Geiser M. / University of Berne, Switzerland

Distribution and clearance of inhaled ultrafine titanium dioxide particles in rat lungs

Experimental studies in animals using radio labeled ultrafine particles have provided a great body of evidence for particle translocation from the lung surface into and beyond the epithelium, even into secondary organs. Consequently, lung distribution patterns as well as clearance pathways for particles in the nanometer size range may significantly differ from those of larger ones. It the presented study, we investigated the distribution as well as the clearance of the particles within the lungs for the first time quantitatively at an individual particle level. Rats inhaled an aerosol of 22-nm titanium dioxide particles by negative-pressure ventilation through an intratracheal cannula. The inhalation lasted one hour and 4-5 micrograms of titanium dioxide were deposited in each lung. The intrapulmonary distribution of particles was analyzed 1 hour and 24 hours after the end of exposure using energy filtering transmission electron microscopy for elemental microanalysis of individual particles. The majority of the inhaled ultrafine titanium dioxide particles, on average 79%, were found on the luminal side of airways and alveoli. The remaining particles were found in all major lung tissue compartments and cells, as well as within capillaries. Particles within cells were not membrane-bound, indicating an uptake by a non-endocytic pathway. Particles penetrating into the lung tissue may affect cellular and eventually organ functions, those entering capillaries may easily reach secondary organs. The relative distribution of the particles within the lungs remained almost unchanged within 24 hours, there were no indications for accumulation of ultrafine titanium dioxide particles in any specific tissue compartment or cell type. Since free particles were still found on the lung surface 24 hours after their inhalation, the question about the role of airway and alveolar macrophages in the clearance of ultrafine particles remains open. First approaches to resolve the clearance mechanisms and pathways of inhaled ultrafine titanium dioxide particles will be shown.

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