characterizes the *in vitro* toxicity the BDE-153, assessed in different hepatic cell lines using monolayer (2D) and tridimensional cell culture by hang drop (3D cell culture) for more predictive data, in an attempt to elucidate the mechanism of toxicity in different cell lines. HepG2 cells were maintained in DMEM medium and plated in 12-well plate for adhesion or in 96-well hanging drop plate for 3D cell culture. Hepatocytes were isolated from healthy Wistar rats; after cannulating the portal vein, the liver was perfused with Krebs-Henseleit buffer. All cell were exposed to BDE-100 (0.1-25μM). After 24 and 48 hours of exposure to BDE-153 cell viability was assessed using 0.5% MTT. In addition, the determination of mitochondrial membrane potential (Dψ) was performed using the TMRM, and also the total protein/cell mass was evaluated using the SRB assay. Finally, we assessed the damage caused by BDE-153 in HepG2 3D-cultures using the fluorescent dyes Hoechst and Ethidium. BDE-153 has been shown to cause cellular dysfunctions by dissipating Dψ and decreasing cell viability and all cultures in monolayers. Additionally, it was observed an increase in the number of cells labeled with ethidium in HepG2 3D-culture, also indicating cell death. We concluded that the exposure to BDE-153 induces significant damage in both, immortalized and in primary cells, and demonstrated to induce cell death in 3D culture too, a new cell culture model that has been growing in recent years. This damage corroborate with the induction of mitochondrial damage data previously submitted. Supported by: Capes - Proc. PVE A018/2013; FAPESP - Proc. 2012/13123-0.

1128 Liver Transcriptomic and Metabolic Reprogramming After Exposure to Diesel Exhaust

G. Ramanathan[2], Y. Zhao[1], F. Yin[2], M. E. Rosenfeld[3], X. Yang[1] and J. A. Araujo[2]. *[1]Integrative Biology and Physiology, University of California, Los Angeles, Los Angeles, CA; [2]Medicine, UCLA School of Medicine, Los Angeles, CA and [3]Pathology and Environmental and Occupational Health Sciences, University of Washington, Los Angeles, CA.* Sponsor: M. Campen.

Background: Exposure to air pollution has been shown to associate with cardiovascular morbi-mortality, insulin resistance and type 2 diabetes. We investigated the mechanisms how air pollution induces metabolic abnormalities in the liver using a combination of ohmics approaches. Methods: Apolipoprotein E (ApoE) null mice were exposed to either diesel exhaust (DE) or filtered air (FA) for 2 weeks. For transcriptomics, RNA was extracted from livers, n=8 per group, and used for Illumina microarrays. Metabolomics analysis of the livers, n=5 per group, was performed by Metabolon Inc. Illumina data was analyzed using the Genomestudio software. *In vitro* experiments used HepG2 cells treated with a methanol extract of diesel exhaust particles (DEP) vs. media. mRNA expression levels were quantified by qPCR. Glucose and glycogen content were determined by biochemical and histological determinations. Results: Liver cholesterol and triglyceride content were significantly increased following DE exposure. Microarray analysis showed differential expression of 477 genes in the DE group compared to FA ($p< 0.05$). Pathways significantly dysregulated by DE included lipid and lipoprotein metabolism, lysosome, oxidative phosphorylation and the citric acid cycle. Metabolomics identified 118 biochemicals with significant differences in their levels between the DE and FA groups. Important pathways enriched with these metabolites included glutathione metabolism, citric acid cycle, glycogen metabolism and glycerolipid metabolism. We identified several key driver genes from the transcriptomic analysis, including PEPCK for biological validation by *in vitro* experiments. HepG2 cells treated with 100ug/ml DEP extract for 8 hours showed a marked increase in PEPCK expression suggesting enhanced gluconeogenesis. DEP treatment also resulted in depletion of glycogen content in HepG2 cells. Conclusion: Integrated analysis of liver transcriptomic and metabolomic data from mice exposed to diesel exhaust for 2 weeks indicated several alterations in metabolic pathways involved in lipid and carbohydrate metabolism, resulting in increased synthesis of triglycerides, increased gluconeogenesis and glycogenolysis.

1129 Extrapolating Salivary Acinar Cell *In Vitro* Pesticide Transport to Whole Animals Using Computational Modeling

C. Timchalk, Z. A. Carver, T. J. Weber and J. N. Smith. *Pacific Northwest National Laboratory (PNNL), Richland, WA.*

Non-invasive biomonitoring with saliva has potential to significantly advance quantitative dosimetry as an integral component of epidemiology. However, predictions of which chemical and/or metabolites are excreted into saliva at detectable concentrations remain a challenge. In order to predict salivary clearance, a combination experimental and computational approach has been developed with 3,5,6-trichloro-2-pyridinol (TCPy) (the major chemical-specific metabolite of chlorpyrifos) to predict potential salivary levels. A Transwell *in vitro* rat salivary acinar cell system was utilized, where protein levels in the basolateral (27.2 mg/mL) and apical (1.3 mg/mL) culture chambers, which represent blood and saliva compartments respectively, were altered using bovine serum albumin to more closely mimic physiological levels. TCPy was dosed to the basolateral chamber at two concentrations (250 and 2500 μM), and both chambers were sampled over time up to 24 hr. The rat salivary cell system maintained the protein gradient and tight junctions over the duration of the experiment as evidenced by consistent transepithelial electrical resistance levels. Levels of TCPy were quantified using gas chromatography-mass spectrometry, and at 24 hr, the predicted median saliva/blood concentration ratio was similar to published values measured *in vivo* (0.021 vs. 0.049). TCPy concentrations were modeled using a mechanistic computational cellular transport model. The resulting model simulations fit the data reasonably well, and fit parameters suggest that TCPy is transported across basolateral and apical cell membranes by passive diffusion. Model parameters were integrated into a physiologically based pharmacokinetic model, and reasonably predicted TCPy concentrations in rat saliva after intravenous administration of TCPy. This poster demonstrates the utility of this combination experimental and computational approach to predict chemical transport in saliva. Supported by CDC/NIOSH grant R01 OH008173.

1130 Non-Invasive Saliva Human Biomonitoring: Development of a Transwell Assay to Support Exposure Science Assessment and Health Impacts

T. J. Weber, J. N. Smith, Z. A. Carver and C. Timchalk. *Health Impacts & Exposure Science, Pacific Northwest National Laboratory, Richland, WA.*

The use of saliva as a biomonitoring matrix can significantly advance quantitative dosimetry as an integral component of epidemiology. A major limitation has been an inability to identify which chemicals are readily cleared in saliva, at levels that can be quantified. To address this limitation, we have developed a primary salivary gland serous-acinar cell model that can be used for chemical transport studies *in vitro*. Serous-acinar biomarkers detected by Western blot include alpha amylase and aquaporin 5 which are uniformly expressed in confluent cultures. Serous-acinar cells express the tight junction marker zona occludens-1 and measurements of transepithelial electrical resistance (TEER) demonstrate exceptional tight junction formation (routinely >2000 Ω/cm2) in a relatively short period of time (6-8 days) in Transwell inserts. When TEER values are > 2000 Ω/cm2, lucifer yellow transport from apical to basolateral chambers is ~ 0.1%/hr. The insecticide chlorpyrifos (CPF) and its primary metabolite trichlorpyridinol (TCPy) can be quantified in saliva at concentrations that are less than, but parallel to blood levels. Results from the Transwell assay indicate that chlorpyrifos transports by diffusion with transport rates that are linear among doses tested. Lucifer yellow passage across the epithelial barrier was clearly disproportional to chlorpyrifos transport. Primary serous-acinar cells showed a low level of CPF metabolism to TCPy, which subsequently localized to both apical and basolateral chambers, consistent with a diffusional process and lack of TCPy concentration gradient. These experiments establish the feasibility of utilizing an *in vitro* cell based uptake/clearance assay coupled with pharmacokinetic modeling as a novel chemical screening strategy to identify ideal chemical candidates for saliva biomonitoring. Future studies will begin linking the transwell assay to higher content chemical screening capabilities to increase throughput. Supported by CDC/NIOSH grant R01 OH008173.

1131 2, 4 - Dichlorophenoxyacetic Acid (2, 4-D) Transport Across an *In Vitro* Salivary Acinar Cell System: A Novel Approach to Biomonitoring

Z. A. Carver, C. Timchalk, J. N. Smith and T. J. Weber. *Health Impacts & Exposure Sci, Pacific Northwest National Laboratory, Richland, WA.*

The non-invasive use of saliva for biomonitoring has the potential to significantly advance quantitative dosimetry as an integral component of public health. A major limitation for this approach has been an inability to identify which chemicals are readily cleared in saliva, at levels that can be quantified at relevant exposure levels. 2, 4-D is a widely used herbicide and its renal clearance mechanism involves both glomerular filtration and active organic ion transport. 2, 4-D was dosed in the basolateral chamber at 2 different concentrations (10 or 100 μg/mL), and both chambers were sampled longitudinally up to 24 hr post dosing. At these doses and time-points cells were viable and maintained tight junction function based upon: transepithelial electrical resistance (TEER) and lucifer yellow permeability (LY) testing. 2, 4-D concentrations in the apical chambers increased over time, and 2, 4-D concentrations in both

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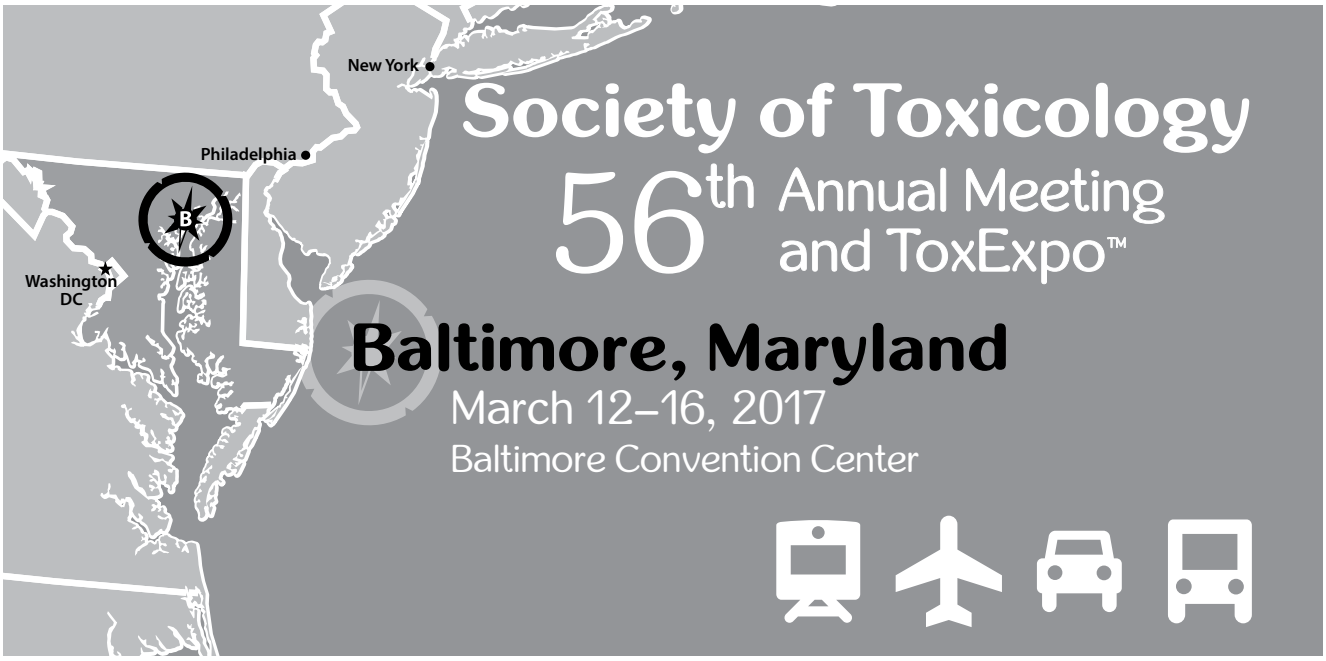

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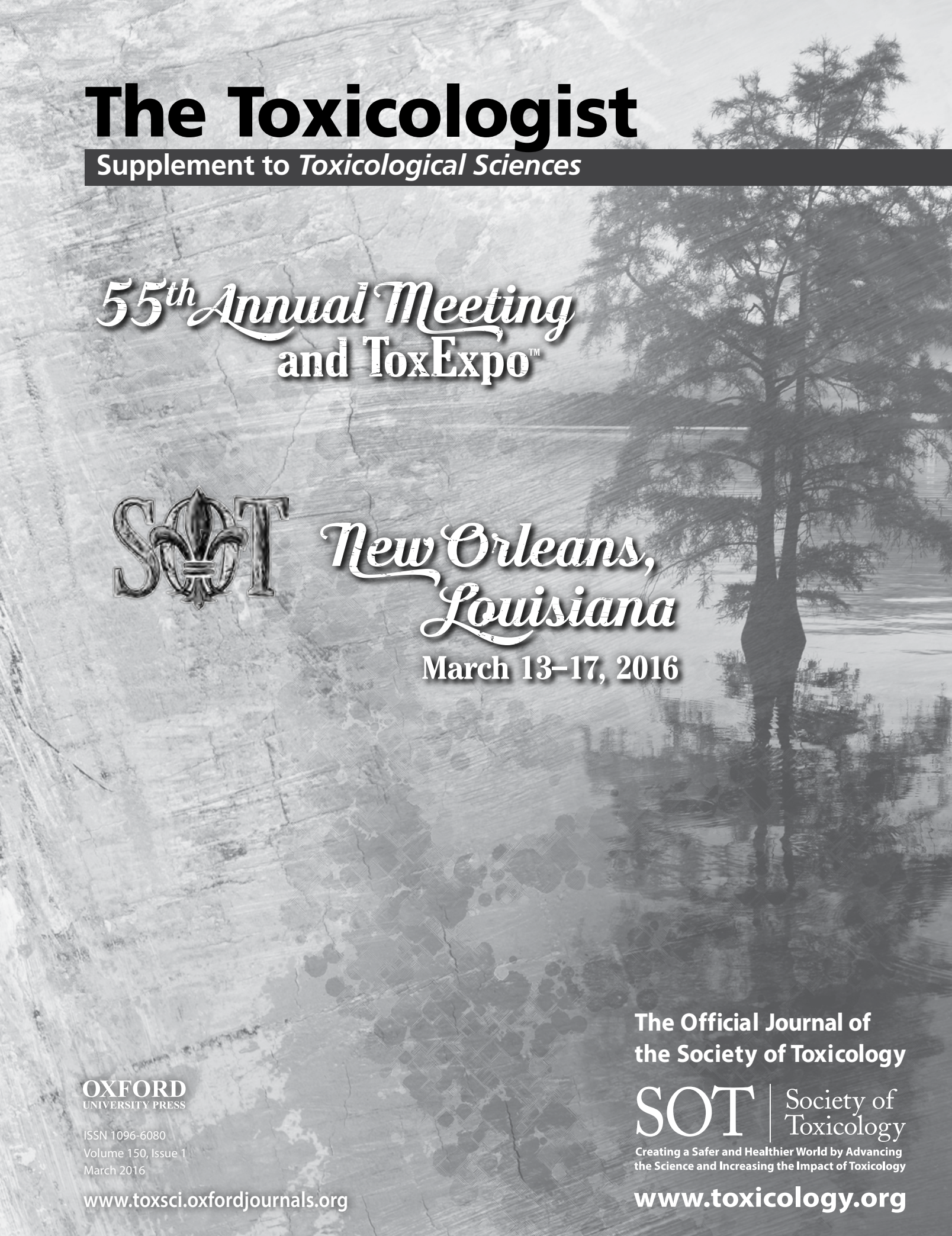

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Preface

This issue is devoted to the abstracts of the presentations for the Continuing Education courses and scientific sessions of the 55th Annual Meeting of the Society of Toxicology, held at the New Orleans Ernest N. Morial Convention Center, March 13–17, 2016.

An alphabetical Author Index, cross referencing the corresponding abstract number(s), begins on page 603.

The issue also contains a Keyword Index (by subject or chemical) of all the presentations, beginning on page 629.

The abstracts are reproduced as accepted by the Scientific Program Committee of the Society of Toxicology and appear in numerical sequence. Author names which are underlined in the author block indicate the author is a member of the Society of Toxicology. For example, J. Smith.

Scientific Session Types:

- CE Continuing Education Courses
- EC Education-Career Development Sessions
- FS Featured Sessions
- HH Historical Highlights Sessions
- IS Informational Sessions
- PL Platform Sessions
- PS Poster Sessions
- RI Regional Interest Sessions
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