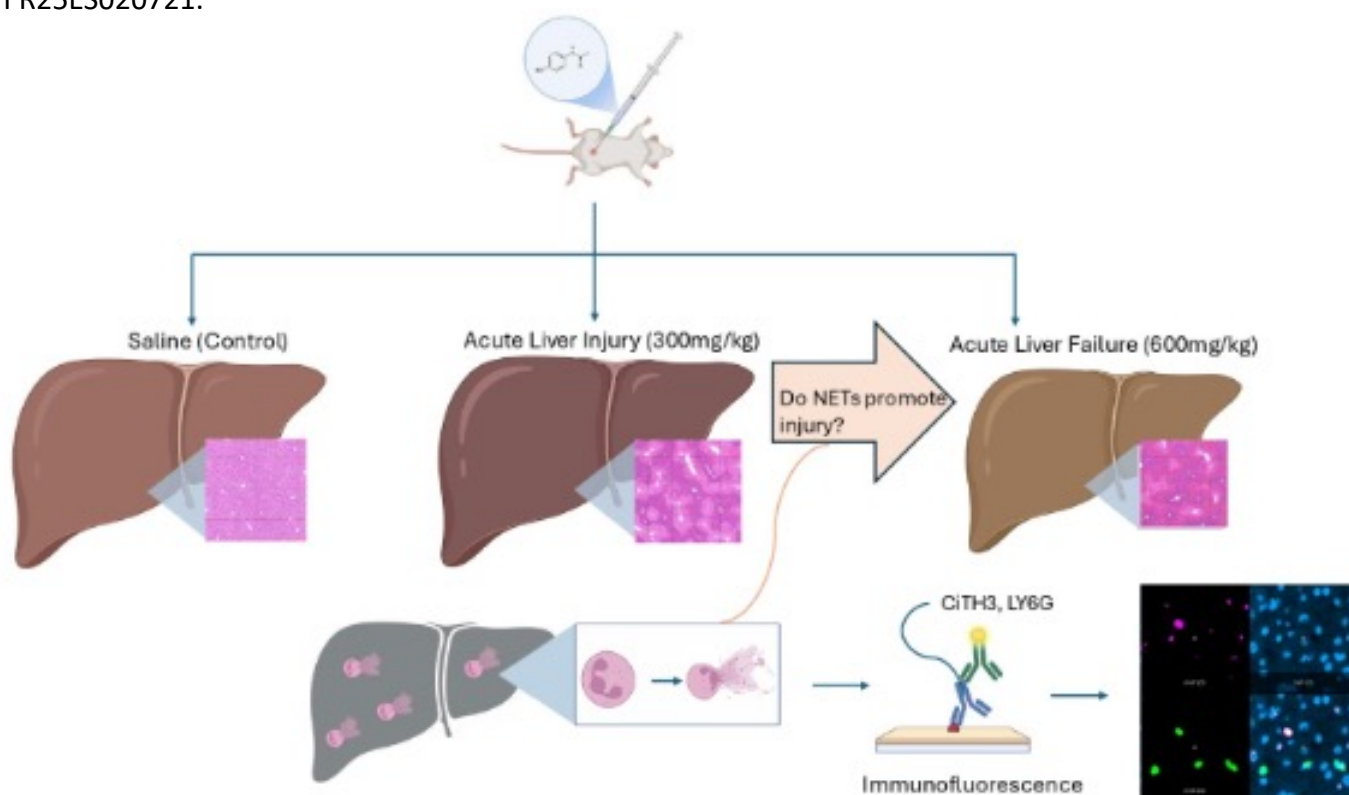


Neutrophil Extracellular Trap (NET) Formation in Experimental Acetaminophen-Induced Acute Liver Injury/Failure

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¹Rutgers, Department of Pharmacology and Toxicology; ²Kean University

Background: Overdose on acetaminophen (APAP), one of the most common over-the-counter pain relievers, can cause acute liver injury (ALI), which may progress to fatal, acute liver failure (ALF). Therapies for ALI/ALF are limited; experimental evidence suggests neutrophils drive APAP-induced ALF. During injury or inflammation, neutrophils have been shown to release neutrophil extracellular traps (NETs), consisting of networks of extracellular DNA, citrullinated histones, and neutrophil proteins. NET markers have been detected in patients after APAP overdose, suggesting NETs may play a role in APAP-induced ALI/ALF. However, the role of NETs during APAP-induced ALI and ALF is still unknown. **Purpose:** The purpose of this study was to quantify the injury and neutrophil extracellular trap formation in APAP-induced ALI and ALF. **Hypothesis:** Intrahepatic NET formation occurs in experimental APAP-induced ALF. **Methods:** Formalin-fixed, paraffin-embedded (FFPE) liver tissues from mice challenged with saline or APAP (300mg/kg, 600mg/kg) for 6-12 h were sectioned and stained with hematoxylin and eosin (H&E) or immunolabeled for NETs. Quantitation of hepatocyte necrosis was performed on H&E-stained tissues using QuPath software. Immunolabeled liver sections for NET components Ly6G (neutrophil surface marker), citrullinated histone H3, and DAPI (DNA) were scanned on a fluorescence microscope and quantified using thresholding methods in QuPath software. **Results:** As anticipated, hepatocyte necrosis was significantly increased following APAP challenge compared to vehicle controls at 6 h and 12 h. NETs were significantly increased at both doses of APAP compared to vehicle. **Conclusion:** NETs were detected in experimental APAP overdose warranting further study of their contribution to liver injury. Supported by NIH R25ES020721.

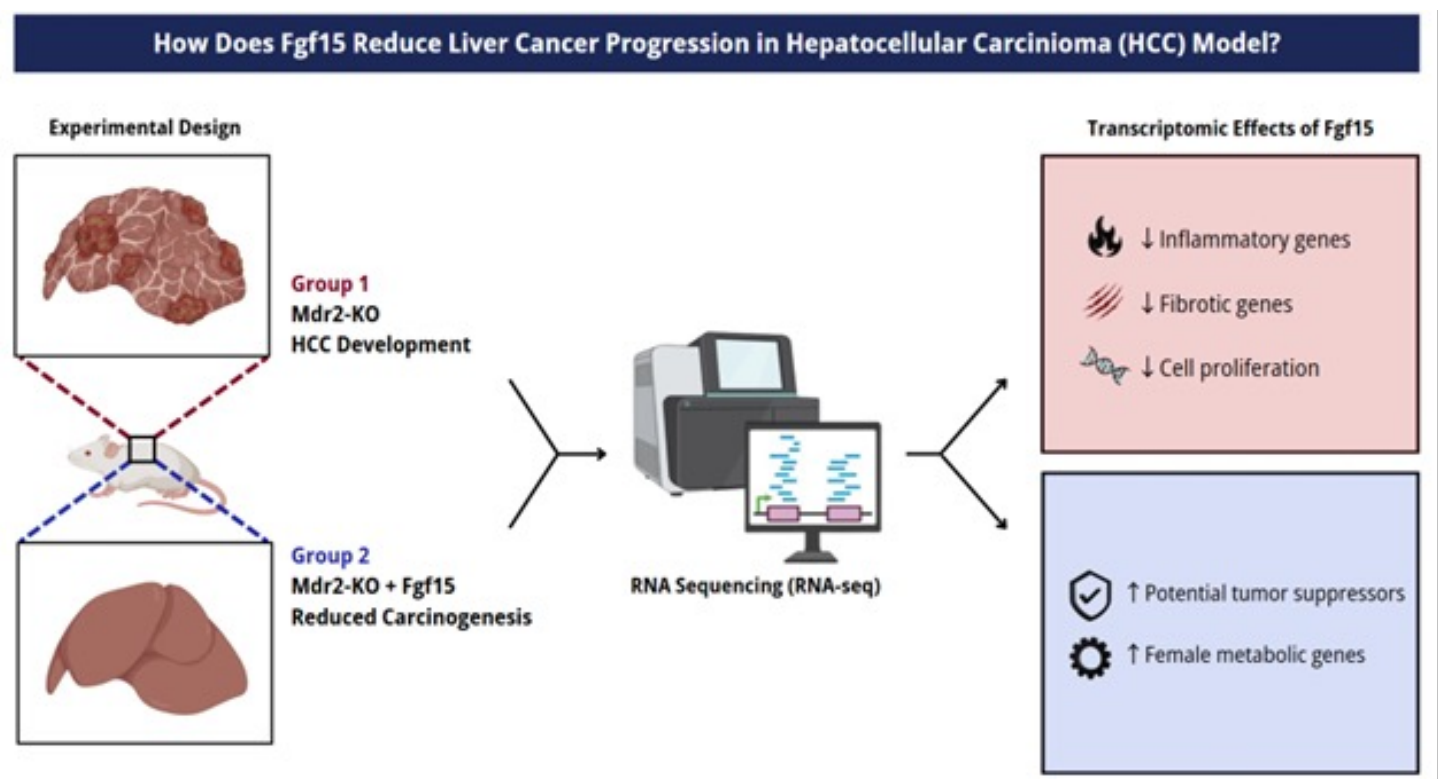


Investigating the Protective Mechanisms of Fgf15 Against Hepatocellular Carcinoma (HCC) in Mdr2-KO Mouse Model: A Review of RNA-seq Analysis

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Hepatocellular carcinoma (HCC) is the most common form of primary liver cancer, and can develop in the setting of chronic liver inflammation and cirrhosis. Dysregulation of bile acids (BAs), as seen in conditions like cholestasis, is a contributor to inflammation-driven HCC. An important regulator of BA homeostasis in mice is the *Fgf15* gene that encodes Fibroblast growth factor 15 (FGF15). *Fgf15* regulates BA synthesis through negative feedback within the enterohepatic circulation system. FGF15 suppresses the synthesis of BAs, which could reduce cholestasis and therefore the severity of inflammation that drives HCC development. Using gene expression profiling, we sought to uncover key molecular mechanisms by which *Fgf15* overexpression protects against carcinogenesis in Mdr2-knockout (KO) mice, a model of cholestasis/inflammation-driven HCC. Livers were collected from male and female mice at 12-13 months of age, with and without the *Fgf15* transgene (four groups; n=3 per group). RNA sequencing (RNA-seq) was performed in each group to identify differentially expressed genes and examine enriched pathways. In male mice, *Fgf15* overexpression was associated with decreased expression of cell proliferation, inflammatory, and fibrotic genes, while potential tumor suppressor genes and metabolic regulators were upregulated. Interestingly, overexpression of *Fgf15* increased the expression of the female biased metabolic enzymes *Cyp2b9* and *Cyp2b13*, consistent with a previous study showing altered growth hormone signaling by *Fgf15* overexpression in male mice. These findings open new avenues of study for understanding *Fgf15* as a therapeutic target for cholestasis and liver injury and for identifying biomarkers. Supported by NIH R25ES020721.

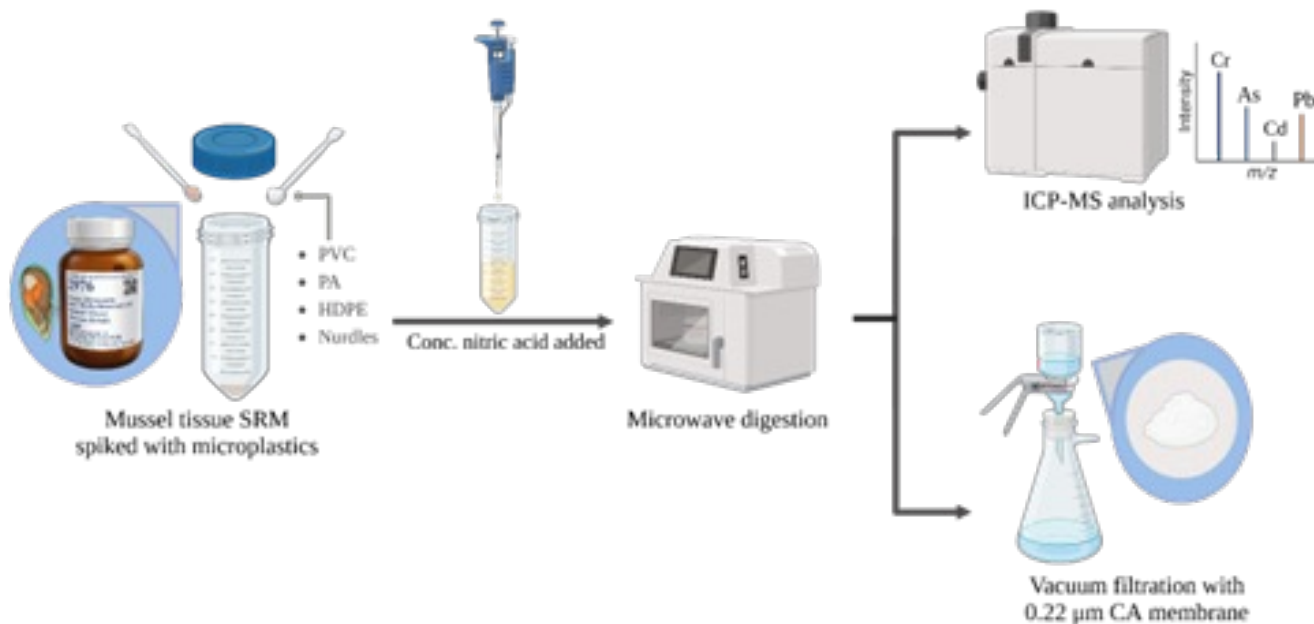


Developing a Method of Microplastic Extraction from Acid Digested Environmental Samples

Joan Dischert, Dr. Cathleen Doherty, Dr. Rachel Buckley, Dr. Brian Buckley

Rutgers University, Environmental and Occupational Health Sciences Institute, Piscataway, NJ

Rampant use and manufacturing of plastic-based products in the last century has left pervasive microplastic (<5 mm) and nanoplastic (<1 μm) contaminants in its wake. Microplastics behave as adsorbent transporters of other environmental pollutants, such as heavy metals. In order to generate accurate and comparable quantitative data, a more standardized method of digestion and separation of plastics from environmental samples must be established. The purpose of this study was to establish a microwave-assisted method of tissue digestion that sufficiently oxidizes organic material while preserving microplastic contaminants for subsequent analysis for heavy metals with inductively-coupled plasma mass spectrometry. Freeze-dried mussel tissue samples (NIST SRM 2976) were spiked with powdered polyamide (PA), polyvinyl chloride (PVC), high-density polyethylene (HDPE), and nurdles. They were then reacted with concentrated nitric acid and heated in a Mars 5 microwave system. Samples were then filtered under vacuum and microplastic recovery was measured by the change in filter mass. An aliquot was analyzed with ICP-MS to measure concentrations of Pb, Cd, Cr, and As. Mussel tissue being digested in the presence of microplastics did not significantly alter the recovery of heavy metals (>90%). Digestion conditions appeared to partially melt the PA and HDPE microplastic powders during digestion. More acid resistant plastics, like PVC, withstood digestion and displayed no obvious visual changes upon recovery. These findings act as a step towards developing a microwave-assisted digestion method that strikes a balance between plastic preservation and metal leaching for ICP-MS analysis. Supported by NIH R25ES020721.

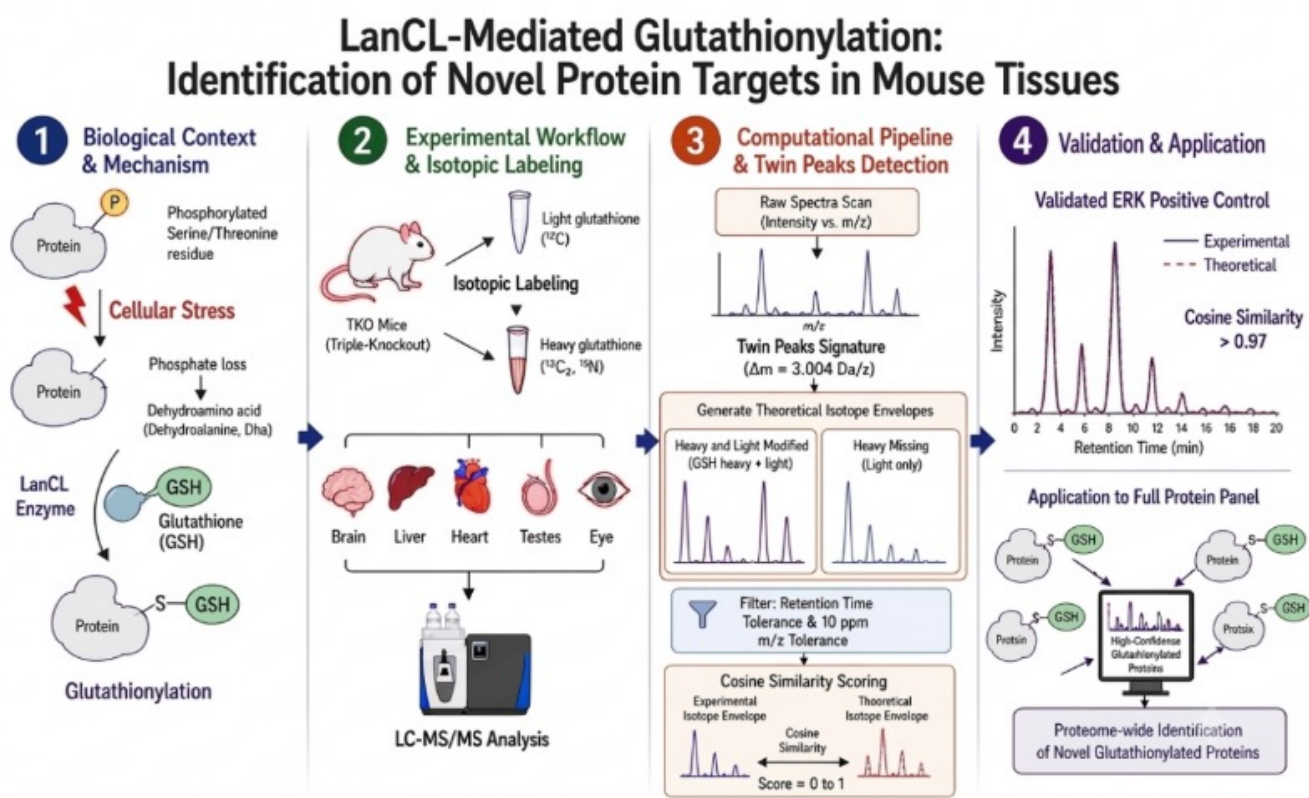


Identification of LanCL-Mediated Glutathionylation Targets in Mouse Tissues

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Department of Medicinal Chemistry, Rutgers University

Glutathione (GSH), the cell's most abundant antioxidant, is known for neutralizing reactive species but can also be enzymatically attached to proteins as a post-translational modification. Under cellular stress, phosphorylated serine and threonine residues can lose their phosphate groups, forming the highly electrophilic dehydroamino acids dehydroalanine (Dha) and dehydrobutyrine (Dhb), which may dysregulate kinase signaling. LanC-like (LanCL) enzymes irreversibly add GSH to these damaged residues through glutathionylation, potentially preventing further signaling disruption. However, the full range of proteins LanCL modifies in living tissue remains unknown. This project aims to identify LanCL-mediated glutathionylation targets across male and female mouse brain, liver, heart, testes, and eye tissues. Triple-knockout tissues were isotopically labeled with light and heavy (+ ≈ 3.00374 Da) forms of GSH and analyzed by liquid chromatography/mass spectrometry. Authentic heavy and light modifications appear as characteristic "twin peaks" separated by ≈ 3.00374 Da per charge, distinguishing them from absent heavy modifications. To detect these events, we developed a computational pipeline that scans raw spectra for peptides carrying both the GSH modification and its isotopic partner. Candidate peptides are grouped by sequence and charge, theoretical light and heavy isotope envelopes are procedurally generated from composition, and experimental spectra are filtered by retention time and a 10-ppm m/z tolerance. Cosine similarity scoring against modified and unmodified theoretical spectra ranks candidates and exports the highest-confidence scans. Validated using a glutathionylated ERK positive control, the framework achieved a cosine similarity greater than 0.97 with its reference spectrum and is now being applied across the full tissue panel. Supported as a Grover Scholar by Dr. and Mrs. Gary Grover.



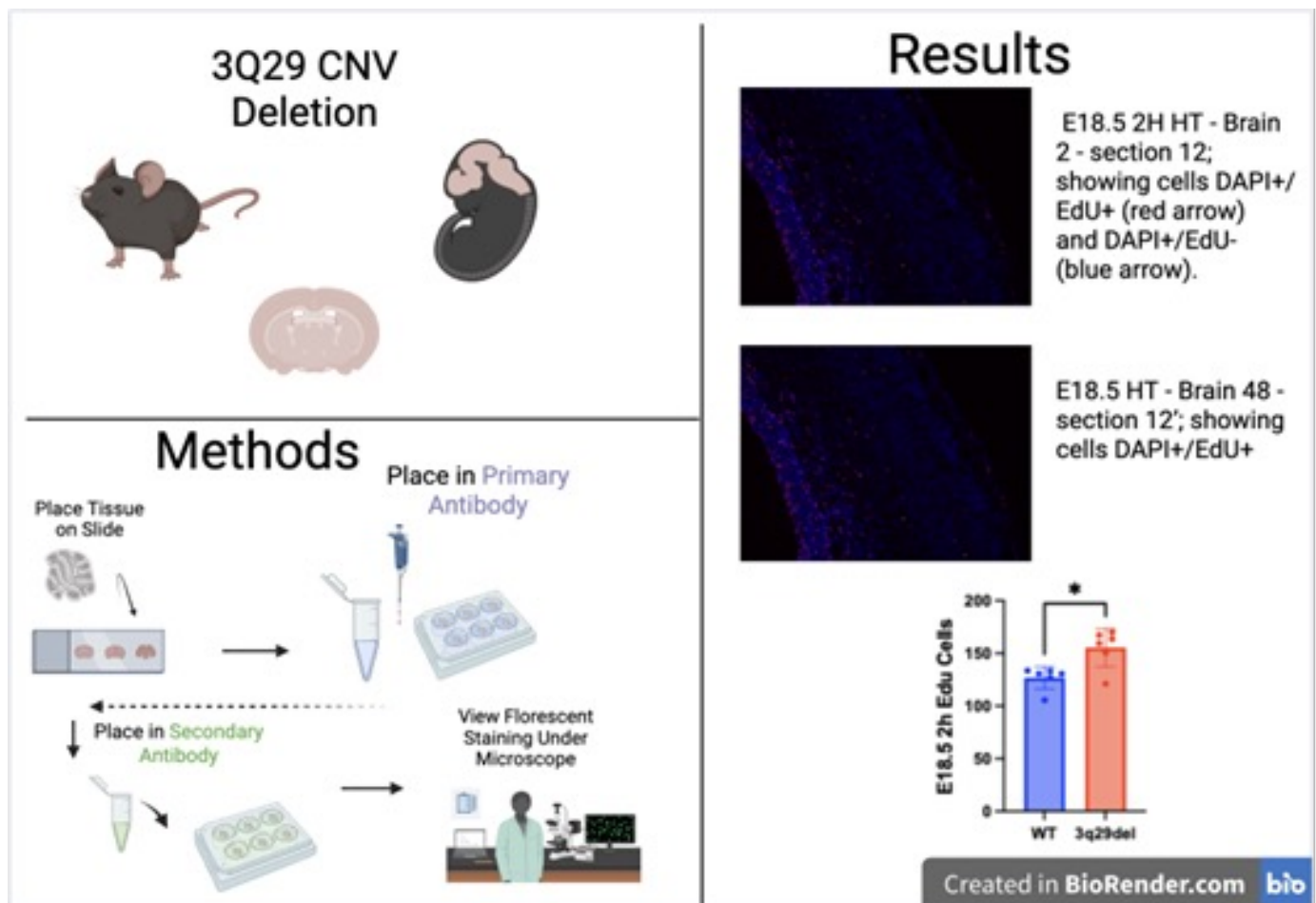
Supported as a Grover Scholar by Dr. and Mrs. Gary Grover.

Disordered Proliferation in Embryonic Mouse Cortex in 3q29 CNV Deletion Model of Neurodevelopmental Disorders

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¹Department of Neuroscience and Cell Biology, Rutgers Robert Wood Johnson Medical School

Neurodevelopmental disorders (NDD) include conditions in which the brain grows and develops abnormally, impacting an individual's behavior, emotions, and/or learning. These disorders may emerge in many different stages of development, ranging from embryonic development to adolescence, and can occur as a result of abnormalities in varying regions of the brain. Deletion of the 3q29 copy number variant gene induces intellectual disability and increases risk for autism spectrum disorder and schizophrenia, and in the mouse model it shows abnormalities beginning in the embryonic period. Neurogenesis was assessed in timed-pregnant mice at embryonic Days (E) E13.5–E17.5 via incorporation into DNA of injected EDU and tissue immunohistochemistry for Pax6, Ki67, and PH3 to assess precursors, proliferation and, mitosis. At E14.5 and E15.5, EdU+ cells were elevated in 3q29del embryos (E14.5: 18% increase $p=0.005$; $N=5$ /genotype; WT from 3 litters, 3q29del from 4 litters; E15.5: 37% increase; $p<0.003$; $N=5-7$ /genotype from 3 litters). There was no significance at E16.5 and an apparent decrease at E17.5. The purpose of this study was to assess whether there were proliferation differences at E18.5. At E18.5, embryos were injected with EdU, a marker to quantify S-phase cell entry, followed by sacrifice 2 hours later. We observed a 22% increase in EdU+ cells in the subventricular zone in 3q29 embryos compared to wildtype embryos. These observations suggest that the program of neurogenesis is disrupted in 3q29 CNV embryonic cortex, potentially identifying mechanisms contributing to brain structural and behavioral phenotypes. Supported as a Scala Scholar by Dr. Robert A. Scala.

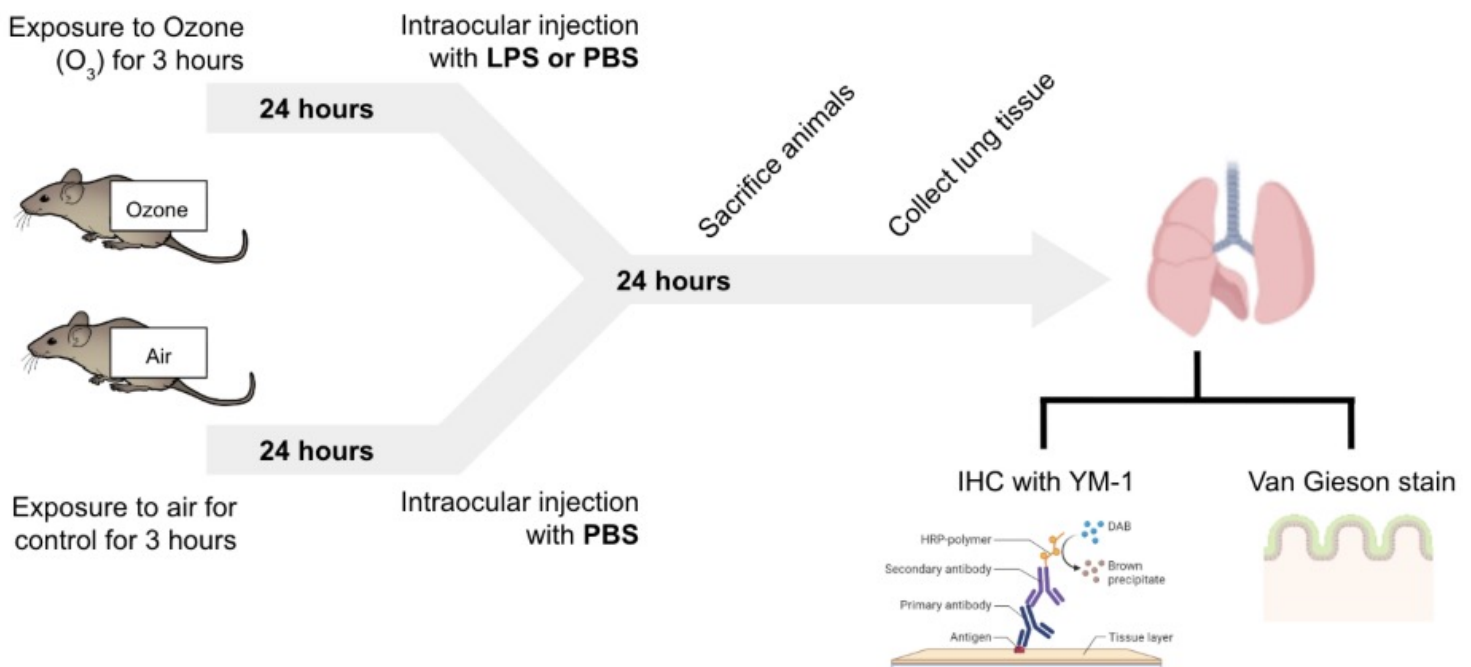


Ozone and LPS Effects on Lung Airway Elastin Fibers and Macrophages

K. Simeon Wong, Sethu Arunachalam, Kyeongseo Kim, Peihong Zhou,
Jared Radbel, Laurie B. Joseph

Rutgers University, Ernest Mario School of Pharmacy, Piscataway, NJ

Exposure to ozone (O_3) is a risk factor for the development of acute respiratory distress syndrome (ARDS), a severe form of acute lung injury (ALI) with sepsis. ARDS causes inflammation in the lung, and pro-inflammatory macrophages produce elastase that breaks down elastin fibers, compromising lung structure and function. In this study, we investigated the effects of O_3 and lipopolysaccharides (LPS) on lung structure. LPS models ALI, triggering inflammation by mimicking sepsis. We hypothesize that exposure to O_3 and LPS induces changes in elastin fibers in the lung. C57BL/6 male 13-week-old mice were exposed to O_3 (800ppb, 3hrs) or air. Twenty-four hours post-exposure, animals were intraocularly injected with LPS (3mg/kg) or PBS (control) and sacrificed 48 hours post- O_3 or air exposure. Lungs were excised, fixed, embedded and 6-micron sections cut for histology and immunohistochemistry. Elastin fibers were evaluated using Verhoeff-Van Gieson stain. Proinflammatory M1 macrophages were identified in the large airway epithelium and alveoli using YM-1 (Chitinase-like protein 3). Both O_3 /PBS and O_3 /LPS induced degradation of elastin fibers in the large airways, whereas elastin fibers were contiguous in the control animals. YM-1 was expressed in both large airway and alveolar macrophages; O_3 /LPS > O_3 /PBS > Air/PBS. These data suggest that O_3 /LPS plays a role in the degradation of elastin fibers, possibly through the release of elastase from M1 macrophages. Future studies will investigate the effects of O_3 /LPS on M1 macrophage elastase production and the role of elastin fiber integrity on lung function in mice. Supported by NIH R25ES02072.



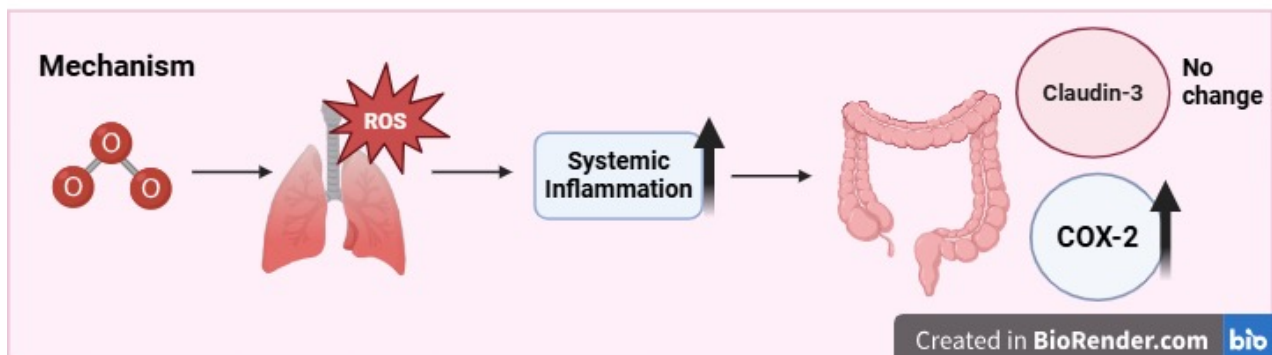
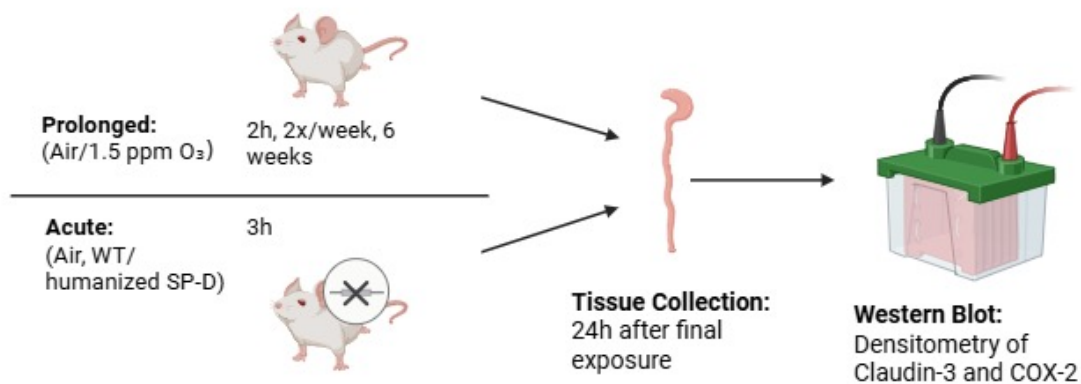
The Effects of Ozone and SP-D on Epithelial Barrier Integrity and Inflammation in the Colon

Natalia Kalinowska, Candace R. Longoria, Benjamin Gelfand-Titiyevskiy,
Jared Radbel, Debra L. Laskin

Rutgers, the State University of New Jersey, Piscataway, NJ

Ozone is a reactive air pollutant that induces lung injury and systemic inflammation, resulting in intestinal oxidative stress and epithelial barrier disruption. Surfactant protein D (SP-D), a protein associated with macrophage efferocytosis, may contribute to intestinal inflammation. Thus, the purpose of this study was to examine the effects of prolonged ozone exposure on the colonic epithelium and the onset of inflammation, and to explore the role of SP-D in the colon. Adult C57/BL6 mice were exposed to filtered air or ozone for 2h, 2x/wk for 6wk; humanized wild-type (WT), SP-D homozygous, and SP-D heterozygous mice generated using CRISPR-cas9 were acutely exposed to filtered air for 3h. Colon samples were collected 24h after final exposures for western blotting. Tissues were homogenized and protein measured using a BCA assay. For western blotting, loaded protein volumes were normalized and membranes probed for expression of COX-2, an inflammatory marker, and claudin-3, a tight junction protein. Densitometry was performed using ImageJ Fiji and protein expression normalized to GAPDH with $p < 0.05$ considered statistically significant. No significant differences in claudin-3 expression were detected in acute or prolonged exposure groups. Expression of COX-2 was significantly increased in female mice following ozone exposure compared to air-exposed controls, and in SP-D homozygous mice compared to WT mice. In conclusion, increased COX-2 expression was observed in female, but not male mice following prolonged ozone exposure. Mutation of the SP-D gene in mice increases basal COX-2 levels. Future studies will determine whether ozone exposure in SP-D humanized mice exacerbates colonic inflammation. Supported by NJ ACTS CREST Program funded by NIH R25TR004777.

Methods



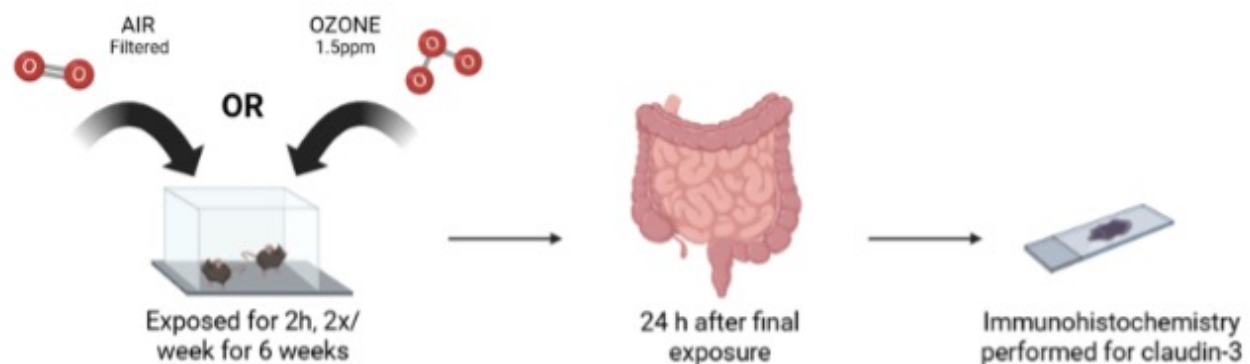
The Effects of Prolonged Ozone Exposure on Intestinal Tight Junction Protein Expression

Bridget Broncales¹, Candace R. Longoria², Debra L. Laskin²

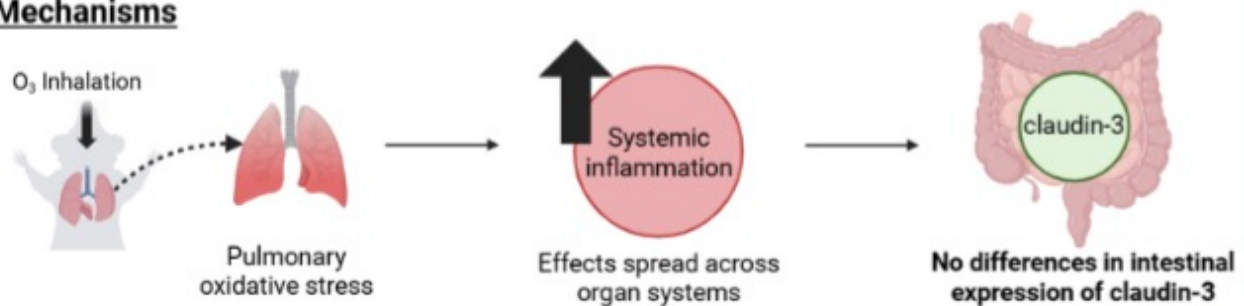
¹School of Environmental and Biological Sciences, Rutgers University, ²Department of Pharmacology and Toxicology, Ernest Mario School of Pharmacy, Rutgers University

Ozone is an urban air pollutant known to induce pulmonary injury, oxidative stress, and systemic inflammation. Increases in circulating inflammatory molecules following ozone inhalation have been linked to intestinal epithelial barrier disruption and gastrointestinal distress. Tight junction proteins, specifically claudins, are located between intestinal endothelial and epithelial cells and are important mediators of intestinal permeability and health. Disruption of these tight junction proteins is associated with gastrointestinal diseases. However, little is known regarding the effects of prolonged ozone exposure on intestinal tight junction protein expression and thus represent the focus of these studies. Wild type C57BL/6J male and female mice were exposed to filtered air or ozone for 2 h, 2x/wk, for 6 wks in whole body exposure chambers; intestinal samples were collected 24 h after the final exposure. Ileum and colon tissues were fixed in a 3% paraformaldehyde 2% sucrose solution, paraffin-embedded, and sectioned for claudin-3 using immunohistochemistry. Stained slides were scanned on a VS-120 microscope, and images were evaluated using Olympus software. Following prolonged ozone exposure, no visible differences in claudin-3 expression were identified in the ileum or colon of male or female mice to air-exposed animals. Future studies will assess other tight junction proteins, such as zonulins and occludins, to better understand the impact of ozone on the intestinal epithelial barrier. Funding was supported by NIH R25ES020721

Methods



Mechanisms



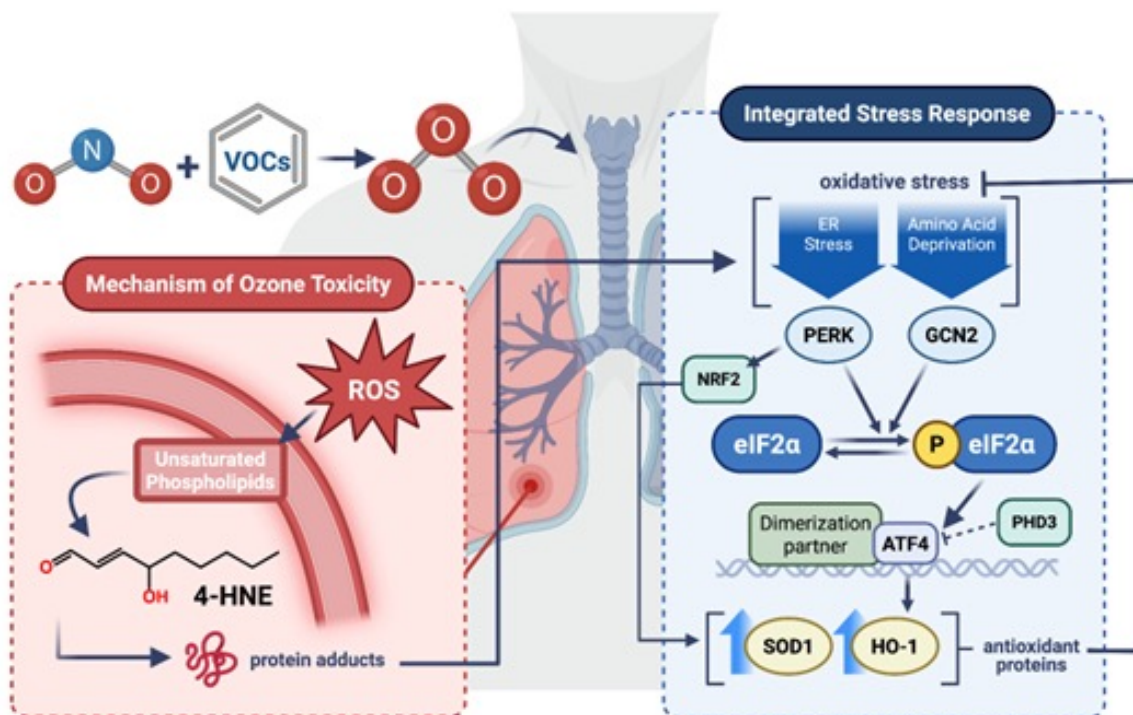
In Vitro Investigation of Integrated Stress Response Activation by 4-Hydroxynonenal

Chung, Jaein¹; Rodriguez, Jessica R.²; Laskin, Debra L.²

¹Dartmouth College, Hanover, NH

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Ground-level ozone is a harmful air pollutant associated with 300,000 deaths annually. Inhaled ozone reacts with airway epithelial membranes and pulmonary surfactant to generate lipid peroxidation products, including aldehyde 4-hydroxynonenal (4-HNE), which forms adducts with proteins and disrupts function. Although ozone-induced oxidative injury has been explored, the cellular pathways promoting recovery from this damage remain less understood. One promising mechanism is the integrated stress response (ISR). In response to cellular stress, various kinases phosphorylate eukaryotic translation initiation factor 2 alpha (eIF2 α) to reduce global protein translation and selectively upregulate protective genes. Because the oxidative effects of 4-HNE can trigger ISR kinases, the ISR may be a protective mechanism following ozone exposure. To investigate this potential role, murine macrophages (RAW 264.7) and alveolar epithelial type 2 (MLE-15) cells were treated with 25 μ M 4-HNE for 3 hours. Protein was then isolated and examined through western blotting. Both RAW and MLE cells exhibited increased phosphorylation of eIF2 α and increased expression of nuclear factor erythroid 2-related factor 2 (NRF2), an antioxidant transcription factor activated by ISR kinases. Additionally, 4-HNE increased prolyl-4-hydroxylase domain 3 (PHD3), a negative regulator of activating transcription factor 4 (ATF4) -mediated ISR signaling. The increase in PHD3 expression suggests that there may be ISR-mediated transcription independent of ATF4. Among antioxidant proteins, heme oxygenase-1 (HO-1) expression increased, whereas superoxide dismutase (SOD1) expression remained unchanged. These data demonstrate that 4-HNE activates the ISR to promote an antioxidant response, supporting a potential protective role of the ISR following ozone-induced oxidative stress. Supported by NIH grants ES004738, ES005022, R25ES020721, the Society of Toxicology, and the Air Pollution Educational and Research Grant (APERG) Scholarship Program.

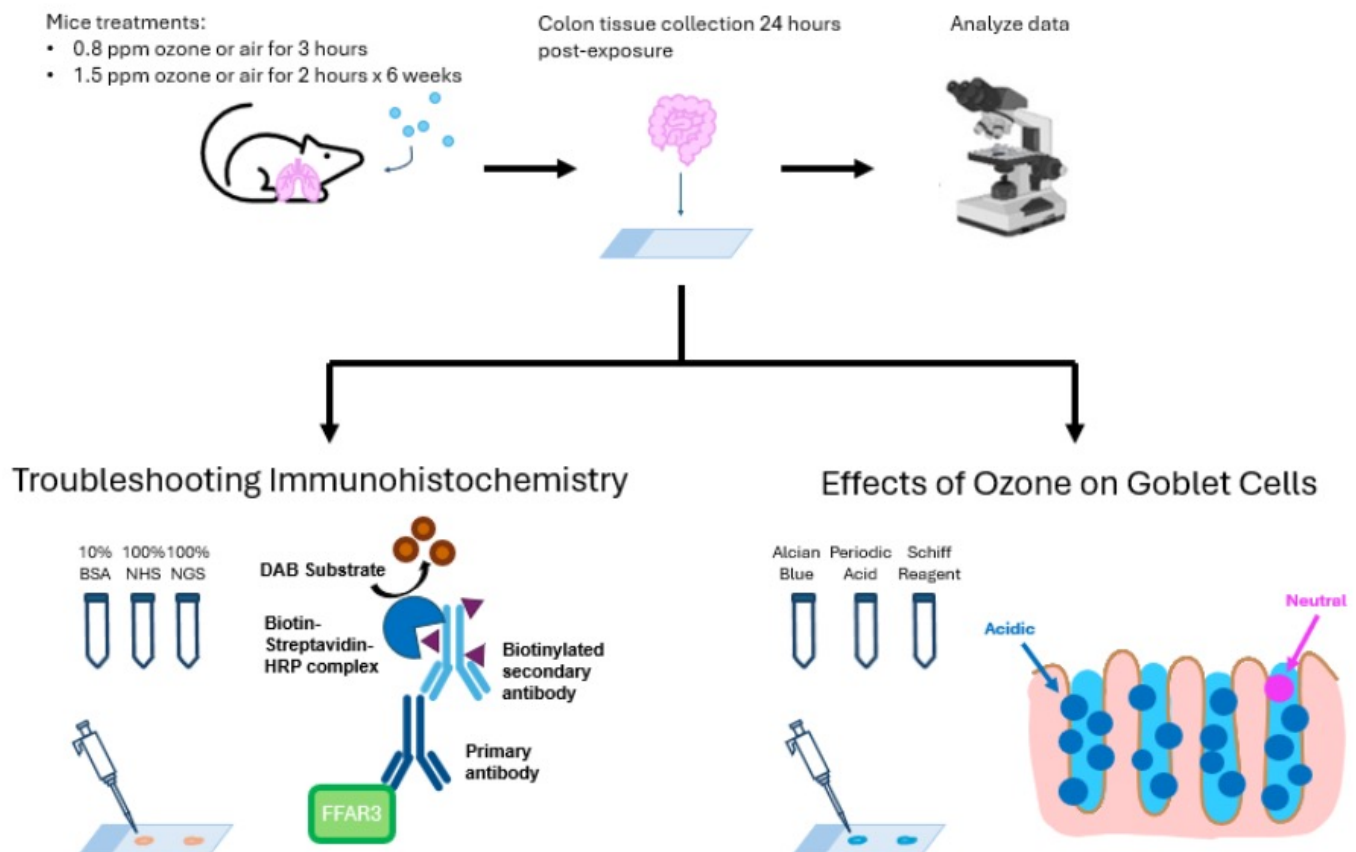


Impact of Ozone Exposure on Mouse Colon

Jessica Wangsa, Kyeongseo Kim, Peihong Zhou, Laurie B. Joseph, Sara C. Campbell

Rutgers, The State University of New Jersey

There is growing concern about the health effects of ozone pollution. Through the gut-lung axis, ozone creates oxidative stress and damage in the lungs that may induce changes in the intestines. This study evaluated intestinal changes following ozone exposure. Free fatty acid receptor 3 (FFAR3) is a G protein-coupled receptor activated by short-chain fatty acids (SCFAs), metabolites produced from fermentation of fiber by gut bacteria. Activation of the receptor triggers regulation of immune cell activity. Goblet cells secrete mucins, which help maintain gut health. We hypothesized that ozone exposure alters intestinal function by changing FFAR3 expression and goblet cells in the distal colon of mice. C57BL6 male and female mice were exposed to 0.8 ppm ozone or air for 3 hours, or 1.5 ppm ozone or air for 2 hours over 6 weeks. Colon tissues were biopsied for histology and immunohistochemistry (IHC) after 24h. IHC was performed on acute air exposed female mice to visualize FFAR3 in the colon. We tested several blocking reagents with FFAR3 antibody and IgG control to determine the best FFAR3 staining. Colonic goblet cells in male and female mice exposed to air and ozone were visualized with Alcian Blue/Periodic Acid- Schiff. IHC revealed FFAR3 expression in the colon of air exposed mice. However, the data is inconclusive because the IgG showed positive staining. Interestingly, there appeared an increased number of goblet cells following ozone exposure. Future studies will enumerate goblet cell number and FFAR3 in the colon following acute and chronic ozone exposure. Supported by NIH R25ES020721, Ernest Mario School of Pharmacy

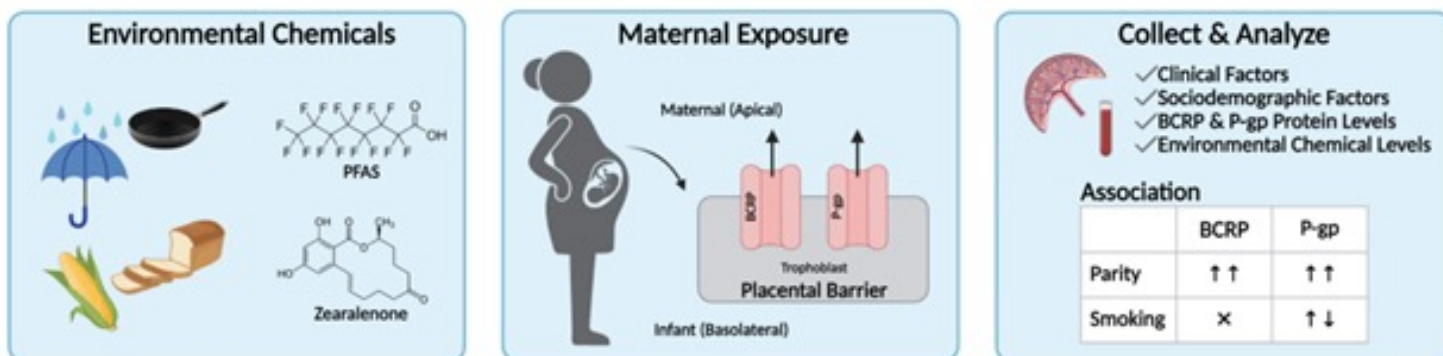


Regulators of the Placental Barrier: Insights from the UPSIDE Birth Cohort

Emma Andrechek^{1,5}, Chenghui Jiang¹, Kylie Getz¹, Ranran Zhang¹, John K. Fallon², Rani J. Qasem², Jacqueline B. Tiley², Philip C. Smith², Jessica Brunner³, Richard K. Miller³, Thomas G. O'Connor³, Nicholas P. Illsley^{1,4}, Pamela Ohman-Strickland¹, Zorimar Rivera-Núñez¹, Emily S. Barrett^{1,3}, Lauren M. Aleksunes¹

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Placental efflux transporters, such as BCRP and P-gp, regulate fetal exposure to nutrients and xenobiotics, including endocrine disrupting compounds such as per- and polyfluoroalkyl substances (PFAS) and mycoestrogens such as zearalenone (ZEN). While human birth cohort studies have linked maternal exposure to these chemicals with adverse pregnancy outcomes, the extent to which exposure to PFAS or ZEN impacts transporter expression levels in human placentas has not been well characterized. The purpose of this study was to analyze relationships between sociodemographic and clinical factors, environmental chemicals such as PFAS and mycoestrogens, and BCRP and P-gp transporter proteins. Placentas (n=251) were collected at term in the Understanding Pregnancy Signals and Development cohort (Rochester, New York, USA). BCRP and P-gp proteins were quantified in membrane fractions using quantitative targeted absolute proteomics. ZEN and metabolites were measured in placentas, and levels of 5 PFAS chemicals were quantified in second trimester serum samples. Statistical analyses with correlations, nonparametric tests, and regression models using R were conducted to evaluate these relationships. In extended models, there were no significant associations between BCRP/P-gp expression and concentrations of PFAS/mycoestrogens, whereas parity was significantly positively associated with both transporters. Smoking was significantly negatively associated with P-gp levels. Future studies looking at how environmental chemicals impact additional placental transporters including those responsible for fetal delivery of nutrients could help further understand the role of transporters in adverse pregnancy outcomes. Supported by NIH R25ES020721, the Society of Toxicology, and the Ernest Mario School of Pharmacy.

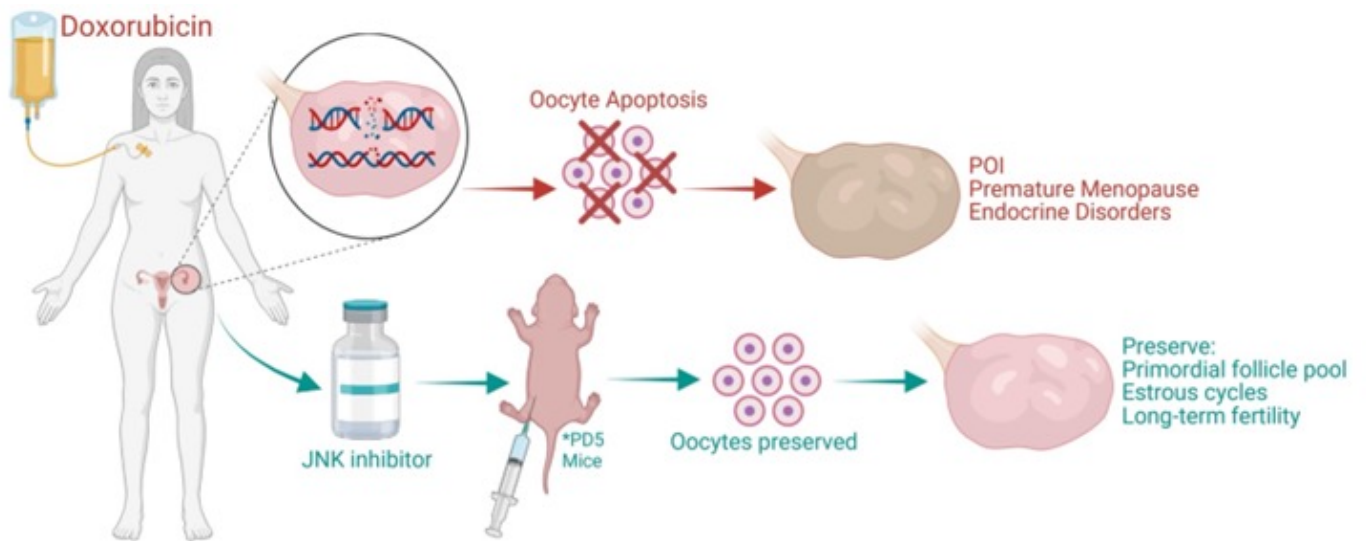


Pharmacological Inhibition of the JNK Cellular Stress Pathway Protects Ovarian Follicle Reserve from Chemotherapy-Induced DNA Damage and Apoptosis

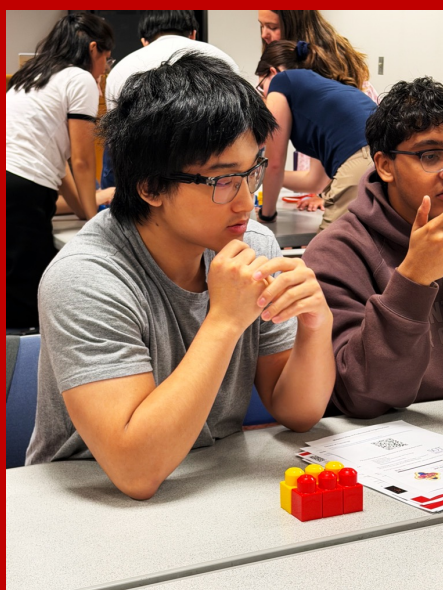
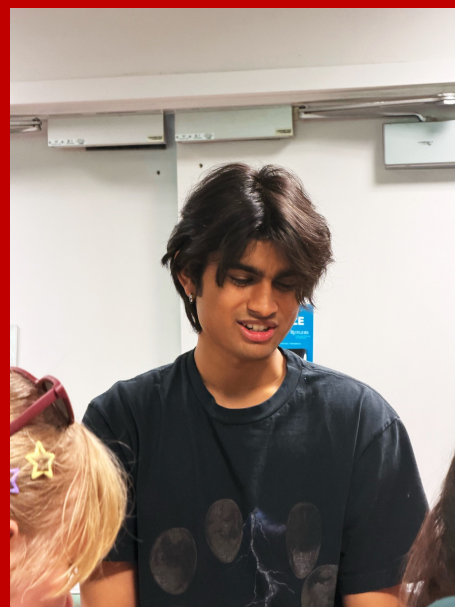
Jenny Chen^{1,2,7}, Wenlong Zhao^{1,2,3}, Jiyang Zhang^{1,2}, Yingnan Bo^{1,2}, Yingzheng Wang^{1,2,4},
Mi Ran Choi^{1,2}, Shichao Liu^{1,2}, Qiang Zhang⁵, So-Youn Kim⁶, Shuo Xiao^{1,2}

¹Environmental and Occupational Health Sciences Institute, Rutgers University; ²Ernest Mario School of Pharmacy, ³Hangzhou Women's Hospital, ⁴Weill Institute for Cell and Molecular Biology, ⁵Rollins School of Public Health, Emory University; ⁶New Jersey Medical School, ⁷Williams College

Advances in cancer treatment have improved patient survival, but young female cancer survivors face chemotherapy-induced primary ovarian insufficiency (POI), endocrine dysfunction, and infertility. Cryopreservation-based fertility preservation methods are invasive, delay cancer treatment, and are unsuitable for prepubertal patients. Pharmacological ovarian protectants offer a non-surgical alternative to preserve ovarian function during chemotherapy. This research investigated the c-Jun N-terminal kinase (JNK) pathway, which regulates cell survival, and is activated in oocytes in response to DNA-damaging chemotherapy. We hypothesized that pharmacological JNK inhibition would protect primordial follicles from chemotherapy-induced apoptosis, preventing POI. The objectives were to determine whether small-molecule JNK inhibitors protect ovaries from chemotherapy-induced follicle loss and elucidate how chemotherapy activates JNK and downstream apoptosis molecules, including Tap63 α , PUMA, and NOXA. To investigate this, mice were treated with doxorubicin, with or without JNK inhibitor. Histological staining and follicle counting assessed ovarian morphology and follicle preservation, while qPCR quantified expression of genes involved in DNA damage response and apoptosis. Results showed that JNK inhibition protected the ovarian follicle reserve and maintained normal puberty onset, estrous cyclicity, and long-term fertility. Importantly, JNK inhibition did not compromise chemotherapy efficacy in breast cancer-bearing mice (Zhao *et al.*, 2026). Future studies will use RNA sequencing and qPCR to further characterize the JNK pathway, define mechanistic differences between oocytes and somatic cells, and evaluate surviving oocyte genetic integrity. Overall, this work advances our understanding of chemotherapy-induced POI, supporting further development of JNK inhibitors as ovarian protectants to preserve fertility and ovarian hormones in young female cancer survivors. My research was supported by NIH R25ES020721, the Society of Toxicology, and the Ernest Mario School of Pharmacy, through the Rutgers SURF and RISE programs.









Thank you to all mentors and advisors,
researchers, sponsors, and department
administrators!



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*Dr. and Mrs. Gary
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