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Observations of *in vivo* Processing of Metal Oxide Nanoparticles by Analytical TEM/STEM

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High resolution transmission/scanning transmission electron microscopy (HRTEM/STEM) imaging coupled with advanced detectors allow one to probe nanomaterials in biological tissue sections in unprecedented detail. Here we report analytical TEM/STEM observations of different metal oxide nanoparticles (NPs) and compare their *in vivo* processing behavior: their breakdown, reactivity, and structural and chemical transformations. It was previously reported by Graham *et al.* that cerium oxide (CeO_2) NPs, which have relatively low solubility even under extreme, controlled laboratory conditions (e.g., very low or high pH, varying ionic strength, high temperature), undergo *in vivo* processing in cellular structures.[1] This finding was evidenced through analytical STEM observations. In addition to CeO_2, the occupational exposure risks of other widely used metal oxide NPs must be assessed. This research will lead to a better understanding of the role that *in vivo* processing plays with regards to toxicity or therapeutic effects of NPs.[2,3] Prepared tissue sections from inhalation studies of rats exposed to either silica (SiO_2) or alumina (Al_2O_3) NPs were examined. SiO_2 and Al_2O_3 NPs were selected based on relative solubility, much greater than and similar to CeO_2, respectively, and for their industrial relevance and reported biological effects. After residence in rat lung tissue, metal oxide NPs underwent morphological changes and size variations, with some instances of significant reaction rims on their surfaces that are indicative of *in vivo* processing. Electron energy loss spectroscopy (EELS) and energy dispersive x-ray spectroscopy (EDS) in scanning (STEM) mode were utilized for elemental point analysis to provide profiling and mapping of compositional variations, phase changes, and oxidative states. Analyses were typically extended into areas adjacent to the NP (primary) deposits to detect any changes in elemental composition. The surface is thought to be main site of biological interaction, while the NP core is more isolated. The small probe (~0.2 nm) used allows compositional variations to be identified that span from the particle surface towards the NP core, while minimizing beam effects. Thus, reaction rims of the metal oxide NPs' surfaces were studied at nano and sub-nano scales. The surrounding tissue zones were also examined for any traces of *in vivo* processed NPs such as released ions and precipitates. The EDS/EELS spectrum images were collected on a 200 kV JEOL 2100F TEM/STEM. Figures 1 and 2 show precursor and *in vivo* processed lung SiO_2 NPs respectively. EDS spot analysis of areas near NP deposits revealed migration of Si into the nearby tissue and intracellular environments, as indicated by the bright halo surrounding the SiO_2 nanoparticles (Figure 3).

References:

[1] Graham U. M. *et al.*, ChemPlusChem, **79**, (2014), 1083.
[2] Cassee, F. R. *et al.*, Crit. Rev. Toxicol., **41**, (2011), 213.
[3] Zhao L. *et al*, Vaccine, **32** (2014), 327-337

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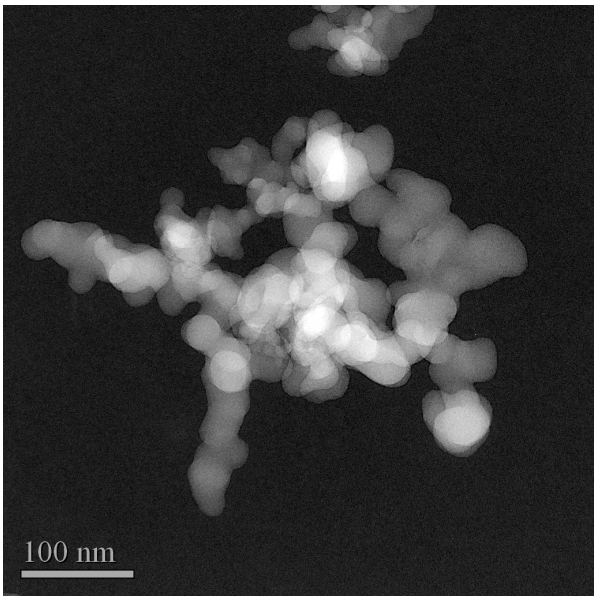

Figure 1. Precursor silica.

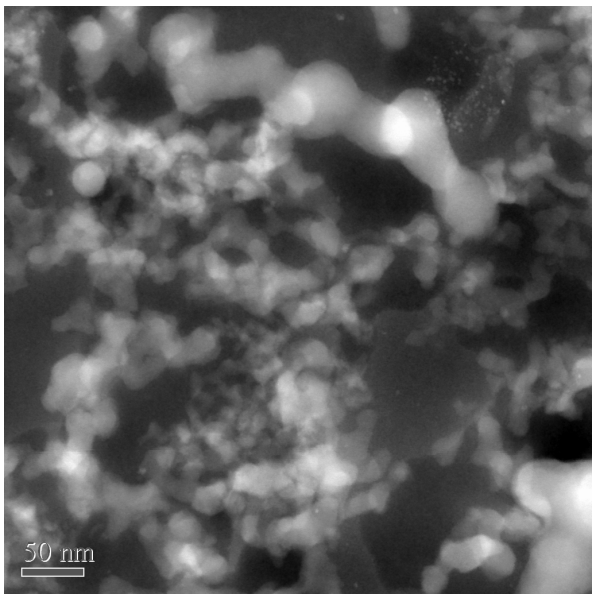

Figure 2. Silica transformation in lung.

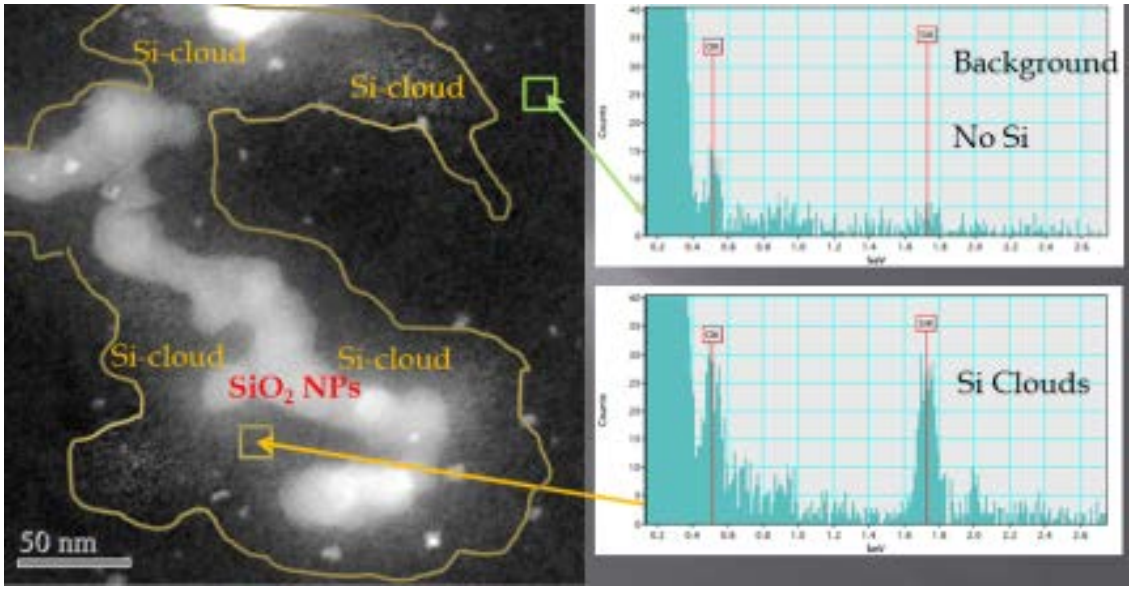

Figure 3. Dark Field STEM image showing bright cloud around lung silica particles. EDS analysis reveals cloud has a high silicon content.

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