72, 2011). The purpose of this study was to determine whether LPS isolated from the freshwater cyanobacterial species *Scytonema javanicum*, *S. ocellatum*, *Nostoc sp.*, *Anabaena sp.*, and *Hapalosiphon fontinalis* (CyaLPS) "classically" activated BMG *in vitro* and concomitant release of thromboxane B_2 (TXB_2), superoxide anion (O_2^-) and tumor necrosis factor-α (TNF-α). CyaLPS was isolated by hot phenol/water extraction. BMG were isolated from neonatal rats, and treated *in vitro* with 0.1-10^5 ng/mL CyaLPS for 17 hours at 35.9 °C. TXB_2 and TNF-α were determined by ELISA, O_2^- by cytochrome C reduction, and lactate dehydrogenase (LDH) by enzyme activity. The study revealed that CyaLPS was cytotoxic to BMG at greater than 10^3 ng/mL as shown by concentration-dependent LDH release. Furthermore, O_2^- and TNF-α generation were observed at CyaLPS ≥ 0.1 ng/mL and > 10^3 ng/mL, respectively, while in contrast TXB_2 production was variable and observed at CyaLPS ≥ 10-10^3 ng/mL. We conclude that CyaLPS classically activated BMG in our *in vitro* experimental conditions, thus extending our published findings with *M. aeruginosa* LPS to other cyanobacterial species. Our results provide further insight into proinflammatory mediators released by CyaLPS-treated BMG that may contribute to self-injury and/or neuronal toxicity *in vivo*. Continued investigation of CyaLPS chemistry as well as its *in vitro* immunotoxicology are currently ongoing in our laboratories. Supported by Midwestern University and the University of Hawaii at Manoa.

PS 715 DOES AFGHANISTAN SAND DUST INHALATION INFLUENCE MILD BLAST-INDUCED IMMUNE AND COGNITIVE RESPONSES?

P. Gunasekar, S. Prues, D. Stoffregen, A. James, S. McInturf and A. Osterburg. *Naval Medical Research Unit, Wright-Patterson AFB, Dayton, OH.*

Soldiers have significant exposure to particulate matter, including when they are subjected to a blast injury. Evidence suggests that inhalation of sand induces an inflammatory response in rats, and if borne out, may indicate a potential response in humans. Additionally, there exists a possibility that inhaled dust containing potentially harmful metals and chemical components may enter the brain and contribute to blast-trauma induced damage and to the development of neurological disorders. Identifying relevant blast injury pathogenic pathways and neurobehavioral deficits is vital for development of mild injury diagnostic biomarkers. In this study, rats were exposed to shock wave pressure to simulate mild traumatic brain injury (mTBI) with and without Afghanistan sand pre-exposure by nose inhalation. Prior to sacrifice, neurobehavioral tests were performed on 7, 14 and 28 days post-trauma animals. MWM tests revealed no significant difference among groups for amount of time taken to locate the platform. Animals that were exposed to dust PM alone or with blast did not appear to have learning and memory deficits at all time points studied. Flow cytometric analysis of splenocytes immunophenotyped with lymphocyte antibodies demonstrated reduction in activation of cytotoxic and helper T-cells in blast/sand exposed rats 3 days after trauma. The ratio of cytotoxic and helper T-cells decreased which indicate the vulnerability of the animals in response to blast/sand dust exposure. At 7 days post injury, significant increases in numbers of B-cell lymphocytes by sand exposure, blast or both compared to control. However, mTBI or sand alone has no significant influence on cytotoxic T-cells, helper T-cells and NK cells. Further, blast trauma rats pre-exposed to sand did not influence or exacerbate B-cell activation or subpopulations of immune cells. Thus, data on mTBI model demonstrates that some immune cells are potentially modulated at early time points due to neuroinflammatory insult during blast injury in conjunction with sand dust.

PS 716 DEFICIENCY IN CD44S ENHANCES DEXTRAN SODIUM SULPHATE (DSS)-INDUCED COLITIS AND INFLAMMATORY TOXICITY IN THE COLON.

I. Altamemi, M. Nagarkatti and P. Nagarkatti. *Pathology, Microbiology, and Immunology, University of South Carolina, School of Medicine, Columbia, SC.*

Inflammatory bowel disease (IBD) is a chronic, relapsing and remitting inflammatory condition. CD44 is a widely expressed family of adhesion receptors. The most common form of CD44, referred to as CD44 standard form (CD44s) does not contain differentially spliced exons.
The objective of this study is to find out the role of CD44s form on inflammation associated with dextran sodium sulphate (DSS)-induced colitis in mice. To this end, CD44s knockout (KO) mice and wildtype C57BL/6 mice were used to induce colitis with 3%DSS. Survival rates, body weight, extent of tissue damage were assessed. In addition, serum amyloid A (SAA) and inflammatory cytokine IL-6 were quantitated. Splenic and mesenteric lymph node cells were analyzed for expression of CD3, CD4, CD8, NK1.1, CD69, and CD19. In addition, CD11b+Gr-1+ MDSCs were also enumerated.
Our current study shows that CD44s KO mice exhibited increased DSS-induced acute colitis, as reflected by high lethality, weight loss, and histological scores compared to wild type mice. Also, SAA level in CD44s KO mice were higher. In addition, IL-6 showed high levels of expression in CD44s KO DSS-treated group, whereas undetectable levels were found in other groups. The flow cytometry results demonstrated that the proportions of MDSCs, CD19+ cells, and activated T cells (CD3+CD69+) in mesenteric lymph node were higher in CD44sKO DSS-treated group compared to wild type DSS-treated mice, whereas NKT (CD3+NK1.1+) cells were lower in CD44sKO DSS-exposed group when compared to wild-type mice. In conclusion, CD44s deficiency enhances inflammation in the colon thereby suggesting that targeting CD44 may serve as a novel approach to treat colitis (Supported in part by VA Merit BX001357, NIH grants R01AT006888, R01ES09098, P01AT003961, and R01ES019313; Iraqi Government).

PS 717 PULMONARY PATHOGENICITY OF AMBIENT PARTICULATE DUST FROM IRAQ MILITARY FIELDS.

N. R. Fix[1], D. L. Pack[1], L. A. Battelli[1], M. W. Barger[1], A. J. Kenyon[1], T. G. Meighan[1], J. A. Lewis[2], D. A. Jackson[2], V. Castranova[1] and S. S. Leonard[1]. *[1]National Institute of Occupational Safety and Health (NIOSH)/CDC, Morgantown, WV and [2]US Army Center for Environmental Health Research, Fort Detrick, MD.*

The pathological response in relation to physical/chemical and morphological properties of ambient particulates from Iraq has become an area of great interest. This study investigated the role of metal contaminants present in ambient dust in the induction of pulmonary injury and examined the potential pulmonary risks from exposure to Iraqi particulate matter. Adult male Sprague-Dawley [Hla(SD) CVF] rats were dosed via intratracheal instillation (IT) with phosphate buffered saline (PBS) as control, ambient dust collected from Camp Victory, Iraq (CV), or NIST SRM1649b U.S. urban particulate matter suspended in PBS at doses of 2.5, 5, or 10 mg/kg/body weight. Responses were then examined at 60, 120, and 150 days post IT. Blood collection via cardiac puncture and bronchoalveolar lavage (BAL) were performed. Measurement of lactate dehydrogenase (LDH), albumin, TNF-α, and cell differentials were conducted to access lung damage and inflammation. Differences in lung cell proliferation were examined via BrdU assay. Histopathological analysis was investigated using Mason's Trichrome, Alcian Blue PAS, and H & E grading. The results from the LDH, albumin, and TNF- α showed no significant differences from control in all exposures. However, a significant difference was found in macrophage and neutrophil response in NIST (10mg/kg) at 150 days and CV (10 mg/kg) at all exposures compared to control. CV (5 mg/kg) dose also showed a significant difference in macrophages and neutrophil response at the 150 day time point compared to control. Our results indicate that a high dose of CV and NIST can induce pulmonary inflammation, but to a lesser degree than a highly fibrogenic particle (Min-U-Sil) at the same time point and concentration as determined by a previous study.
Opinions, interpretations, conclusions, and recommendations are those of the authors and are not necessarily endorsed by the US Army or NIOSH.

PS 718 ASIAN SAND DUST ENHANCES MURINE LUNG INFLAMMATION CAUSED BY *KLEBSIELLA PNEUMONIAE.*

M. He[1, 4], T. Ichinose[1], S. Yoshida[1], S. Yamamoto[2], K. Inoue[2], H. Takano[2], R. Yanagisawa[2], M. Nishikawa[3], I. Mori[3], G. Sun[4] and T. Shibamoto[5]. *[1]Department of Health Sciences, Oita University of Nursing and Health Sciences, Oita, Oita, Japan, [2]Pathophysiology Research Team, National Institute for Environmental Studies, Tsukuba, Ibaraki, Japan, [3]Environmental Chemistry Division, National Institute for Environmental Studies, Tsukuba, Ibaraki, Japan, [4]Department of Environmental and Occupational Health, College of Public Health, China Medical University, Shenyang, Liaoning, China and [5]Department of Environmental Toxicology, University of California Davis, Davis, CA.* Sponsor: Y. Sun.

Concomitant inhalation of Asian sand dust (ASD) and pathogen may result in exacerbation of pneumonia by the pathogen. The exacerbating effect of ASD on pneumonia induced by *Klebsiella Pneumoniae* (KP) was investigated in ICR mice. The organic substances adsorbed onto ASD collected from the atmosphere of Iki-island in Japan were excluded by heat treatment at 360°C for 30 min. ICR mice were instilled intratracheally with ASD at doses of 0.05 mg or 0.2 mg/mouse four times at 2-week intervals and were administrated with ASD in presence or absence of KP at the last intratracheal instillation. Pathologically, ASD caused exacerbation of pneumonia by KP as shown by increased inflammatory cells within the bronchiolar and the alveolar compartments. ASD enhanced dose dependently neutrophil number and expression of cytokines (IL-1β, IL-6, IL-12, IFN-γ, TNF-α,) and chemokines (KC, MCP-1, MIP-1α) in BALF related to KP. In an in vitro study using RAW264.7 cells, the treatment of ASD and KP increased gene expression of IL-6, IFN-β, TNF-α, KC, MCP-1 and MIP-1α and tend to increase the protein level of IL-1β, TNF-α, MCP-1 and MIP-1α in culture medium compared with each alone treatment. The combined treatment tends to increase the gene expression of Toll-like receptor 2 (TLR2), and NALP3, ASC and caspase-1 compared with KP alone. These results suggest that the exacerbation of pneumonia by ASD + KP could be due to the enhanced production of pro-inflammatory mediators via activation of TLR2 and NALP3 inflammasome pathway in alveolar macrophages.

The Toxicologist

Supplement to *Toxicological Sciences*

51st Annual Meeting and ToxExpo™

March 11–15, 2012 • San Francisco, California

SOT 2012 San Francisco California

An Official Journal of the Society of Toxicology

SOT | Society of Toxicology

Creating a Safer and Healthier World by Advancing the Science of Toxicology

www.toxicology.org

OXFORD UNIVERSITY PRESS

ISSN 1096-6080
Volume 126, Issue 1
March 2012

www.toxsci.oxfordjournals.org