PS 1279 CARBON NANOTUBES INDUCE IMMUNE SUPPRESSION VIA DIRECT EFFECTS ON DENDRITIC CELLS.

A. Tkach[1], G. V. Shurin[2], M. R. Shurin[2], E. R. Kisin[1], A. R. Murray[1, 4], S. H. Young[1], A. Star[2], B. Fadeel[3], V. E. Kagan[2] and A. A. Shvedova[1, 4]. *[1]NIOSH, Morgantown, WV, [2]University of Pittsburgh, Pittsburgh, PA, [3]Karolinska Institutet, Stockholm, Sweden and [4]West Virginia University, Morgantown, WV.*

Mounting evidence indicates that exposure to nanoparticles (NP) is able to modify immune responses. However, cellular and molecular mechanisms of immune responses elicited by NP are poorly understood. In the current study, we evaluated site-specific pulmonary inflammation and systemic immune response in mice after pulmonary exposure to single walled carbon nanotubes (SWCNT). SWCNT exposure caused inflammation, pulmonary damage and an altered cytokine network in the lung. SWCNT-induced inflammation facilitated the recruitment of dendritic cells (DC) to the lung tissues, increasing chances of direct DC/SWCNT interactions. Local inflammatory response in vivo was accompanied by modified systemic immunity as documented by decreased proliferation of splenic T cells. To assess if DC could be responsible for modulation of systemic immunity in SWCNT-treated mice, we evaluated the ability of SWCNT-exposed DC to alter T cell responses in vitro. Here we demonstrate that co-culturing of T cells with SWCNT- exposed DC suppressed the T cell proliferation response upon re-stimulation with freshly generated, unexposed DC. Further, exposure of DC to SWCNT did not alter DC phenotype. Exposure of DC to E. coli LPS induced phenotypical maturation of DC. When LPS-exposed DC were mixed with T cells we observed facilitated T cell proliferation. Administration of LPS + SWCNT to DC did not change LPS-induced DC phenotypical maturation. Indeed, when T cells were mixed with LPS+SWCNT treated DC we observed decreased proliferation. Combined, these findings suggest that SWCNT do not interfere with recognition of LPS by DC. We can speculate that SWCNT exposure may intervene with antigen capture/processing and/or presentation, thereby leading to compromised DC/T cell interactions. Overall, our data suggest that exposure to SWCNT modifies systemic immunity by modulating DC function.

PS 1280 DESIGN AND CHARACTERIZATION OF A NANOPARTICLE AEROSOL GENERATOR.

J. Yi[1], T. Knuckles[1], B. Chen[2], E. Sabolsky[3], V. Castranova[2] and T. Nurkiewicz[1]. *[1]Center for Cardiovascular and Respiratory Sciences, West Virginia University, Morgantown, WV, [2]National Institute for Occupational Safety and Health, Morgantown, WV and [3]Mechanical Engineering Department, West Virginia University, Morgantown, WV.*

The generation of nanoparticle aerosols for inhalation toxicology studies is challenging because nanoparticles tend to agglomerate due to very strong inter-particle forces and form large fractal structures in tens or hundreds of microns in size, which are difficult to be broken up. To perform inhalation toxicology studies with nanoparticles, the aerosols in an environmental chamber housing the animal subjects must have: 1) a consistent concentration maintained at a desired level for the entire exposure period; 2) a homogenous composition free of contaminants; and 3) a stable size distribution with a geometric mean diameter < 200 nm and a geometric standard deviation σg < 2.5. We designed and tested a nanoparticle aerosol generator that consists of a vibrating fluidized bed with a baffle, a vibrating Venturi disperser, and a cyclone separator. Nano-sized titanium dioxide (TiO2) dry power (P25, Evonik, Germany) with primary diameter of 21 nm and density of 3.8 g/cm3, and Cerium oxide (CeO2) dry powder with primary diameter of 3 nm and density of 7.1 g/cm3 were used to test the aerosol generator. The aerosols were delivered into a 0.5 m3 inhalation exposure chamber at a flowrate of 90 LPM and measured with a scanning mobility particle sizer and an electric low pressure impactor. The mass concentration of the aerosols was verified gravimetrically. The nanoparticle aerosol generator created TiO2 and CeO2 aerosols with: 1) stable mass concentrations during a 4-hour-study (6.2 mg/m3 and 3.9 mg/m3 for TiO2 and CeO2 aerosols, respectively); and 2) stable particle size distributions during a 4-hour-study (count-median aerodynamic diameters of 157 nm and 145 nm for TiO2 and CeO2 aerosols, respectively). These results indicate that our system has the capability to generate nanoparticle aerosols for inhalation toxicology studies.
NIH-ES015022 and ES018274 (TRN)

PS 1281 AUTOMATED SPRAY CAN AEROSOL EXPOSURE SYSTEM DEVELOPED FOR INHALATION STUDIES INVOLVING PRODUCTS CONTAINING TITANIUM DIOXIDE NANOPARTICLES.

W. McKinney, M. Jackson and D. Frazer. *NIOSH, Mograntown, WV.* Sponsor: V. Castranova.

Inhalation exposure systems are necessary tools for determining the dose response relationships of inhaled toxicants under a variety of exposure conditions. An inhalation exposure system was designed and assembled that could house up to 12 rats and deliver respirable aerosols that were representative of those formed while using a pressurized spray can to their breathing space. A custom generator and support software were developed which could automatically keep the spray can's contents mixed and could precisely time the on / off cycle of the spray to achieve desired exposure levels. The inhalation exposure system also utilized a combination of air flow controllers, particle monitors, data acquisition devices, and custom software with automatic feedback control to achieve constant and repeatable exposure chamber temperature, relative humidity, pressure, and aerosol mass concentration. The automatic control algorithm was capable of delivering median aerosol concentrations to within +/- 0.2 mg/m3 of a user selected target value, ranging from 0.5 to 4 mg/m3, for inhalation exposures lasting 2 to 4 hours. The system was capable of reaching 95% of the target value in less than 8 minutes during the start up phase of an inhalation exposure. Particle distribution and morphology of the spray aerosol delivered to the exposure chamber were measured to verify that a fully dispersed and respirable aerosol was being delivered to the animals' breathing space. This exposure system provides a highly automated tool for exposing small laboratory animals to precise concentrations of aerosols produced by spray can products.

PS 1282 ASSESSMENT OF PULMONARY TOXICITY OF FUNCTIONALIZED MULTIWALL CARBON NANOTUBES *IN VITRO.*

A. Mishra[1, 2], T. Stueckle[1], R. Derk[1], D. Schwegler-Berry[1], N. Wu[2], Y. Rojanasakul[2], V. Castranova[1, 2] and L. Wang[1, 2]. *[1]Pathology & Physiology Research Branch, CDC NIOSH, Morgantown, WV and [2]Pharmacological & Pharmaceutical Sciences, West Virginia University Health Sciences Center, Morgantown, WV.*

Multi-walled Carbon nanotubes (MWCNT), with their unique physico-chemical properties such as diameter less than 100 nm and a large surface area, have a number of current and proposed applications in health care and consumer products. MWCNT can also be toxic due to fiber shape and large surface area. Previous studies have reported that MWCNT exposure in mice caused rapid and progressive interstitial lung fibrosis within a few weeks. Physical-chemical properties of MWCNT e.g. solubility, dispersion status etc certainly mediate their bio-effects. However, mechanisms involved are largely unknown. Therefore, *in vitro* methods should be developed which allow mechanistic studies. For this present study, two types of MWCNT were used: purified (p) and COOH-functionalized (f) MWCNT. Particle characterization was performed by scanning electron microscopy (SEM), Fourier transform infrared spectroscopy (FTIR) and zeta potential measurement. Cultured human bronchial epithelial cell and lung fibroblast cells were exposed to p-MWCNT or f-MWCNT. Cytotoxicity was measured using the tryphan blue assay & lactate dehydrogenase (LDH) assay. Levels of collagen, an indicator of fibrogenicity, were evaluated by ELISA and western blotting. Results showed that 1) f-MWCNT was more hydrophilic than p-MWCNT due to the presence of surface attached COOH functional groups; 2) at physiologically relevant exposure concentrations (0.02-0.6 μg/cm^2), f-MWCNT showed less cell damage compared to p-MWCNT in lung epithilial cells *in vitro*; 3) both p-MWCNT and f-MWCNT induced collagen I in fibroblast cells *in vitro*. Our data suggests that COOH-functionalization modulates the bio-effects of MWCNT in vitro which have important implications in nanotoxicology.

PS 1283 SEMICONDUCTOR NANOPARTICLES EXHIBIT DIFFERENTIAL CYTOTOXICITY THROUGH MITOCHONDRIAL ROS STIMULATION IN A459 CELLS.

V. Escamilla-Rivera[1], M. Uribe-Ramirez[1], V. Subramaniam[2], L. Arreola-Mendoza[3], O. Barbier[2] and A. De Vizcaya-Ruiz[1]. *[1]Toxicology, Cinvestav-IPN, Mexico City, Mexico, [2]SEES, Cinvestav-IPN, Mexico City, Mexico and [3]Biosciences and Engineering, CIIEMAD-IPN, Mexico City, Mexico.*

Copper indium gallium diselenide (CIGS) and cadmium sulfide (CdS) nanoparticles (NP), are semiconductors manufactured for next generation photovoltaic cells, with a better solar energy to electricity conversion. Due to the growing concern on

The Toxicologist

Supplement to *Toxicological Sciences*

51st Annual Meeting and ToxExpo™

March 11–15, 2012 • San Francisco, California

SOT 2012 San Francisco California

An Official Journal of the Society of Toxicology

SOT | Society of Toxicology

Creating a Safer and Healthier World by Advancing the Science of Toxicology

www.toxicology.org

OXFORD UNIVERSITY PRESS

ISSN 1096-6080
Volume 126, Issue 1
March 2012

www.toxsci.oxfordjournals.org