

(with and without cells) showed a slight interaction with the aB assay. UV-Vis spectra determined for aB with the three C₆₀(OH)_x showed no effect. Cytokine analysis for all C₆₀(OH)_x showed a slight increase in IL-8 but was not statistically significant. These results suggest that hydroxylation of C₆₀ causes minimal cytotoxicity at high hydroxylation levels and no inflammatory response in HEK. (Supported by NIH RO1 ES016138)

PS 1177 THE TRANSCRIPTIONAL PROFILING IN RESPONSE TO C(60) FULLERENES OF RAT LUNGS FOR IDENTIFICATION POTENTIAL BIOMARKERS.

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In various industrial fields, the use of C(60) fullerenes is expected to increase, however, little is known about the potential toxicological mechanism of action. In our previous study, the transcriptomic profiling data closely matched the pathological findings that C(60) fullerenes caused no serious adverse pulmonary effects after whole-body inhalation exposure. Taking advantage of this, we attempted to characterize time-dependent changes in the gene expression profiles after intratracheal instillation with C(60) fullerenes at different dosages and to identify the candidate expressed genes as potential biomarkers. The hierarchical cluster analysis revealed that the up- or downregulation of genes after intratracheal instillation with 1.0mg C(60) fullerene particles in rat lung tissue was significantly over-represented in the "response to stimulus" and "response to chemical stimulus" categories of biological processes and in the "extracellular space" category of the cellular component. These results were remarkable for 1 week after the instillation with C(60) fullerenes. In the lung tissues instilled with 1.0mg C(60) fullerene particles, many representative genes involved in "inflammatory response" and in "matrix metalloproteinase activity" were upregulated for over 6 months. The expression levels of 89 and 21 genes were positively correlated with the C(60) fullerene dose at 1 week and 6 months after the instillation, respectively. Most of them were involved in "inflammatory response", and the Ccl17, Ctsk, Cxcl2, Cxcl6, Lcn6, Orm1, Rnase9, Slc26a4, Spp1, Mmp7, and Mmp12 genes were overlapped. Microarray-based gene expression profiling revealed that the expression of some genes is correlated with the dose of intratracheally instilled C(60) fullerenes. We suggest that these genes are useful for identifying potential biomarkers in acute-phase or persistent responses to C(60) fullerenes in the lung tissue.

PS 1178 EFFECT OF SURFACE MODIFICATION ON THE BIOAVAILABILITY AND INFLAMMATORY POTENTIAL OF MULTI-WALLED CARBON NANOTUBES.

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Manufactured nanoparticles display physiochemical characteristics and impart unique electrical, thermal, mechanical, and imaging properties that are highly desirable for applications within the commercial, medical and environmental sectors. Carbon nanotubes exhibit excellent electrical, optical and chemical properties with a broad range of applications. In addition, surface modification of carbon nanotubes with organic functional molecules extends their already broad applications. The addition of organic coatings such as -COOH terminated coatings alter the charge, functionality, and reactivity of the nanotube. However, the development of these engineered carbon nanotubes has surpassed evaluation of the potential health impacts. Therefore, this study examines whether carbon nanotubes with different surface chemistry affects pulmonary toxicity. Mice (C57BL/6J, male, 7 weeks old) were given 0-40 ug/mouse of either bare multi-walled carbon nanotubes (MWCNT) or COOH-coated MWCNT via pharyngeal aspiration. Inflammatory and cytotoxic potential of each particle type was analyzed at 1 and 7 days post-exposure. The findings of this study show both the bare and the COOH-modified MWCNTs produced a dose dependent increase in PMNs harvested by whole lung lavage at both 1 and 7 days post-exposure. However, even though the COOH-modified MWCNT did produce a dose dependent increase in PMN number at all doses and at all post-exposure time points, the inflammatory response produced by the COOH-modified MWCNT was lower than the inflammatory response generated by the bare MWCNT. In conclusion, altering the surface functionality of the

MWCNT, i.e. bare versus COOH-modified MWCNT lowered the inflammatory properties of the MWCNT. Supported in part by grant RC2 ES-018742 (A. Holian, PI) and NSF grant CBET-0834233 (N. Wu, PI).

PS 1179 OXIDATIVE LIPIDOMICS REVEALS SELECTIVE, BUT NOT RANDOM, PULMONARY PHOSPHOLIPID PEROXIDATION AFTER INHALATION OF CARBON NANOTUBES.

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It is commonly accepted that lipid peroxidation is a mechanism of cell/tissue damage and death by nanoparticles, including single walled carbon nanotubes (SWCNT). We performed global lipidomics/oxidative lipidomics analysis of all molecular species in major classes of phospholipids and established that random free radical peroxidation does not happen in the lung of mice at 3 different time-points after SWCNT inhalation. C57BL/6 mice were exposed to SWCNT via inhalation (5mg/m³, whole body inhalation for 4 consecutive days, 5 h/day) and sacrificed 1, 7 and 28 days thereafter. We found that two most abundant and susceptible phospholipids - phosphatidylcholine and phosphatidylethanolamine - that constitute more than 75% of total phospholipids, do not undergo peroxidation at all. In addition, we demonstrated that three relatively minor anionic phospholipids - cardiolipin, phosphatidylinositol, and phosphatidylserine get oxidized in a very selective way: only few molecular species out of many in each class (10 out of 25 for CL, 3 out of 5 for PI, 1 out of 7 for PS) were converted into oxygenated species. Moreover, the selectivity was also detected towards fatty acids of the respective oxidized anionic phospholipids (not most polyunsaturated fatty acids but most abundant). We speculate that SWCNT-induced phospholipid peroxidation in lung is involved in the production of selective precursors of pro-resolving mediators of inflammation rather than in non-specific oxidative damage. Supported by NIOSH OH008282; NIH NIAID U19 AI068021, HL70755, HL094488, EC-FP7-NANOMMUNE-214281.

PS 1180 COMPARATIVE GENOTOXICITY OF FIBROUS PARTICLES: CARBON NANOFIBERS, SINGLE-WALLED CARBON NANOTUBES, AND ASBESTOS.

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Carbon nanofibers (CNF) are generating great interest in industrial sectors such as energy production and electronics, where alternative materials may have limited performance or are produced at a much higher cost. However, despite the increasing industrial use of carbon nanofibers, information on their potential adverse health effects is limited. In the current study, we examine the cytotoxic and genotoxic potential of CNF (Pyrograf®-III) and compare it with the effects of asbestos fibers (crocidolite) or single-walled carbon nanotubes (SWCNT). The genotoxic effects in hamster lung fibroblast (V79) cell line were examined using two complementary assays: comet and micronucleus (MN). In addition, we utilized fluorescence *in situ* hybridization to detect the chromatin pan-centromeric signals within the MN. The use of this probe allows the classification of MN as being centromere positive or centromere negative indicating their origin by anagenic (chromosomal missegregation) or clastogenic (chromosome breakage) mechanisms, respectively. Results from cytotoxicity tests revealed a concentration- and time-dependent loss of cell viability after exposure to all tested materials in the following sequence: asbestos>CNF>SWCNT. Additionally, cellular uptake and generation of oxygen radicals was seen in the murine RAW264.7 macrophage cell line following exposure to CNF or asbestos but not after administration of SWCNT. Comet and MN assays demonstrated the induction of DNA damage and MN after exposure to all tested materials with the strongest effect seen for CNF. Moreover, the chromatin pan-centromeric signals within the MN were positive after cell exposure to CNF suggesting that the mitotic spindle and the segregation of the chromosomes were affected. Supported by NIOSH OH008282, NORA OHELD015, and EC-FP-7-NANOMMUNE-214281.

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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.

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