SYMPOSIUM 6: Nanoparticles Toxicology

S23

Toxicogenomic Analysis of Nanoparticles. Chen FF. Lawrence Berkley National Laboratory, Berkeley, CA, United States.

With the rapid development of nanotechnology and its broad applications, a new wave of industrial revolution is underway. At nanoscale, the physico-chemical properties of matter change significantly from the bulk material. New properties emerge that are unimaginable for conventional bulk material, with dramatically enhanced mechanical, electrical, optical, magnetic, catalytic, and other desirable properties. The benefits of nanotechnology to human society and economy have been very promising, however, the population using and exposed to nanoparticles is expanding quickly with the surge in global production and distribution of nanomaterials. Like any technologies in their infancy stage, the potential toxicity of the nanomaterials is poorly characterized and understood. The potential for risks to human health and environment have been brought to the attention of reserachers within the field of nanotechnology in recent years and have created headlines, in both the popular media and the scientific publications. The unique characteristics that make nanomaterials novel and could potentially be the properties that have profound adverse impacts on human health and environment. I will discuss the global production of the most popular and widely applied nanomaterials, and the risk assessment strategy that should be employed for dealing with them, especially the molecular profiling techniques used for comprehensive nanotoxicological assessments.

S24

Concepts of Nanotoxicology. Oberdörster G. University of Rochester, Rocheser, NY, United States.

Engineered nanomaterials are produced at an increasing rate for many uses, including incorporation into consumer products. Contrasting the many beneficial aspects of nanotechnology are potential risks associated with intended and in particular unintended exposures of humans and the environment. A toxicological assessment of potential nanomaterial associated hazards is essential, and this presentation will address several concepts which are of importance for nanotoxicological evaluations. Among those is the propensity of nanoparticles (<100 nm) to enter cells and translocate cell barriers, thereby targeting tissues and organs that are remote from the portal-of-entry. The high number per given mass as well as the large surface to volume ratio of nanoparticles are other physical properties that impact on biological/toxicological properties of nanoparticles. The large surface and associated chemistry is particularly important for nanoparticle-cell interactions, which can be manipulated through purposeful surface functionalization but also secondary through coating with proteins/lipids once in contact with biological fluids at the portal-of-entry. Given the toxicological importance of particle number, surface and mass the question needs to be considered which of these might be the appropriate dosemetric. Since a major mechanism of nanoparticle-induced effects is the induction of oxidative stress in cells, the intrinsic potential of nanoparticles to generate reactive oxygen species in a cell-free system may contribute to their *in vivo* activity. These diverse aspects of nanomaterial-induced biological/toxicological effects will be discussed in the context of nanoparticle biokinetics and responses in target organs such as the lung and the brain.

S25

New Fuels, New Particles, New Risks? Lucas D[1], Holder A[1], Koshland CP[2], Goth-Goldstein R[1]. [1]LBNL, Berkeley, CA, United States, [2]UC Berkeley, Berkeley, CA, United States.

While diesel exhaust is known to cause human health effects, it is not clear what chemical or physical properties associated with these nanoscale particles and/or their associated gas products are of the greatest risk. Complicating the issue is the current increased focus on modifying the composition of diesel and other liquid fuels to establish a renewable fuel source. Prominent candidates include biodiesel, a fatty acid methyl ester, methanol, ethanol, butanol, and other oxygenated species, as well as mixtures of these compounds with conventional fuels. Since the diesel exhaust is a complex mixture of particles and gases that depend on the fuel composition, engine type, loading, after-treatment and dilution, measuring the biological impacts of these combustion products is not a simple procedure, as there may be too many variables to assess using conventional *in vivo* methods. *In vitro* studies can be employed, but it is necessary to accurately determine appropriate exposure methods and doses. We found it necessary to involve researchers in combustion, aerosol physics and chemistry, as well as biologists to examine many of the issues involved. This presentation will focus on how small particles are formed and transformed from the engine to a biological system. We are using air-liquid interfaces with human lung cells to assess the toxicity of different exhaust mixtures, including engine exhaust and a controlled diffusion burner where the particle characteristics are more readily controlled. This method mimics the inhalation route and provides a realistic exposure to engine exhaust necessary to screen the toxicity of different conditions in reasonably short times. The air-liquid interface system could also be used to screen manufactured nanomaterials that may result in inhalation exposure.

S26

Nanotoxicity Evaluation Platforms. Hobson DW. nanoTox Inc., Houston, TX, United States.

Nanomaterials and nanodevices promise major innovations and technological advances in many areas including manufacturing, electronics, medicine and environmental remediation. Along with their potential utility, there are also significant questions being raised with respect to their safety, whether it be in the development and manufacturing aspect or in their use or disposal. The unusual and unique physical and chemical characteristics of nanoparticles and nanostructures are being shown to create special considerations in the design and development of appropriate test platforms for toxicity assessment. There is reason to believe that at least in some cases, the toxicity of nanomaterials, nanotoxicity, may create special situations with regard to their toxicity testing, including mutagenicity testing. The familiar platforms previously designed for chemical substances may now need to be reconsidered or re-designed for the evaluation of nanomaterials safety. In addition, the sheer number of new nanomaterials and nanodevices that are being developed on a daily basis is overwhelming, and requires that nanotoxicity evaluation platforms have the ability to screen some types of materials quickly so that selections can be made from a variety of potential nanomaterials having differential structures and/or compositions. As a result, many panels have been convened on a worldwide basis to consider and recommend approaches and procedures for the assessment of toxicity from nanomaterials.