phenyl (4-ABP). For this purpose, the cells were co-incubated for 24 h with 1 μM B[a]P + 10-100 μM 4-ABP and 1 μM B[a]P + 10-100 μM 2-NA. Compared to 1 μM B[a]P alone, co-treatment with 2-NA resulted in enhanced CYP1A1 activities (luminescent assay) and induction (immunoblots), whereas decreased activities and induction were observed for co-incubation with 4-ABP. In contrast, increased *anti*-BPDE-DNA adduct rates were observed for both co-exposures of B[a]P + 2-NA and B[a]P + 4-ABP and compared to 1 μM B[a]P alone. The effect was even more pronounced for co-exposures with 4-ABP than for 2-NA. We repeated the experiments in the presence of a specific arylhydrocarbon receptor (AhR) antagonist. Although, as expected, CYP1A1 activities and protein were no longer measurable, *anti*-BPDE-DNA adducts were still detectable. In case of co-exposures of B[a]P and 2-NA, the observed *anti*-BPDE adduct rates were even higher than in the absence of the AhR antagonist. Our results suggest that additional enzymes are responsible for the enhanced formation of *anti*-BPDE adducts in the presence of 2-NA and 4-ABP rather than CYP1A1 alone. Since the highest adduct rates were observed when CYP1A1 activities were low (4-ABP without AhR inhibitor) or completely inhibited (2-NA with AhR inhibitor), CYP1A1 appears to even have some detoxifying properties in the used cell model.

2087 Coupling *In Vitro* and Computational Methods to Investigate the Transport of Herbicide/Insecticide Mixtures into Saliva

A. A. Han[1], Z. A. Carver[2], T. J. Weber[1], C. Timchalk[1], and J. N. Smith[1]. [1]*Pacific Northwest National Laboratory, Richland, WA; and* [2]*Columbia Basin College, Pasco, WA.*

Portable sensors and PBPK models have previously been developed to describe the relationship between salivary and plasma concentrations of a commonly applied herbicide and insecticide metabolite: 2,4-Dichlorophenoxyacetic acid (2,4-D) and 3,5,6-trichloro-2-pyridinol (TCPy). These efforts not only offer a better understanding of potential adverse health effects elicited by common household chemicals but further provide justification for biomonitoring saliva to assess risks associated with chemical exposures. While understanding the pharmacokinetics of a single chemical is necessary, chemical mixtures are more reflective of the reality of everyday exposures. An *in vitro* system was employed to evaluate the chemical transport of a simultaneous dosing of 2,4-D and TCPy across a monolayer of serous-acinar cells cultured from the submaxillary saliva gland of Sprague-Dawley rats. The transport of chemicals across the cell layer (via passive diffusion) was influenced by the binding of proteins (i.e. unbound chemicals were able to pass through the cell layer). At a constant concentration of TCPy (200 μM), levels of protein bound to TCPy in cell culture media (Advanced DMEM:F12 supplemented with 2% fetal bovine serum) decreased as much as 52% with an increasing co-exposure to 2,4-D (0-2300 μM), indicating that these chemicals compete for common binding sites on proteins. This suggests that exposure to chemical mixtures may influence measureable levels of herbicides/insecticides in saliva samples. Additional protein binding (at physiological conditions) and kinetic cellular transport experiments quantifying chemical transport and binding rates were conducted to further explore implications of chemical mixtures transport. *Supported by Centers for Disease Control-National Institute for Occupational Safety and Health (CDC-NIOSH) grant R01 OH011023.*

2087a Combined Cytotoxic Effects of Lead (Pb) and Disinfection Byproducts (DBPs) on Chinese Hamster Ovary (CHO) Cells and Heterogeneous Human Epithelial Colorectal Adenocarcinoma (Caco-2) Cells

J. Liu[1], V. K. Sharma[1], and C. M. Sayes[2]. [1]*Texas A&M University, College Station, TX; and* [2]*Baylor University, Waco, TX.*

Disinfection aimed at inactivating pathogens is an essential process in drinking water treatment plants. Chlorine and chloramine are common disinfectants used in this process today. During disinfection, halogenated disinfection byproducts (DBPs) can be generated from the reactions of chlorine with natural organic matter (NOM) and bromide ions in source water. Halogenated DBPs have been shown to induce chronic adverse effects on cells in culture and rodent models. A certain amount of disinfectant residue is maintained in the water distribution system to prevent the regrowth of microorganisms. Lead (Pb)-containing plumbing materials are widely present in water distribution pipelines in the U.S. Disinfectant residues can react with the pipe materials and enable the release of lead (in the form of Pb^{2+}) in into water. Pb^{2+} is an abundant toxic metal ion that primarily affects the peripheral and central nervous systems, kidneys, red blood cells, and calcium metabolism after ingestion. In this study, we measured the toxicity of lead (Pb^{2+}) and halogenated DBPs on Chinese hamster ovary (CHO) cells and heterogeneous human epithelial colorectal adenocarcinoma (Caco-2) cells separately as well as the synergistic toxic effects of Pb^{2+} and DBPs co-exposures. Data was collected over a dose-response and time-response experimental design and compared to series of controls. The results showed the combined toxic effect of lead and each DBP on the cell cultures were both dose and time dependent. Our data suggest that lead (in the form of Pb^{2+}) affects the formation of DBPs and the overall quality of drinking water.

2087b Report of the 2017 Society of Environmental Toxicology and Chemistry (SETAC) Conference on Risk Assessment of Chemical Mixtures

M. Mumtaz[1], M. Johnson[2], E. Genderen[3], M. Ottinger[4], A. Beasley[5], E. Furlong[6], K. Brix[7], T. Schlekat[8], and T. Backhaus[9]. [1]*CDC/ATSDR, Atlanta, GA;* [2]*US Army, Aberdeen Proving Ground, MD;* [3]*International Zinc Association, San Rafael, CA;* [4]*University of Houston, Houston, TX;* [5]*The Dow Chemical Company, Midland, MI;* [6]*US Geological Survey, Denver, CO;* [7]*EcoTox, Miami, FL;* [8]*SETAC, Pensacola, FL; and* [9]*University of Gothenburg, Gothenburg, Sweden.*

Exposure to complex mixtures, sequentially or simultaneously, has the inherent potential to impact our health and that of the environment. Presence does not mean risk, hence assessments are conducted to evaluate the degree of risk(s) and when necessary mitigate exposures. SETAC recently held a Focused Topic Meeting on mixtures to review the current state of the science for conducting and interpreting the risk of chemical mixtures using a "One Health" approach. International experts invited from Asia, Europe, and the United States presented their perspectives and opinions on various facets of the risk assessment paradigm for mixtures of pharmaceuticals, pesticides, industrial organic pollutants, and metals. Examples and case studies from the conference included reasonableness of the dose additivity assumption, incidence of non-additive interactions, approaches for assessing undefined mixtures, use of adverse outcome pathway (AOP), and priority mixtures warranting specific attention. A general conclusion was that mixtures matter, and the dose addition approach was considered to be generally applicable for mixture toxicity assessments using a variety of human and ecological toxicity assays. Currently available methods and guidance provide the necessary degree of flexibility, including the use of *in vitro* data as research continues to fill data gaps. However, additional empirical data are needed to prudently regulate mixtures in environmental as well as human health contexts. *The findings and conclusions in this presentation have not been formally disseminated by the Centers for Disease Control and Prevention/the Agency for Toxic Substances and Disease Registry and should not be construed to represent any agency determination or policy.*

2088 Computational Association of Chronic Phosphate Exposure, Askaf Consumption, and Celiac Disease in the Saharawi People of Western Sahara

S. Kumar, L. Lau, S. Tran, H. Do, M. Tawiah, and D. E. Johnson. *University of California Berkeley, Berkeley, CA.*

Celiac disease (CD) is a long-term autoimmune disease affecting 1% of people globally; whereas, the Saharawi people of Western Sahara have an unusually high incidence of 5.6%. The Saharawi possess the HLA-DQ2 isoform, making them genetically predisposed to CD. A change in dietary habits over the last few decades may also be responsible for the Saharawi's high incidence of celiac disease. Prior to the introduction of the European diet, the Saharawi subsisted on mainly camel meat and milk. While it is possible that the increased consumption of gluten-heavy foods may play a role in elevated disease incidence, other populations have a much lower prevalence of CD with similar diet consumption and HLA-DQ2 frequencies. The aim of this study was to determine whether there is an additional environmental component that increases the susceptibility of the Saharawi. The Saharawi live on 75% of the world's phosphate rock and consume a local plant Askaf in large amounts, primarily in camel milk. A systems approach was used to determine chemical-gene interactions for phosphate and relevant phytochemicals in Askaf. Research shows that phosphate can stimulate Akt signaling, leading to increased downstream T-cell activation, B-cell activation and antibody production, resulting in greater CD pathology. In addition, flavonoids in Askaf can increase the expression of CTLA-4, an inhibitory receptor on regulatory T-cells, thereby suppressing the immune system. Saponins in Askaf can decrease Akt signaling, thereby decreasing T-cell activation and B-cell antibody production. From these findings, it was concluded that chronic phosphate exposure may contribute to a high incidence of CD in the Saharawi, and the decreased

The Toxicologist

Supplement to
Toxicological Sciences

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San Antonio, Texas
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OXFORD
UNIVERSITY PRESS

ISSN 1096-6080
Volume 162, Issue 1
March 2018

www.academic.oup/toxsci

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the Society of Toxicology

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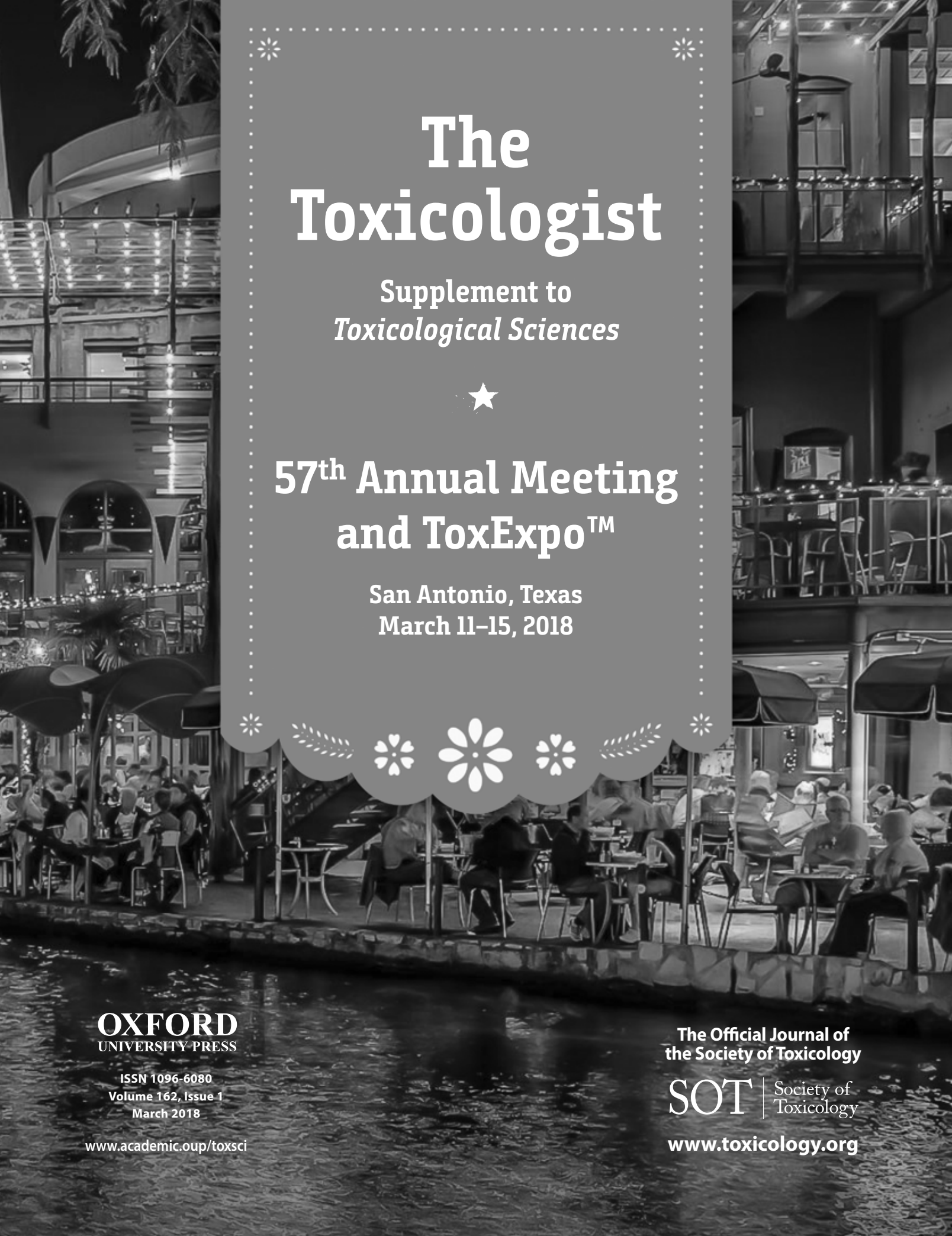

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