alone on Day 1 immediately following dAb X administration. A single dose of dAb X at 20 mg/kg had no effect on the robust anti-KLH memory IgG response in this study. It is likely the large magnitude of memory IgG response to clinical grade KLH as compared to the primary IgG response in the first study prevented suppression by dAb X.

## 1122 Withdrawn by Author

## 1123 Role of the AhR in Immunoglobulin Expression and Antibody Isotopic Profile in a Human B Cell Line

V. Enukonda, C. Buckner, N. Alhamdan, and C. Sulentic. *Wright State University, Dayton, OH.*

B cells play a crucial role in the immune response, but several xenobiotics such as 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) have been shown to affect the function of these cells. In animal models, TCDD inhibits immunoglobulin (Ig) expression and secretion in an aryl hydrocarbon receptor (AhR)-dependent mechanism. The effect of TCDD on human B cells is less clear with studies showing interindividual variation in the effect on IgM secretion. Using a human B cell line (CL-01) and ELISA analysis, we have shown negligible effects of TCDD on stimulation-induced IgM expression, but significantly inhibited IgG expression. Compared to stimulation alone, a co-treatment with the AhR antagonist CH223191 (AhRA) induced significantly higher IgG expression. This effect was antagonized by TCDD co-treatment. The objective of the current study is to determine the role of the AhR in the effects of TCDD and AhRA on IgG secretion and the expression of all eight isotypes (IgM, $IgG_{1\text{-}4}$, $IgA_{1\text{-}2}$, IgE). To evaluate the AhR, we utilized CRISPR/Cas9 gene-editing to generate CL-01 subclones that either have a significant knockdown of AhR expression (AhR KD) or express an AhR with or without a functional transactivation domain (TAD+ or TAD-). The functional status of AhR transactivation was confirmed for each subclone using a luciferase reporter plasmid regulated by six dioxin response elements linked in tandem. The inhibitory effect of TCDD on IgG secretion was similar in both the TAD+ and TAD- subclones. In contrast, IgG secretion was dramatically inhibited in the AhR KD cells. These results suggest that the AhR has a physiological role in IgG secretion and that altered IgG secretion by TCDD involves a nonclassical AhR signaling pathway. Ongoing efforts are focused on evaluating the expression of all antibody isotypes via quantitative real-time PCR in all three CL-01 subclones (AhR KD, AhR TAD+, AhR TAD-). This study will determine how the AhR affects the Ig isotypic profile and the role of classical DRE-mediated signaling vs. nonclassical signaling. Altered expression of specific antibody isotypes could significantly impact immune responses to pathogens or inappropriate immune responses, such as hypersensitivity or autoimmune disease.

## 1124 Computational Association of Polychlorinated Biphenyl Bioaccumulation in Great Lakes Regions and Potential Risk of Inflammatory Bowel Disease

J. M. Hendricks, L. S. Afonso, J. L. Shu, M. Vora, K. M. Koh, and D. E. Johnson. *University of California Berkeley, Berkeley, CA.*

Polychlorinated biphenyls (PCBs), as industrial byproducts, continue to contaminate the Great Lakes and bioaccumulate in wildlife and humans in areas of Michigan. In addition, certain Michigan populations have increased incidences of inflammatory bowel disease (IBD), a chronic, relapsing intestinal inflammatory disease due to irregular intestinal mucosal immune system activation. This current study probes the potential association of PCB contamination and IBD in specific areas of Michigan where PCB river contamination continues to be problematic. Using a computational systems disease read-across approach incorporating comparative inflammatory-related diseases prevalent in the study area including colorectal cancer (CC), and the two principal types of IBD, inflammatory ulcerative colitis (UC) and Crohn's Disease (CD), disease-gene networks were developed and common nodes among the disorders were analyzed. Detailed disease incidence maps were developed for the region and genetic susceptibilities through inflammatory cytokine regulation were proposed for both CC and IBD based on local heritage. Of major interest was a SNP of the transporter ABCB1 which is crucial for cellular efflux of chemicals. Potential PCB and ABCB1 interaction was confirmed with a computational chemical/protein docking model. In addition, in this area Mycobacterium avium subspecies paratuberculosis (MAP) infection has been linked to CD. Studies in animals have shown a decrease in MAP IgG after PCB exposure thereby decreasing immunity to IBD. Based on the comparative networks and association analyses, a molecular initiating event for potential PCB-associated-IBD was proposed: PCB induces ABCB1 disruption, which would lead to bioaccumulation of xenobiotics and inflammatory mediators within intestinal cells, exacerbated by MAP infection and resulting in sustained inflammation.

## 1125 Ethanol-Induced Gastric Ulcer: Molecular Ulcerogenic Mechanism

M. W. Owonikoko, and K. O. Ajeigbe. *Igbinedion University, Okada, Benin, Nigeria.* Sponsor: C. Alimba

Ethanol is one of the numerous gastrointestinal toxicants to which humans are consciously and deliberately exposed daily. Ethanol-induced gastric ulcer is one of the widely studied experimental ulcers among other ulcer models. The fulcrum for this established fact is due both to pathological semblance of the model with most of the symptoms observed in gastric ulcers and most importantly in alcoholics and easy reproducibility of the method. For instance, many bioactive compounds in different plants have been known to show gastric anti-ulcer potencies against ethanol-induced gastric ulcer. This may be attributed to the ability of these agents to interfere with one or more of the cascade of steps involved in the pathogenesis of gastric ulcer as they have been variably reported to be cytoprotective or gastroprotective. However, despite replete simulation of the gastric ulcer method in literature, very little is known about the mechanism involved in its pathogenesis. A thorough literature search through medline was made between year 1997 and 2017 for this purpose and was used as the basis for this review. The review holistically analyse the mechanism, at the molecular level, involved in ethanol induced gastric ulcer model in relations to the healing.

## 1126 *In Vitro* Cytotoxicity and Inflammatory Responses Elicited by Different Types of Rock Dust: Similarities and Material-Specific Differences

A. A. Shvedova[1,2], A. Menas[1], N. Yanamala[1], S. Guppi[1], D. Schwegler-Berry[1], T. Lee[3], M. Harper[4], and E. R. Kisin[1]. [1]*NIOSH, Morgantown, WV;* [2]*West Virginia University, Morgantown, WV;* [3]*NIOSH, Pittsburgh, PA; and* [4]*Zefon International, Ocala, FL.*

Rock dusting in underground coal mines helps to prevent the propagation of coal dust explosions. The commonly used rock dust refers to limestone or marble dusts which may be utilized as is or treated to prevent clumping under high humidity conditions. Although potential occupational exposures to rock dust are real, safety or toxicity information on such exposures are largely lacking. The aim of this study was to evaluate the cytotoxicity, cellular damage and inflammatory responses of respirable untreated limestone (UL) and marble (UM) rock dust as well as to examine whether the treatment of dust affects the outcomes. Human lung epithelial cells (A549) were exposed for 24 and 72 h to various concentrations (0 - 1mg/ml) of four rock dust samples. The results showed dose- and time-dependent cytotoxicity and cell damage with the least effect upon exposure to treated limestone (TL). The extent of inflammatory responses evaluated by the number of cytokines produced and released, increased with the concentration of tested materials. Clustering analysis of the inflammatory cytokines/chemokines revealed an overall stronger effect of marble compared to limestone samples. Furthermore, untreated rock dust induced a greater inflammatory response as compared to treated samples in both cases. Similar to the cytotoxic and cell damage results, treated limestone revealed the lowest inflammatory response compared to other samples. Overall, our results unveiled treatment related differences as well as material dependent changes in biological responses.

## 1127 Defining Interstitial Macrophage Populations in Lungs and Changes Based on Nanomaterials

A. T. Lanphear, P. Fletcher, P. Shaw, and C. Migliaccio. *University of Montana, Missoula, MT.*

Nanoparticles are increasingly utilized in fields such as medicine, agriculture, and industry. Carbon nanotubes have important uses in many of these fields, so understanding their potential for adverse effects is vital. Macrophages are a key component of the immune system and are known to separate into functional subsets that generate distinct responses in the body. Pulmonary macrophages, key regulators of immune responses to respiratory exposures, have yet fully to be sep-

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OXFORD
UNIVERSITY PRESS

ISSN 1096-6080
Volume 162, Issue 1
March 2018

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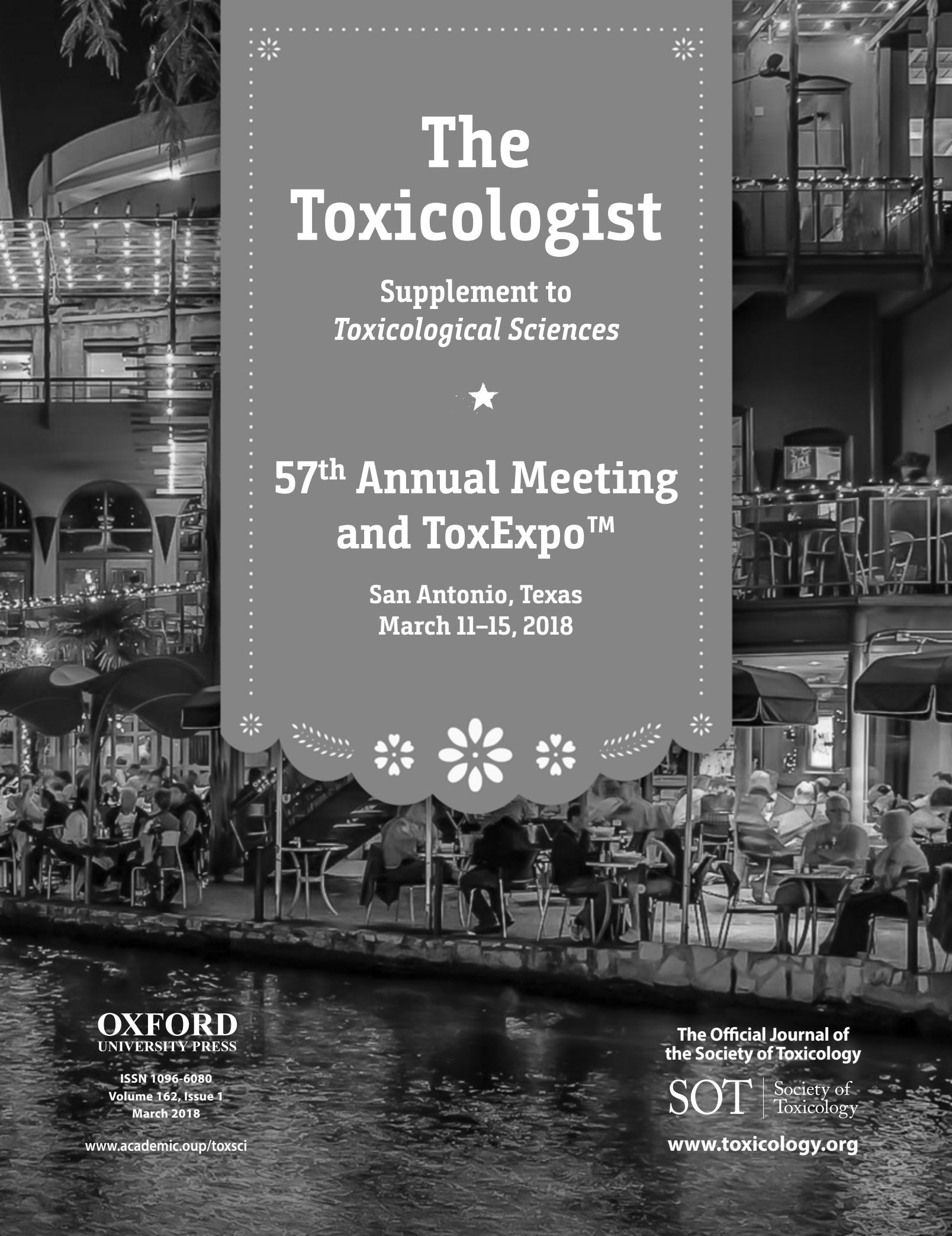

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