properties which result from their fibrous shape and small size. The most common technique for manufacturing SWCNT relies on the use of iron as a transition metal catalyst and can result in the presence of up to 30% metal catalyst in raw SWCNT. The low density of SWCNT may lead to inhalation as well as deposition on exposed skin, which provide routes of exposure that are important to consider when evaluating toxicity. We hypothesized that SWCNT are toxic to the skin, and this toxicity is dependent on the ability of SWCNT to interact with the skin and initiate oxidative stress, and the induction of transcription factors leading to inflammation. To test this hypothesis, the effects of SWCNT were assessed both *in vitro* and *in vivo*. Engineered skin exposed to SWCNT showed increased epidermal thickness and accumulation and activation of dermal fibroblasts, which resulted in increased collagen as well as release of pro-inflammatory cytokines. Exposure of JB6 cells to unpurified SWCNT resulted in the production hydroxyl radicals as detected by ESR and caused a significant dose-dependent activation of AP-1 and NFκB, while partially-purified SWCNT activated only NFκB. Topical exposure of SKH-1 mice (5 days, 40, 80, 160 μg/mouse/day) to SWCNT caused oxidative stress, depletion of GSH, oxidation of protein thiols and carbonyls, elevated MPO activity, and an increase of dermal cell numbers resulting in skin thickening. Altogether, these data indicated that topical exposure to unpurified SWCNT induced free radical generation, oxidative stress, and inflammation, leading to dermal toxicity. Acknowledgements: supported by NIOSH OH008282, NIH HL70755, NORA 927000Y, 927Z1LU and EC-FP-7-NANOMMUNE-214281

PS 2202 PULMONARY EFFECTS OF SINGLE-WALLED CARBON NANOTUBES: INHALATION VS ASPIRATION.

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Health effects and occupational risk of exposures associated with manufacturing and application of nanoparticles are critical points for the safe and sustainable development of nanotechnology. The toxic effects of nanoscale materials have not been fully characterized and the limited *in vivo* studies indicate the urgent necessity for further toxicological assessments of nanomaterials. Some argue that pharyngeal aspiration – a single exposure to a bolus of SWCNT - is an artificial exposure where the single large dose contributes to the pulmonary response. Moreover, aspiration studies reported thus far have been relatively high dose exposures, which may not be relevant to chronic lower dose seen in occupational settings. Inhalation of SWCNT more closely mimics occupational and environmental venues than the above mentioned administrations providing more dispersed SWCNT structures while bolus effects are avoided. By applying a new technique to aerosolize SWCNT, we obtained stable and uniform SWCNT dispersions with a concentration of 5 mg/m^3 and a count mode aerodynamic diameter of 240 nm for the inhalation experiments. In the current study, we utilized non-purified SWCNT containing up to 17.7% of iron for both inhalation (5 mg/m^3, 5 hrs/day for 4 days) and aspiration (varying doses of 5-20 μg/mouse) exposures. Pathological events in both exposure routes were realized through qualitatively similar synergized interactions of early inflammatory response and oxidative stress culminating in the development of multifocal granulomatous pneumonia and interstitial fibrosis. Quantitatively, SWCNT inhalation was more effective than aspiration in causing inflammatory response, oxidative stress, collagen deposition and fibrosis as well as mutations of K-*ras* gene locus in the lung of C57BL/6 mice. Acknowledgements: supported by NIOSH OH008282, NIH HL70755, NORA 927000Y, and EC-FP-7-NANOMMUNE-214281.

PS 2203 SINGLE-WALLED CARBON NANOTUBES INDUCE PULMONARY AND VASCULAR RESPONSE FOLLOWING INTRATRACHEAL INSTILLATION.

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Carbon-based nanotubes have been shown to induce varying degrees of pulmonary response in rodents influenced by the dose, the extent of agglomeration, and the functional properties. We hypothesized that low concentrations of non-modified or acid-functionalized (AF) single walled carbon nanotubes (SWCNT) will cause distinct pulmonary and aortic effects on markers of inflammation, coagulation, vasoconstriction following pulmonary exposure. Male Wistar Kyoto rats (12 week old) were intratracheally instilled with pre-characterized freshly sonicated suspensions of SWCNT or AF-SWCNT at 0, 100 or 500 μg/kg in saline. Pulmonary injury and inflammatory effects were small as determined by bronchoalveolar lavage fluid (BALF) analysis and were concentration-dependent. Small increases in BALF protein were noted with high dose of both types of tubes while albumin increased only with AF-SWCNT. Surprisingly, small but significant increases in BALF γ-glutamyl transferase activity (marker of cell membrane damage) were noted only with high concentrations of SWCNT but not AF-SWCNT. LDH activity was increased 4-d at high concentration of both types of SWCNT. Both types of nanotubes moderately increased BALF neutrophils at high concentration while no increase in macrophages occurred (1-d>4-d). Real-time PCR for mRNA markers of oxidative stress, inflammation, vasoconstriction, thrombosis and cell filamentous components in rats exposed to AF-SWCNT revealed pulmonary induction of HO-1, MIP-2, endothelin-1, PAI-1 and β-catenin at both time points (1-d>4-d). However, mRNA expression for any of the biomarkers was not altered in the aorta at either time points. Pulmonary instillation of SWCNT produces acute pulmonary inflammatory, vasoconstrictive and prothrombotic effects in rats, whereas these effects are not evident within 4 days in the aorta. (Does not reflect US EPA policy). Supported in part by EPA SEE Program and EPA/UNC CR833237).

PS 2204 PULMONARY EFFECTS FROM ACUTE EXPOSURE TO AEROSOLIZED SINGLE-WALLED CARBON NANOTUBES.

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Although nanotechnology is still an emerging field and the enthusiasm for the potential societal benefits of engineered nanomaterials continues, concerns are being raised about whether our knowledge of possible health risks is keeping pace with products going to market. Single-walled carbon nanotubes (SWCNTs) have gained notable attention for application in a number of industries because of their unique electronic, optical, mechanical, chemical, or even biological properties. Due to the potential for human exposure, toxicological studies are needed to understand the potential health hazards of these nanomaterials. To better understand the biological responses associated with acute SWCNT exposure, Sprague Dawley rats were exposed to either aerosolized SWCNTs (300 or 1000 μg/m3, raw [FeSWCNT or purified cSWCNT) or fresh air via nose-only inhalation for 6 hours for 1 day. Cytotoxicity markers (total protein, lactate dehydrogenase [LDH], and gamma-glutamyl transferase [GGT]) in bronchoalveolar lavage and mucin and collagen staining in lung tissue were used as a means to assess immediate and persistent (0, 1, 3, 7 and 28 d post-exposure [PE]) effects of acute exposure to SWCNTs. Results showed that markers for cytotoxicity (LDH, GGT) were acutely increased up to 7 d PE, whereas mucin staining in proximal airways initially increased and then decreased at 7 and 28 d PE, and collagen staining in the alveoli increased at 7 d PE. Effects in all cases were transient, influenced by dose and particle composition (e.g., iron content), and generally were resolved by 7-28 d PE. While these data suggest that exposure to aerosolized SWCNTs may induce cytotoxic and structural responses in the lungs, further research is needed to evaluate whether these changes are suggestive of precursor events to pathological changes or lung remodeling that might develop under more severe or prolonged exposure conditions and may have implications for human health risk for persons potentially exposed to airborne SWCNTs.

PS 2205 INHALED MULTI-WALLED CARBON NANOTUBES STIMULATE A PLEURAL INFLAMMATORY RESPONSE IN THE LUNGS OF MICE.

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Carbon nanotubes have recently been reported to have asbestos-like properties since they stimulate the formation of pleural granulomas when injected into the abdominal cavity of mice. This has raised legitimate concerns over the safety of nanotubes because mesothelial granulomas that form on the pleural surface have the potential to develop into mesothelioma, a type of cancer associated with the inhalation of asbestos fibers. Here we report that male C57BL6 mice that inhaled an aerosol of multi-walled carbon nanotubes (6-hr exposure at 100 mg/m3) developed inflammatory foci on the pleural surface of the lung, even though very little inflammation or fibrosis was observed within the lung parenchyma. These foci were primarily monocytic and persisted at 14 days post-exposure. We observed nanotubes dispersed throughout the lung at 1 day post-exposure with some embedded within the pleural wall. Most of the carbon nanotubes (>90%) were contained within macrophages throughout the 14 day study period. Inhalation is the most relevant route of occupational exposure to carbon nanotubes, and our findings are the first to demonstrate that inhaled carbon nanotubes cause pleural inflammation. We emphasize that further work is urgently needed to assess whether longer term, lower concentration nanotube exposures cause similar pleural responses as seen with this

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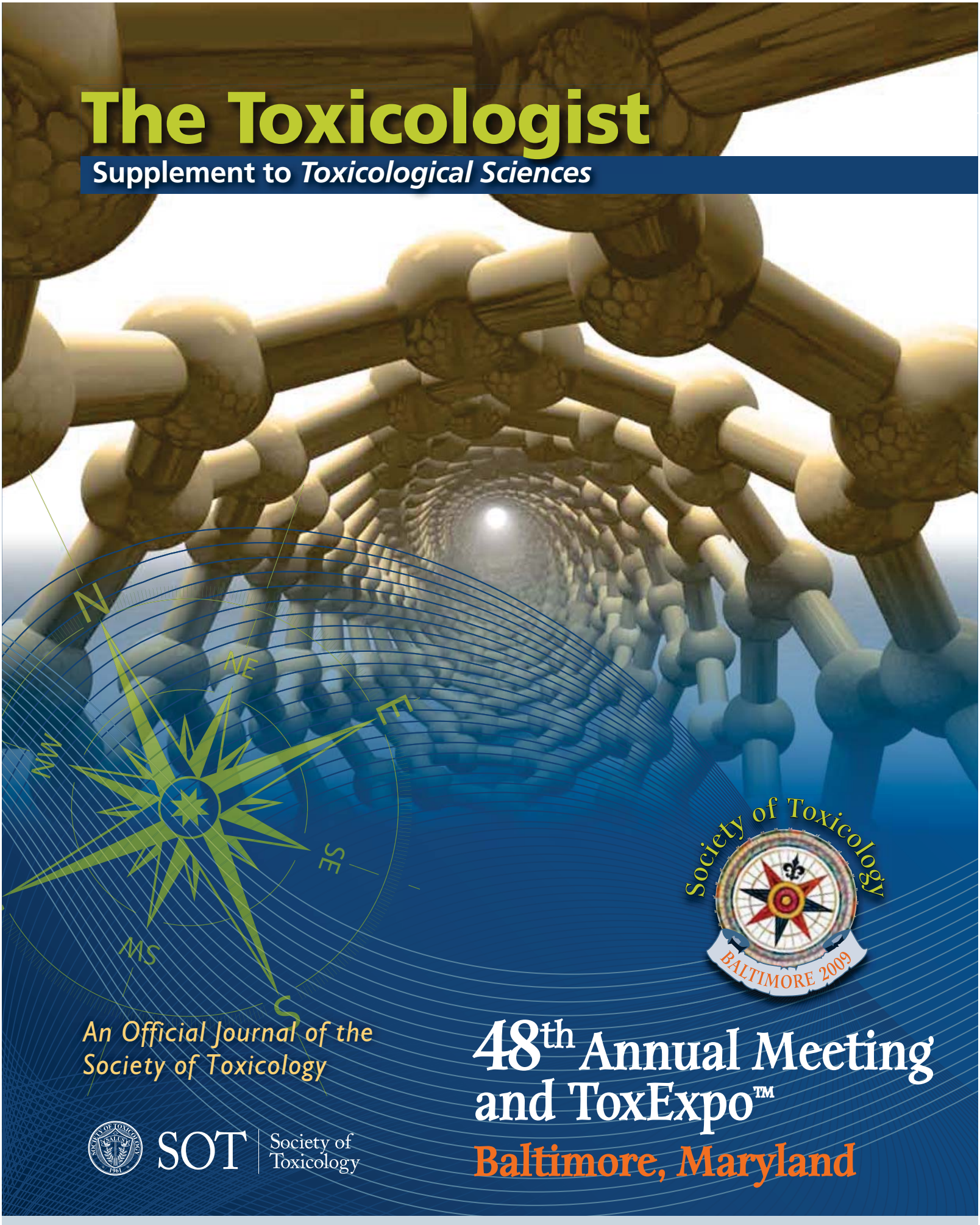

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Deadline for Proposals for SOT 2010 Annual Meeting Sessions: April 30, 2009

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.

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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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