Southern California Society of Toxicology

37th Annual Fall Symposium

Advancements in Toxicology – From Mechanisms to Biotherapeutics

Ionis Conference Center, Carlsbad, CA

October 15, 2025

Southern California Society of Toxicology
37th Annual Fall Symposium

Advancements in Toxicology – From Mechanisms to Biotherapeutics

Morning Agenda

Time	Topic	Speaker/(s)
8:00 – 8:55 am	**BREAKFAST AND ONSITE REGISTRATION**	
8:55 – 9:00 am	Welcome and Introduction **Advancements in Toxicology – From Mechanisms to Biotherapeutics**	**Tejas Lahoti** *SCCSOT President*
9:00 – 9:15 am	SCCSOT Council Updates	**SCCSOT Council**
9:15 – 9:50 am	*Therapeutic Promise of Antibody-Oligonucleotide Conjugates for Rare Muscular Disease: The Development of Del-desiran (AOC 1001) for the Treatment of Myotonic Dystrophy Type 1*	**Laura Leung** *Avidity Biosciences*
9:50 – 10:25 am	*Transient Acute Neuronal Activation Effects with Oligonucleotides*	**Hao Chen** *Ionis Pharmaceuticals*
10:25 – 10:45 am	**COFFEE BREAK**	
10:45 – 11:20 am	*Nonclinical and Translational Safety Strategies for T cell engagers*	**Kristen Holbrook** *JNJ*
11:20 – 11:30 am	***Postdoc Trainee Talk 1:*** *Eye fibrosis-related pathology in male but not in female mice after chronic exposure to quasi- ultrafine particulate matter*	**Jose Arturo Jimenez Chavez**, UCI
11:30 – 11:40 am	***Student Talk 1:*** *Impaired Glo1 Detoxification Drives Sex- and Age-Dependent Metabolic Dysregulation*	**Ingrid Cely,** UCLA
11:40 – 12:00 pm	***Platinum Sponsor Talk 1:*** *From Tradition to Transformation: Interpreting Regulatory Announcement in an Evolving Digital Landscape*	**Mike Templin** CRL
12:00 – 1:30 pm	**LUNCH BREAK**	

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Afternoon Agenda

Time	Topic	Speaker/(s)
1:30 – 2:05 pm	*Developmental Risk Assessment of Teprotumumab, an Ocular Biotherapeutic for Thyroid Eye Disease*	**April O'Connell** *Amgen*
2:10 – 2:20 pm	***Student Talk 2:*** *Perfluorooctanesulfonamide-induced epiboly delay is associated with decreased ATP production within zebrafish embryos*	**John Hoang,** UCR
2:20 – 2:30 pm	***Student Talk 3:*** *Sertoli-Leydig Cell Crosstalk is Disrupted by Acetaminophen, Genistein, and Their Mixture in Juvenile Rodents*	**Nicole Mohajer,** USC
2:35 – 2:55 pm	***Platinum Sponsor Talk 2:*** *HEPATOPAC®, A Long-term* In Vitro *Platform for Assessing Drug-Induced Steatosis and MASLD Pathogenesis*	**Karissa Cottier** *BioIVT*
3:15 - 5:15 pm	**POSTER SESSION AND NETWORKING EVENT**	
5:00 - 5:15 pm	Poster awards and closing remarks	**Christine Hoffmaster** *SCCSOT Vice-President*
5:30 pm	**MEETING ADJOURNS**	

2025-26 SCCSOT EXECUTIVE COUNCIL

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For questions or additional information please contact the SCCSOT at southerncaliforniaSOT@gmail.com
Or Visit the Chapter's Website: https://www.toxicology.org/groups/rc/SouthernCal/index.asp

Farewell to the 2024-25 Outgoing Officers!

Gina Yanochko-Hoffman
Past President

Hemraj Dodiya
Councilor

Stacy Schkoda
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For questions or additional information please contact the SCCSOT at southerncaliforniaSOT@gmail.com
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2026-27 SCCSOT Call for Nomination

SCCSOT Council is currently recruiting for the following positions:

1. Vice President-Elect (4-year term, Presidential chain)
2. Treasurer (2-year term)
3. Secretary (2-year term)
4. Councilor (2-year term)
5. Postdoctoral representative (1-year term)
6. Student representative (2-year term)

Deadline to nominate is November 10th

For questions or additional information please contact the SCCSOT at southerncaliforniaSOT@gmail.com
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Prizes to be awarded at 5:00 pm, during the awards recognition.

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Student Mentoring Event

Thank you, Mentors, for Your Time!!
Trainees: Sign up for event at Registration Desk

Joseph Piccotti, PhD
Research Fellow, Toxicology
Schrödinger

Eric McDuffie, PhD, DABT
Senior Director, Toxicology
Neurocrine Biosciences

Dahea You, PharmD, PhD, DABT
Assoc. Director, Toxicology
Ionis Pharmaceuticals

Patrick Allard, PhD
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UCLA

Michael Boyle, DVM, PhD, DACVP
Head of Toxicology,
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Kumquat Biosciences

Jenny Cohen, PhD, DABT
Immunology TA Lead
Johnson and Johnson

Swati Rawat PhD, DABT
Director, Toxicology & Quality
BD

Elana Elkin, PhD, MPH
Assistant Professor
SDSU

ABSTRACT COMPETITION

Southern California Society of Toxicology
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Poster #	Authors	Title
1	I. Cely, M. Blencowe, G. Diamante, et al.,	**Impaired Glo1 Detoxification Drives Sex- and Age-Dependent Metabolic Dysregulation**
2	Maggie Drelichman and Elana Elkin	**Toxicity assessments of Perfluorobutane sulfonic acid in three *in vitro* human placental models**
3	Adam Filipowicz, Max Levenson, Summer Kelso, Patrick Allard	**Metaboloepigenetic mechanisms of transgenerational alcohol-seeking behavior**
4	Dylan Hatai, Cuining Liu, Ying Wang, et al.,	**Sex-Specific Pulmonary and Reproductive Effects of Perinatal E-cigarette Exposure**
5	John Hoang, Nicholas Jimenez, Keivon Faizi et al.,	**Perfluorooctanesulfonamide-induced epiboly delay is associated with decreased ATP production within zebrafish embryos**
6	Sophia Horn, and Ying-Hsuan Lin	**Fluorotelomer and Perfluoro Aldehyde Reactivity and Lung Cell Toxicity: Implications for Indoor Exposure to Volatile PFAS**
7	Nneamaka Iwobi, and Nicole R.L. Sparks	**Investigating the Developmental Toxicity of Bisphenols on human Embryonic Stem Cell Osteoblast Differentiation**
8	Jiménez-Chávez, A., Morales-Rubio, R., Herman, D., et al.,	**Eye fibrosis-related pathology in male but not in female mice after chronic exposure to quasi-ultrafine particulate matter**

ABSTRACT COMPETITION

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Poster #	Authors	Title
9	Karishma Khanal, Madeline KM Vera-Colon, Aarna Verma et al.,	**Disruption of Bone Homeostasis by Airborne Ultrafine Particulate Matter**
10	Taehee Kim, Catherine Chen, and Alice Soragni	**A Tumor–Liver Organoid Platform for *Ex Vivo* Assessment of Drug Metabolism and Toxicity**
11	Siri Langmo, Haoxuan Chen, Karah Lee, and Yifang Zhu	**Associations between air pollutant exposures from electronic cigarette usage in vape shops and respiratory mechanics**
12	Allen Louie; Russell Chuang; Eric Y. Lin et al.,	**Genetic and Chemical Modulation of Heme Oxygenase-1 Regulates Ultrafine Particle-Induced Inflammation in Macrophages**
13	Nicole Mohajer, Nicander Truong, and Martine Culty	**Sertoli-Leydig Cell Crosstalk is Disrupted by Acetaminophen, Genistein, and Their Mixture in Juvenile Rodents**
14	M.P. More, S. Roy, A. Trivedi, and S. Chatterjee	**Metabolic Dysfunction Worsens *Vibrio vulnificus* Sepsis and Kidney Injury: Intersection of Climate Change and the Obesity Epidemic.**
15	Anthony Rios, and Linlin Zhao	**Elucidation of Mitochondrial Nucleic Acid Signals Under Genotoxic Stress**
16	Gabriel Romo and Elana R. Elkin	**Effects of Tris(4-chlorophenyl)methanol Exposure in the HTR-8/SVneo Placental Cell Line**
17	J.Y.C. Sullivan, H.X. Huang, J.C. Heidmann et al.,	**Cigarette smoke and e-cigarette aerosol extracts disrupt hematopoiesis and suppress macrophage inflammatory cytokine production**

ABSTRACT COMPETITION

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Poster #	Authors	Title
18	Rene Toribio, Luis Trejo, Michael Zepeda, and Nicole Bournias-Vardiabasis	**Evaluating the Effect of Nicotine Exposure on *Drosophila melanogaster*, a Model for Respiratory Diseases**
19	Ance Trapse, Maggie Drelichman, Gabriel Romo et al.,	**Syncytialization and prolonged exposure to DCVC or S – (1,2- dichlorovinyl)- L – cysteine) measuring mitochondrial respiration in BeWo Cells**
20	Madeline K.M. Vera-Colón Desiree Williams, David Herman et al.,	**Transcriptomic pathway analysis reveals mechanisms linking fine particulate matter to skeletal and developmental defects**

INVITED SPEAKERS' ABSTRACTS

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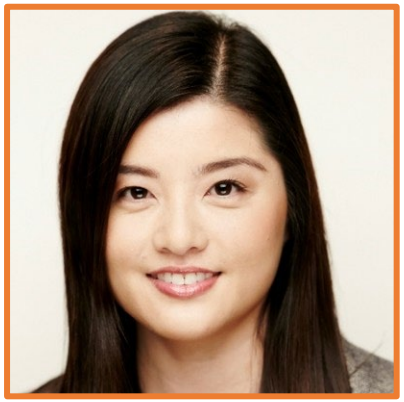
Therapeutic Promise of Antibody-Oligonucleotide Conjugates for Rare Muscular Disease: The Development of Del-desiran (AOC 1001) for the Treatment of Myotonic Dystrophy Type 1



Laura Leung, PhD *Avidity Biosciences, San Diego, CA*

Antibody oligonucleotide conjugates (AOCs) combine the tissue specificity of monoclonal antibodies with the precision and potency of oligonucleotides to enable the targeted delivery of oligonucleotides to previously untreatable tissues and cell types. AOC 1001 is comprised of a siRNA conjugated to an antibody targeting human transferrin receptor 1 (TfR1), designed for functional delivery to muscle cells, where it can reduce the levels of myotonic dystrophy protein kinase (DMPK) mRNA implicated in myotonic dystrophy type 1 (DM1) pathogenesis. DM1 is a rare dominantly inherited progressive neuromuscular disease caused by toxic gain-of-function mutation in the DMPK gene. The nonclinical safety strategy and regulatory feedback of AOC 1001 supporting IND through late-stage clinical trials will be discussed.

Transient Acute Neuronal Activation Effects with Oligonucleotides

Hao Chen, PhD, DABT *Ionis, Carlsbad, CA*

The intrathecal administration of a high concentration of antisense oligonucleotides (ASOs) to the CNS can induce a spectrum of predictable, acute behavioral responses in rodents and nonhuman primates. One such phenotype resembles hypocalceima and/or hypomagnesemia in humans, including muscle twitching/cramping, tremors, and/or convulsions that appear associated with neuronal activation. This "acute activation" phenotype typically resolves shortly after dosing, with no apparent sequelae. The severity of the acute activation phenotype can represent a dose-limiting finding during preclinical safety evaluation of intrathecally administered ASOs. Our work demonstrates that the acute activation phenotype is related to the binding properties of ASOs, specifically to divalent cations. ASOs contain negatively charged backbone linkages, such as phosphate and phosphorothioate, that when delivered at high and concentrated doses intrathecally and not appropriately supplemented with divalent cations can elicit an acute activation response. Optimization of divalent cations in the delivery formulation mitigated these acute phenotypes with no impact on oligonucleotide distribution or pharmacological efficacy. The acute activation response thus likely represents a local effect related to transient chelation of divalent cations near the injection site. As most human formulations exceed the divalent cation to oligonucleotide ratios used preclinically, the translatability of these findings is predicted to be low.

Nonclinical and Translational Safety Strategies for T cell engagers

Kristen Holbrook, PhD *Johnson & Johnson, San Diego, CA*

Innovation in nonclinical safety assessment for T-cell engagers is driving forward due to lack of appropriate nonclinical species, new molecular design, and urgency to bring safe and effective therapies to patients. Nonclinical safety strategy to support T-cell engager clinical development requires considering potential risks based on modality, mechanism of action, and product characteristics. New approaches, including animal models, in silico, and in vitro approaches can be scientifically justified and have an important place in toxicology strategy to identify mechanistic pathways underlying toxicities and to characterize poorly understood clinical toxicities. Our understanding of the translatability of innovative models and regulatory strategy integrating these approaches is developing over time, and these approaches are helping to bring safe and transformational T-cell engager therapies to patients.

Developmental Risk Assessment of Teprotumumab, an Ocular Biotherapeutic for Thyroid Eye Disease

April O'Connell, PhD, DABT *Amgen, Thousand Oaks, CA*

Teprotumumab is a human IgG1 monoclonal antibody administered intravenously for the treatment of thyroid eye disease (TED). While antagonism of the insulin-like growth factor receptor 1 (IGF-1R) signaling provides therapeutic benefit in TED, it also intersects with pathways critical for skeletal development. Nonhuman primate (NHP) embryo-fetal developmental (EFD) and juvenile animal studies (JAS) were conducted for an oncology indication by a prior sponsor in the late 2000s. In 2020, this toxicology package was repurposed to support a rare disease indication.Repeat-dose toxicology studies, including an NHP EFD study and a JAS in cynomolgus monkeys, supported the nonclinical safety evaluation for rare disease submissions. These studies showed test article-related skeletal abnormalities at delivery, and decreased bone parameters and body weights in developing juvenile NHPs. Body weight decreases were also observed in treated groups versus controls. The studies confirmed that teprotumumab is a mechanism-based teratogen. The strength of the data supported an FDA waiver for additional studies and informed the risk and margin language in product labeling, with country-specific variations. Teprotumumab is approved for patients with TED in the U.S. (2020), Japan (2024), Canada and the EU (2025).

From Tradition to Transformation: Interpreting Regulatory Announcement in an Evolving Digital Landscape.

Mike V. Templin, PhD *Charles River Laboratories, Reno, Nevada*

The FDA Modernization Act 2.0 set the stage for a paradigm shift in drug development and has been followed by FDA 3.0 as well as formal and informal announcements. Statements by individuals within regulatory bodies are increasingly being disseminated, and rapidly interpreted, within the digital landscape. Most recent, the announcement by the US FDA outlining a development pathway for monoclonal antibodies that is focused on “human-relevant methods” or New Approach Methodologies (NAMs). Other regulatory bodies, such as the EMA, have also proposed alternative pathways and a move away from traditional in vivo model-centric programs. The implications of this shift in drug development are extensive but have also raised tough questions on exactly how the proposed changes will become reality. This talk will focus on highlighting the challenges and opportunities that arise as traditional regulatory guidance and rapid communications evolve in a more real-time interpretation, and the expectations of immediate application.

HEPATOPAC®, A Long-term *in Vitro* Platform for Assessing Drug-Induced Steatosis and MASLD Pathogenesis

Karissa Cottier, PhD *BIOIVT, Baltimore, MD*

Drug-induced steatosis (DIS), a form of drug-induced liver injury (DILI), occurs when drugs impair hepatic fatty acid metabolism and can worsen underlying metabolic dysfunction-associated steatotic liver disease (MASLD). HEPATOPAC®, a long-term micropatterned hepatocyte co-culture (MPCC) system that retains physiologic metabolic and transporter function for at least 28 days, was used to model MASLD. In these studies, treatment with free fatty acids (FFA) or high glucose fructose (HGF) was used to induce a fatty-liver disease phenotype. These models showed reversible changes in lipid accumulation and fatty liver-related gene expression which were responsive to steatosis reducing compounds. Studies using these models show that valproic acid (VPA) induces steatosis, which is exacerbated in the presence of free fatty acids (FFA) or high glucose and fructose (HGF). Notably, the clinical Cmax for VPA overlaps with the lower concentrations tested in these models, where DIS potential was observed at these clinically relevant levels only in the FFA-induced steatotic background. These observations highlight the importance of disease-relevant backgrounds for DIS screening. Overall, HEPATOPAC provides a robust platform for studying DIS, MASLD/MASH pathogenesis, and drug toxicity, enabling more accurate screening and therapeutic development in metabolic liver diseases.

STUDENT ABSTRACTS

Southern California Society of Toxicology
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(Presenter at poster: 3:10 - 3:50 pm)

#1

Impaired Glo1 Detoxification Drives Sex- and Age-Dependent Metabolic Dysregulation

I. Cely, M. Blencowe, G. Diamante, I. Ahn, G. Zhang, R. Liu, L. Shu and X. Yang.
University of California Los Angeles, Los Angeles, CA, USA.

Abstract:
Glyoxalase 1 (Glo1) is the principal detoxification enzyme for methylglyoxal, a highly reactive dicarbonyl formed as a byproduct of glycolysis. When not effectively cleared, methylglyoxal modifies proteins, lipids, and nucleic acids, leading to oxidative stress and the generation of advanced glycation end products (AGEs). These reactive metabolites are endogenous toxicants that perturb metabolic homeostasis and contribute to metabolic disease such as obesity, cardiovascular disease (CVD), and type 2 diabetes (T2D). These metabolic diseases represent a global epidemic, and environmental toxicants may further exacerbate risk by impairing detoxification systems such as the glyoxalase pathway. While impairment of the glyoxalase pathway has been linked to AGE accumulation, the toxicological consequences of *Glo1* insufficiency independent of AGEs remain poorly understood. This study examined how partial loss of *Glo1* alters susceptibility to metabolic toxicity in a sex- and age-dependent manner in mice. By identifying AGE-independent pathways of dicarbonyl stress, our findings provide mechanistic insight into disease risk and may reveal novel targets for therapeutic intervention.
Methods: A longitudinal toxicological assessment was performed in female and male *Glo1* heterozygous knockdown (*Glo1*+/-) mice with ~50% gene expression, a model reflecting reduced detoxification capacity seen in metabolic disease and stress. Systemic toxicity markers (body weight, adiposity, glycemic control, plasma lipids) and tissue endpoints (atherosclerotic burden, AGE accumulation, transcriptomics) were evaluated across liver, adipose, muscle, kidney, and aorta.
Results: *Glo1* reduction produced sex- and age-dependent metabolic toxicity. Females *Glo1*+/-mice showed impaired glycemic control and elevated triglycerides linked to dysregulated adipogenesis, PPARγ, and fatty acid pathways compared to WT mice. In contrast, male *Glo1*+/-mice developed increased skeletal muscle mass and visceral adiposity with parallel lipid alterations. In addition, qPCR analysis revealed that lipid metabolic pathways were significantly reprogrammed in liver, adipose, muscle, kidney, and aorta, with sex-specific alterations in key enzymes (e.g., *Fasn, Dgat, Scd1*) consistent with the observed phenotypes. Despite the metabolic toxicity, AGE accumulation and RAGE signaling were largely unchanged, suggesting that the adverse effects occurred through AGE-independent mechanisms. Instead, gene expression for compensatory detoxification via *Akr* and *Aldh* was upregulated in a tissue-specific manner, leading to altered production of downstream metabolites such as pyruvate, which may further drive metabolic reprogramming. Moreover, transcriptomic profiling demonstrated widespread gene expression changes across metabolic tissues, including enrichment of pathways related to lipid metabolism, insulin resistance, and oxidative stress. Importantly, toxicology-relevant transcription factors were perturbed, including *Hnf4a* (metabolic and xenobiotic regulation) and *Arntl/Bmal1* (circadian control of detoxification), suggesting a mechanistic link between *Glo1* deficiency, environmental stress responses, and metabolic dysfunction.
Conclusion: Our results indicate that partial loss of *Glo1* increases susceptibility to metabolic toxicity and perturbs metabolic pathways in a sex- and age-dependent manner without significant changes in AGEs across metabolic tissues. These findings highlight toxicology-relevant transcription factors such as *Hnf4a* and *Arntl*, along with shifts in pyruvate metabolism from alternative methylglyoxal detoxification, as likely contributors to metabolic dysregulation in *Glo1+/-* mice.

(Presenter at poster: 3:10 - 3:50 pm)

#2

Toxicity assessments of Perfluorobutane sulfonic acid in three *in vitro* human placental models

Maggie Drelichman, Elana Elkin
San Diego State University

Perfluorobutane sulfonic acid, PFBS, is a compound belonging to the class of human made chemicals, Per- and Polyfluoroalkyl Substances, PFAS, with its greatest source of exposure through drinking water. In humans, maternal PFBS exposure can be associated with adverse birth outcomes and complications for mothers-to-be. Prior studies associate PFBS exposure with preeclampsia, a pregnancy-specific disease characterized by shallow trophoblast invasion and subsequent placental ischemia with PFBS exposure. Despite epidemiological evidence, the toxicological mechanism underlying this association is not clearly known. The aim of the research is to understand dose-response threshold and gene expression results related to reproductive toxicity in three in vitro human placenta models exposed to concentrations relevant to maternal exposure. We measured cell viability in the HTR-8/SVneo cell line using the Promega MultiTox-Glo Cytotoxicity Assay at 0μM, 100nM, 1μM, 10μM, 20μM, 50μM, 100μM PFBS, which showed no dose-response relationship in the live-dead cytotoxicity assay in the cell model. Transcriptomic via RNAseq analysis was performed by the DESeq2 analysis method in R programming for all three models, demonstrating concentration dependent effects in the third trimester tissue model, as evidenced by the magnitude of altered gene expression with 20μM versus 5μM versus 0μM PFBS (FDR > 0.05 + |LogFC| > 1 [FC>2]). Gene set enrichment pathway analyses identified upregulation in cell cycle proliferation in cells with 5μM treatment, both 5μM and 20μM in third trimester tissue, and 5μM in second trimester. Gene set enrichment pathway analyses identified downregulation in inflammation and immune response across all models and doses. This study advances understanding of potential risks of PFBS exposure during pregnancy by identifying differentially expressed genes and subsequent pathways in placental cells and tissues.

(Presenter at poster: 3:50 - 4:30 pm)

#3

Metaboloepigenetic mechanisms of transgenerational alcohol-seeking behavior

Adam Filipowicz, Max Levenson, Summer Kelso, Patrick Allard
University of California, Los Angeles.

Background and Purpose: The fetal brain is particularly vulnerable to ethanol's neurotoxic effects. Exposure during fetal development can cause irreversible damage, leading to long-term cognitive and behavioral deficits that fall under the umbrella of fetal alcohol spectrum disorders (FASD). Human studies on the multi- and transgenerational effects of alcohol have suggested
that neurobehavioral FASD features, including alcohol preference, can be passed across generations. However, the underlying mechanisms of transgenerational FASD inheritance remain largely unknown.
Methods: We used the model organism Caenorhabditis elegans to test the hypothesis that ethanol metabolism directly leads to increased, transgenerationally stable histone acetylation that affects ethanol-related behaviors. Wild-type animals and animals carrying loss-of-function mutations in conserved ethanol metabolism genes (alcohol dehydrogenase, adh-1, and acetyl
coenzyme A synthetase 2, acs-19) were exposed to physiological ethanol levels (0.05%, 0.1%, and 0.5%) and tested using behavioral and molecular assays including ethanol preference, crawling speed, food race, Western blotting, fluorescence microscopy, and mass spectrometry.
Results: While ethanol acted as a mild aversive cue for naïve animals, 48-hour exposure to all tested doses induced attraction to ethanol. This switch from aversion to attraction persisted to the F3 generation following a single parental exposure at the two higher doses. The ethanol preference switch was not merely a result of decreased locomotion, as crawling speed showed no decrease or increased 1 hour after exposure in P0, F1, and F3 generations. Animals tested on a more complex locomotory task (moving towards a food source) showed ethanol-dependent performance decreases at P0 and F1, though not F3, generations. Animals lacking functional adh-1 or acs-19 did not display an ethanol preference switch at P0, F1, or F3 generations, indicating that metabolism of ethanol into acetyl-CoA—the key molecule used to acetylate histones—is required for transgenerational ethanol-seeking behavior. Unbiased mass spectrometry of over 80 histone post-translational modifications revealed that H3K5ac, but not H3K9ac, increased in P0 and F3 generations after 0.5% ethanol exposure at P0. H3K27 modifications could not be examined due to protein sequence differences; however, preliminary Western blot and germline immunofluorescence results suggest that H3K27ac also increases upon 0.5% exposure in P0.
Conclusions: Ongoing studies are validating the mass spectrometry results and identifying histone post-translational modifications to target for epigenomic analysis using CUT&TAG methods. We will also elucidate the epigenetic requirements, including timing and cellular distribution, that direct alcohol's effects on behavior across generations using pharmacological and RNAi-based approaches. This research will identify the metaboloepigenetic mechanisms underlying alcohol's transgenerational effects.

(Presenter at poster: 3:10 - 3:50 pm)

#4

Sex-Specific Pulmonary and Reproductive Effects of Perinatal E-cigarette Exposure

Dylan Hatai, Cuining Liu, Ying Wang, Gourav Chandan, Jie Liu, Celia Yu, Sujit Silas, Samiksha Deme, Sabrina Madrigal, Reiko Sakurai, Patrick Allard, Virender Rehan
University of California Los Angeles, Los Angeles, CA, USA.

E-cigarette use remains popular among pregnant women with some estimates reporting as many as 15% of women have used e-cigarettes during their pregnancy. Our research tests the hypothesis that perinatal e-cigarette exposure alters the lungs and germ cells of F1 pups, and whether this effect persists until the F3 generation. Using an *in vivo* rat model, pregnant Sprague Dawley rats were exposed daily to e-cigarette vapor, resulting in similar serum cotinine levels of a habitual smoker. F1 pups were subjected to pulmonary function testing and lungs were collected for RNA sequencing. Additionally, to investigate the potential germline effects that may mediate transgenerational asthma, we collected the testes and ovaries from F1 pups and performed single nucleus RNA sequencing (snRNAseq).

Evidence of perinatal e-cigarette-induced asthma is supported by increased total airway resistance and decreased compliance in F1 pups by pulmonary function testing in both sexes (N=6-10; $p<0.05$). Furthermore, analysis of RNA sequencing in e-cigarette treated lungs (N=4) revealed that male pups (461 total DEGs, FC >1.5, padj<0.05) had a higher number of differentially expressed genes than females (84 total DEGs) compared to controls. Notably, differentially expressed genes were associated with cilia assembly and organization in both sexes. snRNAseq of pup ovaries and testes (N=3) captured all major cell types and analysis revealed that nuclei from earlier developmental stages of spermatogonia and spermatocytes had more differentially expressed genes than later stage spermatids. Taken together, these data provide molecular characterization of the pulmonary and reproductive effects of vaping over multiple generations.

(Presenter at poster: 3:50 - 4:30 pm)

#5

Perfluorooctanesulfonamide-induced epiboly delay is associated with decreased ATP production within zebrafish embryos

John Hoang, Nicholas Jimenez, Keivon Faizi, Qibo Xiang, Emma Fencl, Rebecca Yates, Jay Gan, David C. Volz
University of California, Riverside, CA 92521, United States

Background and Purpose: Per- and polyfluoroalkyl substances (PFAS) have been widely used within various industrial processes and consumer products, such as food packaging and fire-fighting foams. PFAS persistence within environmental media has led to ubiquitous exposure within humans and wildlife. We previously conducted a high-content toxicity screen of 38 different PFAS within the first 72 h of zebrafish development. This screen identified perfluorooctanesulfonamide (PFOSA) as the most potent developmental toxicant among the 38 PFAS tested. At non-lethal concentrations, exposure to PFOSA from 0.75 to 6 h post-fertilization (hpf) – a developmental window that includes cleavage, blastulation, and early-gastrulation – resulted in a concentration-dependent delay in epiboly (blastoderm migration and spreading) by 6 hpf. Therefore, for this study, we determined whether 1) PFOSA delays epiboly by inhibiting actin polymerization within the yolk, as epiboly progression is reliant on yolk-associated actin networks, and/or 2) PFOSA-induced effects are associated with a decrease in embryonic ATP, as PFOSA is a potent uncoupler of oxidative phosphorylation *in vitro*.

Methods: To accomplish this objective, we first tested whether there was an association between the uptake of PFOSA into the developing embryo, and whether the timing and magnitude of PFOSA-induced epiboly delay were similar to CCB-induced epiboly delay. Next, we employed phalloidin-based staining of F-actin and high-resolution laser-scanning confocal microscopy to determine if CCB and PFOSA inhibited yolk-associated actin polymerization throughout the entire embryo. Third, using mRNA-sequencing, we tested whether the potential impacts of PFOSA on the transcriptome were similar to CCB during epiboly progression. Finally, we determined whether 1) PFOSA-induced epiboly delay was associated with a decrease in embryonic ATP and 2) co-exposure to exogenous ATP mitigated PFOSA-induced delayed epiboly.

Results: Although PFOSA and CCB induced a similar magnitude of epiboly delay beginning at 4 hpf following initiation of exposure at 0.75 hpf, PFOSA did not, contrary to CCB, significantly decrease yolk-associated actin within embryos. Using mRNA-sequencing, we also found that, consistent with chemical-specific differences in effects on actin polymerization, PFOSA-exposed embryos were also transcriptionally different from CCB-exposed embryos. Moreover, phenotypically matched, PFOSA-exposed embryos at 6 hpf were transcriptionally similar to vehicle-exposed embryos at 5 hpf, and PFOSA delayed the maternal-to-zygotic transition (MZT) beginning at 5 hpf. Finally, PFOSA-induced delayed epiboly was associated with decreased ATP levels *in vivo*, an effect that was partially mitigated by co-exposure to exogenous ATP.

Conclusions: Overall, our findings suggest that PFOSA exposure during early embryonic development decreases ATP production in the absence of effects on actin polymerization *in vivo*, an effect that is associated with PFOSA-induced delays in epiboly and the MZT.

(Presenter at poster: 3:10 - 3:50 pm)

#6

Fluorotelomer and Perfluoro Aldehyde Reactivity and Lung Cell Toxicity: Implications for Indoor Exposure to Volatile PFAS

Sophia Horn, Ying-Hsuan Lin
University of California, Riverside

Background

Per and poly-fluoroalkyl substances (PFAS) are a family of persistent emerging contaminants of concern. FTOHs are a volatile subclass of this family and have been ubiquitously detected indoors emitted from various industrial and consumer products, such as food contact materials, weatherproof clothing, personal care products, and more. FTOHs are not toxic via inhalation themselves, but are known to transform in the atmosphere first into aldehydes and then into toxic PFAAs. However, the indoor exposure risks for the fluorotelomer aldehyde (FTAL) and perfluoro aldehyde (PFAL) intermediates are unknown.This study aims to examine chemical reactivity and in-vitro toxicity of these aldehydes.

Methods

To access effects on lung cell viability, acute exposure of 4:1 PFAL and 6:1 PFAL was carried out on BEAS-2B, immortalized human epithelial lung cells using XTT colorimetric assays to measure light absorption of metabolized salts by living cells. Cells will be exposed to FTALs and parent FTOHs in cell media with 1% DMSO to facilitate solubility. To predict reactivity of FTOHs, FTALs, and PFALs with biological nucleophiles, electrophilicity indexes were calculated using DFT/B3LYP/6-311+G(d, p) level of theory on Gaussian 16W software, and will be compared to GSH depletion rates in assays of aldehyde standards. Standard aldehyde-GSH adducts will be characterized using LCMS, and exposed cells will be screened for aldehyde-GSH adducts.

Results

4:1 and 6:1 PFAL significantly reduced lung cell viability in the micromolar range in a dose dependent manner. We expect carbon chain length of the tested aldehyde compounds to influence the cell viability and the rate of GSH depletion, as well as the detection of carbonyl-GSH adducts in cells to correlate with cell viability. The presence of FTALs and PFALs in indoor air could contribute to overall PFAS exposure. The results from this study have implications for their inhalation exposure risks.

(Presenter at poster: 3:50 - 4:30 pm)

#7

Investigating the Developmental Toxicity of Bisphenols on human Embryonic Stem Cell Osteoblast Differentiation

Nneamaka Iwobi, and Nicole R.L. Sparks
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Bisphenols (BPs), particularly bisphenol A (BPA), are a well-known endocrine disruptors with pervasive environmental presence. While the adverse health effects of BPA exposure are well studied, leading to restrictions on its use, increased usage of bisphenol F (BPF) and bisphenol S (BPS) as substitutes necessitates further investigation on its toxicity and effects on bone development. Studies have shown BPA to inhibit osteoblast differentiation and promote osteoblast apoptosis, impacting long-term bone health. However, the embryonic developmental bone toxicity of BPF and BPS remains unclear. Here, we explore the developmental toxic effects of BPA, BPF, and BPS on osteoblast development using human embryonic stem cells (hESCs) of the H9 line osteogenically differentiated with 1,25(OH)2 vitamin D3 (VD3), β-glycerophosphate (βGP), and ascorbic acid (AA). Human ESCs were exposed to increasing concentrations (0.0001-100 μM) of BPs during osteogenic differentiation. BPA and BPF dose-dependently inhibited hESC osteoblast cell viability and osteoblast differentiation, measured by MTT and alkaline phosphatase (ALP) assays. Alarmingly, BPS did not cause cell death at 100 μM but did decrease osteoblast differentiation. These findings highlight the need for further research into the mechanistic effects of bisphenols exposure on osteoblast differentiation and emphasize their potential to cause embryonic developmental bone toxicity.

(Presenter at poster: 3:10 - 3:50 pm)

#8

Eye fibrosis-related pathology in male but not in female mice after chronic exposure to quasi-ultrafine particulate matter

Jiménez-Chávez, A., Morales-Rubio, R., Herman, D., Hasen, I., Kleinman, M., De Vizcaya-Ruiz A.
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Background and Purpose: Currently, about 90 million U.S. adults have been diagnosed with an eye or vision disorder. Eyes are especially vulnerable to air pollutants like particulate matter (PM) due to direct exposure. This exposure has been linked to a higher risk of conditions such as dry eye, glaucoma, and age-related macular degeneration. Various effects, including the activation of inflammatory responses, oxidative stress, and damage to DNA and mitochondria, have been observed in the eyes after PM exposure. However, the activation of fibrotic pathways in the eye that lead to ocular pathologies remains unclear. Activation of the SMAD pathway by TGF-β can cause upregulation of α-SMA expression and fibrosis in the eye. Additionally, structural damage caused by particulate matter within ocular tissues may play a role in the development of eye diseases. This study aims to examine the effect of quasi-ultrafine particulate matter (qUFP) on eye tissue health, focusing specifically on structural damage in the retinal and corneal layers of the mouse eye, as well as the activation of fibrotic pathways.
Methods: Male and female C57BL/6 mice were exposed to filter air (FA) or concentrated qUFP (≤ 180 nm) in a whole-body exposure chamber for 6 months (5 hours/day, 4 days/week). After this time, animals were euthanized, and their eyes were removed. The right eye of each animal was flash-frozen in liquid nitrogen for mRNA analysis, and the left eye was placed in formalin to be fixed, stained with hematoxylin/eosin or α-smooth actin protein (α-SMA) antibody for fluorescence analysis, to determine structural and fibrotic changes.
Results: Histopathological alterations in the structural architecture of the cornea and retina were examined. Male eyes showed reduced thickness in the cornea and retina, as well as a decrease in corneal stroma thickness. In contrast, females exhibited increased thickness in both the cornea and stroma. The mRNA analysis revealed higher levels of markers associated with inflammation, oxidative stress, lipid metabolism, epithelial-mesenchymal transition, and neovascularization in male mice. Conversely, females only showed increased markers of inflammation and proliferation. Finally, an increase in α-SMA aggregates was observed only in the retina of male mice.

(Presenter at poster: 3:50 - 4:30 pm)

#9

Disruption of Bone Homeostasis by Airborne Ultrafine Particulate Matter

Karishma Khanal, Madeline KM Vera-Colon, Aarna Verma , David Herman , Andrea De Vizcaya-Ruiz, Michael T.Kleinman , Nicole R.L. Sparks
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Air pollution remains a critical public health issue, with particulate matter (PM) responsible for ~4.2 million premature deaths each year from cardiovascular and respiratory diseases. Among these pollutants, ultrafine particles (PM0.1) are of particular concern because their small size and reactive surfaces enable them to penetrate deeply into biological tissues. Although links between PM exposure and reduced adult bone health have been documented, the effects of ultrafine PM on skeletal structure are still poorly understood. In this study, we examined the long-term impact of airborne PM0.1 on bone integrity using $LDL^{-/-}$ and $ApoE^{-/-}$ mice. Animals were exposed to concentrated PM0.1 or filtered air for 6 hours per day, 5 days per week, over 18 weeks, while maintained on either a standard chow diet (16% fat) or a high-fat diet (40% fat). Histological evaluation of the femoral head metaphysis was performed on decalcified, paraffin-embedded, and H&E-stained sections. Our findings show that chronic PM exposure increased bone marrow adiposity, with large lipid-filled vacuoles especially prominent in high-fat diet groups. $ApoE^{-/-}$ mice displayed the greatest vulnerability, with severe trabecular bone loss, inflammatory cell infiltration, and compromised bone architecture. Even under standard diet conditions, PM exposure was sufficient to cause cortical thinning and loss of trabecular connectivity. These results suggest that ultrafine PM disrupts bone homeostasis through mechanisms likely involving oxidative stress, systemic inflammation, and lipid dysregulation. Given the central role of maternal bone turnover in supplying calcium for fetal skeletal development, such disturbances may also impair fetal bone formation and elevate the risk of congenital skeletal abnormalities. Together, this work emphasizes the need to consider environmental exposures in the context of maternal and developmental bone health, and highlights dietary and metabolic pathways as potential targets for intervention.

(Presenter at poster: 3:10 - 3:50 pm)

#10

A Tumor–Liver Organoid Platform for *Ex Vivo* Assessment of Drug Metabolism and Toxicity

Taehee Kim, Catherine Chen, Alice Soragni
University of California, Los Angeles

Several anti-cancer agents, including chemotherapies such as ifosfamide and irinotecan, are administered as prodrugs that require hepatic metabolism to become pharmacologically active. Because most cancer cells lack the enzymes needed for this activation, preclinical testing of prodrugs has been limited to animal models, which capture systemic metabolism but are costly, time-consuming, and unsuitable for high-throughput studies. To overcome this limitation, we developed a co-culture platform that integrates patient-derived tumor organoids with liver organoids in a miniaturized, high-throughput format. As proof of concept, we evaluated irinotecan, which is converted to the active metabolite SN-38 by hepatic carboxylesterases. We optimized dosing conditions that permit metabolic conversion, established hepatocyte culture conditions that preserve viability and CES1/CYP activity, and validated tumor organoid mini-ring assays with appropriate controls. Incorporating hepatocytes enabled irinotecan activation and sensitized tumor organoids to treatment, demonstrating the feasibility of prodrug testing in this system. This co-culture model expands the range of drugs that can be tested ex vivo, providing a scalable tool for drug discovery and personalized therapy selection.

(Presenter at poster: 3:50 - 4:30 pm)

#11

Associations between air pollutant exposures from electronic cigarette usage in vape shops and respiratory mechanics

Siri Langmo, Haoxuan Chen, Karah Lee, Yifang Zhu
University of California Los Angeles

Exposure to secondhand smoke from tobacco cigarettes has been associated with a plethora of acute respiratory symptoms, including changes in respiratory mechanics. However, similar studies on electronic cigarettes (e-cigs), the most popular tobacco product for youth in the United States, remain limited. This study investigated the effects of pollutant exposure on respiratory mechanics in vape shops where e-cigarettes are frequently vaped. It builds upon the few studies that have measured these effects in a controlled laboratory setting, utilizing our previous work that showed poor air quality and environmental e-cig aerosol exposure within and around vape shops. Healthy non-e-cig users visited a vape shop for six hours, during which they were exposed to environmental e-cig aerosol, measured through observation notes and real-time monitoring. Pre- and post-visit airway mechanics were measured using Impulse Oscillometry. No significant difference was found between the participants' pre- and post-visit measurements, consistent with previous studies. However, each participant experienced a unique exposure, as shown by real-time sampling data and observation notes. We identified a significant relationship between the number of observed puffs and the percent change in distal airway respiratory mechanics, as well as between particle number concentration and the percent change in distal airway respiratory mechanics. Our results suggest that airway mechanics are impacted by exposure to environmental e-cig aerosol within vape shops, and the extent of the impact is dependent on the level of exposure. These results underscore the importance of utilizing real-world settings to investigate environmental e-cigarette aerosol exposures.

(Presenter at poster: 3:50 - 4:30 pm)

#12

Genetic and Chemical Modulation of Heme Oxygenase-1 Regulates Ultrafine Particle-Induced Inflammation in Macrophages

Allen Louie; Russell Chuang; Eric Y. Lin; Srihari Prabu; Aishwarya Nair; Alexander Moroz; Matthew Sanchez; Neel Fulton; Emiliano Olivo Cauberghs; Mehdi Badami; Yashar Aghaei; Constantinos Sioutas; Jesus A. Araujo
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Introduction: Ambient air pollution is a well-recognized, major risk factor for atherosclerosis, a chronic inflammatory disorder of the vasculature. Epidemiological, in vivo, and in vitro studies have supported a mechanism of inflammation and atherogenesis linked to the exposure of fine particles (or particulate matter (PM) with a diameter ≤2.5μm). However, ultrafine particles (UFP; PM with a diameter ≤0.1μm) are likely to pose a greater health risk due to their smaller size and greater adsorbed surface material, but the mechanisms are still unclear. It has been shown that upregulation of systemic Heme oxygenase-1 (HO-1) offers cytoprotection against vascular atherogenesis due to its important antioxidant and anti-inflammatory properties. With macrophages playing a central role in inflammation, atherogenesis, and PM clearance in the most distal regions of the lungs, it is pertinent to understand how PM, and more importantly UFP, can affect inflammation. We hypothesize that UFP activate inflammatory processes via the upregulation of cytokines and the activation of the inflammasome in macrophages, all of which can be modulated by HO-1 expression.
Methods: RAW 264.7 macrophages were seeded at 300,000 cells/well at passage 12 and grown overnight. Macrophages were pretreated with cobalt protoporphyrin (CoPPIX) (10μM), tin protoporphyrin (SnPPIX) (10μM), UFP (25μg/mL) or a combination of chemical treatment and UFP for 24 hours. After the exposure duration, RNA was isolated from the cells and cDNA was synthesized. Bone marrow-derived macrophages (BMDMs) were harvested from the femurs of myeloid-specific Heme oxygenase-1 knockout mice (mHO-1-KO) and transgenic overexpressing Heme oxygenase-1 mice (mHO-1-Tg). For controls, BMDMs were harvested from their respective floxed counterparts. Briefly, marrow was extracted from the femurs of multiple mice and pooled (n=6-8) using complete RMPI media and frozen in 90% FBS and 10% DMSO until needed for experiments. BMDMs were cultured and differentiated in RPMI supplemented with M-CSF from L929 conditioned media. BMDMs were seeded at 500,000 cells/well and grown overnight. BMDMs were treated with UFP (25μg/mL) for 24 hours. After the treatment duration, RNA was isolated from the cells, and cDNA was synthesized. The expression of cytokines and inflammasome were assessed by quantitative PCR (Roche LightCycler 480) using Taqman probes on 384-well plates.
Results: Our data show that exposure to UFP induced robust cytokine and inflammasome activation in RAW 264.7 macrophages ($p<0.05$). The data supports that chemical induction and inhibition of HO-1 modulates cytokine and inflammasome components expression in macrophages, as evidenced by the significant reduction or exacerbation in the expression of specific cytokines and NLRP3 ($p<0.05$). In BMDMs from control floxed mice, UFP treatment significantly increased cytokine expression. In BMDMs harvested from mHO-1-KO mice, there is an exacerbation of these respective cytokines ($p<0.05$) and NLRP3. On the contrary, BMDMs from mHO-1-Tg mice had a significant reduction in inflammatory cytokines ($p<0.05$) as well as decreased expression of NLRP3.

(Presenter at poster: 3:10 - 3:50 pm)

#13

Sertoli-Leydig Cell Crosstalk is Disrupted by Acetaminophen, Genistein, and Their Mixture in Juvenile Rodents

Nicole Mohajer, Nicander Truong, Martine Culty
USC Alfred E. Mann School of Pharmacy and Pharmaceutical Sciences

Background: Testosterone-producing Leydig (LC) and Sertoli cells (SC) are somatic cell types within the testis that work together to support spermatogenesis. We previously determined that juvenile SCs and LCs are sensitive to acetaminophen (APAP), a widely used analgesic, and genistein (GEN), a dietary phytoestrogen, as well as their mixture. Preliminary analysis revealed differential expression of SC-secreted factors which target on LCs. Thus, we hypothesize that APAP, GEN, and their mixture disturb the cell-cell interactions between Sertoli and Leydig cells. Disruption of this SC–LC crosstalk may compromise testicular development.

Methods: Murine TM4 Sertoli and MA10 Leydig cell lines, along with postnatal day 8 (PND8) rat SCs and LCs, were treated for 24h with APAP (50 μM), GEN (50 μM), and their mixture alongside selective Cox inhibitors, antagonists of estrogen receptors, with/without hCG in the case of LCs. RNA-seq analysis identified altered genes and functional pathways using KEGG and Ingenuity Pathway Analysis (IPA). We validated target genes by RT-qPCR, analyzed selected proteins by immunofluorescent (IF) and measured testosterone by ELISA.

Results: The expression of LC genes involved in steroidogenesis, such as Star and Tspo, were significantly altered by APAP, GEN, and their mixture, and testosterone production was disrupted. We also observed differential gene expression of SC-secreted factors including *Dhh* and *Pdgfa* in SCs and LCs, and changes in their receptors (*Ptch1* and *Pdgfra*) in LCs in response to treatments with/without hCG. Expression of SC factors known to affect steroidogenesis in LCs, including *Timp1,* were altered. Additionally, secreted factors relevant to SC and LC functions, including Inhba and Igf2 were altered at the gene and/or protein level.

Conclusions: These data strongly suggest that APAP and GEN, in isolation and combined, disrupt SC-LC crosstalk, which can subsequently alter the functionality of the testicular microenvironment, and contribute to poor reproductive outcomes in males.

(Presenter at poster: 3:50 - 4:30 pm)

#14

Metabolic Dysfunction Worsens *Vibrio vulnificus* Sepsis and Kidney Injury: Intersection of Climate Change and the Obesity Epidemic.

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Climate change–driven increases in *Vibrio vulnificus* infections, together with the global obesity epidemic, present converging threats that heighten susceptibility to sepsis and its complications. Obesity and high-fat diet (HFD) consumption induce chronic inflammation and immune dysregulation, which may exacerbate sepsis-associated acute kidney injury (SAKI). Here, we investigated the mechanistic role of HFD-induced metabolic dysfunction in *V. vulnificus* sepsis–associated AKI using a murine model. Adult C57BL/6J mice were fed either standard chow or 60% kcal HFD for six weeks before oral, intragastric challenge with *V. vulnificus*. Infection markedly elevated serum TNF-α levels, with the HFD + *V. vulnificus* group displaying a synergistic three-fold increase over HFD alone and 1.6-fold increase over infection alone, indicating amplified systemic inflammation. Consistent with renal dysfunction, serum creatinine was significantly higher in the HFD + *V. vulnificus* group compared to either condition alone. Flow cytometry revealed that while Th17 cell expansion was infection-driven, HFD profoundly reduced Treg populations, resulting in a skewed Th17/Treg ratio that favored inflammation. This imbalance was reflected in elevated IL-17A levels in serum and kidneys of HFD + *V. vulnificus* mice, coupled with suppressed IL-10 and IL-4, highlighting impaired immunoregulatory capacity. Together, these findings demonstrate that diet-induced metabolic stress exacerbates *V. vulnificus* sepsis by amplifying systemic cytokine production, disrupting Th17/Treg homeostasis, and aggravating kidney injury. This work underscores the intersection of climate change and metabolic disease as critical drivers of infectious disease severity.

(Presenter at poster: 3:10 - 3:50 pm)

#15

Elucidation of Mitochondrial Nucleic Acid Signals Under Genotoxic Stress

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Mitochondria are vital organelles in higher eukaryotic cells, playing a crucial role in energy production, cell signaling, and biosynthesis. The mitochondrial DNA (mtDNA) genome, which encodes key components of the oxidative phosphorylation system, is susceptible to damage by endogenous and exogenous chemicals. When compromised, both mtDNA and mitochondrial double-stranded RNA (mt-dsRNA) can be released into the cytosol, where they act as damage-associated molecular patterns (DAMPs), triggering innate immune and inflammatory responses. While their role as signaling molecules is recognized, the relative contributions of mtDNA and mt-dsRNA under different genotoxic chemicals are not well understood. We hypothesize mtDNA and mt-dsRNA molecules contain signaling codes to inform different cellular defense mechanisms.

This study aims to quantify the contributions of mtDNA and mt-dsRNA in the mitochondrial homeostasis and innate immune response to various genotoxic agents. The initial phase of the project focuses on mitochondria-targeting chlorambucil (mtChlor), a proprietary compound developed in my laboratory that selectively alkylates mtDNA without damaging nuclear DNA. We used human bronchial epithelial (BEAS-2B) cells as a model system, which is relevant to inhalation exposures. Quantitative PCR was used to quantify the abundance of mtDNA and mt-dsRNA in the cytoplasm and assess the mtDNA integrity, as well as to determine the effects on the mitochondrial network and activation of an immune response downstream of the sensors cGAS and RIG1. Immunofluorescence using the J2 anti-dsRNA antibody was used to verify the release of mt-dsRNA species. Changes in mitochondrial homeostasis were measured as a function of respiration efficiency using the mitochondrial stress tests by the Seahorse apparatus.

Our findings revealed that exposure to mtChlor led to a significant increase in mitochondrial copy number and a concomitant decrease in mtDNA integrity. Release of both mtDNA and mt-dsRNA into the cytosol was confirmed, accompanied by changes in mitochondrial and cellular dynamics. We observed the upregulation of both fission and fusion genes, indicative of a shift in mitochondrial dynamics. Furthermore, a significant increase in the transcription of cytosolic sensors and immune response components was observed. Seahorse assays revealed that respiration efficiency was negatively affected after a 24-h exposure. Taken together, this research establishes a robust and quantitative platform to assess the distinct contributions of mtDNA and mt-dsRNA in mitochondrial respiration, dynamics, and innate immunity under genotoxic stress. Future work will extend this platform to decode the mitochondrial nucleic acid signals from additional genotoxic chemicals and cell models, particularly at doses relevant to human exposure.

(Presenter at poster: 3:50 - 4:30 pm)

#16

Effects of Tris(4-chlorophenyl)methanol Exposure in the HTR-8/SVneo Placental Cell Line

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Introduction: Tris(4-chlorophenyl)methane (TCPM) and tris(4-chlorophenyl)methanol (TCPMOH) are anthropogenic environmental pollutants that are believed to be byproducts of the organochlorine pesticide dichlorodiphenyltrichloroethane (DDT). TCPMOH is thought to be a metabolite of TCPM. These chemicals persist in the environment, and have been found to accumulate in aquatic mammal tissue and in human breast milk. They are also potential endocrine disruptors, yet no studies evaluating potential toxic effects have been conducted in the placenta, a transient organ with many endocrine functions critical for fetal development. In this study, TCPMOH was screened for its cytotoxic effects, differential gene expression, and invasion capacity.
Materials and Methods: For cell viability and cytotoxicity, HTR-8/SVneo cells were treated with medium plus DMSO (control) or TCPM or TCPMOH (1 μM – 1 mM) for 24-hours and cytotoxicity was measured using Multitox Cytotoxicity Assay. RNA sequencing of HTR-8/SVneo cells was used to measure gene expression after being treated with medium plus DMSO (control) or TCPMOH (1 μM or 10 μM). Differential gene expression was analyzed using DEseq2 in R. For invasion capacity, HTR-8/SVneo cells treated with medium plus DMSO (control) or TCPMOH (1 μM or 10 μM) in transwell inserts and evaluated by fluorensence microscopy.
Results: Placental cells significantly decreased in cell viability when exposed to concentrations of 50 μM or greater ($p < 0.0001$). Differential gene expression for 1 μM and 10 μM concentrations yielded 3 shared significantly upregulated pathways: Inflammatory response, Interferon gamma, and KRAS signaling. Invasion capacity for 1 μM concentrations reduced cell count by 38% ($p = 0.0229$), and for 10 μM concentrations cell count was reduced by 62% ($p = 0.0019$).
Conclusions: Placental cell viability was significantly reduced by concentrations of TCPMOH 50 μM and greater. Differential gene expression showed an upregulation of pathways related to inflammation as well as cell proliferation at sublethal concentrations. Low concentrations of TCPMOH also affected the invasion capacity of the placental cells. Future studies will further investigate the underlying toxicological mechanism of cytotoxicity and reduced invasion capacity.

(Presenter at poster: 3:10 - 3:50 pm)

#17

Cigarette smoke and e-cigarette aerosol extracts disrupt hematopoiesis and suppress macrophage inflammatory cytokine production

J.Y.C. Sullivan, H.X. Huang, J.C. Heidmann, J.H. Chen, N. Iwobi, D. Herman, N. Sparks, M. Kleinman, A.G. Fleischman
University of California, Irvine

Background: The widespread consumption of nicotine and tobacco is the leading cause of cancers attributable to modifiable lifestyle choices. Direct and secondhand exposure to traditional cigarettes or electronic nicotine devices impacts many processes throughout the body, including immune responses and healthy blood formation. Here, we examine the effects of e-cigarette vapor and combustible cigarette smoke on inflammatory responses in cells in vitro and long-term hematopoietic stem cell (HSC) differentiation in vivo. We hypothesize that dual exposure to both cigarettes and e-cigarettes worsens inflammation more than exposure to each alone, and that these exposures provide a selective advantage for the proliferation of hematopoietic driver mutations.

Methods: Cigarette smoke extracts (CSE) and e-cigarette vape extracts (EVE) were prepared by using an impinger to draw combustible smoke (Kentucky research cigarettes) or e-cigarette vapor (commercially available Naked brand melon-flavored vape liquid) into DMEM + 10% FBS. RAW264.7 macrophages, THP-1-differentiated macrophages, human PBMCs, and wild-type (WT) and Tet2-/- macrophages were stimulated with LPS and CSE or EVE for 24 hours. ELISA was used to quantify TNF-α secretion. Colony formation assays were performed by incubating WT or Tet2-/- HSCs with CSE or EVE overnight, washing and plating them in cytokine-supplemented methylcellulose media, and enumerating colonies 7 days later. To examine the impact of CSE or EVE on the proliferation of mutant HSCs, we performed competitive bone marrow transplants using cells pre-exposed to CSE, EVE, or both. Flow cytometry was used to quantify peripheral blood subsets and WT or Tet2-/- chimerism.

Results: Exposure to cigarette smoke and e-cigarette vape extracts inhibits LPS-induced TNF-α secretion in primary mouse and human cells. CSE and EVE also significantly reduce colony formation in both wild-type and Tet2-/- HSCs, with a greater effect in WT cells. In a competitive bone marrow transplant (BMT) model, a single dose of CSE or EVE before transplantation increases myeloid cell frequencies and suppresses the proliferation of Tet2-deficient cells.

Conclusions: Impairment of LPS-induced TNF-α production indicates that cigarettes and e-cigarettes inhibit the ability to respond to an immune stimulus. The higher clonogenic potential of the Tet2-/- HSCs suggests that Tet2 deficiency confers relative resistance to the suppressive effects of cigarette smoke on hematopoietic progenitors. Using a BMT model, we demonstrate that exposure to cigarette or e-cigarette extract reprograms HSCs to shift toward enhanced granulopoiesis and myelopoiesis. Taken together, these results demonstrate how exposure to cigarettes and e-cigarettes has distinct but impactful effects on the phenotype of both mature myeloid cells and their HSC progenitors.

(Presenter at poster: 3:50 - 4:30 pm)

#18

Evaluating the Effect of Nicotine Exposure on *Drosophila melanogaster*, a Model for Respiratory Diseases

Rene Toribio, Luis Trejo, Michael Zepeda, Nicole Bournias-Vardiabasis
California State University, San Bernardino

Nicotine consumption through vaping has seen a concerning rise in recent years, particularly prevalent among high school students despite declines in cigarette use. In 2023, 10.0% of high school students reported regular e-cigarette use, according to the FDA's National Youth Tobacco Survey (CDC). Numerous studies highlight the negative side effects of nicotine, such as COPD, respiratory disease, heart disease, and early death among consumers. To evaluate the effects of vape products on respiratory health, we investigated how vaping impacted the trachea of *Drosophila melanogaster* 3rd instar larvae. *Drosophila* is a well-established model organism due to its genetic tractability, short life cycle, and similarities in fundamental biological processes to humans. The larvae provide a useful model for studying respiratory diseases due to structural and functional similarities with mammalian respiratory systems. The *Drosophila* tracheal system has been widely utilized to uncover mechanisms behind tube morphogenesis, which can be linked to structural changes observed in COPD, making it a valuable tool for studying COPD-related alterations. We conducted assays to assess nicotine-laced food effects on the viability of *Drosophila* 3rd instar larvae, using this data to determine appropriate nicotine concentrations for vaping exposure. The effects on viability, development, and respiratory damage were assessed, with ingestion and inhalation resulting in a substantial, dose-dependent decrease in larval survival. Dissections and histological analysis of the trachea revealed significant morphological differences, indicating structural damage. Additionally, we utilized flow cytometry to further analyze cellular changes in tracheal tissue after exposure, providing detailed insights into the impact of nicotine on respiratory cell populations.These studies demonstrate *Drosophila melanogaster* as a viable model for investigating the impact of nicotine ingestion and inhalation, revealing both macroscopic and cellular-level alterations associated with respiratory damage, and contributing to a deeper understanding of the health risks posed by e-cigarette use

(Presenter at poster: 3:10 - 3:50 pm)

#19

Syncytialization and prolonged exposure to DCVC or S – (1,2- dichlorovinyl)- L – cysteine) measuring mitochondrial respiration in BeWo Cells

Ance Trapse, Maggie Drelichman, Gabriel Romo, Chris Cellini, Kya Vulgamott, Elana Elkin
San Diego State University School of Public Health

Trichloroethylene (TCE) is a widely used industrial solvent and recognized environmental pollutant, present in spray adhesives, paint removers, tool cleaners, and other common household products. It has remained persistent in the environment globally, causing a risk to human health. TCE can be metabolized into the reactive and toxic metabolite S-(1,2-dichlorovinyl)-L-cysteine (DCVC), which induces mitochondrial-mediated apoptosis in trophoblast cells, known to play a crucial role in the early stages of pregnancy and placental development. Mitochondrial metabolism plays a crucial role in trophoblast differentiation, and little is known about how DCVC exposure affects this process. The current study aims to investigate the effects of different environmentally relevant DCVC concentrations on inducing mitochondrial stress and disruptions to the fusion process, known as syncytialization, in BeWo syncytiotrophoblast cells. To assess the effects of DCVC on the BeWo cell line, we measured live-cell metabolic function using the Agilent Seahorse XF HS Mini Analyzer, conducting a Mito Stress Test assay. This test measures key parameters such as the oxygen consumption rate (OCR) of cells, allowing for real-time monitoring of plate-based live assays. Prior to the assay, BeWo cells were exposed to 10 and 20 μM DCVC and incubated for 24 hours. Following the exposure period, oxygen consumption rate (OCR), proton efflux rate (PER), extracellular acidification rate (ECAR), and seven other parameters were measured via the Seahorse XF Analyzer. A one-way ANOVA was conducted for the basal respiration results for the three trials to assess changes in mitochondrial activity. So far, preliminary data have shown no significant results identified in the DCVC-treated BeWo cells. Experiments continue with the fused version of these cells for further insight into the mitochondrial dysfunction caused by DCVC in this placental cell line.

Conclusion: Overall, our results showed a sex-specific pattern of corneal and retinal degeneration in the eye after qUFP exposure. In males, changes in the corneal and retinal layers, along with TGF-β–mediated upregulation of α-SMA, which is closely linked to fibrosis-related eye pathology. In females, the structural and molecular damage appears to be connected to ocular surface inflammatory disease caused by qUFP exposure. Understanding these sex-specific eye changes induced by qUFP exposure can help clarify how fibrotic eye diseases develop and support the development of new treatments and preventive strategies to reduce α-SMA upregulation and prevent ocular fibrosis and vision loss.

(Presenter at poster: 3:50 - 4:30 pm)

#20

Transcriptomic pathway analysis reveals mechanisms linking fine particulate matter to skeletal and developmental defects

Madeline K.M. Vera-Colón, Desiree Williams, David Herman, Andrea De Vizcaya-Ruiz, Michael T. Kleinman, and Nicole R.L. Sparks
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Air pollution, particularly particulate matter (PM), poses a significant public health risk, with established links to respiratory disease, cancers, and cardiovascular diseases. Emerging evidence suggests that PM exposure is a risk factor for poor adult bone health, such as osteoporosis. Additionally, prenatal PM exposure has been associated with adverse birth outcomes, including increased risk for skeletal defects, though the underlying mechanisms remain unclear. Osteogenesis, the formation of bone, is governed by a complex network of epigenetic mechanisms, microRNAs, and transcription factors that are susceptible to environmental perturbations and can manifest embryonic skeletal defects. We sought to investigate how PM exposure alters embryonic molecular signatures in human embryonic stem cells (hESCs) before cell fate commitment, potentially predisposing to skeletal birth defects. Using the H9 hESC line, we differentiated cells into osteoblasts and exposed to fine PM (PM2.5) or urban dust at concentrations inhibiting differentiation by 25% (ID25) or 50% (ID50). Fine PM exposure inhibited osteogenesis in a dose-dependent manner, as evidenced by reduced protein expression, alkaline phosphatase activity, matrix mineralization, and cell viability. Transcriptomic profiling revealed that fine PM triggered strong gene induction at ID25, with ID50 yielding the highest number of differentially expressed genes (DEGs). UpSet plot analysis showed minimal DEG overlap between conditions, highlighting distinct toxicity mechanisms at different exposure levels. Pathway enrichment analysis of fine PM DEGs identified pathways relevant to bone-, metabolism- and toxicity-related pathways. Our findings provide mechanistic insight into how fine PM impairs embryonic osteoblast differentiation, underscoring the need for interventions to mitigate environmental risk factors for skeletal birth defects

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Prizes to be awarded at 5:00 pm, during the awards recognition.

Southern California Society of Toxicology

37th Annual Fall Symposium

Advancements in Toxicology – From Mechanisms to Biotherapeutics

Ionis Conference Center, Carlsbad, CA

October 15, 2025

Thank You for Attending!

For questions or additional information please contact the SCCSOT at
southerncaliforniaSOT@gmail.com

Or Visit the Chapter's Website:
https://www.toxicology.org/groups/rc/SouthernCal/index.asp

SOT 2026

See you all in San Diego, CA