Conference abstract L08

A 3D model of the epithelial airway barrier to study uptake, cell responses and intracellular distribution of nanoparticles

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Sci Pharm. 2010; 78: 548 doi:10.3797/scipharm.cespt.8.L08

Understanding the intracellular localisation of biomedical nanoparticles (NPs), such as their co-localisation within cellular organells, e. g. endosomes, lysosomes, mitochondria or nuclei, or, alternatively free in the cytosol, can provide essential information in regard to the potential toxicity of NPs.

Polymer coated iron-platinum and gold NPs with a fluorescent dye embedded in the polymer shell were used to investigate their intracellular localization in lung cells, i. e. epithelial cells, macrophages as well as dendritic cells [1], and their potential to induce a pro-inflammatory response dependent on concentration and incubation time [2]. In addition, a quantitivate method [3] was used to evaluate the intracellular gold NP distribution by transmission electron microsopy within time (1h, 4h and 24h).

By laser scanning microscopy it was shown that the iron-platinum NP were taken up by all three cell types but macrophages and dendritic cells to a higher extent than epithelial cells. In both cell types of the defence system but not in epithelial cells, a particle dose-dependent increase of tumor necrosis factor-α is found. By comparing the iron-platinum- and the gold NPs as well as the shell only it was shown that the cores combined with the shells are responsible for the induction of inflammatory effects and not the shells alone. The quantitative analysis revealed a significant, non-random intracellular gold NP distribution. No particles were observed in the nucleus, mitochondria, endoplasmatic reticulum or golgi, and the cytosol was not the preferred NP compartment. A significant increased gold NP localization in large vesicles (lysosomes) was found with prolonged post-incubation times, indicating intracellular particle trafficking.

In conclusion, by using sophisticated cell culture and microscopic methods, it is possible to determine if NPs exposed to cultured lung cells can penetrate into these cells, inducing an effect and furthermore, in which intracellular compartments they are subsequently localized (trafficking).

This work was supported by the German Research Foundation (DFG SPP 1313), the Swiss National Foundation (Nr. 3100A0_118420), the Doerenkamp Zbinden Foundation and the AnimalFreeResearch.

[1] Lehmann AD, Parak WJ, Zhang F, Ali Z, Röcker C, Nienhaus GU, Gehr P, Rothen-Rutishauser B. Fluorescent-magnetic hybrid nanoparticles induce a dose-dependent increase of the pro-inflammatory response in lung cells in vitro correlated with intracellular localization. Small. 2010; 6: 753–762. doi:10.1002/smll.200901770