ation based on real-world exposure scenarios is desirable. Nanomaterial concentrations in air (particle mass or count per air volume) are being measured in manufacturing and R&D lab settings. We reviewed nanomaterial levels reported across facility types for different nanomaterial classes. Using particle number concentration data from these studies, we calculated nanomaterial mass retained in the tracheobronchial and alveolar regions of the human lung using the open-source Multiple-Path Particle Dosimetry (MPPD) model. These estimates of inhalation dosimetry were performed for carbon nanotubes (CNTs), titanium dioxide (TiO_2) and silver nanoparticles. The key model input parameters that affect the alveolar mass retained after 24 hours of nanoparticle exposure were particle size and size geometric standard deviation, aspect ratio, breathing conditions (resting, light or heavy exercise), and aerosol concentration. These key parameters were varied to further calculate alveolar mass retained per alveolar surface area ($\mu g/cm^2$) for different particle sizes (ranging from 5 to 100 nm), aerosol concentrations (0.1 and 1 mg/m^3), and exposure times (24 hours and a full working lifetime of 45 years at 8 hours per day, 5 days per week of aerosol inhalation). The alveolar mass retained per surface area for silver and TiO_2 nanoparticles for *a full working lifetime* exposure duration was similar to the high-end concentrations (~ 100-200 µg/mL) typical of *in vitro* testing for silver and TiO_2 nanoparticles. The amount retained per surface area after 24 hours of exposure equated to approximately 0.5 µg/mL. *This abstract may not necessarily reflect U.S. EPA policy.*

PS 2157 NANOTOXICOLOGY – QUO VADIS?

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Nanosafety considerations become a substantial part of many funding programs, international conferences, regulatory activities worlwide and many international working groups are taking care of this topic. Since the term "Nanotoxicology" appeared the first time within a title of a publication [1] confusion about its implementation and the objectives starts. One year later, the relationship to the former research on ultrafine particles has been highlighted [2] and the "new discipline" started its success story. Whereas the number of publications regarding nanotoxicological issues from that time increases dramatically each year (from around 150 in 2004 to nearly 1300 in 2009) clarity about possible risks dropped. Besides the fact that more and more products contain nanoparticles (NP) and thus have to be tested to be safe for the customer there is no general opinion how to approach this target. It has been shown that many of the used methods are not adapted for NP and thus results are often false-positive or false-negative. Not only we could demonstrate the interference of NP with the assay systems which often is neglected [3], solvent problems have not been addressed and the appropriate controls are missing as well as the characterization of the materials tested. Taking all these critical points into account especially nanotoxicology has to establish a new strategy in the future as has been postulated last year [3] on the basis of important recommendations [4]. [1] Donaldson K, Stone V, Tran CL, Kreyling WG, & Borm PJ (2004) Nanotoxicology. Occup Environ Med 61: 727-728; [2: Oberdörster G, Oberdörster E, & Oberdörster J (2005) Nanotoxicology: an emerging discipline evolving from studies of ultrafine particles. Environ Health Perspect 113: 823-839; [3] Wörle-Knirsch JM, Pulskamp K, & Krug HF (2006) Oops they did it again! Carbon nanotubes hoax scientists in viability assays. Nano Lett 6: 1261-1268; [4] Hartung T (2009) Toxicology for the twenty-first century. Nature 460: 208-212; [5] Krug HF & Wick P (2010) Nanotoxicology – an interdisciplinary challenge. Angew Chem Int Ed, accepted

PS 2158 A NOVEL COMPREHENSIVE EVALUATION PLATFORM TO ASSESS NANOPARTICLE TOXICITY *IN VITRO.*

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The unique properties of engineered nanomaterials (ENM) render them suitable for various applications. However, even though studies on biological effects of ENM are available standardized and validated test systems are still missing. Furthermore, inappropriate ways of suspending ENM and their interference with different assays frequently lead to false results. Comparing data to profoundly estimate nano-related toxicity is thus virtually impossible. Hence, harmonized, robust and comprehensively validated tools to assess toxicological effects of ENM are urgently needed. Our novel in vitro evaluation system addresses four key aspects of cytotoxicity: viability, inflammation, genotoxicity and oxidative stress. Special emphasis is laid on careful reassessment and validation of the tests and a thorough characterization of the ENM. Interlaboratory comparisons will subsequently verify the reliability, reproducibility and robustness of the testing platform.

Cell viability was assessed using AnnexinV/Propidium Iodide double-labeling of lung epithelial cells treated with increasing concentrations of ZnO nanoparticles (NP). We find a dose-dependent increase in the number of late apoptotic/necrotic cells. To distinguish effects caused by Zn-ions from NP-related ones we compared dose-response curves of ZnCl2 and NP treated cells. Preliminary results indicate that ZnO NP toxicity is at least to some extend caused by dissociating Zn-ions. Genotoxic effects of different ENM were analyzed by the Comet and Micronucleus assay. At higher concentrations the tested ENM interfere with the system by either quenching or enhancing the fluorescence signal.
We conclude that it is crucial to control for interference of ENM with the assay system as well as for nano-specific effects in comparison to bulk material caused effects. Accordingly, critical concentrations of ENM mustn't be exceeded and additional tests that circumvent the mentioned problems are needed.

PS 2159 PROTEOME PROFILING OF BEAS-2B CELLS TREATED WITH TITANIUM DIOXIDE REVEALS POTENTIAL TOXICITY OF AND DETOXIFICATION PATHWAYS FOR NANOMATERIALS.

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Oxidative stress is known to play important roles in nanomaterial-induced toxicities. However, the proteins and signaling pathways associated with nanomaterial-mediated oxidative stress and toxicity are largely unknown. To identify oxidative stress-responding toxicity pathways and networks that are associated with exposure to nanomaterials, an integrated redox proteomic study was conducted using human bronchial epithelial cells (BEAS-2B) and titanium dioxide. Utilizing two-dimensional gel electrophoresis (2-DE) and mass spectrometry (MS), we identified 46 proteins that were altered at protein expression levels. The protein changes detected by 2-DE/MS were verified by functional protein assays. These identified proteins include some key proteins involved in cellular stress response, metabolism, adhesion, cytoskeletal dynamics, cell growth, cell death, and cell signaling. The differentially expressed proteins were mapped using Ingenuity Pathway Analyses™ (IPA) canonical pathways and IPA tox lists, and these proteins were found to be involved in 20 proteomic pathways/lists. The protein-generated IPA canonical pathways and IPA tox lists were compared to signaling pathways generated from genomic analyses of BEAS-2B cells treated with titanium dioxide. There was a significant overlap in the specific pathways and lists generated from the proteomic and the genomic data. In addition, we also analyzed the phosphorylation profiles of protein kinases in titanium dioxide-treated BEAS-2B cells for a better understanding of upstream signaling pathways in response to the titanium dioxide treatment and the induced oxidative stress. In summary, the present study provides the first protein interacting network maps and novel insights into the biological responses and potential toxicity and detoxification pathways of titanium dioxide. This abstract does not necessarily reflect EPA policy.

PS 2160 SWCNT EXPOSURE OF ALVEOLAR EPITHELIAL CELLS AND MACROPHAGES INDUCED OPN AND TGF-β1 RESPONSE.

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Exposure of the lung to carbonaceous nanoparticles: single walled carbon nanotubes (SWCNT) leads to the development of pulmonary fibrosis (PF) and induction of a network of pro-fibrotic/pro-inflammatory cytokines including TGF-β1 and osteopontin (OPN). TGF-β1 is involved in fibrotic remodeling including fibroblast differentiation and enhanced deposition of collagen in the extracellular matrix. As part of the inflammatory cascade, OPN acts as a chemoattractant to guide polymorphonuclear neutrophils (PMN) and macrophages (MΦ) to the area of insult/injury and is also involved in collagen deposition. Potential interactions between OPN and TGF-β1 have not been investigated even though both cytokines have been shown to be upregulated in response to SWCNT. We hypothesize that OPN increase in response to SWCNT potentiate TGF-β1 production in lung cells. To test our hypothesis two cell types, alveolar epithelial cells (MLE-15) and RAW 264.7 MΦ were treated with SWCNT (6 $\mu g/cm^2$ – 48 $\mu g/cm^2$, for 24 hours). Exposure of the cells to SWCNT resulted in significantly enhanced OPN released found in the incubation medium (39.1% for MLE-15 and 38.6% for RAW 264.7 MΦ vs. respective controls). Using an OPN antibody we demonstrated an inhibition of OPN production in response to SWCNT. Further studies are needed to evaluate interplay between OPN and TGF-β1 and their role in SWCNT induced pulmonary fibrosis.

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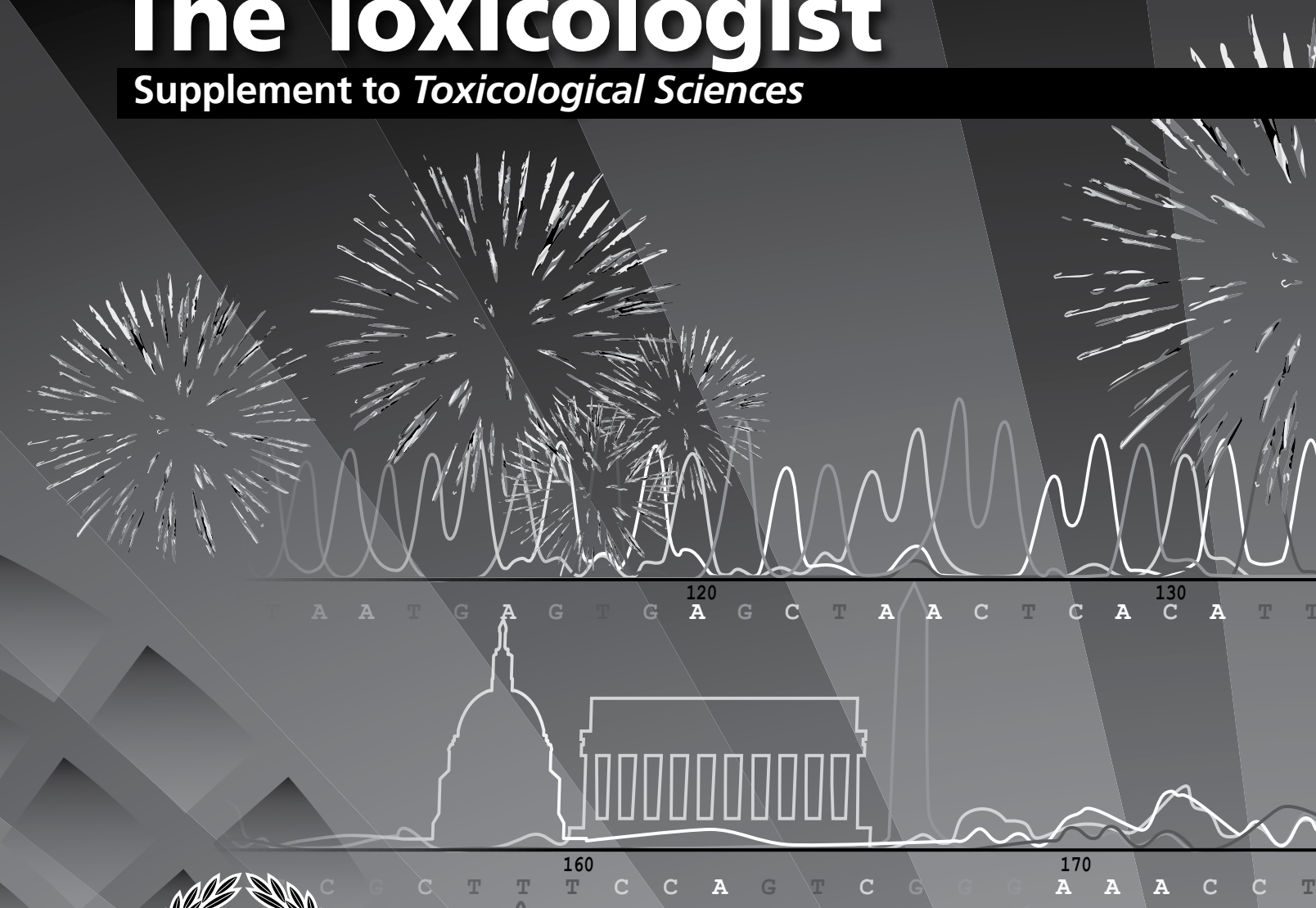

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Preface

This issue of *The Toxicologist* is devoted to the abstracts of the presentations for the Continuing Education courses and scientific sessions of the 50th Annual Meeting of the Society of Toxicology, held at the Walter E. Washington Convention Center, March 6–10, 2011.

An alphabetical Author Index, cross referencing the corresponding abstract number(s), begins on page 578.

The issue also contains a Key Word Index (by subject or chemical) of all the presentations, beginning on page 606.

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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