their genotoxic effects remain under-explored. This study aims to elucidate the toxic effects and biological responses and provide the possibility of application for cancer therapy by attractive nanomaterial QDs. In this study, CdSe/ZnS core/shell QDs-induced cell death type in A549 cells was evaluated via MTT, apoptosis, and LDH assay and analyzed differential mRNA levels involved in apoptosis with/without UVA/UVB irradiation. The genotoxic effect of CdSe/ZnS QDs was measured, for the first time, by comet and micronucleus assay based on human cancer cell in the present study. The extent of cell death was the most severe in CdSe/ZnS QDs treatment under UVB irradiation group, which indicated the strong induction of phototoxicity by CdSe/ZnS QDs with UVB and it led to both apoptotic and necrotic cell death. In the induction of olive tail moment and micronucleus formation, significant increases were also investigated in CdSe/ZnS QDs under UVB irradiation group. Here, we estimated the genotoxic effect and mechanistic details on the CdSe/ZnS QD-induced cell death pathway and suggest, furthermore, it might be used to apply for cancer therapy using UVB radiation.

PS 331 ROLE OF DOSE RATE ON NANOPARTICLE-INDUCED INFLAMMATORY RESPONSES *IN VIVO*.

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The increased production of nanomaterials has caused a corresponding increase in concern about human exposures in consumer and occupational settings. Numerous *in vivo* studies in rodents have evaluated dose-response relationships following respiratory tract (RT) delivery of nanoparticles (NPs) in order to identify potential hazards. These studies often use high doses and bolus delivery methods that do not reflect real world scenarios. We hypothesized that the delivered dose rate is a key determinant of the induction of the inflammatory response in the RT. These studies aim to re-evaluate the predictive power of *in vivo* bolus delivery for NP hazard identification. F-344 rats (175-270 μg) were exposed to the same deposited dose (200 μg) of TiO_2 (80% anatase, 20% rutile; 21 nm) by high dose rate (bolus) intratracheal instillation or by low dose rate (aerosol) whole body inhalation over 4 hrs. Controls were exposed to saline or filtered air. The impact of dose rate was also examined in the context of repeated instillation and inhalation exposures (one quarter the dose on each of 4 consecutive days). The greatest post-exposure (24 hrs) increases in bronchoalveolar lavage fluid (BALF) neutrophils were found after single (31.1% ± 2.6% (SD)) and repeated (16.8% ± 3.6%) bolus TiO_2 NP exposures. Aerosol delivery resulted in lower inflammation (6.2% ± 1.5%, single; 1.6% ± 0.6%, repeated exposure). For both bolus and aerosol delivery, there was an attenuation of the neutrophil response when the dose was delivered over 4 days. Similar trends were found for changes in BALF lactate dehydrogenase and β-glucuronidase activities. We conclude that high dose rate NP delivery elicits significantly greater inflammation compared to realistic low dose rate delivery and that bolus delivery overestimates the NP-associated hazard. This research was funded by NIH R01CA134218, P30ES01247, T32E07026, and 5RC2ES018741.

PS 332 SILVER NANOPARTICLE TOXICITY TO RETINAL PIGMENT EPITHELIAL CELLS *IN VITRO* IS INFLUENCED BY PARTICLE SIZE AND COATING, BUT NOT UVA RADIATION.

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Silver nanoparticles (AgNP) are used in textiles, medical devices, cleaning products and ocular devices because of their antibiotic properties. Because the retina is the only part of the nervous system exposed to light and because other nanoparticles have demonstrated phototoxicity, human retinal pigment epithelial cells (ARPE-19) were used to test the potential cytotoxicity and phototoxicity of PVP- and citrate-coated silver nanoparticles (Ag-PVP and Ag-CIT, respectively). ARPE-19 cells were grown to confluence in DMEM/F12 + 10% FBS and dosed with 0, 3, 10, 30, 55, 100, & 200 μg/ml of 10, 50, and 75nm Ag-PVP or Ag-CIT(nanoComposix). For phototoxicity tests, the cells were exposed to 2 hrs of either UVA, visible light, or no light exposure 24 hrs after dosing. Cell viability(calcein AM/propidium iodide) was measured either 24 hrs after dosing (cytotoxicity) or 24 hrs after dark/light/radiation exposure (phototoxicity). Flow cytometry showed dose-related increased side-scatter consistent with cellular uptake of AgNP. silver particles were observed in the cytoplasm of ARPE-19 cells under darkfield microscopy. The cytotoxicity of nano-silver was dose-dependent, and inversely proportional to particle size. Nano Ag-PVP was more potent than equivalent-sized Ag-CIT for 50 or 75 nm particles. No differences in cytotoxicity were observed between 10 nm Ag-PVP and 10 nm Ag-CIT. No differences were observed between cells treated 10 nm Ag-PVP or 50 nm Ag-CIT and co-exposed to darkness, visible light or UVA. Thus, the toxicity of Ag nanoparticles was influenced by particle size and coatings, but no evidence of phototoxicity was observed. This abstract does not reflect EPA policy.

PS 333 *IN VITRO* MODEL TO MIMIC THE LUNG EPITHELIAL BARRIER FOR NANO-TOXICOLOGY STUDIES.

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Previous data have shown that upon alveolar deposition, dispersed carbon nanotubes (CNT) can penetrate into the interstitium or pleural area which may indicate a specific mechanism of CNT induced pulmonary toxicity. Our hypothesis is that physicochemical properties of CNT could play a key role in determining the penetration mechanism of CNT into deep lung tissue. However, this would be difficult to determine *in vivo*. Lung epithelial cells typically form tight junctions which serve as a protective barrier against external particulates and can be monitored through resistance measurement *in vitro*. An experimental model was developed using an immortalized human lung epithelial cell line [Calu-3 cells (HTB-55), ATCC, Manassas, VA] and Transwell ® inserts (Costar 6.5 mm polyester membrane with 3.0 μm pores). Calu3 cells were cultured at 10, 20 or 50 x 10^3 per insert in Eagle's Minimum Essential Medium (EMEM) containing 15% Fetal Bovine Serum (FBS). After two days, medium was changed to EMEM that contained 2, 5, 10, or 15% FBS to assess serum effects on tight junction formation. Resistance (ohms) of the cell monolayer was monitored every day from days 3 - 18 in culture using the Epithelial Voltohmeter and STX2 electrode (World Precision Instruments). A subset of Transwell inserts were collected at various resistances and days in culture and tight junctions were immunofluorescence stained using the ZO-1 antibody. Tight junctions were observed using confocal microscopy after the resistance reached 2000 ohms in all concentrations of FBS tested. Resistance reached and maintained > 4000 ohms in 5 days at 50k, in 12 days at 20k and 14 days at 10k cell density. Establishment of Calu3 cell monolayers with functional tight junctions is dependent on filter size, seeding density and serum concentration. The Transwell Calu-3 model represents a potential rapid assessment *in vitro* model to test the effects of nano-material exposure on cell tight junction integrity.

PS 334 GENOTOXIC STRESS RESPONSE GENES ARE DYSREGULATED BY SILVER NANOPARTICLES IN TK6 CELLS.

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Silver nanoparticles (AgNPs) are presently the most used engineered nanomaterials due to their antimicrobic nature. AgNPs have been used in dressings to reduce infections in burns, and as antimicrobials in air fresheners, water purifiers, food storage containers, and in coatings for clothing. However, their genotoxicity has not been well examined. In this study, 4 genes involved in the genotoxic stress response, p21, GADD45, ATF3, and DDB2, were used to evaluate the genotoxicity of AgNPs. Cells were treated in triplicate for 24 hours with different concentrations of 5 nm AgNPs coated with polyvinylpyrrolidone (PVP) or tannic acid (TA). The cytotoxicity of the AgNPs increased with dose and the doses causing relative cell counts 50% of the control cell count were about 3 ug/ml for PVP-AgNPs and 4 ug/ml for TA-AgNPs. There were dose-dependent increases in the expression of all 4 genes except for those at concentrations causing very high cytotoxicity. The fold changes induced by the AgNPs were small and the highest induction over the control was 2.5-fold that occurred in the p21 gene. The gene expression was significantly altered by the treatment of the both types of AgNPs for least one concentration in all the 4 genes ($p < 0.05$). The response of these genotoxic stress genes to the AgNP treatment was correlated well with our other genotoxicity studies showing that AgNPs induced DNA adducts, DNA breaks, micronuclei and mutations in TK6 or mouse lymphoma cells.

PS 335 CEREBROVASCULAR TOXICITY OF PCBS BOUND TO NANOPARTICLES IN THE EXPERIMENTAL STROKE MODEL.

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Polychlorinated biphenyls (PCBs) are among the most persistent and widespread environmental pollutants. Recent evidence suggests that exposure to PCBs may increase the incidence of stroke and worsen stroke outcomes. PCBs released from environmental sources are capable of binding onto nanoparticles present in the environment and be taken up by humans. However, very little is known about the toxic effects of PCBs assembled onto nanoparticles. In the current study, we hypothesize

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