Amber Nagy  
PhD Candidate  

“Characterization and Interaction of Nanoparticles in Biological Systems”  

11/2/10  
Graves Hall 1175  
10:00am
VITA

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AWARDS AND HONORS

OSUMC Trainee Research Day Travel Prize April, 2010
OSU Alumni Grant for Graduate Research and Scholarship May, 2009

FUTURE PLANS

Amber plans to pursue postdoctoral training in the field of immuno-nanotoxicology.
ABSTRACT

Nanoparticles are particles with at least 1 dimension less than 100 nm in size. Many consumer products already contain nanoparticles; however the risks and consequences of acute and chronic nanoparticle exposure have not yet been adequately evaluated. Additionally, nanoparticle manufacturing plants are becoming more prevalent around the world. As such, there is cause for concern regarding the effects of nanoparticle related occupational hazards and also incidental nanoparticle exposure to the general public.

This communication sought to further investigate nanoparticle/cell interactions, ensuing toxicity and cellular responses within biological systems. Three model nanoparticles were synthesized: quantum dots (QDs), modified carbon nanoparticles (CNPs) and a zeolite substrate containing silver nanoparticles.

QDs were chosen to model mechanisms of nanoparticle internalization and compartmentalization. It was found that QDs interact with scavenger receptors, and enter cells via a clathrin coated pit mediated pathway. The kinetics of QD internalization was established; QDs were found to associate with macrophage cell membranes within 2.5 minutes, and are confined to lysosomes 9 minutes after exposure. QDs were found to be approximately 9 nm in size and were found to aggregate when subjected to acidic conditions. Cadmium ions were found to leach from the core at low pH. Macrophages exposed to quantities 20 times greater than needed for imaging were found to induce TNF-α secretion and cytotoxicity, via apoptosis.

To understand how the surface functional groups on nanoparticles drives inflammation and cytotoxicity, CNPs were modified with iron species, benzo(a)pyrene or ozone. Experiments utilizing primary human monocyte-derived macrophages revealed large variability in individual cell responses, ranging from increases in cytokines including TNF-α, to upregulation of complement factors. Carbon nanoparticles were added to cultures...
of murine alveolar macrophages and those modified with iron or B(a)P had little proinflammatory response. However, treating CNPs with O₃ immediately prior to exposing macrophages resulted in a significant decrease in TNF-α secretion that was found to be a result of changes in the oxidative state of modified CNP surfaces. Additionally, free radical content was sustained after ozonated CNPs were suspended in cell culture media, indicating that mechanisms other than oxidative stress may drive CNP mediated cell responses.

Finally, a novel antimicrobial zeolite support containing silver nanoparticles was created. These supports were found to have superior antimicrobial activity against E. coli. Zeolite micropatterning was not found to be a significant factor in bacterial killing. In addition, antibacterial activity was not found to be contact dependent. The upregulation of genes involved with metal transport, ATPase efflux pumps and multiple antibiotic resistance was revealed using gene microarrays. Increased antioxidant gene expression, including superoxide dismutase, glutaredoxin and thioredoxin was also noted, indicating that oxidative stress may be driving the antimicrobial activity of zeolite silver nanoparticle supports. Lastly, these supports were also found to be significantly cytotoxic to macrophages, and research is ongoing to determine if the mechanism of silver nanoparticle toxicity is similar to bacteria.

Physicochemical properties of nanoparticles, including charge and surface functional groups were found to play a role in nanoparticle-cell interactions. However, more definitive studies regarding specific pathways that are involved with nanoparticle internalization, inflammatory responses and toxicity are warranted before proper guidelines regarding nanoparticle exposure are established.