POSTER ABSTRACTS

Exposure to Arsenic and Uranium in Drinking water alters Gastrointestinal Health

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Metal exposure poses a serious environmental threat to the Native American community in New Mexico. From 1944 - 1986, the United States extracted 4 million tons of Uranium and other metal ores from native Navajo territories and consequently left over 10,000 abandoned mines. This mining and subsequent abandonment of mines caused random dispersion of heavy metals, windblown dust dispersal, and the contamination of drinking water with arsenic and uranium. This gastrointestinal exposure can have detrimental effects on gut health. We sought to understand how these heavy metals influenced the gut microenvironment. Metagenomic analysis of stool samples collected from mice exposed to both uranium and arsenic had alterations in α-diversity as well as changes in specific bacterial phyla and species that have differences in arsenic-related pathways. An oxidative metabolic state in mature intestinal epithelial cells (IEC) is critical for intestinal homeostasis and a diverse gut microbiota. This metabolic state is highly energy dependent and this energy is mainly derived from oxidative metabolism and fatty acid oxidation that subsequently preserves an obligate anaerobic microbial community. Thus, we furthered assessed if the heavy metals affected the metabolic state of IEC. Exposing the colonic cell line, Caco-2, to metals particles derived from environmentally relevant locations showed a higher glycolytic phenotype as indicated by higher basal glycolysis and higher compensatory glycolysis compared to controls. These data highlight the impact of metal exposure on intestinal barrier metabolism which influences the gut microbiota. Numerous metabolic disorders such as metabolic syndrome, type II diabetes, and non-alcoholic fatty liver disease have been linked to GI health and the gut microbiota. Taken together our data shows metal exposure causes alterations in the gut which may be a predisposing factor for metabolic disorders such as metabolic syndrome, type II diabetes, and non-alcoholic fatty liver disease.

Genomic basis for individual differences in susceptibility to the neurotoxic effects of diesel exhaust

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Air pollution is a known environmental health hazard. A major source of air pollution includes diesel exhaust (DE). Initially, research on DE focused on respiratory morbidities; however, more recently, exposures to DE have been associated with neurological disorders and neurodegeneration. In this pilot study, we investigated the effects of sub-chronic inhalation exposure to DE on neuroinflammatory markers in two inbred mouse strains of both sexes, including whole transcriptome examination of the medial prefrontal cortex. We exposed aged male and female C57BL/6J (B6) and DBA/2J (D2) mice to DE, which was cooled and diluted with HEPA-filtered compressed air for 2 hours/day, 5 days/week, for 4 weeks. Control animals were exposed to HEPA-filtered air. The prefrontal cortex was harvested and analyzed for proinflammatory cytokine gene expression and transcriptome-wide response by RNA-sequencing. We observed differential cytokine gene expression between strains and sexes in the DE-exposed vs. control-exposed groups for Il1b, Tnfα, and Il6. We identified 150 differentially expressed genes between air and DE groupswhichrelated to natural killer cell-mediated cytotoxicity per Kyoto Encyclopedia of Genes and Genomes pathways. Overall, our data show differential strain-related effects of DE on neuroinflammation and neurotoxicity and demonstrate that B6are more susceptible than D2 to gene expression changes due to DE exposures. These results are important because B6 mice are often used as the default mouse model for DE studies and strain-related effects of DE neurotoxicity warrant expanded studies.All procedures were approved by the Louisiana State University Institutional Animal Care &Use Committe

Does inhalation of tungsten particulates affect the heart and increase the risk of cardiovascular disease?

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Inhalation of tungsten particulates is a relevant route of human exposure, especially in occupational settings where airborne tungsten concentrations have been reported as high as 3.1 mg/m3. In the hard metal manufacturing industry exposure to tungsten particulatesleads to increased incidence of interstitiallungdisease, characterized by pulmonary inflammation and fibrosis.In vivostudieshavealsoshown that inhalation of tungsten and tungsten-mixed metal alloy particulatesinduces inflammation and fibrotic changes in the lungs leading to impairedlung function. However,the systemic consequencesofthis pulmonary damagehave not been investigated.Multiple epidemiological studies have found an association between urinary tungsten levels and increased incidence and/or mortality of cardiovascular diseases. However, no studies have investigatedhow tungsten exposure affects the heart of the risk of developing cardiovascular disease.Using a whole-bodyinhalation exposure system 4, 4-hour exposuresto tungsten metal particulates (1.5± 0.32mg/m3; <1 μm),over the course of two weeks,resulted in changes in cardiac function including a decrease in cardiac output and an increase inthe amount of work required by the atria to fill the heart (A'). E'/A' ratio, an indicator of diastolic relaxation,also showed a decreasing trend.Gene expression profiling of tungsten-exposed hearts revealed a significant up-regulation in multiple pro-inflammatory, cardiac remodeling, and oxidative stress genes. These data strongly

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