MED of UVA. Cell viability was determined 24 hr post-irradiation by the MTS assay. Preliminary results indicate that there was no difference in cytotoxicity between nanosized or bulk ZnO (200 nm) and Zn^{2+} alone, in both sham- and UV-irradiated skin cells. However, Zn^{2+} and all ZnO filters were more cytotoxic in HaCaT cells than most organics, at doses >10 μg/mL. In immune cells, organics decreased viability at similar doses in both cell types. Comparatively, organics were equally cytotoxic to ZnO NP in monocytes, but less cytotoxic in macrophages. Following UVA exposure of macrophages, there was a trend towards increased cytotoxicity with Zn^{2+} and 30 nm ZnO NP. Conversely, the cytotoxicity of organic UVA blocker butylmethoxydibenzylmethane, but not organic UVB blockers, was partially reduced by UVA. Our data indicate that the relative cytotoxicity of ZnO NP in this *in vitro* test system is comparable to that of Zn^{2+} alone, and is similar to organic UV blockers.

PS 2180 TITANIUM NANOPARTICLES INDUCE EXPRESSION OF ADHESION MOLECULES IN VASCULAR ENDOTHELIAL CELLS.

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Atherosclerosis is a chronic inflammatory disease and still the number one cause of death in the United States. Numerous risk factors for endothelial cell dysfunction and the development of atherosclerosis have been identified, including air pollution and inhalation of ambient nano-size ultrafine particles. Recently, engineered nanoparticles (NPs) such as metal NPs have attracted a great deal of attention due to their potential applications. However, there are also great concerns for their potential to cause adverse health effects in vascular systems because engineered NPs are similar in size and characteristics in comparison to ambient ultrafine particles. Among a variety of metal NPs, titanium NPs are receiving increasing attention due to their wide range of applications and mass production. To test the hypothesis that metal NPs can induce adhesion molecules in the endothelium, endothelial cells were treated with metal NPs. Among selected metal NPs, titanium NPs strongly, and in a concentration-dependent manner, induced mRNA and protein levels of vascular cell adhesion molecule-1 (VCAM-1). In addition, monocyte chemoattractant protein-1 (MCP-1) mRNA levels were increased after exposure to titanium NPs in a concentration-dependent manner. Titanium NPs with two different surface area (45 vs. 210 m2/g) showed similar effects in the induction of VCAM-1 and MCP-1. Exposure of endothelial cells with titanium NPs and pharmacological inhibitors, e.g., a JNK inhibitor, SP600125 and a PI3K inhibitor, LY294002, resulted in a decrease of VCAM-1 and MCP-1 expression, suggesting both JNK and PI3K are critical mediators of these proinflammatory responses. Furthermore, disruption of lipid rafts by cholesterol depleting agents did not influence titanium NP-induced VCAM-1 expression. These data show that titanium NPs can induce a cardiovascular disease risk via increased proinflammatory responses, such as adhesion molecule expression in vascular endothelial cells. This work was supported in part by NIH/NIEHS grant P42ES007380 and the UKAES.

PS 2181 SILVER NANOWIRES INDUCED INFLAMMATION IN AN *IN VITRO* HUMAN ALVEOLAR LUNG MODEL.

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The goal of this study was to evaluate the biological response following inhalation exposure to silver nanowires (Ag-NWs). Nanomaterials have been shown to penetrate deep into the alveolar regions of the lung, so we used a human alveolar lung co-culture model previously established in our lab as our model for inhalation exposure. The Ag-NWs were synthesized by nanoComposix and were 4 and 20 μm in length, with a similar diameter of ~90 nm. Changes in cellular morphology and the cellular interaction of the Ag-NWs with the cells was assessed using ultra-resolution microscopy after a 24 h exposure to 200 ng/ml of the Ag-NWs. The cell morphology and interaction of the Ag-NWs demonstrated that both lengths of Ag-NWs were interacting with the cells, but normal morphology indicated that they were not toxic. In addition, the co-cultures were exposed to Ag-NWs (concentrations ranging from 0-200 ng/ml) and cell viability was assessed using MTS to evaluate mitochondrial function. Our viability assays indicated that both Ag-NWs did not alter cell viability and that there was no toxicity. In addition, inflammatory responses were evaluated using ELISA assays to determine the secretion of 12 different cytokines. Of the cytokines evaluated, the Ag-NWs demonstrated an increase in secretion of several of them including IL-6, IL-8 and Interferon Gamma indicating that the Ag-NWs caused inflammation. Therefore, while the Ag-NWs were not toxic to the cells, they did cause irritation and an inflammatory response.

PS 2182 EVALUATING THE TOXICITY OF NANOMATERIALS USING A 3D NEURONAL CO-CULTURE MODEL.

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Use of unicellular in vitro models to represent complex tissues, such as the brain, has received criticism since these models cannot provide a modest to often needed exact depiction of how a multi-cellular tissue responds. However, in vitro cultures are key tools for preliminary foundation studies that assess dosing ranges, probable mechanisms of toxicity and that lower animal use by refining techniques prior to progressing to in vivo studies. As a bridging model system, the use of cell matrixes and multi-cell co-cultures such as those including more tissue specific cells or their resident immune cells may provide a linkage between in vitro to in vivo responses. Major players within the body's immune system include localized phagocytic cells that patrol and remove foreign materials they encounter to include toxic nanomaterials. In some cases, specific proteins called cytokines will signal phagocytic cells to a particular site within the body to aid in an immune response. This study focused on establishing in vitro neuronal co-cultures, neurons and their microglia, to evaluate the response effects of nanoparticle (NP) exposures. Co-cultures of neurons and microglia were grown on poly-l-lysine coated plates in Matrigel to simulate a 3D environment. Following exposure to 40 nm and 1 μm manganese NPs, there was a greater decrease in cell viability in the unicellular cultures, compared to when microglia cells were present. In addition to cellular viability, gene expression changes were evaluated as well as secretion of dopamine, norepinephrine and glutamate. When these endpoints were compared between the unicellular and co-cultures there was a drastic difference in the response. This model demonstrated the importance of normal phagocytic cells within the matrix for evaluating the biological responses to NPs, and suggests that the development of in vitro model systems, which more accurately simulate in vivo conditions, should be considered in order to obtain an accurate evaluation of tissue sensitivity from NP exposures.

PS 2183 CYTOTOXICOLOGICAL AND PATHWAY-FOCUSED PERTURBATIONS IN DERMAL CELLS EXPOSED TO QUANTUM DOT SYSTEMS.

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Quantum Dot (QD) nanocrystals have received attention due to their unique electronic and optoelectronic properties. QDs are increasingly being used for a wide variety of industrial and consumer-based applications, including biomedical imaging agents, inks, and solar panels. QDs may also pose risks to human health due to heavy metal exposure and/or the production of reactive oxygen intermediates. However, it is largely unknown which specific pathways or subcellular mechanisms of action are triggered as a result of exposure to QDs. First, inflammatory and non-inflammatory immune responses were measured in HDF cells by probing for protein and mRNA expression with western blots and pathway-focused gene profiling. Cellular effects from QD (CdSe/ZnS-COOH) exposure induced upregulation of apoptotic, inflammatory and immunoregulatory proteins including TNFα, IL-1B and IL-10. QDs also caused modulation of genes known to be associated with inflammatory (IL1-β), immune (IL-1, IL-6, IL-10), cellular stress (HMOX1), and apoptotic (CASP1, ADORA2A, NLRC4) responses. QDs caused dose (1 to 120 nM exposure concentrations) and time (8 hr vs. 48 hr) dependent cell death, as evidenced by resazurin-based metabolic activity assays. Differential cytotoxicity in HEK and HDF cells was seen over a range of exposure concentrations. By 48hrs, viability of HEK cells was reduced to 12% vs. 57% in HDFs when exposed to 120nM concentrations. Additionally, we probed the differential cytotoxicological and morphological response in HDFs exposed to cadmium-containing QDs (CdSe/ZnS-PEI) or microencapsulated QDs, as measured by fluorescence microscopy, metabolic activity, and western blots. Results show that microencapsulated QDs induced less toxic response as compared to unencapsulated QDs, while still offering the desirable optic characteristics. This data suggests that the cytotoxic response of cells exposed to these materials is dependent upon size and surface coating. In addition, the observed toxic response can be mitigated by altering these physical features.

PS 2184 *IN VITRO* DNA DAMAGE, MUTATION, AND CYTOTOXICITY AND SUBCHRONIC CELL GROWTH STUDIES OF QUANTUM DOT NANOPARTICLES.

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Quantum dots are engineered nano-materials whose composition and toxicology profile are wholly dependent on the method of synthesis. Because of their ease of use and unique advantages over traditional fluorescent probes, quantum dots have

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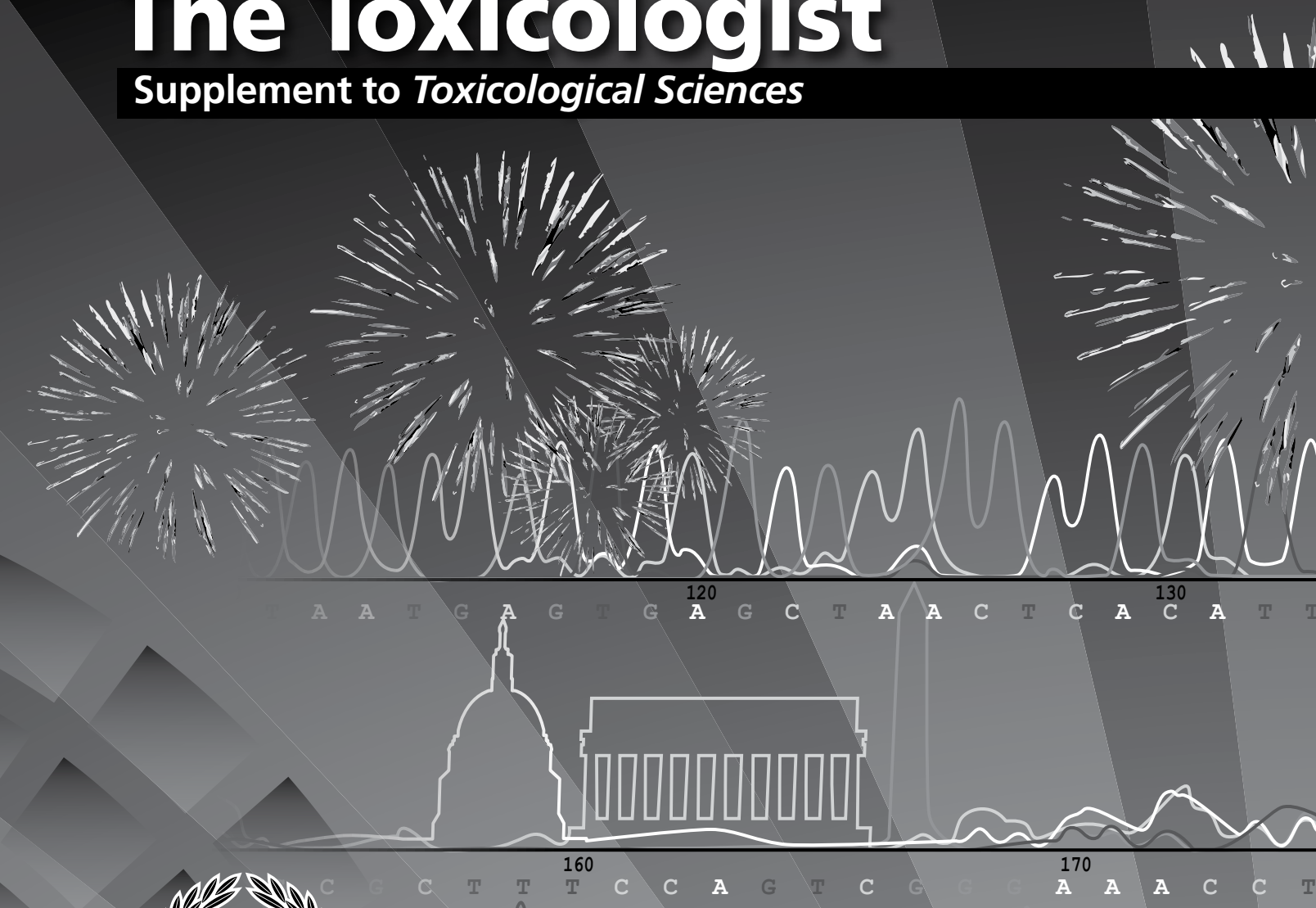

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Preface

This issue of *The Toxicologist* is devoted to the abstracts of the presentations for the Continuing Education courses and scientific sessions of the 50th Annual Meeting of the Society of Toxicology, held at the Walter E. Washington Convention Center, March 6–10, 2011.

An alphabetical Author Index, cross referencing the corresponding abstract number(s), begins on page 578.

The issue also contains a Key Word Index (by subject or chemical) of all the presentations, beginning on page 606.

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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