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Interaction of nanoparticles with cells of the airway tissue barrier: A study with cell culture models

So far, little is known about the interaction of nanoparticles with lung cells and their transport by the vascular system to other organs. The uptake of different nanoparticles consisting of different materials and of different charges was studied in cell culture models: (1) cultured porcine macrophages, as a model for phagocytic cells; (2) human red blood cells, which do not have any receptors on their surface and which served as a model for non-phagocytic cells; (3) a triple cell co-culture model of the human airway barrier to simulate the cellular part of the air-blood barrier of the respiratory tract, represented by macrophages, epithelial cells, and dendritic cells. Since ultrafine particles have the size of small cell components (e.g. ribosomes), their identification in cells is very difficult. We combined different microscopic techniques to visualise nanoparticles in cultured cells: (1) fluorescent particles were analysed by confocal laser scanning microscopy combined with digital image restoration; (2) gold particles were analysed by conventional transmission electron microscopy and after silver enhancement with energy filtering transmission electron microscopy; (3) titanium dioxide particles were analysed by energy filtering transmission electron microscopy. In addition, the amount of TNF- α , a pro-inflammatory mediator, produced by cells upon entering nanoparticles was determined as an estimate for specific cell reactions using the triple cell co-culture model. TNF- α concentrations in the supernatants after applying gold particles was twice as high than in controls or after applying ultrafine polystyrol and titanium dioxide particles. Using different cell culture models and advanced microscopic techniques, we have been able to visualize and detect nanoparticles in cultured cells. We have shown that particles entering cells under *in vitro* conditions did not occur by any of the existing endocytic processes, but rather by diffusion or adhesive interaction. The surface charge and the material of the particles did not influence their penetration into cells and intracellular, the particles were not membrane bound. However, an inflammatory response is induced in the co-culture model depending on the particle material.

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