strongest activation of nuclear factor-κB (NF-κB). In conclusion, we show that 1-NP and 1-AP induce different cytokine/chemokine expression patterns in BEAS-2B cells. This seems to be linked to differential activation of transcription factors including NF-κB and AP-1. Furthermore we hypothesize that the effects of silencing AhR and ARNT on chemokine release are due to interactions between AhR and NF-κB.

PS 737 DEVELOPMENT OF A MODIFIED GLUCAN-SPECIFIC LIMULUS AMEBOCYTE LYSATE METHOD WHICH CORRELATES MURINE PULMONARY INFLAMMATION INDUCED BY FLOOR DUST COLLECTED FROM A WATER-DAMAGED BUILDING.

S. Young, J. M. Cox-Ganser, E. S. Shogren, M. G. Wolfarth, S. Li, J. M. Antonini, V. Castranova and J. Park. *NIOSH, Morgantown, WV.*

1Ç3-β-glucan, a major cell wall component of fungi, induces pulmonary inflammation. There is inconsistency in correlation between the levels of glucan measured by current detection methods and the respiratory inflammation observed in people or laboratory animals exposed to fungi. There is a need for a method that better assesses the inflammatory potential of 1Ç3-β-glucans in environmental samples. We used the glucan-specific (G-specific) Limulus Amebocyte Lysate (LAL) method after extraction with dimethyl sulfoxide (DMSO), sodium hydroxide (NaOH), or water to analyze the glucan content in floor dusts from a water-damaged building. C3HeB/FeJ mice, an endotoxin-sensitive strain, were treated with different dusts (2.5 mg/kg of body weight), or saline (vehicle control) by pharyngeal aspiration. At 18 hr after aspiration, bronchoalveolar lavage (BAL) was performed, and lung inflammation and injury were assessed by measuring: (1) neutrophil (PMN) infiltration, (2) inflammatory cytokines (IL-6, IL-10, MCP-1, IFN-γ, TNF-α, and IL12-p70) levels and (3) albumin and lactate dehydrogenase in recovered BAL fluid. Both DMSO and NaOH extaction increased the detection of glucan by ~20 fold compared to water extraction. Only the DMSO extraction method showed a statistically significant correlation ($p<0.05$) between 1Ç3-β-glucan levels and albumin, total BAL cells, PMNs recovered, TNF-α, MCP-1, and IL-6. As expected, significant positive correlations ($p<0.05$) were also found comparing endotoxin levels and BAL cell numbers, PMNs recovered, IL-6, IFN-γ and MCP-1. In conclusion, DMSO extraction for glucan analysis may prove useful in understanding the impact of environmental contamination of glucans on lung disease.

PS 738 ROLE OF SURFACTANT PROTEIN D IN OZONE-INDUCED LUNG INJURY AND INFLAMMATION.

A. M. Groves[1], A. Gow[1], J. D. Laskin[2] and D. L. Laskin[1]. *[1]Rutgers University, Piscataway, NJ and [2]UMDNJ-RWJ Med School, Piscataway, NJ.*

Ozone is a ubiquitous urban air pollutant known to induce lung injury and inflammation. This is associated with the release of nitrogen species (RNS) which contribute to toxicity. Surfactant protein-D (SPD)functions to down regulate inflammation. We examined the role of SPD in ozone-induced lung toxicity. Exposure of mice to ozone (0.8 ppm, 3h) resulted in RNS-mediated posttranslational modifications of SPD causing it to become a pro-inflammatory mediator, a possible mechanism whereby RNS induce pulmonary inflammation. To investigate this, we used SPD-/- mice. Ozone inhalation resulted in increased BAL protein levels and macrophage content, markers of lung inflammation and injury in both wild type and SPD-/- mice, 72 hr post exposure. These effects were more pronounced in SPD-/- mice. Greater levels of NOx were also detected in BAL from SPD-/- mice, as well as increased numbers of iNOS positive macrophages in lung tissue. Using a SCIREQ FlexiVent, we next analyzed pulmonary function. Total lung resistance (RL) increased in both WT and SPD-/-mice in response to increasing positive end expiratory pressure (PEEP). This was due to increases in central airway resistance (Rn) and static compliance (Cst). Whereas RL was greater in SPD-/-mice when compared to WT mice, at all PEEPs, Cst values were only greater at low PEEPs. These results are consistent with an emphysematous morphology in lungs of SPD-/- mice. Exposure of WT mice to ozone resulted in increased RL with little change in Cst. At low PEEPs, Rn also increased in WT mice following ozone inhalation. These findings indicate that ozone induces restrictive lung disease. Exposure of SPD-/- mice to ozone resulted in decreases in RL, Rn and Cst to levels observed in ozone exposed WT mice, indicating that the effects of ozone on respiratory mechanics are more significant than the loss of SPD. These results suggest that SPD plays distinct roles in ozone-induced pulmonary inflammation and altered lung functioning. Supported by ES007148, GM034310, ES004738, CA132624, AR055073, HL074115 and ES005022.

PS 739 IDENTIFICATION OF CYTOKINES AND GROWTH FACTORS ASSOCIATED WITH EXPOSURE OF MESOTHELIAL CELLS TO ASBESTOS AND PROGRESSION OF MESOTHELIOMA GROWTH IN MICE.

J. M. Hillegass[1], A. Shukla[1], M. MacPherson[1], S. Beuschel[1], S. Lathrop[1], C. Steele[2] and B. Mossman[1]. *[1]Pathology, University of Vermont, Burlington, VT and [2]Medicine and Microbiology, University of Alabama at Birmingham School of Medicine, Birmingham, AL.*

The mechanisms by which pathogenic particulates such as asbestos cause injury to lung and pleural cells remain unclear, although chronic inflammation has been linked to initiation and progression of numerous cancers, including malignant mesothelioma (MM). The purpose of the studies described here was to examine the ability of a contact-inhibited hTERT-immortalized human peritoneal mesothelial cell line (LP9/TERT-1) and two human MM cell lines (PPM Mill, Hmeso) to release cytokines/growth factors in response to either crocidolite asbestos exposure *in vitro*, or inoculation of MM cells into immunodeficient SCID mice. *In vitro* Bio-Plex studies demonstrated that exposure of LP9/TERT-1 cells to asbestos increased the amount of IL-1β, IL-6, IL-13, bFGF, G-CSF, and VEGF secreted into medium, suggesting that asbestos may elicit a number of autocrine growth factor pathways in mesothelial cells. Peritoneal xenograft studies in SCID mice using PPM Mill and Hmeso cells revealed enhanced cell injury as illustrated by increases in peritoneal lavage fluid (PLF) lactate dehydrogenase levels, neutrophilia as determined by cell differential counts of PLF cytospins, and increases in IL-1β, IL-6, IL-7, IL-8, IL-12 (p70), MCAF, and VEGF at 4 weeks post-inoculation as shown via Bio-Plex analysis of PLF. These changes corresponded with the time-dependent establishment of tumor spheroids and mesenteric masses within the peritoneal cavity. Overall, these results demonstrate that human mesothelial and MM cells have independent roles in producing cytokines/growth factors linked to inflammation and carcinogenesis. Additionally, determining early molecular responses to crocidolite asbestos exposure and MM tumor formation may directly contribute to understanding the etiology of this disease and aid in identifying targets for therapeutic intervention. Support: NIEHS T32ES0071, Mesothelioma Applied Research Foundation.

PS 740 INHIBITION OF CF AIRWAY HMGB1 REDUCES *P. AERUGINOSA* INFECTION AND NEUTROPHILIC INFLAMMATORY LUNG INJURY.

L. Mantell[1, 2], T. Zaher[1], D. Weiss[3], E. Miller[2] and K. J. Tracey[2]. *[1]Pharmaceutical Sciences, St. John's University, Queens, NY, [2]Center for Lung and Heart Research, The Feinstein Institute for Medical Research, NS-LIJ Health System, Manhasset, NY and [3]Medicine, University of Vermont College of Medicine, Burlington, VT.*

Despite advances in the understanding of the pathogenesis of CF and the improvement in its management, the average life span of individuals with CF remains short. Chronic pulmonary infection with *Pseudomonas (P.) aeruginosa* and persistent neutrophilic lung inflammation contribute to the morbidity and mortality associated with CF patients. High mobility box group 1 (HMGB1), a proinflammatory cytokine, has recently been implicated in mediating neutrophilic inflammation in CF in the absence of infection. We show here that HMGB1 levels were elevated in bronchoalveolar lavage fluids (BAL) of CF patients and CFTR-/- mice. In both WT and CF mice infected with P. aeruginosa, treatment with neutralizing monoclonal anti-HMGB1 antibody significantly reduced neutrophilic infiltration, bacterial burden and injury in the lung. Notably, recombinant HMGB1 directly inhibited the ability of isolated macrophages to phagocytose and kill P. aeruginosa. A similar suppression in macrophages' ability to phagocytose bacteria was invoked by BAL from CF patients and this suppression was reversed by HMGB1-neutralizing antibodies. Interestingly, toll-like receptor 4 (TLR4) on macrophages plays an essential role in signaling HMGB1-mediated macrophage dysfunction. These findings suggest that HMGB1 and downstream signaling molecule TLR4 could provide novel therapeutic targets for reducing both lung inflammation and bacterial infection in CF patients.

PS 741 RODENT INHALATION STUDIES AND CIGARETTE SMOKE: INFLAMMATION-MEDIATED PROMOTION OF TUMOR CELLS.

G. M. Curtin and J. E. Swauger. *Regulatory Oversight, RAI Services Company, Winston Salem, NC.*

A rodent inhalation model capable of reproducibly demonstrating dose-dependent increases for lung tumor development in response to cigarette smoke exposure has yet to be developed. Model development efforts have generally presumed that cigarette smoke mediates lung tumor development primarily through genetic damage.

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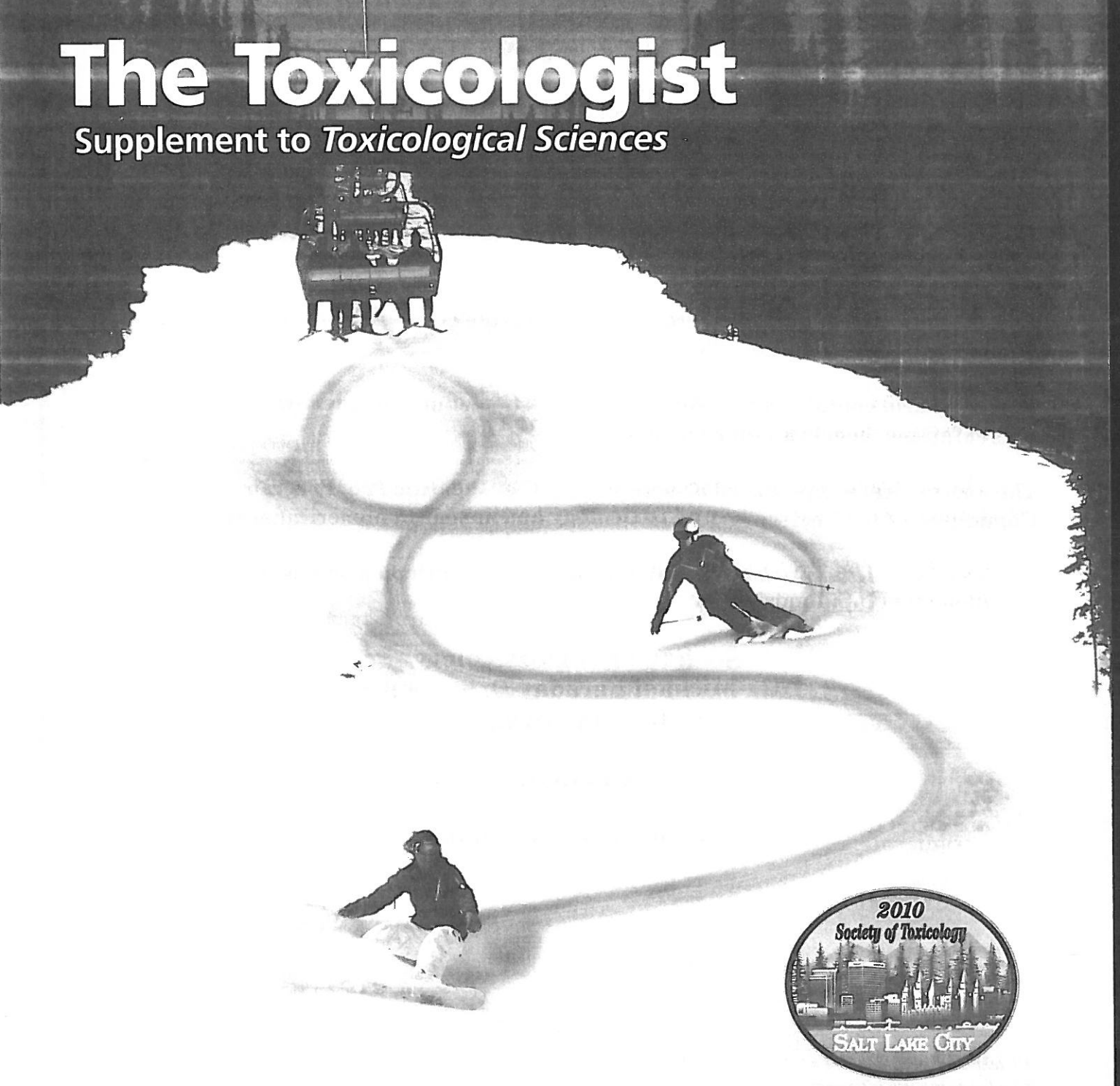

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Preface

This issue of *The Toxicologist* is devoted to the abstracts of the presentations for the Continuing Education courses and scientific sessions of the 49th Annual Meeting of the Society of Toxicology, held at the Salt Palace Convention Center, March 7–11, 2010.

An alphabetical Author Index, cross referencing the corresponding abstract number(s), begins on page 473.

The issue also contains a Key Word Index (by subject or chemical) of all the presentations, beginning on page 496.

The abstracts are reproduced as accepted by the Scientific Program Committee of the Society of Toxicology and appear in numerical sequence.

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