exposure. However, the magnitude of inflammatory response was significantly higher in rigid rod-like MWCNT exposed TLR5 KO mice. In conclusion, these results demonstrate a potential role of TLR5 in mediating MWCNT induced lung injury. Further studies are underway to explore the mechanistic basis of observed responses.

2734 Mouse Pulmonary Dose- and Time Course-Responses Induced by Exposure to Nitrogen-Doped Multi-Walled Carbon Nanotubes

D. W. Porter[1], N. Wu[2], M. Orandle[1], B. T. Chen[1], M. G. Wolfarth[1], L. Battelli[1], M. Andrew[1], S. Tsuruoka[3], M. Endo[3], R. Cruz-Silva[3], M. Terrones[4], and V. Castranova[2]. [1]*NIOSH, Morgantown, WV;* [2]*West Virginia University, Morgantown, WV;* [3]*Shinshu University, Nagano, Japan; and* [4]*Pennsylvania State University, University Park, PA.*

Multi-walled carbon nanotubes (MWCNT) can be modified by doping them with other elements. These modifications change the intrinsic properties of MWCNT and may also alter their bioactivity. In this study, we compared the *in vivo* bioactivity of nitrogen doped multi-walled carbon nanotubes (NDMWCNT) to pristine MWCNT to test the hypothesis that nitrogen doping would alter their bioactivity. First, characterization of the MWCNT and NDMWCNT was conducted. High resolution TEM confirmed the multilayer structure of MWCNT with an average layer distance of 0.36 nm, which was not altered by nitrogen doping. TEM analyses indicated the nanomaterials had similar widths (NDMWCNT=53 nm, MWCNT=49 nm) and lengths (NDMWCNT=4.73 µm, MWCNT=3.86 µm). Comparison of MWCNT and NDMWCNT XPS spectra demonstrated presence of a N1S peak, while FTIR spectra indicated the presence of N-H bonding only in the NDMWCNT sample. For *in vivo* studies, male C57BL/6J mice received a single dose of either dispersion medium (DM: vehicle control), 2.5, 10, or 40 µg/mouse of NDMWCNT, or 40 µg/mouse of MWCNT. Animals were euthanized at 1 and 7 days post-exposure for whole lung lavage (WLL) studies. NDMWCNT caused time- and dose-dependent pulmonary inflammation. However, on an equivalent mass basis, it is less than that caused by MWCNT. Activation of the NLRP3 inflammasome was assessed in mice exposed to 40 µg MWCNT or NDMWCNT by measuring cathepsin activity and cytokine production in acellular WLL fluid at 1 day post-exposure. In comparison to DM-exposed mice, cathepsin activity, as well as IL-1β and IL-18, was significantly increased in MWCNT- and NDMWCNT-exposed mice. Comparison of MWCNT- to NDMWCT-exposed mice showed that cathepsin activity, IL-1β and IL-18 were significantly higher in MWCNT-exposed mice. At 56 days post-exposure, histopathological analyses determined lung fibrosis in MWCNT-exposed mice was greater than that determined for NDMWCNT-exposed mice. These data indicate that nitrogen doping of MWCNT decreases their bioactivity, and that lower activation of the NLRP3 inflammasome by NDMWCNT relative to MWCNT may be responsible.

2735 Multi-Walled Carbon Nanotube Inhalation Alters Expression of SP-D and Inflammation in the Rat Lung

J. M. Bustamante[1], C. H. Flayer[1], C. Bautista[1], E. Laing[1], A. Gupta[2], J. Richey[2], G. L. Baker[2], M. Stout[3], K. Pinkerton[1], A. Haczku[1], and L. S. Van Winkle[1]. [1]*University of California Davis, Davis, CA;* [2]*Battelle, West Jefferson, OH; and* [3]*NIEHS, Research Triangle Park, NC.*

When aerosolized, multi-walled carbon nanotubes (MWCNT) pose an inhalational hazard. Previous studies have shown that rats exhibit a dose dependent acute inflammatory response without altering mucous distribution and abundance and that MWCNT are retained in the lungs for up to 30 days. Surfactant protein-D (SP-D) is an airway epithelial cell-derived lung collectin, an important modulator of the innate and adaptive immune response, and a regulator of apoptotic cell clearance in the lung. The objective of this study was to examine the effects of long term MWCNT exposure via inhalation, on levels of SP-D expression. Male Sprague Dawley rats were exposed to aerosolized MWCNT at 0, 0.06, 0.2, and 0.6 mg/m3 for a total of 22 days over the course of one month. Bronchoalveolar lavage (BAL) fluids were taken 5 days post-exposure to obtain BAL differential cell counts and total protein concentration. Additional lung samples were analyzed for SP-D gene expression and accumulation of neutrophils and macrophages. Native gel electrophoresis and Western blot analysis for SP-D levels in cell-free BAL fluid were performed and BAL cell counts and SP-D levels were correlated by regression analysis. Exposure to MWCNT's induced a significant change in BAL neutrophil counts and SP-D protein expression. Rats exposed to 0.2 mg/m^3 of aerosolized MWCNTs had significantly lower levels of SP-D than control rats exposed to ambient air. However, rats exposed to a concentration of 0.6mg/m^3 MWCNTs expressed significantly more SP-D when compared to the control group. The increase in SP-D level in this group coincided with a significant increase in numbers of neutrophils found in BAL cell differentials. Additionally, there was a negative correlation between numbers of macrophages in the BAL of this high concentration exposure group and the levels of SP-D in BAL supernatant. This data suggests that chronic exposure to MWCNT contributes to increased expression of SP-D which may modulate macrophage uptake of MWCNT and attenuation of inflammatory cell accumulation in BAL. *Supported by: P30 ES023513, T32 ES007059, U01 ES020127.*

2736 Kinetic Time Courses of Inhaled Silver Nanoparticles in Rats

S. Andriamasinoro[1], D. Dieme[1], C. Desvergne[2], S. Alessandra-Maria[3], M. Debia[1], S. Haddad[1], and M. Bouchard[1]. [1]*University of Montreal, Montreal, QC, Canada;* [2]*CEA Grenoble, Grenoble, France; and* [3]*Institute of Research of Hydro-Quebec, Montreal, QC, Canada.*

Silver (Ag) NPs are emerging priority substances closely monitored by main health and safety agencies. Despite their extensive use, there is a lack of data on their *in vivo* behavior in the body, in particular following inhalation, the predominant route of exposure in the workplace. We thus evaluated the toxicokinetics of Ag NPs after inhalation in rats exposed nose-only to 20 nm Ag NPs during 6 h at a concentration of 15 mg/m^3 (218341 ± 85512 particles/cm^3). The generated aerosol showed a uniform size distribution of NP agglomerates with a geometric mean (± SD) diameter of 79.1 ± 1.88 nm. The time courses of Ag element in lungs, blood, tissues and excreta were established over 14 days following the onset of inhalation. All samples were analyzed using inductively-coupled plasma mass spectrometry (ICP-MS). Elimination profiles revealed that feces was the dominant excretion route and represented on average (± SD) 5.1 ± 3.4 % of the inhaled exposure dose compared with urinary excretion, which amounted to 0.01 ± 0.006 %. In the lungs, highest percentage of inhaled dose was observed at the end of the 6-h inhalation and reached 1.9 ± 1.2 %. Blood concentrations increased progressively post-inhalation, reached a maximum at 168 h and decreased thereafter, but values remained 80 times lower than lung levels. In extrapulmonary organs, such as liver, spleen, and kidney, concentrations were also much lower than lung concentrations, representing less than 0.2 % of dose at all times and peak levels were reached at t = 72 h followed by a progressive decrease over the 14-day sampling. Results show that only a small percentage of inhaled dose reached the lungs - the majority of dose most plausibly remained in the upper respiratory tract - and that Ag NPs also poorly translocated to the systemic circulation.

2737 Short-Term Inhalation Study of Graphene Oxide Nanoplates

E. M. Faustman. *University of Washington, Seattle, WA.*

Graphene oxides possessing unique physicochemical properties are expected to be applied within industrial science for electronics, pharmaceuticals and medicine. However, the toxicity of graphene oxide exposure has not been clarified. Therefore, a short-term inhalation toxicity study of graphene oxide was conduct by using a nose-only inhalation exposure system for male Sprague-Dawley rats. A total of four groups (15 rats per group) were exposed: (1) control (fresh air) (2) low concentration (0.76 ± 0.16 mg/m^3) (3) moderate concentration (2.60 ± 0.19 mg/m^3) (4) high concentration (9.78 ± 0.29 mg/m^3). The rats were exposed to graphene oxide for 6 h/day for 5 days followed by recovery 1, 3, and 21 days. The exposure to graphene oxide did not change body weight, and organ weight of the rats after the short-term exposure during the recovery period. Minimal differences were observed in the level of lactate dehydrogenase, alkaline phosphatase, total protein, and albumin between the exposed and control groups suggesting minimal liver and kidney damage. In addition, no significant difference was observed in the bronchoalveolar lavage cell differential such as lymphocytes, macrophages, and PMN. Graphene oxide ingested alveolar macrophages were observed in the lungs of all concentration groups from post 1 day to post 21 days. Thus, these short-term inhalation studies provide important initial information about similarities of toxicities between graphene and graphene oxide following nose-only exposures in lung and lack of toxicity in other organs.

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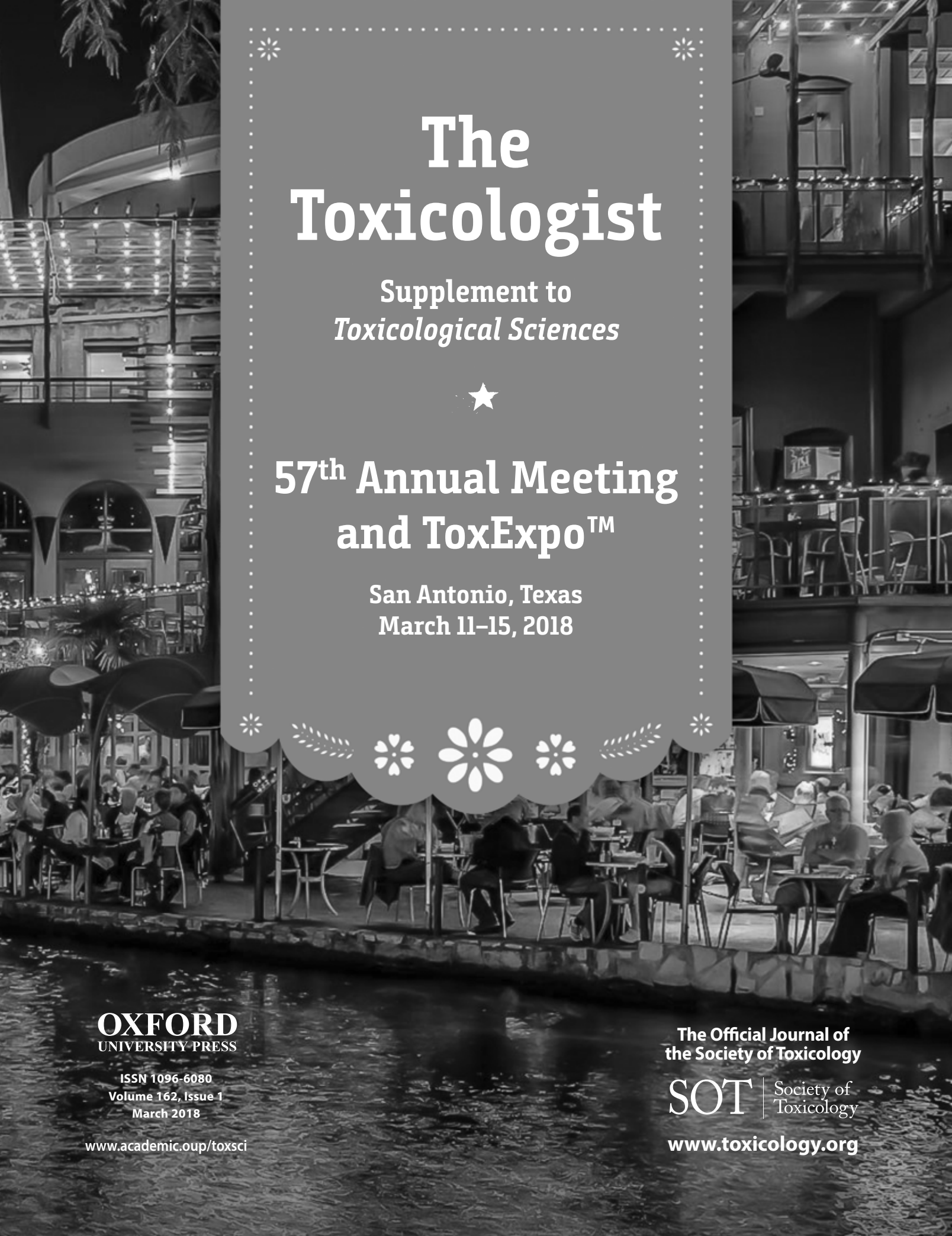

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