sus filtered air, n=7, p<0.05). Taken together, *in vitro* exposure to DEP caused a significant reduction in epithelial barrier function with a corresponding reduction in Tricellulin expression. A similar reduction was seen in whole lungs of neonatal mice two weeks following exposure to aerosolized DEP. Overall, these results suggest that early life exposure to DEP may have lasting impacts on epithelial barrier structure and function.

1133 Effects of Diesel Exhaust on Airway Epithelial Ion Transport and Lung Function in the Rat

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Diesel engines are employed to run drilling rigs and pump fracking fluid down the well bore at hydraulic fracturing worksites. Workers at these sites are routinely exposed to diesel engine exhaust (DE) due to their proximity to the engines. Short-term exposure to DE is associated with headache, dizziness, and irritation of the eye, nose and throat. Long-term exposure increases the risk of cardiovascular disease, pulmonary disease and lung cancer. The effects of a sub-chronic inhalation exposure to DE on lung function, airway reactivity, and airway epithelial ion transport, were investigated. Rats in whole body chambers were exposed to 1 mg/m^3 DE generated from a tier 2 engine for 6 h/d, 4 d/wk. Experimental endpoints were measured at 1, 7 and 27 d post-exposure. Combustion gasses were monitored in real time inside the exposure chamber and had typical values of 4,000 ppm CO_2, 18 ppm NO, 800 ppm SO_2, 28 ppm CO, and 20.2% O_2. Lung resistance (R_L), dynamic compliance (C_{dyn}) and reactivity to inhaled MCh were measured in anesthetized rats. There was no effect of DE on basal R_L or C_{dyn} or reactivity to inhaled MCh at 1 d post-exposure. However, DE increased basal R_L and decreased basal C_{dyn} compared to air-breathing controls at 7 d post-exposure. Transepithelial potential difference (V_t), transepithelial resistance (R_t), and short-circuit current (I_{SC}) were measured *in vitro* in tracheas mounted in Ussing chambers and treated with the ion transport inhibitors amiloride (Na^+ channel blocker; apical), 5-nitro-2-(3-phenylpropylamino) benzoic acid (NPPB; Cl^- channel blocker; apical), and ouabain (Na^+,K^+-pump blocker; basolateral). Exposure to DE had no effect on I_{SC} or R_t at 1 and 7 d post-exposure. Basal I_{SC} and responses to ion transport inhibitors were reduced at 27 d post-exposure; however, there was no effect on R_t. There were no changes in V_t at any post-exposure time. These results indicate that inhalation of DE leads to changes in pulmonary function and airway ion transport.

1134 Characterizing $PM_{2.5}$ Samples with Different Source Contributions

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Ubiquitous fine particulate matter ($PM_{2.5}$) exposures largely impact global public health, yet little is known about the mechanisms causing the known adverse health effects. Oxidative stress due to $PM_{2.5}$ associated chemical constituents, such as polycyclic aromatic hydrocarbons (PAHs) and elements, has been proposed as a possible mechanism for $PM_{2.5}$ mediated health effects. Variations in the ability to induce oxidative stress, or oxidative potential, have been previously identified in $PM_{2.5}$ air filter samples. These variations may be attributed to the differing source contributions and thus chemical constituents of the $PM_{2.5}$ assessed. To test this, $PM_{2.5}$ filters collected at locations with differing predominant sources were assessed for oxidative potential, chemical composition, and developmental toxicity. Sampling locations included outdoor (a rural park across seasons, 2 vehicular traffic influenced locations) and indoor (32 homes in India) samples. $PM_{2.5}$ was extracted from filters via sonication in methanol. Aliquots of individual filter samples were removed for oxidative potential assessment using the dithiothreitol (DTT) assay. Samples were then pooled by location for chemical analysis of PAHs (n=115) and elements (n=20). Pooled samples were also prepared for developmental toxicity testing in zebrafish starting at 6 hours post fertilization (hpf) to assess morphological and behavioral changes at 24 and 120 hpf. Significant differences in oxidative potential were observed between both individual filters and overall groups. Significant variation in chemical constituents between locations of differing sources was observed. Developmental toxicity testing is underway to investigate correlations between the chemical constituents and biological responses. This research will ultimately lead to a greater understanding of health-relevant metrics for $PM_{2.5}$ exposures and the potential impacts of various $PM_{2.5}$ sources.

1135 Marco Regulates *In Vivo* Response to Low Molecular Weight Hyaluronan Fragments

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Ozone is criterion air pollutant, which enhances cardiorespiratory morbidity and mortality and exacerbates preexistent respiratory diseases. Prior work demonstrates that macrophage scavenger receptor (Marco) is critical for the clearance of O3-derived oxidized lipid species. We hypothesize that Marco also regulates biological response to O3-derived low molecular weight hyaluronan (sHA) fragments. We challenged 8-10 weeks old C57BL6 (WT) and Marco-/- mice with 2ppm O3 or filter air for 3 hours. 24h after exposure mice underwent BAL for total cell count, differentials and hyaluronan measurement. We observed significantly increased level of BAL hyaluronan in O3-exposed Marco-/- mice. Moreover, at 6h following oropharyngeal instillation of sHA (1.5mg/ml) versus saline in Marco-/- or C57BL6 mice, we observed that Marco-/- mice had increased cell count and neutrophil influx with increased BAL cytokines (IL6, TNF alpha, MCP1 and KC) in comparison to WT. Alveolar macrophages harvested from sHA instilled WT mice significantly increased their Marco expression. Moreover, in time course experiments with alveolar macrophages harvested from naïve WT and Marco-/- mice using Rhodamine labeled sHA, we observed enhance sHA binding in WT vs Marco -/- after 2h of treatment by confocal microscopy. In these same experiments, we observed a positive correlation between level of binding sHA and Marco receptor expression at the cell surface. Finally, we evaluated baseline levels of TLR4 and CD14 expression in Marco -/- mice and WT by RTPCR and observed increased RNA for TLR4 and CD14 in the Marco -/- alveolar macrophages. In summary, our data suggest a central role for Marco receptor in biological response to low molecular weight hyaluronan. Deletion of this scavenger receptor lead to accumulation of hyaluronan in respiratory system. *In vivo* stimulation with sHA caused increase expression of Marco receptor in WT and more exacerbated inflammation with increased level of cytokines and neutrophil influx in Marco-/- mice. Lack of Marco receptor causes less binding of sHA and disbalances baseline expression of TLR group proteins, which suggests a potential mechanism for this response.

1136 Comparison of Precision Cut Lung Slices and Whole Lungs in Particle-Induced Inflammation

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Precision cut lung slices (PCLS) have been widely used as a 3D organotypic lung tissue model to provide physiologically relevant responses to whole animal exposures while requiring far fewer animals. We previously assessed lung toxicity of airborne particles in both PCLS and mice and sought here to determine whether the responses obtained were linear between the two systems. The particles were categorized into three types: indoor airborne particles from an electronic recycling plant (mechanical process emissions; inorganic-rich particles; IRP), outdoor airborne particles (wildfire smoke; organic-rich particles; ORP), and engineered nanoparticles (SiO_2, CeO_2 and TiO_2; poorly soluble particles; PSP). PCLS were exposed to 22 µg/mL of IRP or ORP and 132 µg/mL of PSP under submerged conditions and assessed for lung toxicity at 24 h post-exposure. Mice were exposed to 100 µg of all the particle samples by oropharyngeal aspiration and assessed for lung toxicity at 4 and 24 h post-exposure. The relationship of proinflammatory cytokine levels (TNF-α, MIP-2, and IL-6) between PCLS and *in vivo* bronchoalveolar lavage fluid of mouse lungs was then examined. We found that ORP exposures show a strong correlation for all cytokines between the two models (TNF-α: r^2 = 0.9997, MIP-2: r^2 = 0.9953, and IL-6: r^2 = 0.9790), followed by IRP exposures (TNF-α: r^2 = 0.9957, MIP-2: r^2 = 0.7150, and IL-6: r^2 = 0.9390). PSP exposures however only showed a strong correlation for IL-6 (r^2 = 0.7948) between PCLS and whole lung models (TNF-α: r^2 = 0.0075 and MIP-2: r^2 = 0.0605). These results suggest that inflammatory responses between PCLS and whole lung models are highly associated with concentrations of organic matter (ORP > IRP > PSP) and water-soluble materials (ORP > IRP > PSP) in the particulate samples. In addition, IL-6 appears to be a more sensitive biomarker in PCLS than other cytokines. Overall our findings demonstrate good concordance in proinflammatory responses between PCLS and whole lung studies following exposures to different types of airborne particles. Notably, PCLS may better predict *in vivo* responses to chemicals (e.g., water-soluble organic matter) released from particles. This information can be used to understand the uses and limitations of PCLS as a screening tool for the lung toxicity of airborne particles. *This abstract does not represent US EPA policy.*

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