highlights the importance of considering G×P effects when identifying sensitive populations, whose underlying genetics or diseases could directly modify their response to AgNP exposures.

2118 The Yin-Yang of Inflammation: Is There a Balance during Nanoparticle Toxicity?

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Nanoparticle exposure is rising due to their versatile utility as drug carriers, mechanical property enhancers in medical devices, consumer products, and food excipients. To name a few multiwalled carbon nanotubes (MWCNT), cobalt oxide (cancer therapy), silver (antibacterial composition), titanium oxide (sunscreen), are routinely used in a variety of formulations. Nanoparticles can accumulate in tissues due to their extremely small size and elicit toxic effects. Despite the tremendous benefit presented, common pitfalls of this technology are its potential short and long-term effects on the human body. High mobility group box-1 (HMGB1) acts as a damage-associated molecular pattern and can work as a necrosis signal for the immune cell activation through the toll-like receptor (TLR). HMGB1 can bind to multiple receptors including TLRs in liver diseases. Our previous differential HMGB1 expression analysis following TiO_2 or MWCNT exposure showed an increase in HMGB1 protein expression in the hepatocyte cell line, HC-04. Tumor necrosis factor α induced protein 3-interacting protein 1 (TNIP1), a cytoplasmic protein, inhibits signaling mediated by numerous trans-membrane receptors, such as TLRs, thus acting as a negative regulator of TLR signaling. Both HMGB1 and TNIP1 converge at TLR signaling: where HMGB1 activates TLRs producing an inflammatory response and TNIP1 restricts TLR mediated inflammation. Thus, in this analysis, our goal was to evaluate the relationship between HMGB1 expression and TNIP1 expression in HC-04 cells exposed to nanoparticles. Interestingly, we evidenced an inverse relation between HMGB1 and TNIP1 protein expression. Hepatotoxicants such as acetaminophen (APAP) and ethanol (EtOH) have been shown to induce HMGB1 expression in the liver. In HC-04 cells, HMGB1 expression also increased due to APAP and EtOH whereas TNIP1 expression decreased. For the first time, we could demonstrate the changes in TNIP1 expression after a xenobiotic exposure and its relationship with a pro-inflammatory signal. In summary, the results suggest that nanoparticle exposure results in an increase in the inflammatory ligand, which in combination with decreased inhibitory control on inflammatory signaling may predispose cells to the inflammatory response to otherwise less toxic xenobiotic exposure.

2119 Formation of Low Molecular Weight Products during Environmental Transformation of Graphene Oxide Modulates Toxicity in Aquatic Species

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Carbon-based nanoparticles (CNPs) are used extensively in industrial, consumer, and mechanical applications. Their unique structural properties provide novel opportunities to develop more robust and innovative commercial products including paints, fabrics, cosmetics and electronics. With increasing commercial use of CNPs, environmental exposure is growing increasingly common. Specifically, graphene oxide (GO) has been shown to compromise cell integrity via interactions with lipid membranes and subsequent induction of oxidative stress *in vitro*. An understanding of GO-membrane interactions and resulting potential of GO to perturb biological systems are crucial for estimating risk. To assess the exposure and toxicological implications of environmental transformations of GO in aquatic species, GO suspensions were photo-irradiated by simulated sunlight for up to 490 hrs. Fathead minnow (FHM) epithelial cells were exposed to both GO/reduced (rGO) suspensions as well as their filtrates. The formation of low molecular weight products (LMWPs) was assessed by mass spectrometry and metabolomic profiling was used to investigate the biological response in this ecologically relevant cell line. GO readily undergoes both direct and indirect photo-transformation processes and increasing time of irradiation increases the biological response of FHM cells. Both decreased size of GO (or rGO formation) as well as the formation of LMWPs are likely contributing to this cellular response. In FHM cells, GO induced changes in numerous markers of oxidative stress. Most biological pathways affected included perturbations in the citric acid cycle, glycolysis and amino acid metabolism. Removal of suspended GO/rGO via filtration still elicited a biological response in our test system. Mass spectral identification of the LMWPs suggested that the photo-production of polycyclic aromatic hydrocarbon (PAH)-like derivatives facilitate the measured response in FHM cells. Ultimately, identifying potential biomarkers of GO exposure and the development of exposure indices of GO and its photoproducts in human and ecologically relevant species will aid in accurately establishing risk.

2120 Liposomal Composition Can Affect Nanoparticle Transport into Epithelial and Endothelial Cells

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Biologically compatible liposomes have value as vehicles for drug delivery. Potential capability of liposomes to cross membrane barriers of epithelial, endothelial, and astrocytic cells was examined using liposomes alone, liposomes with cholesterol, and liposomes with cholesterol and folate. The liposomes were composed of phosphatidylcholine derivatives and surfactants. FITC dye-labeled products were examined in transwell cultures of Caco-2 epithelial cells, HBEC-5i endothelial cells, and astrocyte cultures. With DMSO as a positive control, none of the liposomal products at 10 micromolar concentrations contributed to cell death in any of the cell cultures when examined 6 h after exposure. Cellular uptake measured at 4 h and 24 h demonstrated 34% and 88% of HBEC-5i had taken up the liposomes alone. Uptake of liposomes was 7.8% at 4 h and 34% at 24 h by astrocytes and 18% at 24 h by Caco-2 cells. Liposomes containing cholesterol with or without folate did not take up these FITC-labeled products in any of these cells. Liposomes with folate but without cholesterol resulted in 34% and 30% uptake, respectively, in Caco-2 and HBEC-5i cells after 24 hours. These results suggest that, for this particular liposomal nanomaterial, inclusion of cholesterol was detrimental to cellular uptake. *Supported at Virginia Tech by Luna Innovations, Inc.*

2121 Dermal Toxicity of Nickel- and Cobalt-Based Nanocatalysts

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Nanocatalysis is a fast-growing field involving the use of nanomaterials as catalysts for a variety of applications, specifically, metal nanoparticles (NP) and their compounds, which have a large surface-to-volume ratio compared to bulk materials. Metal/metal oxide (Me/MeO) NP possess unique properties which can be useful in different applications including catalytic processes such as decomposition, reactions of dehydrogenation, oxidation, alkylation, C-C coupling, among others. Nonetheless, the same properties that make these metal nanocatalysts (NCT) very attractive can pose potential health risks. In addition to inhalation exposure route, workers may also be exposed through skin contact. In this study, we evaluated the ability of four different NCT ($NiFe_2O_4$, $CoFe_2O_4$, Ni and Co_3O_4) to initiate oxidative stress, induce redox-sensitive transcription factors and to trigger inflammation in primary human epidermal keratinocytes (HEK). Besides, due to the skin's vulnerability to UV radiation, it is important to assess whether metal NCT augment the adverse effects of UVB. HEKs exposure to the studied Me/MeO NCT (0-20 μg/cm^2) resulted in a dose- and time-dependent reduction in cell viability, cell damage, activation of NF-κB, elevated ROS generation, release of inflammatory mediators, and increase in oxidative stress markers. Co-exposure of HEK to UVB (4KJ/m^2) and Me/MeO caused marked amplification of the observed responses. UVB exposure alone induced significant cytotoxicity and secretion of cytokines/chemokines. Based on the hierarchical clustering analysis of the cytokine/chemokine responses, Co_3O_4 and Ni were segregated from the control and both ferrites-exposed samples. Pre-treatment with UVB resulted in separation of Ni, Co_3O_4 and $NiFe_2O_4$ responses from control and $CoFe_2O_4$ exposure groups. Overall the inflammatory responses in HEK cells induced by exposure to different Me/MeO NPs investigated, with or without UVB pre-treatment, were in order: Ni>Co_3O_4>$NiFe_2O_4$>$CoFe_2O_4$. Altogether, these data indicated that co-exposure of dermal cells *in vitro* to Me/MeO NP and UVB was associated with potentiation of the adverse effects as compared to the cells treated with NCT alone. *Disclaimer: The findings and conclusions of this report are those of the authors and do not necessarily reflect those of National Institute for Occupational Safety and Health.*

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Preface

This issue is devoted to the abstracts of the presentations for the Continuing Education courses and Scientific Sessions of the 59th Annual Meeting of the Society of Toxicology, held at the Anaheim Convention Center, Anaheim, California, March 15–19, 2020.

An alphabetical Author Index, cross-referencing the corresponding abstract number(s), begins on page 542.

The issue also contains a Keyword Index (by subject or chemical) of all the presentations, beginning on page 580.

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