that PBDEs stimulated release of the pro-inflammatory cytokines IL-6 and TNFα. Because these cytokines have been linked with increased prostaglandin release from gestational membranes and onset of term and preterm labor, these results support the need for further investigations of potential risks that PBDEs may pose to pregnant women.

1554 NANO-TIO2 ANATASE PARTICLES VS. RUTILE PARTICLES: A CYTOTOXICITY AND INFLAMMATORY RESPONSE STUDY WITH HUMAN DERMAL FIBROBLASTS AND HUMAN LUNG EPITHELIAL CELLS

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Titanium dioxide on the nanoscale is an important chemical substance in commerce today. Depending on its crystalline phase, however, nano-TiO2 particles may possess different properties. The objectives of this study were to correlate the photocatalytic properties and reactive oxygen species generation of nano-TiO2 particles in its anatase, anatase/rutile, and rutile phases with the cytotoxic response and production of inflammatory mediators in human dermal fibroblasts and immortalized human lung epithelial cells. A dose range of 0-10,000 ppm of nano-TiO2 particles and varying exposure times provided evidence of both dose-response and time-course relationships. A differential cytotoxicity relationship was observed in nano-TiO2 particles of different preparation methods and crystallinity. Each of the nano-TiO2 particle types exhibited differing reactive oxygen species generation, and thus different photocatalytic degradation efficiencies. Correlations were established for each variable. Nano-TiO2 particles in the anatase phase photodegraded Congo Red dye most efficiently, produced the most ROS, and produced the largest cytotoxic response in human dermal fibroblasts and immortalized human lung epithelial cells. When comparing TiO2 samples on the nanoscale, kinetic results indicate that nano-TiO2 anatase particles are a superior photocatalyst to rutile because of differences inherent in the crystal structures of the two phases, not because of anatase's typically higher specific surface area.

1555 RELATIONSHIP BETWEEN PULMONARY EXPOSURE TO MULTIPLE DOSES OF SINGLE WALL CARBON NANOTUBES AND ATHEROSCLEROSIS IN APOE-/- MOUSE MODEL

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Epidemiological studies are demonstrating a link between exposure to air pollutants and cardiopulmonary diseases. Recent studies showed that single installation of single wall carbon nanotubes (SWCNT) into the lung of C57BL/6 mice results in pulmonary granuloma formation and fibrosis. We demonstrated that this response is associated with dose-dependent oxidative effects including mitochondrial DNA damage and protein carbonyl formation in the aortic tissue. Consistently, SWCNT exposure induces similar oxidative modifications in the aortic tissue of ApoE-/- mice. The chronic vascular oxidative modifications might lead to accelerated atherosclerosis. To test this hypothesis, ApoE-/- mice (10 mice per treatment) were exposed by pharyngeal aspiration to SWCNT (20 ug/mouse) or vehicle via multiple exposures (once every other week for 8 weeks). The mice were on a chow diet for four weeks followed by four weeks on a cocoa butter diet (TD 88051; Harlan). At the end of the exposure period the lungs and the atherosclerotic lesions were assessed histopathologically. The experimental treatment resulted in nanotube accumulation in the lung and foci of granuloma formation accompanied with different degree of inflammatory and fibrotic responses. The percent of plaque area in the aortas, measured by en face method, was significantly increased in the SWCNT-treated mice ($p<0.01$). Furthermore, a significant increase in atherosclerotic lesion size was demonstrated by histopatological morphometrical analysis of serial sections of the brachiocephalic arteries ($p<0.001$). The body weight, plasma high/low density cholesterol, and liver enzymes were similar between the controls and the treated mice. In conclusion, pulmonary exposure to multiple doses of SWCNT induces severe lung toxicity and accelerates the progression of atherosclerosis in ApoE-/- mice. The atherogenic effects might be a result of low-grade systemic inflammatory responses related to the lung toxicity and/or translocation of nanotubes into the systemic circulation.

1556 SINGLE WALL CARBON NANOTUBES INDUCE OXIDATIVE STRESS, ACUTE INFLAMMATION, AND PROGRESSIVE PULMONARY FIBROSIS

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Among different types of nano-particles, single-walled carbon nanotubes (SWCNT) with their unique electronic and mechanical properties may also exhibit unique biological interactions, thus necessitating studies of their health effects. Previously, we reported that exposure of human bronchial epithelial cells to SWCNT induced oxidative stress, depletion of antioxidants, morphological changes, and cytotoxicity. In the current study, we investigated pulmonary toxicity of SWCNT after pharyngeal aspiration by C57BL/6 mice. Administration of SWCNT to C57BL/6 mice resulted in a dose-dependent augmentation of biomarkers of cell injury and oxidative stress quantified by cell counts, total protein, lactate dehydrogenase and γ-glutamyltranspeptidase activities, as well as reduced levels of GSH and total antioxidant reserves along with the accumulation of lipid peroxidation products found in bronchoalveolar lavage (BAL) fluid and in the lung. Markers of pulmonary cytotoxicity were associated with early development of acute inflammation, collagen accumulation, and progressive fibrosis. Maximal increase of TGF-β in BAL fluid occurred on day 7 after the exposure of mice to SWCNT and corresponded to a peak of macrophage content as well as robust collagen formation and impaired pulmonary functions. Exposure to SWCNT in mice maintained on a vitamin E deficient diet significantly enhanced collagen deposition as compared to the vitamin E sufficient group. Overall, our data suggest that pharyngeal aspiration of SWCNT elicited a robust acute inflammatory response with early onset of progressive pulmonary fibrosis whose expression and severity was associated with the intensity of oxidative stress in the lung of the exposed C57BL/6 mice.
Acknowledgements: supported by NIOSH OH008282, NORA 92700Y.

1557 OXIDATIVE INTERACTIONS OF SINGLE WALLED CARBON NANOTUBES WITH RAW 264.7 MACROPHAGES: ROLE OF IRON

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Single-walled carbon nanotubes (SWCNT) have unique physico-chemical properties and may exhibit unusual interactions with cells, thus necessitating studies of their toxicity. Manufactured SWCNT usually contain significant amounts of iron that may act as a catalyst of oxidative stress. Because macrophages are the primary responders to different particles that initiate and propagate inflammatory reactions and oxidative stress, we utilized two types of SWCNT: 1) iron-rich (non-purified) SWCNT (26 weight% of iron) and 2) iron-stripped (purified) SWCNT (0.23 weight% of iron) to study their interactions with RAW 264.7 macrophages. Ultrasonication resulted in predominantly well-dispersed and separated SWCNT strands as evidenced by scanning electron microscopy. Neither purified nor non-purifed SWCNT were able to generate intracellular production of superoxide radicals or nitric oxide in RAW 264.7 macrophages as documented by flow cytometry. SWCNT with different iron content displayed different redox activity in a cell-free model system as revealed by EPR-detectable formation of ascorbate radicals. Co-incubation of zymosan-stimulated RAW 264.7 macrophages with non-purifed iron-rich SWCNT generated more hydroxyl radicals (documented by EPR spin-trapping with 5,5-dimethyl-1-pyrroline-N-oxide, DMPO) than with purified SWCNT. Similarly, in the presence of zymosan-stimulated RAW 264.7 macrophages, non-purified SWCNT more effectively converted superoxide radicals generated by xanthine oxidase/xanthine into hydroxyl radicals as compared to purified SWCNT. Iron-rich SWCNT caused significant loss of intracellular GSH and accumulation of lipid hydroperoxides in zymosan-stimulated RAW 264.7 macrophages. Thus, iron in SWCNT may be important in determining redox-dependent responses of macrophages. Supported by NIOSH OH008282, NORA 92700Y.

1558 THE CYTOTOXICITY AND CYTOTOXIC MECHANISMS OF CERIUM OXIDE NANOPARTICLES AGAINST LUNG CANCER CELLS

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With the fast growth of nanotechnology, nanoparticles have been widely used in products of human daily living. However, there is a significant lack of information about potential toxicity of these products, especially metal oxide nanoparticles. In this study, we have investigated the cytotoxicity of the cerium oxide (CeO2) nanoparticles using human lung cancer cells. About 2×105 cells were plated in T-75 flasks and dosed with different concentrations of nanoparticle solutions prepared by dispersing nanoparticles in cell medium and followed by sonication for 5 min. After 24 hours of exposure, the experiments were terminated and the cell viability in each flask was measured by a sulforhodamine B (SRB) method. The experimental results showed that the cell viability decreased with increase of nanoparticle concentrations, the viability of cells exposed by 15μM, 45μM and 100μM were about 94.1%, 86.6%, and 75.2% individually. To study the cytotoxicity mechanism, the

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The Toxicologist

Supplement to *Toxicological Sciences*

An Offical Journal of the Society of Toxicology

45th Annual Meeting and ToxExpo™

San Diego, California

OXFORD UNIVERSITY PRESS

ISSN 1096-6080
Volume 90, Number 1, March 2006

www.toxsci.oupjournals.org

Preface

This issue of *The Toxicologist* is devoted to the abstracts of the presentations for the symposium, platform, poster discussion, workshop, and poster sessions of the 45th Annual Meeting of the Society of Toxicology, held at the San Diego Convention Center, San Diego, March 5–9, 2006.

An alphabetical Author Index, cross referencing the corresponding abstract number(s), begins on page 500.

The issue also contains a Keyword Index (by subject or chemical) of all the presentations, beginning on page 534.

The abstracts are reproduced as accepted by the Program Committee of the Society of Toxicology and appear in numerical sequence.

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