NPs by SR-A involves more than simple anionic charge interactions. High resolution fluorescent microscopy analyses show that the majority of single or small clusters of silica NPs co-localize and traffick intracellularly with SR-A and are internalized through a pathway characteristic of clathrin-dependent endocytosis. In contrast, larger agglomerates (>500 nm diameter) of the same silica NPs show only a low level of co-localization with the receptor, suggesting independent pathways for internalization are involved. Silencing of SR-A expression also results in decreased NP-induced secretion of pro-inflammatory cytokines, suggesting the inflammatory response is triggered by NP internalization rather than by non-specific cell contact. Given the broad expression of this receptor throughout the reticuloendothelial system, the SR-A pathway likely plays an important role in modulating inflammatory responses to NPs and in limiting the effective delivery of therapeutic NPs in vivo.

PS 276 EVALUATION OF TOPO-PMAT MODIFIED QUANTUM DOT UPTAKE AND TOXICITY IN A549 HUMAN LUNG EPITHELIAL CELLS.

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Nanotechnology is becoming increasingly more prevalent in modern society. The ability to engineer various forms of nanoparticles has led to their use in products such as cosmetics and LED displays, and even biomedical imaging. Quantum dots (QDs) are one form of fluorescent nanoparticles. However, their heavy metal composition has given rise to concerns regarding toxicity and persistence in biological settings. The aim of this research is to evaluate the in vitro toxicity of trioctylphosphine oxide, poly(maleic anhydride-alt-1-tetradecene (TOPO-PMAT) coated CdSe QDs on human lung carcinoma epithelial A549 cells. QD uptake was measured following a 24h exposure with doses from 2.5nM to 40nM, using both flow cytometry (FACS) and fluorescence microscopy, which demonstrated a dose-dependent increase. Cell viability was unaffected at these doses, as assessed by MTT reduction to formazan. However, Western blot analysis of heme oxygenase 1 (HMOX) levels showed a dose-dependent up-regulation, suggestive of oxidative stress. Total glutathione (GSH) and total cellular thiols were assayed using NDA and monobromobimane (MBB) fluorescence, respectively. Neither of these measures changed. The induction of HMOX is thus more suggestive of an inflammatory response. While these preliminary results suggest that these amphiphilic QDs are taken up and do not have an adverse affect on cell viability, exposure does cause a stress response in A549 cells. This work was supported by NIEHS grants R01ES016189.

PS 277 SHORT- AND LONG-TERM BIODISTRIBUTION AND OXIDATIVE STRESS EFFECTS OF A SYSTEMICALLY-INTRODUCED 5NM CERIA ENGINEERED NANOMATERIAL.

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Objectives: To characterize the short- and long-term biodistribution and persistence of a 5 nm diameter ceria dispersion from blood and its oxidative stress effects in the spleen. Methods: An ~ 4% aqueous citrate-stabilized ceria dispersion, synthesized and characterized in-house, was intravenously infused into rats (100 mg/kg), which were terminated 1 or 20 h or 30 days later. Ceria concentration and localization in the brain, liver, spleen and whole blood were assessed by ICP-MS and light and electron microscopy. Oxidative stress effects were assessed as protein bound 4-hydroxy-2-trans-nonenal (HNE), 3-nitrotyrosine (3NT), and protein carbonyls (PC). Results: Cerium was quantified in cortex samples 1 and 20 h and 30 d after ceria dosing. However, EM revealed the presence of ceria aggregates in the brain vascular compartment but not in microvascular endothelial or brain cells. Thirty days after the ceria infusion the cerium concentration in the liver and spleen were 60 and 35% of that seen 20 h after infusion. However, there was no significant difference between total cerium in liver and spleen 30 d vs. 20 h after ceria infusion because the liver and spleen weights of treated rats were greater than control rats. At 30 d 44% and 10% of the ceria dose was in the liver and spleen. Giant cells containing ceria were seen in spleen red pulp as well as thickend arterials in white pulp. LM and EM revealed granulomatous formations in the liver. Oxidative biomarkers in spleen revealed 10% elevation of protein oxidation and 10% decreased lipid peroxidation. Conclusions: Contrary to expectation, these small ENMs did not permeate the BBB. Ceria clearance from these organs was slow. More toxicity was seen in the spleen and liver after 30 days than at 1 or 20h, demonstrating the importance of studying long-term retention and effects of engineered nanomaterials.
Supported by U.S. EPA STAR Grant RD-833772.

PS 278 EFFECTS OF PARTICLE SIZE AND ROUTE OF EXPOSURE ON THE BIOAVAILABILITY OF ZINC FROM NANO-SIZED ZINC OXIDE PARTICLES.

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This study utilized nano-sized ZnO to better define the pharmacokinetic and translocation properties of nano-sized particles. To determine the pharmacokinetic and translocation properties of neutron activated ZnO (^{65}Zn) particles, we utilizied two particle sizes (7-13 nm and 40-100 nm) and two routes of exposure (intravenous injection (IV) or intratracheal instillation (IT)). Male Sprague-Dawley rats were given a single dose of neutron activated ^{65}ZnO particles at 1.5 mg/kg body weight. At varying time points, tissues (lungs, brain, heart, spleen, kidney, skeletal muscle, liver, bone marrow and gastrointestinal tract) were collected. The radioactivity in tissues was calculated as % of instilled/injected dose. Results show that at 30 minutes post-IV, the % of injected ^{65}Zn in the liver was significantly higher for 40-100 nm than for 7-13 nm. However, 7 days later, liver uptake was the same for both particle sizes. For the IT-instilled particles, at both 1 and 7 days post-IT, tissue distribution was similar between the 2 particle sizes. At 1 day post, only 10% of the instilled ^{65}ZnO remained in the lung for both particle sizes. At 7 days post, the amount of ^{65}ZnO in the lung decreased to 0.1% for both particle sizes. In conclusion, for the IV-injected particles, particle size has an initial effect on ^{65}Zn uptake in the liver. For IT instilled particles, particle size did not alter lung clearance or distribution. The lack of particle size dependence on translocation and lung clearance of ^{65}ZnO particles may be due to the agglomerated state of the ZnO nanoparticles. Dynamic light scattering revealed that the 7-13 nm and 40-100 nm ZnO particles had a mean diameter of 83.5 nm and 88.3 respectively. Also, the high solubility of ZnO could have obscured any influence of particle size on pulmonary deposition of the particles. The ^{65}Zn measured in collected tissues was most certainly dissolved ^{65}Zn from the particles, especially at later time points.

PS 279 AGGLOMERATION STATUS OF NANO- AND SUBMICRON-SIZED PARTICLES AND THE EFFECT ON PULMONARY TOXICITY.

I. Gosens[1], D. Leseman[1], J. Boere[1], D. Lankveld[2], L. de la Fonteyne[2], F. Cassee[1] and W. de Jong[2]. *[1]MGO, National Institute for Public Health and the Environment (RIVM), Bilthoven, Netherlands and [2]GBO, National Institute for Public Health and the Environment (RIVM), Bilthoven, Netherlands.*

Nanoparticle (NP) toxicity testing comes with many challenges. One of them is agglomeration of nanoparticles in physiological media. In this study, we address the effect of agglomerated versus single particle suspensions of nanosized and submicron-sized gold on inflammatory response in the lung. Colloidal gold was chosen as a model particle to study effects on lung inflammatory markers in broncho alveolar lavage fluid (BALF) after intratracheal instillation in the rat. A single dose of 1 mg of spherical gold particles of 50 nm or 250 nm is diluted 10% either by ultrapure water or by adding 10x phosphate buffered saline (PBS). Particles diluted in ultrapure water are well dispersed, while the citrate shell is disturbed and agglomerates are formed when diluting in PBS. A single dose of 1 mg DQ12 quartz is used as a positive control. Dynamic light scattering (NanoSight) is used to determine the particle size distribution in the suspensions prior to application. Cell differentials, oxidative stress and inflammation are measured in BALF after 24 hrs.
This study focuses on the preparation of particle suspensions, the agglomeration status of particles and the effect this has on pulmonary inflammation.

PS 280 THE PARTICOKINETIC AND PHYSIOLOGICAL BASIS FOR *IN VITRO - IN VIVO* EXTRAPOLATION OF NANOMATERIAL TOXICITY STUDIES.

J. G. Teeguarden, P. Hinderliter, B. Thrall, G. Orr, K. Waters, R. Corley and J. Pounds. *Pacific Northwest National Laboratory, Richland, WA.*

The rapid development, varied forms and potentially vast number of untested nanomaterials pose a significant challenge to time consuming and costly conventional safety assessment paradigms. This challenge will be met with new testing par-

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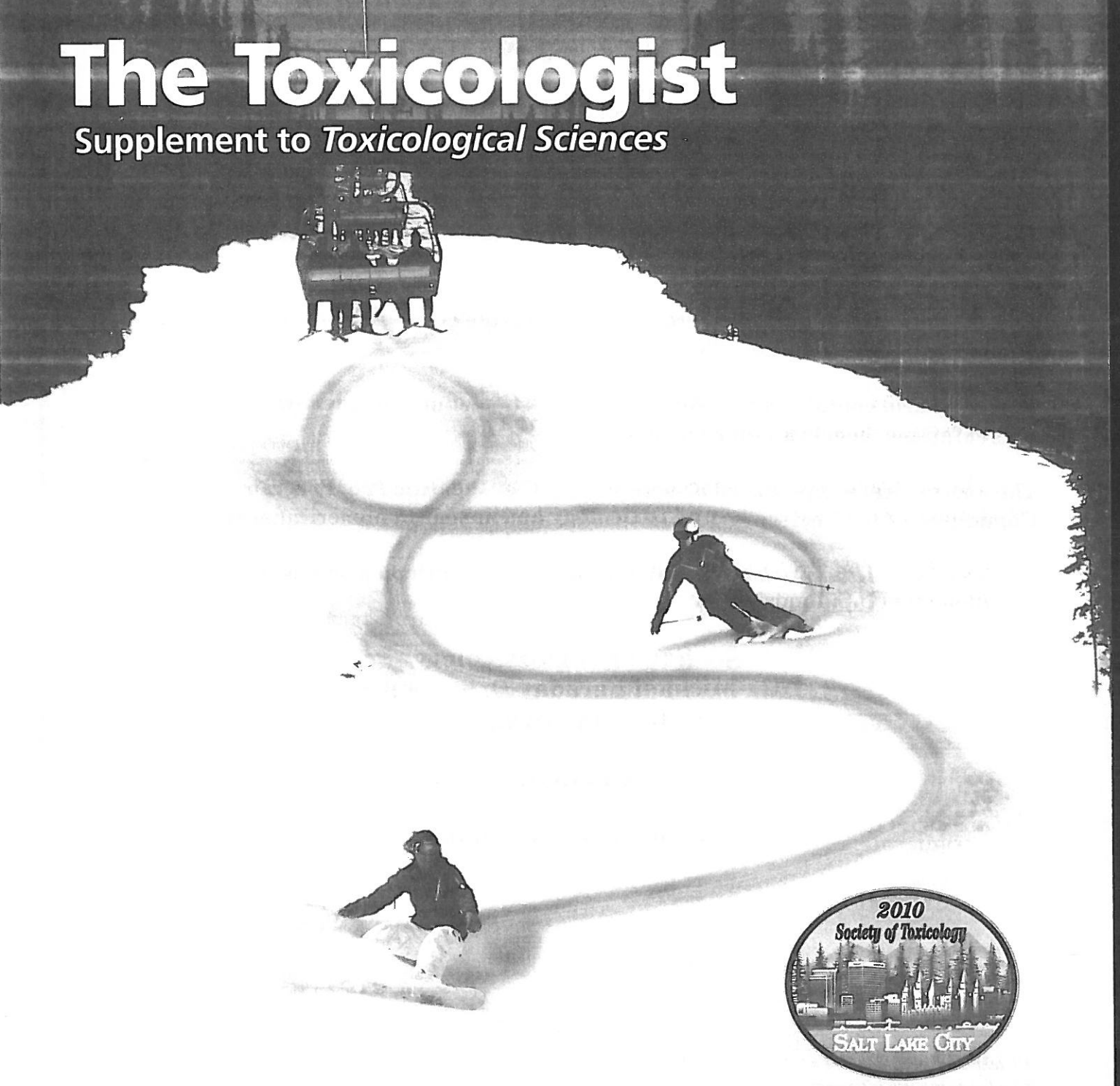

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Preface

This issue of *The Toxicologist* is devoted to the abstracts of the presentations for the Continuing Education courses and scientific sessions of the 49th Annual Meeting of the Society of Toxicology, held at the Salt Palace Convention Center, March 7–11, 2010.

An alphabetical Author Index, cross referencing the corresponding abstract number(s), begins on page 473.

The issue also contains a Key Word Index (by subject or chemical) of all the presentations, beginning on page 496.

The abstracts are reproduced as accepted by the Scientific Program Committee of the Society of Toxicology and appear in numerical sequence.

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