7, 28 and 56 days post-exposure. In bronchoalveolar lavage (BAL) studies, polymorphonuclear leukocytes (PMNs) were assessed to index pulmonary inflammation, BAL fluid lactate dehydrogenase (LDH) activity was measured as a marker of cytotoxicity, and BAL fluid albumin was determined as a marker of the lung air-blood barrier integrity. MWCNT exposure induced dose- and time-dependent changes, with maximum changes occurring at 7 days post-exposure for all three BAL markers. At 7 days post-exposure, mice exposed to 40 μg/mouse MWCNT had increased BAL PMNs (724-fold), BAL fluid LDH activity (2.6-fold) and BAL fluid albumin (2.4-fold) versus vehicle-exposed controls. At 56 days post-exposure, mice exposed to 40 μg/mouse MWCNT still had increased BAL PMNs (22.3-fold), BAL fluid LDH activity (1.9-fold) and BAL fluid albumin (1.6-fold) versus vehicle-exposed controls. Thus, relative to 7 days post-exposure, these BAL markers had decreased, but were still significantly elevated above vehicle-exposed controls at 56 days post-exposure. At 28 and 56 days post-exposure, histopathology confirmed persistent interstitial inflammation and indicated fibrosis. In summary, these data indicate that exposure to MWCNT results in dose- and time-dependent changes in pulmonary inflammation and damage, suggesting that MWCNT may pose an occupational health hazard.

PS 2197 NEUROINFLAMMATION AND BLOOD-BRAIN BARRIER CHANGES FOLLOWING EXPOSURE TO ENGINEERED NANOMATERIALS.

K. Sriram, D. W. Porter, A. M. Jefferson, G. X. Lin, M. G. Wolfarth, B. T. Chen, W. McKinney, D. G. Frazer and V. Castranova. *Centers for Disease Control & Prevention (CDC)-NIOSH, Morgantown, WV.*

The unique physico-chemical properties of engineered nanomaterials influence their ability to aerosolize, and thus inhalation exposure is of major occupational concern. Inhaled nanoparticles can potentially translocate to the brain via olfactory sensory neurons or through systemic circulation and cause irreversible damage to the nervous system. To determine if engineered nanomaterials pose a neurological risk, we evaluated the effects of multi-walled carbon nanotubes (MWCNT) in a murine model. Male C57BL/6J mice were exposed to MWCNT either by pharyngeal aspiration (single dose of 10-80μg/mouse; 1, 7, 28, or 56d post-exposure) or whole-body inhalation (10mg/m^3 x 5h/d x 2, 4, 8 or 12d; 1d post-exposure). MWCNT exposure elicited neuroinflammation, altered blood-brain barrier (BBB) integrity and induced cellular stress in discrete brain areas. Specifically, MWCNT induced (2 to 16-fold) the mRNA expression of several proinflammatory chemokines (Ccl2, Ccl3, Ccl4, Cxcl2), cytokines (Il-1β, Il-6, Tnfα), selectins (Sele, Selp) and markers of cellular stress (Hspb2, Mt1, Mt2). Exposure to MWCNT also decreased the expression of BBB-related markers (Edn2, Vegfa), suggestive of alterations in BBB integrity. In the hippocampus, MWCNT altered the expression of certain Alzheimer's–related genes (Aplp2, Apba2, Apba3, Bace1, Bace2, Ctsc, Ctsd), which interact with or are involved in the processing of amyloid-precursor protein. The neurotoxic responses were comparable between the two routes of exposure and some of the effects persisted until 56d post-exposure. Taken together, our findings suggest that exposure to an engineered nanomaterial like MWCNT, can elicit neuroinflammation, disrupt BBB integrity and cause cellular/molecular changes that could potentially culminate in neurodegeneration.

PS 2198 NANOPARTICLE DISPERSION METHOD USING NATURAL LUNG SURFACTANT.

L. Wang[1,2], V. Castranova[1,2], R. R. Mercer[1,2], N. Wu[2], T. Li[3], S. Li[3], J. Hall[1], M. Li[2] and Y. Rojanasakul[2]. *[1]National Institute for Occupational Safety and Health (NIOSH), Morgantown, WV, [2]West Virginia University, Morgantown, WV and [3]National Institute of Occupational Health and Poison Control, CDC, Beijing, China.*

Nanomaterials, as a class of small-scale (<100 nm) substances with unique mechanical, optical and electrical properties, are increasingly being used in a wide range of industries. Their unique properties present new challenges to understanding the toxicity of these materials to humans and the environment. Lung is the major target organ for airborne nanoparticles. *In vitro* and *in vivo* exposure studies often rely on the use of suspended nanoparticle preparations. However, nanoparticles suspended in culture medium or physiologic saline solution tend to form micrometer-sized aggregates. Increasing evidence indicates that the degree of dispersion of nanoparticles has a strong influence on their biological activities. In this study, we test a new method of nanoparticle dispersion using natural lung surfactant, Survanta®, as a dispersing agent. Dose dependence studies of Survanta® were performed on single-walled carbon nanotube (SWCNT) dispersion. Our results show that Survanta® at a concentration of 150 μg/ml, which is comparable to that found in normal rodent lungs, was optimal in dispersing SWCNT (0.1 mg/ml), producing well dispersed preparations as analyzed by microscopic and light scattering methods. This dose of Survanta® was found to be non-toxic and non-inflammatory *in vivo* and *in vitro* when used alone, and did not mask the bioactivity of SWCNT. We also found that the dispersed form of SWCNT was more effective in inducing cytotoxicity and lung fibrosis than the non-dispersed form, indicating the importance of nanoparticle dispersion on biological activities. Since Survanta® is commercially available and its one step nanoparticle dispersion is simple and rapid, this method provides major advantages over existing methods of nanoparticle dispersion. Furthermore, our stability studies showed that Survanta®-dispersed nanoparticles remain well dispersed for months and upon dilution with aqueous medium.

PS 2199 BIODEGRADATION OF SINGLE WALLED CARBON NANOTUBES THROUGH PEROXIDASE CATALYSIS.

N. V. Konduru[1], I. I. Vlasova[1], B. L. Allen[2], E. R. Kisin[3], A. R. Murray[3], A. A. Kapralov[1], A. Star[2], A. A. Shvedova[3] and V. E. Kagan[1]. *[1]Environmental and Occupational Health, University of Pittsburgh, Pittsburgh, PA, [2]Department of Chemistry, University of Pittsburgh, Pittsburgh, PA and [3]Pathology/Physiology Research Branch, Health Effects Laboratory Division (HELD), NIOSH, Morgantown, WV.*

Management of exposure to bioengineered single walled carbon nanotubes (SWCNT) is becoming a major environmental and health challenge. Because of unique characteristics, SWCNT have found increased applications in various fields of science and technology. With increased risk of human and environmental exposure, strategies to degrade SWCNT are also garnering interest. Here, we show - for the first time - that two peroxidases, namely myeloperoxidase and horseradish peroxidase are effective in catalyzing the biodegradation of SWCNT. A systematic characterization of resulting products of degradation was performed using transmission electron microscopy (TEM), dynamic light scattering (DLS), gel electrophoresis, mass spectrometry, UV-Vis-NIR spectroscopy and thermogravimetric analysis (TGA). We also demonstrate that unlike naïve non-biodegraded nanoparticles, the peroxidase degraded particles did not elicit pulmonary inflammatory response in mice as evidenced by the release of pro-inflammatory cytokines and the content of neutrophils (PMN) in bronchoalveolar lavage. These results mark a novel approach to employ peroxidase catalysis for directed biodegradation of carbon nanotubes in biofluids/tissues as well as in environmental settings. Supported by NIOSH OH008282, NORA 927000Y, National Heart,Lung and Blood Institute Grant HL-70755, The Swedish Research Council, the Swedish Council for Working Life and Social Research, The Human Frontier Science Program (HFSP)and the 7th Framework Program of the European Commission.

PS 2200 PULMONARY AND SYSTEMIC INHALATION TOXICITY OF MULTI-WALLED AND SINGLE WALLED CARBON NANOTUBES.

J. D. McDonald[1], L. Mitchell[1,2], S. Burchiel[2] and A. Gigliotti[1]. *[1]Lovelace Respiratory Research Institute, Albuquerque, NM and [2]University of New Mexico, Albuquerque, NM.*

Inhalation of multiwalled carbon nanotubes (MWCNTs) and single walled carbon nanotubes (SWCNT) at particle concentrations up to 1 mg/m3 did not result in significant lung inflammation or tissue damage, but caused systemic immune function alterations. C57BL/6 adult (10-12 week) male mice were exposed by whole-body inhalation to control air or 0.3 or 1 mg/m3 respirable aggregates of MWCNTs or SWCNTs for 14 days, with either immediate sacrifice or sacrifice of a recovery group 30 days after the end of exposure. Histopathology of lungs from exposed animals showed alveolar macrophages containing significant amounts of black particles; however, there was minimal to no inflammation or tissue damage observed. Bronchial alveolar lavage fluid also demonstrated particle-laden macrophages; however, white blood cell counts were not increased compared to controls. Both types of carbon nanotubes caused systemic immunosuppression after 14 days and after recovery. Immunosuppression was characterized by reduced T-cell-dependent antibody response to sheep erythrocytes as well as T-cell proliferative ability in presence of mitogen, Concanavalin A (Con A).

PS 2201 SINGLE-WALLED CARBON NANOTUBES: SKIN EXPOSURES.

A. R. Murray[1,2], E. Kisin[1], S. S. Leonard[1], S. H. Young[1], C. Kommineni[1], V. E. Kagan[3], V. Castranova[1,2] and A. A. Shvedova[1,2]. *[1]PPRB, NIOSH, Morgantown, WV, [2]Department of Physiology/Pharmacology, WVU, Morgantown, WV and [3]Department of Environmental and Occupational Health, University of Pittsburgh, Pittsburgh, PA.*

Nanotechnology is a newly developing field resulting in the development of unique materials with a variety of applications from electronics to engineered tissue. SWCNT are of the most interest because of their unique mechanical and electrical

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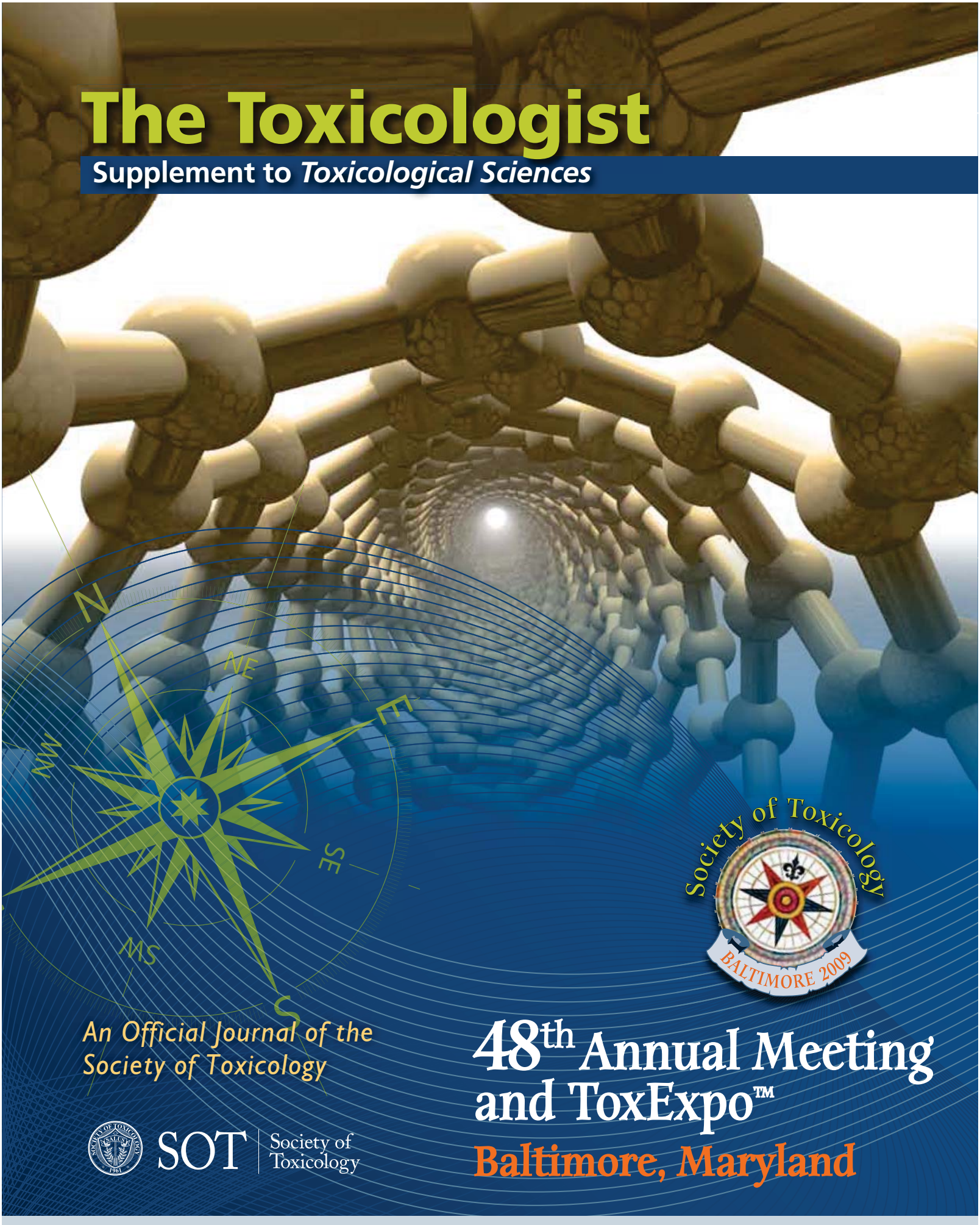

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Deadline for Proposals for SOT 2010 Annual Meeting Sessions: April 30, 2009

WHY SUBMIT A PROPOSAL?

1. To present new developments in toxicology.
2. To provide attendees an opportunity to learn about state-of-the-art technology and how it applies to toxicological research.
3. To provide attendees an opportunity to learn about the emerging fields and how they apply to toxicology.

SESSION TYPES

Continuing Education—Emphasis on quality presentations of generally accepted, state-of-the-art knowledge in toxicology

Note: CE Courses will be held on Sunday.

Symposia—"Cutting-edge" science; new areas, concepts, or data

Workshops—State-of-the-art knowledge in toxicology

Roundtables—Controversial subjects

Historical Highlights—Review of a historical body of science that has impacted toxicology

Informational Sessions—Scientific planning or membership development

Education-Career Development Sessions—Sessions that provide the tools and resources to toxicologists that will enhance their professional and scientific development

2010 Thematic Approach

The Scientific Program Committee will continue the thematic approach for the 2010 Annual Meeting. All proposal submissions will be reviewed for their relevance under the following themes—***Cell Signaling, Gene-Environment Interactions, Metabolic Disease, Mitochondrial Basis of Disease, Toxicity Testing in the 21st Century,*** and ***Translational Toxicology*** for the 2010 meeting. Please note that while we are actively soliciting proposals for the themes listed above, all proposal submissions will be reviewed under the current criteria for their timeliness and relevance to the field of toxicology.

Please refer to the SOT 2009 *Program,* Scientific Program Overview on the fold-out cover for a list of 2009 sessions highlighted under the thematic approach.

You can now submit your proposal on-line at www.toxicology.org

Preface

This issue of *The Toxicologist* is devoted to the abstracts of the presentations for the continuing education, symposia, workshop, roundtable, platform, and poster discussion sessions of the 48th Annual Meeting of the Society of Toxicology, held at the Baltimore Convention Center, March 15–19, 2009.

An alphabetical Author Index, cross referencing the corresponding abstract number(s), begins on page 469.

The issue also contains a Key Word Index (by subject or chemical) of all the presentations, beginning on page 487.

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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