size. Ag coatings were made up of several Ag crystallites that nucleated on the Au producing many highly defective interfaces. In contrast, pure Ag particles were less uniform in shape but had a more ordered 'single' crystal structure with slip plane or grain-boundary defects. Dissolution was studied in RPMI+FBS culture medium by measuring the appearance of Ag in the supernatant as a function of time up to 24 hours. High resolution (HR)-TEM and STEM images after solution exposure showed that the pure Ag particles maintained structural integrity compared to Ag/Au particles where Ag layer had a non-uniform dissolution sometimes exposing the Au core. Dissolution was increased for 20 nm Ag/Au particles in comparison to pure Ag. An equation relating the kinetics of dissolution, the surface area of particles and an effective solubility constant was used to examine dissolution behaviors. For solution concentrations ≥ 10 μg/ml, dissolution parameters within each particle type are consistent regardless of particle concentration. The effective solubility constant for 20nm particles with the Au was higher than that observed for pure Ag particles. At solution concentrations < 10 μg/ml, solution kinetics and rates appear to be less than would be expected from the behaviors at higher concentrations. Reasons for this difference are under study.

PS 1964 Does Microfluidic Dispersion Influence the Toxicity of Geometric TiO2 Nanomaterials?

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Tunable chemical and physical properties of engineered nanomaterials are achievable by changing their geometry and morphology. Titanium dioxide (TiO2) based nanofilaments—nanotubes, nanowires, nanorods—have gained interest in sensing, electrical, and environmental fields due to their superior performance over TiO2 nanoparticles. Their application in the medical field for drug delivery, implant coating, and bioimaging is just now being realized, however their biocompatibility is not fully understood. Thus, safety assessment of geometric TiO2 nanomaterials is critical for protecting workers, patients, and bystanders as these technologies become widely implemented. The tendency of TiO2 based nanofilaments to aggregate and agglomerate make toxicity results controversial because of the challenge in differentiating whether the observed toxicity was caused by the nanofilaments or aggregates. TiO2 nanofilaments aggregate and are difficult to disperse homogeneously in solution by conventional methods, like sonication and voxtexing. In this study, a microfluidic device was utilized to produce the stable, homogeneous dosing solutions necessary for in vitro toxicity evaluation by eliminating any toxicity caused by aggregated TiO2 nanofilaments. The quality of the dispersion provided by this method allows for toxicity results to be directly correlated to the TiO2 nanostructure itself. The biocompatibility of four TiO2 nanogeometries—nanotubes, nanowires, nanorods, and nanoparticles—were assessed in nasal epithelial cells (RPMI 2650). All TiO2 based nanomaterials dispersed by the microfluidic method were biocompatible in RPMI 2650 cells at the concentrations tested. Whereas 100 μg/ml concentrations of nanowires and nanotubes dispersed by sonication reduced viability up to 27%, indicating that in vitro toxicity results may be controlled by the dispersion of dosing solutions.

PS 1965 Low-Level Exposure to Silver Nanoparticles-Induced Hypertrophy, Multinucleation, and Senescence in Lung Epithelial Cells

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Nanotechnology is a rapidly expanding discipline focused on manipulating materials at the nanometer scale. Considerable research has focused on the antibacterial properties of silver nanoparticles (AgNPs), resulting in several commercial products. The bactericidal activity of AgNPs stems from shedding of silver ions and their binding critical biomolecules. The toxic activity in mammalian cells is proposed to derive from oxidative stress caused by the particles and the ions release. In addition, AgNPs may reside in biosystems, producing long-term stress directly or through slow dissolution to ions. As a result, AgNP exposure raises concern over environmental and human health effects. Long-term stress and oxidative damage can induce cellular senescence, or permanent growth arrest. This project tested the potential for AgNPs to induce senescence in A549, epithelial cells during extended exposure at a sub-lethal concentration. Cells were exposed to AgNPs for 1 to 4 days at 10 μg/mL, a level that did not cause overt toxicity by MTS assay but caused oxidative stress measured using a Dichlorofluorescein probe. After 3 to 20 days of recovery, induction of senescence was assessed by observing cell morphology, measuring proliferation, and testing for senescence-associated β-galactosidase (SA-β-Gal) activity. AgNPs caused an increase in the number of hypertrophic cells and cells with SA-β-Gal activity, indicating senescence was induced. Proliferation was relatively unaffected suggesting that many A549 cells were able to subvert full growth arrest; however most hypertrophic cells were multinucleate implying that they could not complete cytokinesis. Taken together, these results indicate that AgNPs induced a senescence-like phenotype in A549 cells despite their resistance to growth arrest.

PS 1966 Evaluation of Tungstate Nanoparticle Cytotoxicity

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Alkaline-earth metal tungstate AWO_4 (A= Ca, Ba, Sr) nanoparticles are currently being used in a variety of applications, including use as components of medical equipment, optical fibers, and scintillator detectors. This versatility may lead to increases in manufacturing within the next 10 years and may subsequently result in more cases of occupational exposure. Therefore, it is important to assess the effects of tungstate nanoparticles on cellular systems. RAW 264.7 macrophage cells were used to assess tungstate nanoparticle toxicity and changes in reactivity based on shape (sphere vs. wire), size, and chemistry. Enhanced dark field microscopy and scanning electron microscopy were used to evaluate nanoparticle-cell association over multiple time points up to 7 hours. To assess uptake, transmission electron microscopy was implemented. Both wires and spheres showed cell surface interactions; however, only spheres were engulfed. To assess intracellular reactive oxygen species (ROS) production, a DCFH assay was performed. Results showed that nanowire-exposed cells had significantly increased levels of ROS over a 7 hour time-course, while nanosphere-treated cells did not. This may be a result of association versus engulfment. Based on ROS production and cell-particle interactions, overall cellular cytotoxicity was measured. A caspase activation assay was used to assess apoptosis, and an MTT assay was employed to determine cell viability. Minimal caspase activity was measured after 24 hours with both spheres and wires. Wire-cell interactions resulted in cell death after 24 hours and sphere treated cells had minimal changes in viability. This data shows that tungstate nanoparticles are not explicitly toxic; however, wires appear to be more reactive than spheres, and have an initial, but manageable toxic effect on cells.

PS 1967 *In Vitro* Cytotoxicity Assay of TiO_2 Nanoparticles in Pulmonary Epithelial and Macrophage-Like Cells

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Recent advances in nanotechnology have increased the development and production of many new nanomaterials, and this raises concerns about possible human health risk. To establish alveolar cell-based assay systems, human epithelial and macrophage-like cell lines (A549 and THP-1) were used.
First, we investigated the A549 cell viability after exposure to the nanoparticles (Φ21 nm TiO_2) at various initial densities. When the cells are cultured at a low density, the drastic decrease of viability (50%) was observed. In contrast, when the cells are cultured at a high density to form cell monolayer, the viability decreased only slightly. In addition, in cocultues of A549 monolayer and THP-1, there were no viability changes, presumably because particles are firstly phagocytized by THP-1 or macrophages. These results show that we have to carefully choose the culture conditions according to the objectives such as screening with high sensitivities or physiological relevancy.
Second, nanoparticles permeation was investigated using A549 and THP-1 cell-based alveolar model formed on semi-permeable membranes and relevant numerical simulation describing dynamic equilibrium among the apical side, alveolar cells, macrophages and basolateral sides. With biological kinetic parameters obtained in the cell-based assay, the numerical model largely described the concentration changes in the assay system. By changing some parameters such as scale of the model to overcome the limitations of existing culture models, it was indicated that the combination use of *in vitro* cell-based tissue models and numerical simulations made us possible to predict the permeation of particles through the alveolar tissue.

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