concerns about possible occupational and environmental health toxicity. To investigate the potential deleterious effects of inhalation exposure to WO_3 NPs, Golden Syrian hamsters were divided into three groups – a control, exposed to aerosolized sterile distilled water and two treatment groups exposed to either 5 or 10 mg/m^3 of aerosolized WO_3 NPs for 4 hrs/day, for 4 days in a whole body exposure chamber. WO_3 NPs were characterized by TEM and the chamber concentration was monitored using the NanoScan SMPS. Animals were euthanized 24 hours post exposure and bronchoalveolar lavage fluid (BALF) was collected. Total LDH activity and TNF-α levels were evaluated biochemically while BALF macrophages were examined by SEM. After collecting BALF, lungs were snap frozen in liquid nitrogen for further analysis. Total LDH activity of control was 2431 ±169.3 μU/mL; while in 5 and 10 mg/m^3 treated groups it was increased ($p<0.05$) to 2996 ±568.9 μU/mL and 4280 ±887.8 μU/mL respectively. Isolated macrophages from BALF of treated hamsters show presence of membrane blebbing compared to control, when observed under the SEM. Level of TNF-α of control was 79 ±8 pg/mL, while that of 5 and 10 mg/m^3 treated groups were increased ($p<0.05$) to 105 ±4 pg/mL, 169 ±52 pg/mL respectively. Western blot analyses of tissue lysate indicated an increase of Caspase-1 and IL-1β in the treatment groups as compared to controls. Results from these experiments indicate that exposure to WO_3 NPs can lead to cytoxicity indicated by increase in LDH and cytokines TNF-α. A possible molecular mechanism is through activation of Caspase-1 induced pyroptotic cell death as indicated by increase in Caspase-1 and IL-1β.

PS 2352 Inhaled TiO_2 Nanoparticles Induce Formation of NLRP3 Inflammasome and Upregulation of IL1-beta Expression in the Lungs of Golden Syrian Hamsters

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TiO_2 is an important metal that is used in diverse applications from paints to aircraft frames. Inhaled metal nanoparticles have been shown to deposit in the parenchyma of the lungs causing inflammation, cell death and fibrosis. NIOSH has recommended an exposure limit of 0.3mg/m^3 for ultra fine TiO_2 while OSHA recommends a permissible exposure limit of 15mg/m^3 of total airborne fraction of respirable dust. Nanoparticles (NP) have been shown to induce the formation of inflammasomes, through the activation of cathepsin B with the consequent release of IL1-β. The current study investigated the toxicity of TiO_2 NP in Golden Syrian hamsters. Hamsters were exposed in a whole body chamber to aerosolized vehicle (control) or aerosolized TiO_2 NP at concentrations of 0.3mg/m^3, 3mg/m^3 or 15mg/m^3 (4 hrs/day for 7 days). Twenty-four hours post exposure, hamsters were euthanized, lungs removed and frozen for biochemical analyses. Frozen tissues were assessed by western blot analysis to detect the levels of Cathepsin B, NLRP3, ASC and IL1-β. Average size of TiO_2 NP was determined to be 36.9 ±14.4nm by TEM evaluation. Tissue from the lungs of hamsters treated with 3 and 15mg/m^3 NP had a 2-fold increase in expression of Cathepsin B as compared to controls and animals treated at 0.3mg/m^3 NP. Lungs from hamsters treated with the above concentrations of TiO_2 NP had 3 fold increase in NLRP3 protein levels when compared to control and 0.3mg/m^3 treated group. Levels of ASC were 3-5 fold higher in pulmonary tissue from hamsters treated with 3 and 15mg/m^3 as compared to controls. There was no significant difference in the levels of expression of IL1-β between control, 0.3mg/m^3 and 3mg/m^3 groups, but there was a 2 fold increase seen in 15mg/m^3 NP treated group when compared to the other groups. These results indicate that inhalation of nanosized TiO_2 particles induce the formation of NLRP3 inflammasome with the subsequent up-regulation of IL1-β protein.

PS 2353 Acute Effects following Inhalation Exposure to Metal Oxide Nanoparticle-Containing Chemical Mechanical Planarization Slurries

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Chemical mechanical planarization (CMP) is an important process in the semiconductor industry in which there is a potential for worker exposure to metal oxide nanoparticle (NP) aerosols. Toxicological evaluation of dispersant-stabilized NP-containing CMP slurries is essential for performing a comprehensive risk assessment. We hypothesized that inhalation exposure to CMP slurries would lead to a dose-dependent acute pulmonary inflammatory response in male F-344 rats (200-300 g). CMP slurries (alumina, ceria or amorphous silica; 10–100 nm) were diluted in water and aerosolized using an ultrasonic nebulizer for whole body inhalation exposures (4-6 hrs; mass median aerodynamic diameter, 0.7-1 μm; geometric standard deviation, 1.5-1.8). Deposited lung doses and acute inflammatory responses were evaluated 24 hrs after exposure and the persistence of response was evaluated 7 days after exposure. The silica slurry produced the largest increases in lavage neutrophils (4.6 - 34.0 mg/m^3 as Si; 7.6% ± 2.7% - 45.1% ± 3.0%) at 24 hrs post-exposure. Alumina and ceria slurries induced more modest neutrophilia (9.7 - 20.9 mg/m^3 as Al, 0.64% ± 0.1% - 5.1% ± 4.6%; 3.5 - 9.5 mg/m^3 as Ce, 2.1% ± 0.6% - 7.6% ± 4.6%) when compared to air-exposed controls (0.8% ± 0.3%). Unlike with silica and alumina, the modest inflammatory response to ceria slurry persisted up to 7 days post exposure (2.3% ± 0.8% - 9.2% ± 1.3%). These data suggest that NP-containing CMP slurries can cause lung inflammation in rats following acute, high-concentration exposures, depending on the type of NP. Further research is needed in order to evaluate lung effects following repeated exposures at lower concentrations. This research was funded by NIH P30 ES01247 and NY State Research Foundation subaward 13-15.

PS 2354 Functional Assessment of the Serome following Pulmonary Exposure to Carbon Nanotubes

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Assessing the mechanisms underlying adverse cardiovascular effects induced by inhaled toxins presents a substantial research challenge. We propose that blood carries an as yet unknown "inflammatory potential" consisting of modified proteins or other biomolecules and reaction byproducts that affects a pathological bioactivity which can be assessed using endothelial cells as biosensors. The approach involves applying serum from exposed animals to cultured primary endothelial cells or *ex vivo* isolated arteries. Mice were exposed to multi-walled carbon nanotubes (MWCNT; 0, 10 or 40 μg) via pharyngeal aspiration and serum was collected at 4 and 24 h post-exposure. Serum from exposed mice increased endothelial cell surface vascular cell adhesion molecule-1 (VCAM-1) and intracellular adhesion molecule-1 (ICAM-1) expression and proinflammatory transcripts, and decreased ATP-stimulated nitric oxide (NO) production. The functional impact of this loss of NO bioavailability was confirmed via myography, in which serum from MWCNT-exposed mice significantly impaired vasodilation to acetylcholine. In addition, serum from MWCNT-exposed mice reduced cell migration in a traditional scratch assay experiment. To identify the bioactive circulating components in the serum, a data-independent 'omic platform enabled reproducible label-free quantitative analysis revealed a diverse set of serum factors in the size range of 500-5000 Da altered due to MWCNT exposure. Each dose was associated with its own independent set of selective factors that differentiated the two MWCNT exposure groups. More compelling was that this particular size fraction had functional effects on endothelial cell function. In conclusion, pulmonary exposure to MWCNT dynamically alters circulating factors, which promotes endothelial cell activation, decreased NO bioavailability, and altered functionality all directionally predicting adverse cardiovascular outcomes.

PS 2355 Heterogeneity in Quantum Dot-Induced Lung Inflammation and Toxicity in Recombinant Inbred Mouse Strains of the Collaborative Cross

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Quantum dots (QDs) are engineered nanoparticles commonly composed of a CdSe/ZnS core/shell and application-specific outer coatings. QDs have uses in electronics, biomedical research and medicine. However, their small size, heavy metal composition and multitude of potential uses have generated concerns regarding their toxicity. The CdSe/ZnS QDs being used in this study are 12 nm in diameter and are coated with an amphiphilic polymer (trioctylphosphine oxide / poly (maleic anhydride-alt-1- tetradecene). We are investigating QD-induced lung inflammation and toxicity with a systems genetics approach utilizing recombinant inbred (RI) mouse strains from the Collaborative Cross (CC). We have observed significant heterogeneity across the RI strains in response to QD exposure 8 h after oropharyngeal aspiration. Specifically, we found significant mouse strain ($p<1 \times 10^{-9}$) and QD treatment ($p<0.05$) related effects in the levels of total protein in bronchoalveolar lavage fluid (BALF). We also found significant background strain variation in the % neutrophils in BALF ($p<1 \times 10^{-4}$), levels of lactate dehydrogenase (LDH) ($p<1 \times 10^{-6}$) in BALF, and in levels of lung tissue heme oxygenase ($p<0.002$). In addition, heme oxygenase levels were significantly correlated with BALF neutrophils ($r^2=0.16$, $p=0.005$) and lung tissue glutathione ($r^2=0.11$, $p=0.02$). This study will provide insight into mechanisms of QD related toxicity,

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