Sunday Afternoon, November 8, 2009

Biomaterials Plenary Session
Room: K - Session BP+NS-SuA

Nanoparticles: Advances in Fabrication, Characterization and Regulatory Challenges

Moderator: K.J. Wahl, Naval Research Laboratory, S. Zauscher, Duke University

3:00pm **BP+NS-SuA1 Using the Fabrication Technologies from the Microelectronics Industry to Address the Unmet Needs in Drug Delivery**, ***J.M. DeSimone***, UNC-Chapel Hill & NC State University **INVITED**

To translate promising molecular discoveries into benefits for patients, we are taking a pharmaco-engineering systems approach to develop the next generation of delivery systems with programmable multi-functional capability. Our laboratory has pioneered the development of a technique called **PRINT** (**P**article **R**eplication **i**n **N**on-wetting **T**emplates). PRINT is a remarkable top-down particle fabrication technique that has its roots in the fabrication techniques used in the microelectronics industry to make transistors. PRINT is a high resolution molding technique that allows the fabrication of precisely defined nano-particles with control over size, shape, deformability and surface chemistry. PRINT allows for the precise control over particle size (20 nm to >100 micron), particle shape (spheres, cylinders, discs, toroidal), particle composition (organic/inorganic, solid/porous), particle cargo (hydrophilic or hydrophobic therapeutics, biologicals, proteins, oligonucleotides, siRNA, imaging agents such as MR contrast agents, positron emitters), particle modulus (stiff, deformable) and particle surface properties (Avidin/biotin complexes, targeting peptides, antibodies, aptamers, cationic/anion charges, Stealth PEG chains).

3:40pm **BP+NS-SuA3 Designing Next Generation Nanoparticles for Self-Assembly and Reconfigurability**, ***S.C. Glotzer***, University of Michigan, Ann Arbor **INVITED**

Nanoparticles comprise a new generation of materials building blocks because of their diversity of shape, material and size, and because they can now be patterned and functionalized down to molecular scales with tailored and programmable interactions. The ability to create designer particles opens up exciting opportunities to create building blocks designed for self-assembly and even reconfigurability, in part through biomimicry. We show how, in the absence of a predictive theory, computer simulations play a critical role in elucidating how particle shape, interactions, and programmability can be exploited to achieve a high propensity for self-assembly into complex structures, including sheets, wires, helices, shells and other biomimetic structures.

4:20pm **BP+NS-SuA5 Nanotoxicology, Including Use of Nanomaterial Structure-Activity Relationships for Nanomaterial Safety Testing**, ***A.E. Nel***, University of California - Los Angeles **INVITED**

Because of the large number of new nanomaterials that are being produced, it is of increasing importance to develop a predictive platform for safety and risk assessment at the scale of technology expansion. The UC Center for the Environmental Impact of Nanotechnology (CEIN) is developing high throughput screening methods that incorporate relevant toxicological injury pathways that relate to the physicochemical properties of nanomaterials. I will discuss the emerging paradigms of toxicity that can be linked to the physicochemical properties of engineered nanoparticles with a view to outlining scientific principles that originate at the nano/bio interface and could determine which bio-physicochemical interactions occur and what leads to biocompatibility or toxicity. The major toxicological paradigm that has emerged from nanoparticle toxicity relates to the semiconductor, electronic, UV activation, and redox cycling chemistry of the particles, leading to biological hazard through the generation of oxygen radicals, electron-hole pairs and oxidant injury. It is possible to follow the oxygen radical generation and oxidant stress injury by abiotic methods as well as a set of hierarchical cellular responses that reflect protective, pro-inflammatory, mitochondrial damaging and pro-apoptotic outcomes. An oxidant injury pathway could translate into adaptive, pro-inflammatory or pro-apoptotic cellular effects in the lung, cardiovascular system, skin and the brain. Another paradigm relates to the ability of nanoparticles to absorb circulatory or cellular proteins as a function of particle size, surface area, functionalized surface groups, charge, hydrophobicity/hydrophilicity etc. This could induce protein unfolding, protein fibrillation, thiol crosslinking and loss of function, which could lead to neurotoxicity, loss of enzymatic activity, and generation of immunological responses. The thermodynamic properties and free surface energy of nanoparticles as a function of particle size, composition, phase and crystallinity could be responsible for particle dissolution in a biological environment, leading to the generation of cytotoxicity through the release of toxic ions or chemicals. ZnO will be discussed as an example of the latter category. I will demonstrate that it is possible to devise high content screening to capture these toxicological mechanisms, which can then be used to rank nanoparticle hazard and establish guidelines for safe design. If used as a preliminary screen for emerging nanomaterials, these predictive science-based approaches can help to determine which materials should undergo priority *in vivo* testing in the CEIN environmental mesocosms. I will also briefly discuss how these principles can be applied to toxicity testing and safe design of therapeutic nanoparticles.

Authors Index

Bold page numbers indicate the presenter