# Towards Understanding Nanoparticle Toxicity

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Material properties at the nano-scale level vary greatly from the macroscopic components due to their small size, motivating a rapid growth in nanomaterials development. Functional nanomaterials have already found application in many consumer products such as apparel, cosmetics, and electronics. However, nanomaterials have the potential to exhibit different properties than shown at the macro-scale in various categories including toxicity[1]. Nanomaterials have shown increasing evidence of elevated toxicity and with that the potential to harm people and the environment. Hence there is an urgent need for a more thorough understanding of the effect of 'nano-sizing' on toxicity[1-2]. This project hypothesizes that supporting or embedding metal nanoparticles on/in a nontoxic support will create less toxic nanomaterials. The goal is to create nanomaterials that are "safer by design" through correlations between structure and toxicity.

Our complex engineered nanomaterials (CENs) combine nickel and silica, i.e. a known toxin (Ni) with a non-toxic matrix (amorphous $SiO_2$). Due to their versatility, modifiable capabilities, and nontoxic properties, porous silica nanomaterials are used in a wide range of applications such as biomedical imaging, catalysis, and drug delivery. Therefore, we hypothesized that embedding nickel in porous silica will reduce the toxicity of nickel by modifying transport and interaction of the embedded nanoparticles with its environment while still providing full access to the metal nanoparticle surface. In this manner, the functionality of the embedded nanoparticle can be maintained while toxicity can be reduced.

Three nickel and silica nanostructures, nhNi@$SiO_2$ (nickel embedded in silica), hNi@$SiO_2$ (nickel encapsulated in a hollow core in silica), and Ni-$SiO_2$ (nickel deposited on silica) were synthesized. Pure $SiO_2$ is used as a negative control, and $NiCl_2$ as a positive control. The latter is chosen both due to its established toxicity and to "represent" nickel ions that dissolve from the nanoparticles. We are employing an in vitro model to test the effects of the synthesized nanomaterials. 3T3 mouse-skin derived fibroblasts are well-suited and well established for nanotoxicity studies because they are inexpensive, robust, and proliferate quickly. 3T3 fibroblasts were exposed to varying nickel concentrations over 24 hours before being analyzed for viability via qualitative and quantitative analysis.

Qualitative analysis included using microscopy and live/dead imaging, while MTS assays were used to quantitatively determine cell viability. As expected, exposure to pure $SiO_2$ did not indicate any toxicity, while $NiCl_2$ showed increasing toxicity with increasing concentrations of nickel exposure. Our Ni/$SiO_2$ showed generally similar toxicity trends to $NiCl_2$. Among the three CENs, nhNi@$SiO_2$ was found to be the least toxic compared to hNi@$SiO_2$ and Ni-$SiO_2$. The MTS assay used for this analysis determines the metabolic activity of cells, which is directly correlated to cell count. Hence there is a possibility of CENs affecting metabolism along with affecting cell viability. In order to eliminate this artifact, we directly measured the cell number by DNA-staining and quantitative fluorescence imaging using Li-cor Odyssey imaging platform. Comparing Li-cor to MTS we confirmed that the NP toxicity was indeed from a reduction in cell number, not a reduction in cell metabolism.

We have successfully used 3T3 cells to study cell viability after exposure to our nanomaterials. As expected, pure silica showed no toxicity, while $NiCl_2$ salt and our NPs exhibited dose-dependent toxicity. Confirming that the porous $SiO_2$ in indeed nontoxic, suggests that the nanomaterial toxicity seen is associated with the nickel nanoparticles. However, since we did not observe a significant mitigation of toxicity through our CENs, we were not about to validate our original hypothesis. Future work includes the study of nanomaterial uptake, and continuing analysis on the nanoparticle toxicity mechanism and persistency.

**References**

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