

and gravimetric instruments requiring daily or weekly attendance, the passive charge devices employed here, once located in the field and supplied with an internet or cell phone connection, required no maintenance, no human intervention and reported their observations to the cloud. This allowed minute by minute display of urban air LDSA concentrations with controlled or open global access. Additional data analysis as well as other comparisons are ongoing and will be reported. *This work was self funded and supported by Pegasor Oy who supplied the measuring devices. The cooperation and hospitality of the staff of the NY DEC is gratefully acknowledged.*

**PS 1089 Developmental Traffic-Related Air Pollution Exposure and Autism-Related Neurotoxicity in Mice**

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Epidemiological findings have suggested that developmental exposure to traffic-related air pollution (TRAP) may be associated with an increased risk of autism spectrum disorders (ASD). In order to further assess this association mechanistically, we carried out a series of studies in C57Bl/6J mice developmentally (E0 to PND21) exposed to 250-300 ug/m<sup>3</sup> of diesel exhaust (DE) or filtered air (FA) in a controlled environment. A series of behavioral, molecular, and brain histological assessments relevant to ASD were carried out in both male and female pups and young adults. Behavioral testing indicated changes consistent with ASD, namely increased repetitive behavior, disrupted social behavior and impaired social communication. Elevated levels of the inflammatory cytokine interleukin-6 (IL-6) were found in fetal brains and placentas of mice exposed to DE. Prompted by findings obtained in the maternal immune activation model of ASD, we also explored a possible biochemical pathway relevant for ASD which may be disrupted by developmental DE exposure. Additionally, increased levels of phosphorylation of STAT3, as well as increased expression levels of DNMT1 (DNA methyltransferase 1) and reelin (RELN) were found to be associated with DE exposure. DNMT1 is a target gene of activated transcription factor STAT3 and has been shown to bind directly to the promoter region of the RELN gene and modulate RELN expression via epigenetic modification. The RELN gene encodes for extracellular protein reelin, which plays a major role in guiding the neuronal migration process during CNS development. Downregulation of RELN due to DE exposure persisted in cortical samples of PND60 male mice. An immunohistochemical analysis was performed with the lamina-specific markers RELN and calretinin to examine the cortical organization in PND60 brains of mice exposed to either DE or FA during development. Significant differences were seen in the cortical distribution of both RELN- and calretinin-positive cells, suggesting a disruption of cortical layering. Altogether these studies suggest that developmental exposure to DE causes behavioral, biochemical and histological changes in mice which are similar to those observed in ASD. *Supported in part by NIEHS grants R01ES22949, and R01ES028273.*

**PS 1090 Mouse Pulmonary Response Induced by Exposure to Dust from Sawing Corian, a Solid-Surface Composite Material**

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Corian®, a solid-surface composite (SSC), is composed of a proprietary blend of powdered alumina trihydrate, methyl methacrylate, and other binders and colorants. The present study evaluated the murine pulmonary toxicity from exposure to dust generated from sawing of SSC. The particle number-based geometric mean diameter and geometric standard deviation  $\sigma_g$  of the airborne fraction SSC sawing dust following suspension in saline was 1.16  $\mu\text{m}$ ,  $\sigma_g = 2.18$ , which is similar to the number-based geometric mean aerodynamic diameter to aerosolized SSC sawing dust of 1.05  $\mu\text{m}$ ,  $\sigma_g = 1.78$ . Inductively coupled plasma and energy dispersive X-ray spectroscopy analyses confirmed that aluminum was the principle inorganic component of SSC sawing dust (29.7  $\pm$  1.3%) and was not different compared to airborne SSC. Mice were exposed to 62.5, 125, 250, 500, or 1000  $\mu\text{g}$  of SSC dust, saline, or 1000  $\mu\text{g}$  silica positive control via oropharyngeal aspiration. At 1 and 14 days post-exposure, the body weights of both 500 and 1000  $\mu\text{g}$  group mice were significantly lower than those of the saline group. Analysis of bronchoalveolar lavage fluid showed that lactate dehydrogenase, inflammatory cells, and pro-inflammatory cytokines were elevated in the 500 and 1000  $\mu\text{g}$  SSC exposure groups at days 1 and 14 post-exposure, indicating that exposure to the SSC sawing dust induced an inflammatory response in mice. Furthermore, lung histopathology indicated inflammation in alveoli at all doses at day 1 post-exposure, and fibrosis in the 1000  $\mu\text{g}$  dose at day 14 post-exposure. Darkfield imaging indicated alveolar particle deposition and granulomatous mass formation

persisting to 14 days post-exposure in all exposure groups. Taken together, these findings suggest that SSC sawing dust exposure may induce pulmonary inflammation and damage that warrants further investigation. *Disclaimer: The findings and conclusions in this report are those of the author(s) and do not necessarily represent the official position of the National Institute for Occupational Safety and Health, Centers for Disease Control and Prevention.*

**PS 1091 Effect of Vinyl Chloride on HNF4 $\alpha$  Expression in a Model of Nonalcoholic Steatohepatitis (NASH)**

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Vinyl Chloride (VC) is an organochlorine compound which is known to cause hepatic steatosis, fibrosis, necrosis and hepatocellular carcinoma. Occupational exposure has been directly associated with hepatic angiosarcoma. Recent studies have shown that inhalation exposure to VC at levels below current Occupational Safety and Health Administration exacerbates liver injury, steatosis and inflammation in mice fed a high fat diet suggesting that VC is a Toxicant Associated Steatohepatitis (TASH) causing agent. Previous studies from our laboratory have shown that decrease in expression and activity of Hepatocyte Nuclear Factor 4 alpha (HNF4 $\alpha$ ) an orphan nuclear receptor produces NASH like pathology in the liver. We hypothesized that VC might be causing these effects by targeting HNF4 $\alpha$ . To test this hypothesis, HNF4 $\alpha$  activity, mRNA and protein expression was measured in livers from mice with and without inhalation exposure to vinyl chloride and fed either normal chow (LFD) or high fat diet (HFD). Western Blot and RT-PCR analyses were used to determine HNF4 $\alpha$  protein expression and activity. Western blot analysis for adult isoforms (P1) of HNF4 $\alpha$  showed no difference in protein expression between treated and untreated LFD fed animals. Interestingly, the adult P1 HNF4 $\alpha$  protein levels were decreased in untreated HFD fed mice but returned to normal levels with VC treatment. Expression of fetal P2 HNF4 $\alpha$  isoforms were not affected by VC treatment but were induced in all mice fed HFD. RT-PCR analysis of HNF4 $\alpha$  and its target genes did not reveal any changes in HNF4 $\alpha$  activity measured using target gene expression except CD36, a lipid importer, which significantly increased in mice on a high fat diet. VC treatment decreased CD36 expression in mice on HFD, but expression was still significantly greater than VC treated and untreated fed LFD. In conclusion, HFD decreased HNF4 $\alpha$  expression and VC exposure along with HFD prevented this decrease. Further, the HFD treatment with and without VC induced expression of the fetal P2 isoform in HFD. Further studies are required to determine the mechanisms behind these observed effects.

**PS 1092 The Effect of Farm Dust Collection Method on the Toxicological Responses in Lung Co-Culture Model**

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Early life exposure to farm environment has been shown to protect from asthma and allergies, whereas exposure during adulthood can increase the risk of respiratory syndromes. To assess the immunological mechanisms behind these phenomena, the focus of research has shifted to *in vitro* stimulations with farm dust. However, the use of authentic farm dust raises questions about the collection methods as different methods might affect the composition of the dust and furthermore alter toxicological and immunological responses. Detailed characterization, such as data on the size distribution of dust particles as well as microbiome and chemical composition of the dust, could also support the identification of causative components. The aim of our study was to assess the impact of dust collection methods on cellular responses. Farm dust samples were collected from 3 different Finnish dairy farms by 1) mechanical scraping (sample matrix 1), 2) settled dust sampling (sample matrix 2), and 3) utilizing DGI impactor (sample matrix 3). Scraped sample was further filtered into two size-fractions (>63  $\mu\text{m}$  and 63-125  $\mu\text{m}$ ). DGI filter samples were extracted and different size fractions were pooled to obtain sufficient mass of particles for the experiments. Co-cultures of lung epithelial cells (A549) and macrophage-like cells (THP-1) were stimulated with different doses (25, 50 and 100  $\mu\text{g}/\text{ml}$ ) of farm dusts. Toxicological and immunomodulatory potential of the dusts was measured. Dusts were also analysed for particle size distribution, microbiome and chemical composition. Cell membrane integrity was not affected by the collection method, whereas oxidative stress and metabolic activity responses were distinct between matrices. The results were dependent of the farm, as responses from samples collected from farm 1 differed more significantly from each other than matrices from other farms. The secretions of IL-6 and TNF $\alpha$  were slightly dependent on matrix. The response profiles were similar whereas the absolute levels



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