further reflected in the kidneys of lupus-prone mice by delayed onset of proteinuria and reduction of glomerulonephritis. The percent energy intake from 3% and 6% DHA-enriched AIN-93G diet were comparable to 2.7% and 5.5% respectively, of dietary intake or pharmacological supplementation in humans. Taken together, these results suggest that consumption of the n-3 PUFA, DHA, might be effective in preventing silica-induced acceleration and exacerbation of autoimmunity.

PS 141 Early Immunomodulatory Effects of Dermal Triclosan Exposure in Mice

N. B. Marshall, S. E. Anderson, K. L. Anderson, C. M. Long, E. Lukomska and B. J. Meade. *CDC/NIOSH, Morgantown, WV.*

It has recently been shown that dermal application of the commonly used antimicrobial compound triclosan, enhanced allergic responses in a mouse asthma model. To help elucidate the mechanisms of this augmented allergic response, we investigated the early immune-related effects of dermal triclosan exposure in mice. Triclosan was applied daily to the dorsal surface of the ears of BALB/c mice at concentrations ranging from 0%-3%, and leukocytes were examined in different organs over time using flow cytometry. Examination of the draining lymph nodes revealed a dose-dependent increase in cell numbers and enhanced GATA-3, IL-4, IL-21 and IL-17 expression suggesting enhanced Th2- and Th17-like effector T cell polarization. Effects on antigen presenting cells were also observed including increased expression of MHC class II, CD80 and CD86. In mice sensitized to ovalbumin (OVA) and subsequently challenged with OVA through pharyngeal aspiration on day 7, mice exposed to triclosan had increased cell numbers in the bronchoalveolar lavage and mediastinal LN by 24 hours compared to vehicle-treated mice. Interestingly, the introduction of OVA into the airway of triclosan-exposed mice was associated with increased swelling of the ear tissue along with an influx of CD11b+ cells and dramatic increase in TSLP and TNF-alpha expression. Taken together, the early immunomodulatory effects of triclosan suggest an adjuvancy-type effect that involves CD4 T cells and antigen presenting cells which may contribute to the augmentation of allergic responses.

PS 142 An Immunologic Role of microRNA 210 in a Murine Model of Dermal Toluene-2, 4-Diisocyanate Sensitization

C. M. Long[1, 2], N. B. Marshall[1], P. D. Siegel[1], B. J. Meade[1], E. Lukomska[1], K. L. Anderson[1], D. Beezhold[1] and S. E. Anderson[1]. *[1]Centers for Disease Control and Prevention-National Institute for Occupational Safety and Health (CDC-NIOSH), Morgantown, WV and [2]Immunology and Microbial Pathogenesis Graduate Program, West Virginia University, Morgantown, WV.*

Diisocyanates, such as toluene 2, 4-diisocyanate (TDI) are the principal cause of occupational asthma induced by low molecular weight chemicals. Recently, the study of immune regulation by microRNAs has revealed the importance of these regulatory molecules in allergic disease. Our laboratory has shown that miRNA 210 (miR-210) expression increases in the draining lymph nodes (DLN) following dermal exposure to TDI in a murine model, however, the role of miR-210 in allergic disease is unknown. These studies were conducted to elucidate the functional role of miR-210 during sensitization to TDI. Female BALB/c mice were dermally exposed to TDI (4%) or vehicle. RNA was isolated from specific cellular subsets (T-cells and B-cells) at four days post exposure and analyzed for miR-210 expression using real-time quantitative polymerase chain reaction analysis. A statistically significant increase in miR-210 expression occurred in the DLN CD4+ cell population of TDI-exposed mice. Confirmed (foxp3) and predicted (runx1t1, runx3, smad4, and stat6) miR-210 transcription factor targets were identified using computational algorithms. Augmentations in foxp3 protein expression and decreases in runx1 and foxp3 mRNA occurred concurrently with expression of miR-210 following dermal TDI exposure. Understanding the immunologic mechanisms of allergic disease is critical for the development of preventative and therapeutic strategies and these studies suggest a functional role for miR-210 in the regulatory T cell pathway and ultimately in the pathogenesis of TDI sensitization.
Funding: This work was supported by internal funds from the Health Effects Laboratory Division of the National Institute for Occupational Safety and Health

PS 143 Differential Susceptibility to Suppression of Human Peripheral Blood T Cells by Sodium Arsenite and Monomethylarsonous Acid

F. T. Lauer[1], D. MacKenzie[1], E. Beswick[2], A. J. Gandolfi[3], L. G. Hudson[1], K. Liu[1] and S. W. Burchiel[1]. *[1]Pharmaceutical Sciences, University of New Mexico College of Pharmacy, Albuquerque, NM, [2]Molecular Genetics and Microbiology, University of New Mexico School of Medicine, Albuquerque, NM and [3]Pharmacology and Toxicology, University of Arizona College of Pharmacy, Albuquerque, AZ.*

Human exposure to arsenic in drinking water is known to contribute to many different health outcomes such as cancer, diabetes, and heart disease. Several epidemiological studies suggest that T cell function is also altered by drinking water arsenic exposure. However, it is unclear how individual responses differ to various levels of exposure to arsenic. Our laboratory has recently identified differential responses of human peripheral blood mononuclear cell (HPMBC) T cells as measured by polyclonal T cell activation following sodium arsenite exposure. Certain healthy individuals exposed to low concentrations (0.1- 100 nM) of arsenic in vitro showed a dose-dependent suppression at low concentrations of arsenite, whereas other individuals were not suppressed at low concentrations. In a series of 30 normal donors, we found that three individuals were sensitive to low dose sodium arsenite-induced inhibition of T cell proliferation produced by phytohemagglutinin (PHA) and anti-CD3/anti-CD28. There also appeared to be a correlation with the amount of IL-2 produced by these cells in culture. Current studies suggest that donors who are sensitive to As+3 may be even more sensitive to monomethylarsonous acid (MMA+3) at concentrations of 0.1-100 nM. Our studies demonstrate for the first time that low doses of As+3 and MMA+3 are immunosuppressive to HPBMC T cells in some individuals.
This work is supported by 1R01ES019968

PS 144 Association of Pro-Inflammatory and Apoptotic-Related Genes Expression with Lymphocyte DNA Telomere Length (LTL) in a Mexican Population Exposed to Arsenic

C. Escudero-Lourdes[1], A. S. Perez-Martinez[1], L. M. Del Razo[2], J. Alegria-Torres[3] and P. Mandeville[1]. *[1]Laboratorio de Inmunotoxicologia, Universidad Autonoma de San Luis Potosi, San Luis Potosi, Mexico, [2]Toxicologia, Centro de Investigación y Estudios Avanzados, México, D.F., Mexico and [3]Laboratorio de Investigación en Nutrición, Universidad del Centro de México, San Luis Potosi, Mexico.*

Long term exposure to inorganic arsenic (iAs) leads to a sustained inflammatory response. Chronic inflammation is frequently associated with oxidative stress which may cause telomere dysfunction, leading to apoptosis or, on the opposite side, to cells malignant transformation. It has been reported that during acute inflammation telomeres length increase temporarily, maybe as a strategy to assure cell expansion and insult elimination. However, telomere length shortening has been reported in peripheral blood lymphocytes as a marker of accumulated effect of oxidative stress and inflammation. In this work we evaluated the expression of inflammation and apoptotic related genes and its association with leucocyte telomere length (LTL) in a Mexican population chronically exposed to iAs (n=128) in drinking water. Results showed a positive association between iAs exposure and granulocyte and macrophage colony stimulating factor (GM-CSF) gene expression (p=0.00305) and LTL was positively associated with urinary concentration of DMA III+V (p= 0.044), but only when variables corresponding to Apaf-1, TGF-β e IL-8 gene expression were included in the multivariate model. These preliminary results suggest that inflammatory responses may contribute to lymphocyte telomere dysfunction and it could represent a mechanism associated with an increased risk for iAs-related diseases development in exposed populations.

PS 145 Inhibition of Early T Cell Cytokine Production by Arsenic Occurs Independently of Nrf2

K. R. VanDenBerg[1] and C. E. Rockwell[1, 2]. *[1]Pharmacology and Toxicology, Michigan State University, East Lansing, MI and [2]Center for Integrative Toxicology, Michigan State University, East Lansing, MI.*

Nuclear factor erythroid 2-related factor 2 (Nrf2) is a stress-activated transcription factor that induces the expression of a variety of cytoprotective genes. Nrf2 has also been shown to mediate immunosuppressive effects in multiple inflammatory models. Upon activation, Nrf2 dissociates from its repressor protein, Keap1, and translocates to the nucleus to induce the expression of Nrf2 target genes. This Nrf2-Keap1 interaction can be disrupted by the environmental toxicant and chemotherapeutic agent arsenic trioxide (ATO). The purpose of this study was to determine the effects of ATO on early events of T cell activation and the role of Nrf2 in those effects. The Nrf2 target genes Hmox-1, Nqo-1, and Gclc were all

The Toxicologist

Supplement to *Toxicological Sciences*

53rd Annual Meeting and ToxExpo™

March 23–27, 2014 • Phoenix, Arizona

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 138, Issue 1
March 2014

www.toxsci.oxfordjournals.org