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Role of macrophages in the clearance of ultrafine titanium dioxide particles from lungs

The importance of macrophages in the clearance of inhaled and deposited particles of micrometer size from the inner surface of the lungs has long been recognized. However, the increasing evidence for particles with diameters < 100 nm (ultrafine or nanoparticles) to rapidly penetrate the lung epithelium and to be translocated even into secondary organs, has led to question the role of macrophages in the clearance of this particle category.

To investigate the uptake of ultrafine particles by lung phagocytes, we analyzed the distribution of 22-nm titanium dioxide particles in systematic samples of rat macrophages, obtained by bronchoalveolar lavage at 1 h and 24 h after aerosol inhalation. We employed energy filtering transmission electron microscopy for elemental microanalysis of individual particles. Particles identified as TiO_2 were recorded with respect to their ultrastructural localization within the cell.

We examined 144 systematic fields on 520 macrophages in the 1-h animal group (n=6) and recorded 51 TiO_2 particles in the cytoplasm and 1 particle within the cell nucleus. In the 24-h animal group (n=6), we analyzed sampled fields on 604 macrophages and identified 71 particles in the cytoplasm and 10 in the nucleus. From the particles in the cytoplasm only 1 and 3, respectively, were found to be enclosed in vesicles, the others and those in the nuclei were not surrounded by a membrane.

Particles within cells that are not membrane-bound are likely to have penetrated the cells by a non-endocytic pathway. Hence, the finding of very few particles in vesicles, even 24h after aerosol inhalation suggest that phagocytic uptake of TiO_2 nanoparticles by lung surface macrophages plays a minor role in the clearance of these particles from the lungs.

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