diopulmonary toxicity. It has been proposed that surface area of ultrafine PM is more closely associated with PM-related toxicity. In this study, we investigated the effect of ultrafine polystyrene particles on inflammation and oxidative stress markers in pulmonary hypertensive rats to determine whether surface area of ultrafine polystyrene particles play an important role in ROS generation in diseased animals. Each exposed group (n=5) were treated with ultrafine polystyrene in the combination of three sizes (64, 202 and 535 nm) and two concentrations (100 and 50 μg/ml) using intratracheal instillation. Control group (n=4) received PBS. Bronchoalveolar lavage fluid (BALF), lung tissue and peripheral plasma were collected 24hr after experiment. The results showed that instillation with 100 and 50μg/ml of ultrafine polystyrene particle can induce increased total cells, neutrophil proportion, total protein and LDH compared to fine polystyrene particle at same mass concentration in pulmonary hypertensive rats. We also observed that ultrafine polystyrene induced significant higher proinflammatory cytokine IL-6 and TNF-α as compared to fine particles. Furthermore, the result revealed that the depletion of total GSH in the lung tissue and formation of plasma 8-OHdG were associated with total surface area of particles instilled. In conclusion, we found inert ultrafine polystyrene may cause lung inflammatory effects on pulmonary hypertensive rats, and the formation of ROS was associated with instilled total surface area of ultrafine PM. The exact mechanism warrants further study.

1385 TOXICOLOGICAL ASSESSMENT OF DIESEL-METHANOL-WATER EMULSION [PURINOX™ (ALL WEATHER) GENERATION 2 FUEL] EXHAUST EMISSIONS.

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A type of fuel shown to decrease combustion emissions vs. traditional diesel is the diesel emulsion. Utilizing a colaborative approach, a toxicological assessment of the exhaust of PuriNOx™ fuel emulsion was recently conducted. Whole exhaust from one of two, 2002 model Cummins 5.9L ISB engines was diluted to exposure levels of 125, 250, and 500 μg particulate matter (PM)/m^3. The engines were operated on a repeating EPA heavy-duty certification cycle. F344 rats were housed in Hazleton H2000 exposure chambers and exposed to exhaust 6 h/day, 5 days/wk for the first 11 weeks and 7 days a week thereafter. Exposure days ranged from 58-70 days. Exposure- start was staggered to account for multiple health endpoints. Toxicological assays were conducted during and following exposures and subsequent to a recovery period. General toxicity (body weight, organ weight, clinical pathology, and histopathology), neurotoxicity (glial fibrillary acidic protein assay, GFAP), genotoxicity (Ames, micronucleus, sister chromatid exchange), and reproduction and development were assessed. Effects observed were mild. Exhaust was not associated with neurotoxicity, reproductive/developmental toxicity, or *in vivo* genotoxicity. Small decreases in serum cholesterol were noted in males and females of the high level exposure. PM accumulation within alveolar macrophages was noted in all exposure groups. Other sporadic statistically significant responses were observed but not clearly treatment related. Exhaust subfractions induced mutagenic responses in S. typh. Based on the cholesterol results, it can be concluded that the 250 μg/m^3 exposure level was the NOAEL. In general, these observations were consistent with rodent and bacteria exposure to petroleum diesel exhaust.

1386 INDUCTION OF IL-6 IN LUNG CELLS BY PM2.5 PARTICLES FROM DESERT SOILS AND COAL FLY ASH.

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Fine particle air pollution is a complex mixture containing materials from geological, combustion, and atmospheric sources. The mechanisms linking various particle types to specific health effects remain elusive, but many studies have associated ambient particles with pro-inflammatory cytokine signaling pathways. In this study, PM2.5 particles were aerodynamically separated from three western United States desert soils and from a sample of fly ash collected at a power plant burning bituminous coal. Cultured human lung epithelial cells (type BEAS-2B) were treated with doses from 10 - 160 microgram/cm2 of the particles. Viable cell count and the interleukin-6 (IL-6) concentration in the media were determined 24 h after treatment. The IL-6 response correlated with negative charge on the particles (zeta potential) but did not correlate with particle surface area or with transition metal content. Capsazepine, an antagonist of the TRPV-1 receptor, decreased the IL-6 response. One desert dust induced an exceptionally high IL-6 response compared to treatment with the other soils, kaolin clay, or soluble metal salts. The LAL chromagenic assay showed that this dust contained the highest level of endotoxin (20-50 EU/mg particles which equals <10 EU/mL as applied to the cells). The measured endotoxin concentration in the dust was considerably lower that the amount of soluble lipopolysaccaride required to elicit a comparable IL-6 response (> 2000 EU/mL). This suggests that either the particles interfere with the LAL endotoxin assay or that other soil dust properties are responsible for the cytokine response. This work was sponsored by NIH research career award 1 K25 ES011281-01A1 by Southwest Center for Environmental Research and Policy project EH-03-03.

1387 EFFECTS OF PARTICULATE MATTER ON GLUTAMATE CYSTEINE LIGASE IN RAW CELLS.

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Epidemiological studies have consistently shown associations between ambient particulate matter (PM) and respiratory and cardiovascular mortality and morbidity. The mechanisms responsible for this association remain unclear. One hypothesis with supportive toxicologic evidence is that PM acts to cause oxidative stress in the lung leading to upregulation and systemic release of pro-inflammatory mediators from immune defense cells such as macrophages. These pro-inflammatory mediators such as cytokines and reactive oxygen species can negatively impact cardiovascular function. Many studies have revealed the importance of antioxidants in protection of the lung from oxidative stress. The thiol antioxidant glutathione (GSH) is a major antioxidant in the lung and inhibition of its synthesis has been shown to exacerbate lung injury by a large number of toxicants. Glutamate cysteine ligase (GCL), a heterodimer composed of a catalytic (GCLc) and a modifying (GCLm) subunits, catalyzes the rate-limiting step in glutathione (GSH) biosynthesis. Exposing the murine macrophage cell line, RAW 264.7 to 100 μg/ml PM1648 for 3-24 hours caused an upregulation of the GCLm protein while exposing cells to 300 μg/ml PM1648 upregulated GCLc protein over the same time course. These data suggest that GCL plays a role in protecting cells in the lung, such as alveolar macrophages from injury caused by PM exposure.

1388 EFFECTS OF COMBUSTION-DERIVED PARTICULATE MATTERS CONTAINING ARSENIC IN NF-κB LUCIFERASE TRANSGENIC MICE.

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Inhalation of combustion-derived particulate matters (PMs) can have a variety of negative impacts on human health. Some heavy metals are also known to play a substantial role in adverse health effects. The potential toxic effects of inhaled combustion-derived PMs containing arsenic, one of the most frequently present heavy metals in the air, were examined usinf NF-KB luciferase reporter mice. The male mice (5-6 weeks old) were exposed to different concentrations of PMs (124±24.5, 220±34.5, 426.4±40.3 μ/m3) for 6h per day, 5 days per week for 4 weeks in 1 m3 whole-body chambers. Significant increase of the luciferase activity in heart, liver, and lung was observed. Among them, the pulmonary luciferase activity was changed dramatically. EMSA indicated that the exposed PMs inhibited NF-kκB DNA binding activity in the lung. Western blot analysis in the lung indicated that p65 and p50 protein levels were increased while IκB was decreased in a concentration-dependent manner. The PMs also induced increase of Akt, Bcl-2, c-Myc and Erk proteins. Our results suggest that combustion-derived PMs containing arsenic can be a significant cause of adverse human health. Supported by BK21 grant

1389 CYTOTOXICITY AND CELL SIGNALING IN MH-S CELLS: RELATIVE POTENCY OF DIESEL AND COAL COMBUSTION PARTICLES.

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Pulmonary exposures to combustion source particulate matter (PM) are known to induce inflammatory lung diseases, however it is not well understood how these particles exert their effects and how different sources and types of PM rank in potency. We have previously demonstrated in mice that diesel exhaust particles (DEP) high in organic carbons produced macrophage influx, while DEP, high in elemental carbon, induced neutrophilic inflammation in the lung. In the present study we tested the *in vitro* effects of these DEP (SRM-DEP, A1-DEP) along with a third

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Preface

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