neuronal cells may be important in understanding a potential link between metal oxide nanoparticles exposure and the development of various neurological diseases in humans.

ABSTRACT FINAL ID: 2783 Poster Board #107
TITLE: CELLULAR EFFECTS OF NANOSILVER IN HUMAN MACROPHAGES: UPTAKE, OXIDATIVE STRESS, LIPID ALTERATIONS AND FUNCTIONAL IMPAIRMENT

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KEYWORDS: silver nanoparticles, protein carbonyls, TOF-SIMS.

ABSTRACT BODY: Silver nanoparticles (SNP) belong to the most commercialized nanoparticles. Here we monitored the biological effects of SNP of different sizes (20 nm, 40 nm) and coatings (citrate, peptide) in human macrophages in vitro. We used THP-1 derived macrophages as a model because of their particle-clearing role in vivo. The cellular uptake was analyzed by confocal Raman microscopy, TEM or Laser postionization secondary neutral mass spectrometry (Laser-SNMS). Cellular responses upon SNP treatment were studied by time-of-flight secondary ion mass spectrometry (TOF-SIMS) and several biological endpoints were evaluated, i.e., cytotoxicity, protein carbonyl formation and induction of heme oxygenase-1 (HO-1). Toxicity of SNP was dependent on exposure time, dose and particle coating. Nanogold proved mainly inert. All kinds of nanoparticles were efficiently taken up by cells. Aggregates and single particles could be detected throughout whole cells, including nuclei and lysosomes. With TOF-SIMS and Laser-SNMS we visualized intracellular SNP and detected significant changes in the membrane lipid pattern indicating oxidative stress and fluidity changes. We measured strong induction of HO-1 and formation of protein carbonyls with different time patterns. Each type of SNP induced a characteristic carbonylation pattern as resolved by 2D gel electrophoresis. SNP but not nanogold significantly affected the phagocytic activity of macrophages. Some of the particle-mediated effects could be reversed depending on the time and doses applied. Conclusion: SNP exert adverse effects in human macrophages already at subcytotoxic doses. Different kinds of SNP induce distinguishable effects at cellular and biochemical levels.

ABSTRACT FINAL ID: 2784 Poster Board #108
TITLE: INTRATRACHEAL INSTILLATION OF NANOCERIA INDUCE SYSTEMIC TOXICITY IN RATS

AUTHORS (LAST NAME, FIRST NAME): Nalabotu, Siva krishna[1]; Ma, Jane[2]; Triest, William[3]; Kolli, Madhukar[1]; Wehner, Paulette[4]; Blough, Eric[1]
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KEYWORDS: Cerium oxide nanoparticle toxicity.

ABSTRACT BODY: Nanotechnology is a broad interdisciplinary field that is centered on the use of materials that range in size from 1- 100 nm. The extensive use of nanomaterials in various sectors such as electronics, consumer goods, transportation and health industries poses an increased risk of exposure to both humans and the environment. Cerium oxide nano particles are shown to scavenge reactive oxygen species thereby they are proposed to use for the treatment of cardiovascular disease, neuronal injury and radiation induced damage. However, the systemic toxicity after cerium oxide nanoparticles exposure is not well understood. Herein, we investigate if intratracheal instillation of nanoceria is associated with alterations in blood biochemistry and histopathology of liver, kidney, spleen, and heart.

Compared to control animals, cerium oxide instillation increased serum ALT levels [Saline control: 58.29±10.73 vs. CeO2 7.0 mg/kg: 130.50±94.46; p< 0.05], reduced albumin levels [Control 4.17±0.17 vs. CeO2 7.0 mg/kg 3.54±1.14] and diminished the sodium-potassium ratio [Control: 25.78±1.98 vs. CeO2 7.0mg/kg: 22.78±2.54; p< 0.05]. An analysis of the blood lipid profile indicated a reduction in the triglyceride levels [Control: 142.86±53.0 vs. CeO2 7.0 mg/kg: 93.14±22.33; p< 0.05]. Compared to control animals, animals exposed to cerium oxide exhibited a reduction in liver weight [Control: 14.55±0.57 vs. CeO2 7.0 mg/kg: 12.50±0.54; p< 0.05] and dose dependent alterations (hydropic degeneration, enlargement of the hepatocytes, sinusoidal dilatation and the accumulation of granular bodies) in liver histology. No gross histopathological alterations were observed in the kidney, spleen and heart. Taken together, these data suggest that cerium oxide nanoparticles may exit the lung after deposition producing toxicological effects in the liver.

ABSTRACT FINAL ID: 2785 Poster Board #109

TITLE: TIME-COURSE DETERMINATION OF CELLULAR STRESS RESPONSES ELICITED BY ENGINEERED NANOMATERIALS

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KEYWORDS: Nanotoxicology, Pathways, Inflammation.

ABSTRACT BODY: Engineered nanomaterials are being incorporated continuously into consumer products, resulting in increased human exposures. The study of engineered nanomaterials has focused largely on oxidative stress and inflammation endpoints without further investigating potential pathways. Here we examine time-sensitive biological response pathways affected by engineered nanomaterials using a battery of stable luciferase-reporter cell lines in HepG2 cells. We measured the activation of three key stress responsive transcription factors: NFκB, Nrf2, and AP-1 by exposure to 6 titanium dioxide nanomaterials (nano-TiO2) with rutile, anatase, and rutile/anatase crystal structures, and 2 cerium oxide nanomaterials (nano-CeO2) from various manufacturers. Exposure concentrations ranged from 1-100 µg/ml per nanomaterial at 6 and 24 h. Cytotoxicity was measured in parallel using the MTT assay. Dynamic light scattering was used to determine the size and zeta potential of the nanomaterials in medium. Our results show that there were significant changes in transcriptional activation at concentrations as low as 1 µg/ml. The 10 nm anatase nano-TiO2 elicited the highest effect, a ~2.5 fold increase in NFkB transcriptional activation at 100 µg/ml after 24 h. Nrf2 showed transcriptional activation by one nano-CeO2, showing ~1.5 fold activation at 100 µg/ml after 24 h. AP1 elicited a ~1.3 fold increase in anatase/rutile nano-TiO2 at 1 µg/ml after 24 h. Both anatase/rutile nano-TiO2 were cytotoxic at 100 µg/ml after 24 h. Our results demonstrate the potential for engineered nanomaterials to elicit cellular stress responses through the NFκB and Nrf2 pathways. [This is an abstract or proposed presentation and does not necessarily reflect EPA policy.]

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