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Size determines the ultrastructural uptake mode of silica nanoparticles into cultured cells

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Silica nanoparticles are widely used in commercial products. As additives in food, drinks, cosmetics and pharmaceuticals they directly get into contact with different human tissues. Therefore, a thorough examination of nanoparticle – cell interactions is of paramount importance.

In our study we applied electron microscopic methods (TEM, SEM, FIB-SEM) to investigate the interaction of differently sized, small silica nanoparticles with cultured cells on the ultrastructural level. For high resolution of the cellular details high pressure freezing was utilized as the fixation method for TEM. Additionally, we used some standard biochemical assays to test for the type of cell death occurring after the exposure to high concentrations of the respective particles.

Our observations clearly indicate that the mode of uptake into cells strongly depends on particle size. For each size of silica particle used we could identify characteristic membrane morphologies during the uptake process (Figure 1, Figure 2). These morphologies have proven reproducible in five completely different cell types and could give a hint at the mechanism of silica nanoparticle toxicity. Interestingly, though it forms large agglomerates in cell culture media, one of the particle sizes we tested enters cells as single particles (Figure 3).

From the electron microscopic evaluation of cell morphology and the findings yielded by analytical TEM and biochemical assays we conclude that high concentrations of small silica nanoparticles induce necrotic cell death. We could not find evidence for apoptosis.

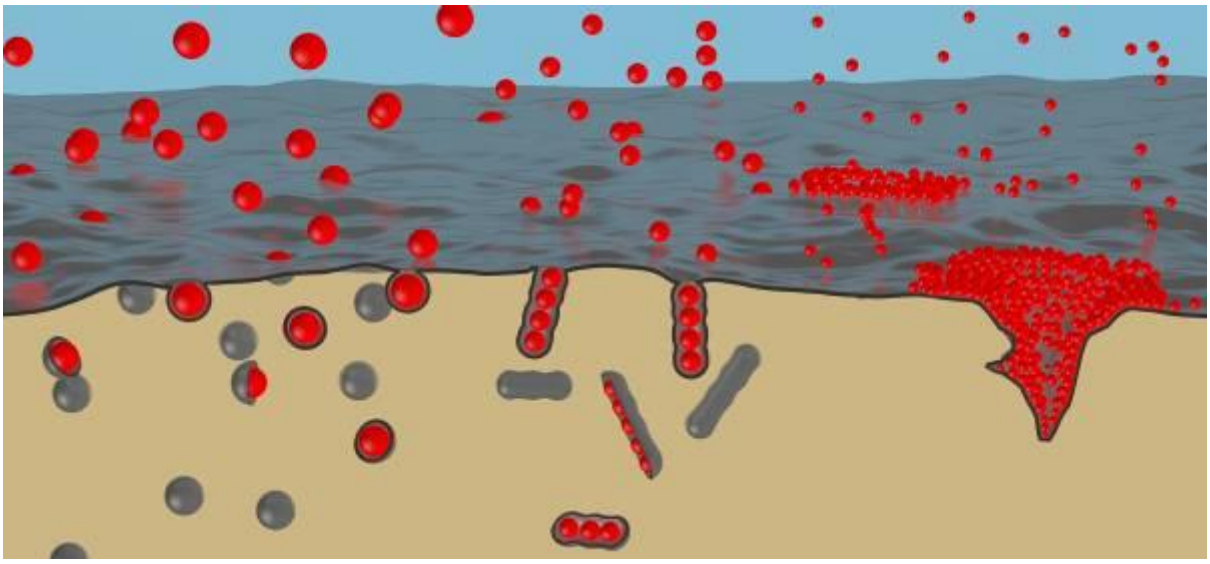

Figure 1. Scheme of the uptake modes observed for three differently sized, small silica nanoparticles (represented by red spheres).

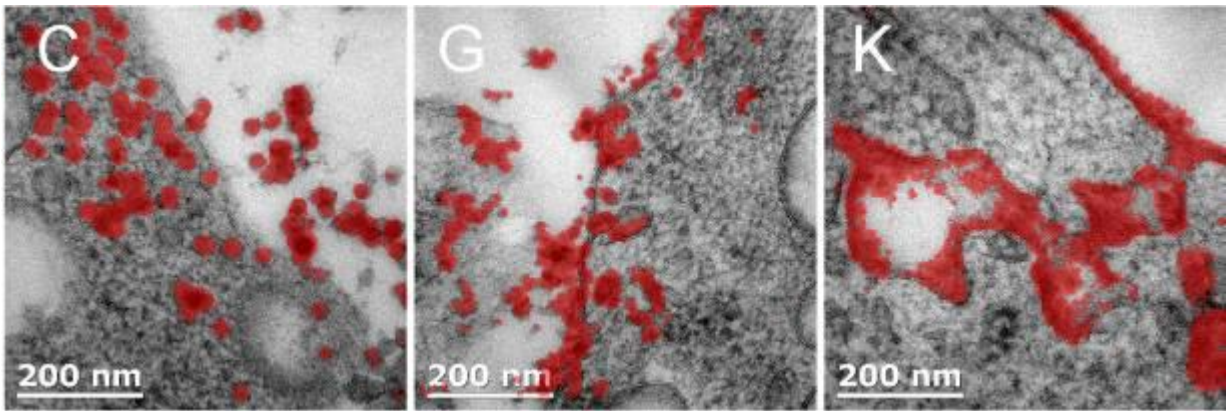

Figure 2. TEM micrographs showing the three different uptake modes observed. Silica nanoparticles are coloured red for better visibility.

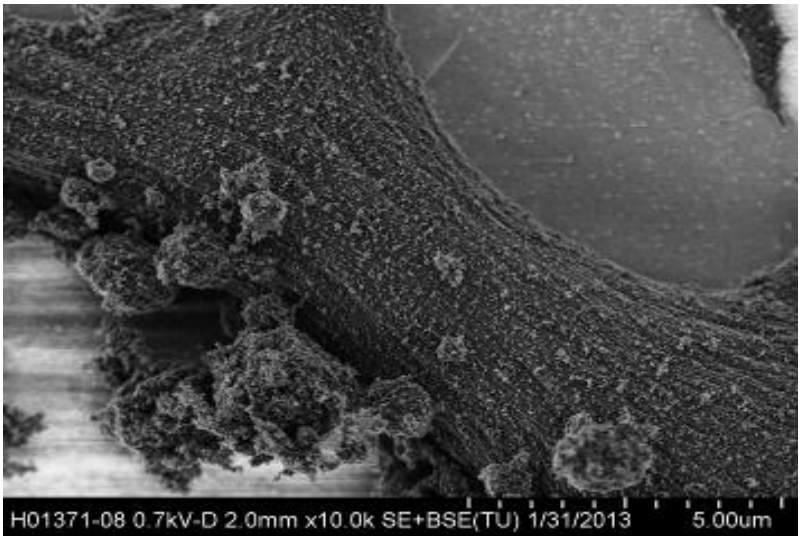

Figure 3. SEM micrograph showing the coverage of a cell membrane with single and aggregated silica nanoparticles.