a positive association between elevated ANA and amphibole exposure. However, enhanced ANA was not correlated with other hallmarks of SAID thus precluding a conclusion on the significance of elevated ANA. Neither anti-Jo-1 antibodies nor myositis has been reported in asbestos-exposed populations, suggesting that the Lewis rat may not be a suitable model for study. This abstract does not reflect EPA policy.

PS 759 TRICHLOROETHENE-INDUCED NITROSATIVE STRESS: PROTEOMIC IDENTIFICATION OF NITRATED PROTEINS IN THE LIVER OF MRL+/+ MICE.

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Exposure to trichloroethene (TCE), a common environmental contaminant, is associated with an autoimmune response, but the mechanisms remain largely unknown. Liver is one of the major organs affected by TCE exposure. Previous studies from our laboratory have shown that TCE exposure in mice leads to increased nitrosative stress in livers, and suggested a potential role of the nitrosative stress in TCE-mediated autoimmunity. To further explore the role of nitrosative stress in TCE-mediated autoimmunity, the current study using proteomic approaches (2D gel, Western blot, MALDI TOF/TOF MS/MS, etc.), was conducted to characterize the nitrated proteins in the livers of TCE-exposed mice. Female MRL +/+ mice were treated with TCE (10 mmol/kg, i.p., every 4th day) for 6 weeks, and liver proteins were extracted for the identification of nitrated protein and iNOS expression. A total of thirty nine proteins were identified in the livers of TCE-treated mice, whereas 21 proteins were found in the livers of both TCE-treated and control mice. The nitrated proteins were found in the molecular weight range of 19.1 to 128.3 kDa and PI range of 4.9 to 8.8. The identified nitrated proteins mainly represented skeletal proteins, enzymes, stress proteins and chaperones. Furthermore, TCE exposure led to significantly increased iNOS protein expression in the livers, suggesting its contribution to increased formation of reactive nitrogen species and thus, contribution to increased nitrated proteins. The identified nitrated proteins provide a global map to further investigate alterations in their structural and functional properties, which will lead to a better understanding of the role of protein nitration in TCE-mediated autoimmunity. Supported by NIH ES016302.

PS 760 INTERRELATIONSHIPS OF PEROXIDATION AND IMMUNOGENICITY OF CARDIOLIPIN: AN OXIDATIVE LIPIDOMICS APPROACH.

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The myriad of neoepitopes formed during lipid peroxidation trigger potent innate and adaptive immune responses. Experimental and clinical studies have been mostly focused on immunogenic properties of oxidized species of phosphatidylcholine (PCox) and phosphatidylserine (PSox). Lately, a mitochondria-specific anionic phospholipid, cardiolipin (CL), particularly its peroxidized molecular species (CLox) attracted attention as innate and adaptive immunogens and predictors of clinical outcomes and novel therapeutic modalities for vaccination. Specific interrelationships between the emergence of individual molecular species of CLs/CLox in circulation and the appearance of the respective antibodies remain unknown. This is due to the lack of specific/sensitive analytical tools to characterize a huge diversity of individual CL and CLox. Using mass spectrometry based oxidative lipidomics, we focused on the analysis of molecular species of CLs and CLox in plasma of mice exposed to total body irradiation (9.5 Gy) or bacterial infection (Pseudomonas aeruginosa, PA103) as well as in plasma from ARDS patients. In the latter cases, we were able to detect the presence of both host and bacterial CLs in LC/MS spectra of plasma lipids. While relatively low molecular mass species (m/z 1376 and 1418) are typical of bacterial CLs, larger CL molecules (with m/z from 1448) dominate in MS of mammalian plasma CLs. Simultaneously, antiCL/CLox antibodies were detected in plasma. We also found that CL-containing liposomes and CL-coated mitochondria were recognized and taken-up by RAW264.7 macrophages. The data are discussed in the context of possible roles that CLs/CLox play as PAMPs/DAMPs regulating adaptive and innate immune responses. Supported by NIOSH OH008282; NIH U19 AI068021, HL70755, HL094488, ES020693, ES021068.

PS 761 COMPARISON OF SERUM AUTOANTIBODY PREVALENCE IN ASBESTOS-EXPOSED POPULATIONS.

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Research suggests that some asbestos exposures trigger autoimmune responses. Asbestos-induced autoimmunity is of particular concern as a novel, non-pulmonary component of asbestos-related diseases (ARDs) and may contribute to the on-set or progression of traditional pulmonary ARDs such as pleural fibrosis. Recent studies in our laboratory revealed an increased number of autoantibodies in patients exposed to amphibole asbestos compared to a control population. Statistical analyses demonstrated a positive and significant correlation between the presence of pleural abnormalities and anti-nuclear antibodies (ANAs) or mesothelial cell autoantibodies (MesCAAs). While a clear association between amphibole-induced autoantibodies and pleural disease exists, amphibole exposure is relatively rare compared to the commercially used chrysotile asbestos fiber. Therefore, we examined serum from a chrysotile-exposed population for the presence of ANAs and MesCAAs. ANAs were detected in <1% of the chrysotile group compared to 62% of the amphibole group while MesCAAs were detected in approximately 19% of serum in each group. However, unlike the amphibole group, pleural disease was not significantly associated with MesCAA presence in the chrysotile group. Instead, the only factor significantly correlated with disease status in the chrysotile group was patient age. These data are consistent with clinical data reporting little or no autoimmune disease in chrysotile-exposed patients and pleural diseases that manifest later in life compared to amphibole-exposed patients. On-going studies are further exploring the relationship between the molecular structure of asbestos fibers and ARD pathology and progression.

PS 762 ASBESTOS-INDUCED MESOTHELIAL CELL AUTOANTIBODIES PROMOTE COLLAGEN MATRIX FORMATION.

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Populations exposed to amphibole asbestos present with various respiratory tract diseases, including cancer and fibrosis, as well as autoimmune diseases. Studies in our laboratory have demonstrated the presence of asbestos-induced autoantibodies against fibroblast and mesothelial cells in amphibole-exposed humans and mice. Mechanistic studies demonstrated that anti-fibroblast antibodies (AFAs) induce cultured fibroblast cells to express a myofibroblast phenotype and up-regulate collagen production. Immunohistochemistry studies revealed increased accumulation of collagen protein in amphibole-exposed mice, but collagen localized with mesothelial, not fibroblast, cells. Subsequently, mesothelial cell autoantibodies (MesCAAs) were identified in sera from amphibole-exposed subjects from Libby, MT. Therefore, we hypothesized that MesCAAs induce a mesothelial-mesenchymal transition resulting in increased collagen synthesis. We incubated cultured human mesothelial cells with sera identified as MesCAA positive (+ive) or negative (–ive) and assayed for mesenchymal transition and collagen production. Serum cleared of MesCAA (IgG isotype) was used as a negative control. Flow cytometric analysis revealed no changes in the expression of the mesothelial cell marker cytokeratin-8 or the myofibroblast cell marker α-smooth muscle actin indicating that MesCAAs do not induce a mesenchymal transition. Increased concentrations of soluble collagen protein were detected in the supernatant of cells incubated with MesCAA+ive or –ive sera but not with cleared sera. However, only MesCAA+ive sera induced formation of a collagen matrix, perhaps through regulation of matricellular proteins. These data indicate that, unlike AFAs, MesCAAs affect matrix-collagen accumulation without inducing phenotypic changes. This study provides a better mechanistic understanding of how autoantibodies may contribute to the progression of asbestos-related fibrosis.

PS 763 USE OF *IN VITRO* AND *IN VIVO* METHODS TO ASSESS THE SENSITIZATION POTENTIAL OF NOVEL AMINO ALCOHOLS.

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The Local Lymph Node Assay (LLNA) is the principle preferred method for assessing the skin sensitization potential for EU REACH regulatory purposes. However, the LLNA has been found to overestimate sensitization potential for various compounds such as surfactants, fatty acids and alcohols. Amino Alcohols, as a class, have been shown to be non sensitizers. We have discovered four alcohol amines; aminocyclohexane (ACyHM), 2-aminopropanol (2-AP), aminomethylcyclohexanol (AMCyHOL) and aminododecane (ADD), that tested positive in the LLNA.

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