silver nitrate (AgNO3) as a positive control in the same soils. Soil exposures lasted for 14 days, after which surviving earthworms were counted and the median lethal concentration for 50% of the population (LC50) was calculated according to the trimmed Spearman-Karber method. PVP- AgNP LC50 in the Memphis Silt soil was 2828.43 mg/kg; in contrast, AgNO3 was much more toxic than PVP-AgNP in the same soil (LC50=223.31 mg/kg). The PVP coating did not contribute to PVP-AgNP soil toxicity (PVP LC50 > 40,000 mg/kg). PVP-AgNP LC50 in Sunev, Camp Shelby, and Big Black soil were all >1000 mg/kg. These data demonstrate that PVP-AgNP is less toxic in a soil environment than the ionic form (AgNO3). Furthermore, by utilizing four soils that cover over 50% of the soil in the contiguous U.S., these data provide quantitative soil toxicity values to better evaluate the effects of PVP-AgNP in soil environments.

PS 841b Transmission Electron Microscopic (TEM) Evaluation of Silver Nanoparticles (AgNP) or Silver Acetate (AgOAc) Deposition in Selected Tissues of Sprague-Dawley (SD) Rats

M. S. Imam[1], M. D. Boudreau[1], G. Olson[2] and A. Paredes[1]. *[1]National Center for Toxicological Research, Jefferson, AR and [2]Toxicologic Pathology Associates, Jefferson, AR.*

This study investigated the deposition of silver (Ag) in selected tissues (ileum, jejunum, colon, kidney, liver, spleen and mesenteric lymph nodes) of SD rats administered AgNP (10, 75, and 110 nm) at 36 mg/kg/day or AgOAc at 56 mg/kg/day by daily oral gavages for 13 weeks. The levels of Ag detected by TEM were highest in the small and large intestine of both male and female rats administered either AgNP or AgOAc. A subtle surface difference between AgNP and AgOAc deposition were observed in the colons and kidneys of rats. Rats treated with AgNP showed fine, spherical, and measurable Ag granules, whereas AgOAc showed irregular, flower-shaped surface depositions. The majority of Ag granules were located within the lamina propria and basement membrane of the intestinal epithelial cells. The localization and distribution of Ag varied in the other tissues, including the kidneys, livers, and mesenteric lymph nodes. Ag granules were entrapped by the macrophages in the mesenteric lymph nodes, whereas in the kidneys, the Ag deposition was observed in the basal lamina of the glomeruli involving podocytes and endothelia cells. In particular, the 10 nm AgNP had greater deposition in mesenteric lymph nodes, kidneys, and colons of both male and female rats suggesting size-dependent bio-distribution. Furthermore, the energy-dispersive X-ray spectral analysis revealed that Ag deposition in the kidneys, colons, and mesenteric lymph nodes consisted of silver and often coexisted with selenium, silicon and sulfur containing granules. A gender-related difference in Ag deposition was noted in the kidneys and colons, with greater Ag deposition in females compared to males. This study provides new insights into the bio-distribution patterns of AgNP or AgOAc in the major tissues and proposes a need for further research. This study is supported, by interagency agreements 224-12-0003 and AES12013 between the NCTR/FDA and NIEHS/NTP

PS 841c Toxicity and Allergy Responses in the Lung following Pulmonary Exposure to Nanoparticle Silver in Mice

C. E. McLoughlin, S. Anderson, K. L. Anderson, D. Schwegler-Berry, B. T. Chen and J. R. Roberts. *NIOSH, Morgantown, WV.*

Silver nanoparticles (AgNP), due to antimicrobial properties, are widely used in medical applications and consumer products. Expansive use of AgNP in manufacturing raises the concern of effects following respiratory exposure in workers. Previous work in the laboratory has shown dose-dependent lung toxicity with inflammation and alterations in lung immune parameters in rodents. The goal of the current study is to characterize effects of AgNP for potential exacerbation/attenuation of respiratory allergy in an ovalbumin (OVA)-induced allergy model in BALB/c mice. For range-finding (RF) studies, mice were exposed to physiological dispersion medium (DM), 6.1μg (LO), 18.2μg (ME), or 73μg (HI) AgNP. AgNP were 20 nm diameter with 0.3% wt polyvinylpovidone coating (NanoAmor, Inc.), were suspended and sonicated before exposures by pharyngeal aspiration (PA) on day 0. For RF studies assays were conducted on days 1, 10, and 29 post exposure—time points chosen to correspond with the allergy paradigm time course. Airway hyperreactivity was measured as PenH, bronchalveolar lavage (BAL) was performed on the whole lung, cells and fluid were retained for analysis of lung-associated injury and inflammation and phenotyping by flow cytometry, lymph nodes (LN) were harvested for enumeration and phenotyping. Changes in PenH did not occur with AgNP alone at any time point. Results indicated a dose-dependent injury and inflammation by day 10 which began to resolve by day 29. For the allergy model, DM and OVA served as controls and ME and HI were chosen for study. Animals received i.p. injections of OVA + aluminum hydroxide gel (alum) during the sensitization phase on days 1 and 10. To elicit an OVA-specific response, 2 PA challenges of OVA were given on days 19 and 29. Dose dependent increases in PenH, BAL and LN cell number were observed in mice exposed to AgNP over OVA controls. Results indicate potential for AgNP to exacerbate allergic response in the lung.

PS 841d Differential Genomic Effects on Signaling Pathways by Two Different CeO2 Nanoparticles in HepG2 Cells

K. T. Kitchin, K. A. Wallace, C. P. Jones, H. Ren, B. T. Castellon, J. Crooks and S. Thai. *US EPA, Durham, NC.*

Nanoparticles composed of CeO2 are of particular interest in toxicological studies due to their growing use in pharmaceutics, biomedical products, cosmetics, polishing materials and as automotive fuel additives. Human liver HepG2 cells were exposed for three days to two different forms of nanoparticles both composed of CeO2 (0.3, 3 and 30 ug/mL) and a genomic study performed. The two CeO2 nanoparticles have dry primary particle sizes of 8 nanometers {(M) made by NanoAmor}and 58 nanometers {(L) made by Alfa Aesar}and differ in various other physical-chemical properties as well. This systems biological genomic study showed that the major altered pathways were protein synthesis, stress response, proliferation/cell cycle, cytoskeleton remodeling/actin polymerization and cellular metabolism. Some of the canonical pathways affected were mTOR signaling, EIF2 signaling, fatty acid activation, G2/M DNA damage checkpoint regulation, glycolysis and ubiquitination. Nanoparticle M showed a normal dose-response pattern with 363, 633 and 1273 differentially expressed genes (DEGs) at 0.3, 3 and 30 ug/mL, respectively. M is more active than L in respect to altering the pathways of mitochondrial dysfunction, acute phase response, apoptosis, 14-3-3 mediated signaling, remodeling of epithelial adherens junction signaling, actin nucleation by ARP-WASP complex, and altered TCA cycle. However, L is more active than M in respect to the pathways of NRF2-mediated stress response and hepatic fibrosis/hepatic stellate cell activation. In summary, these two CeO2 nanoparticles effected both many shared and some differing toxicity pathways. Disclaimer: [This is an abstract or a proposed presentation and does not necessarily reflect EPA policy. Mention of trade names or commercial products does not constitute endorsement or recommendation for use.]

PS 841e Aggregation of Gold Nanoparticles with Thioether-Containing Amino Acids

S. Babu[1], F. Jaetae Seo[1], R. M. Uppu[2] and M. O. Claville[1]. *[1]School of Science, Hampton University, Hampton, VA and [2]Department of Environmental Toxicology and the Health Research Center, Southern University and A&M College, Baton Rouge, LA.*

Gold nanoparticles (Au NPs) have vast applications in drug therapy because of their unique optical, electronic and molecular properties. The toxicity of the Au NPs varies in cellular environment, depending on the physiochemical properties such as size, shape, surface chemistry, and the molecules with which they interact. When blue mussels, *Mytilus edulis*, are exposed to Au NPs of particle size < 5 nm, they exhibit an increase in oxidative stress and decrease in thiol-containing proteins. These organisms also contain methionyl peptides that are hypothetically subject to oxidation due to Au NP exposure. In this present study, we present preliminary findings regarding the interaction of Au NPs with methionyl compounds, L-Methionine(Met), D/L-Met, N-Acetyl-L-Met, L-Met Ethyl Ester, and Met-Glycine. The average sizes of the eight Au NPs used in the study are ~5, ~10, ~15, ~20, ~30, ~32, ~35, and ~40 nm diameters. The UV-Vis spectral studies showed that Au NPs exhibit a strong plasmon at ~530 nm while the methionyl compounds displayed an additional plasmon band at ~785 nm, indicating the formation of Au NPs aggregates. Methionine was found to aggregate Au NPs (conc. $3.487E^{-10}$ M) with size ~35 nm at higher concentration (final 0.125 M) with the color change from red to blue. While lower concentration of L-Met and D/L-Met did not aggregate immediately, N-terminal (N-Acetyl-L-Met) and C-terminal protected Met (Met Ethyl Ester) readily formed Au NPs aggregates. Methionine-Glycine dipeptide was only slightly better than D/L-Met at inducing aggregation of Au NPs. The results provide insight into the impact of NP size, peptide sequence, and concentration of NPs, on aggregation. We strongly believe aggregation size and kinetics may have a role in the etiology of cellular response which needs to be systematically evaluated. [This research is supported by grants from NSF-1230357 (formerly 0847742), NSF HRD–1238838, NSF HRD–1137747, and ARO W911NF-11-1-0177.]

The Toxicologist

Supplement to *Toxicological Sciences*

53rd Annual Meeting and ToxExpo™

March 23–27, 2014 • Phoenix, Arizona

An Official Journal of the Society of Toxicology

SOT | Society of Toxicology

Creating a Safer and Healthier World by Advancing the Science of Toxicology

www.toxicology.org

OXFORD UNIVERSITY PRESS

ISSN 1096-6080
Volume 138, Issue 1
March 2014

www.toxsci.oxfordjournals.org