Prediction of the effects of nanoparticles on humans: Impact of amorphous silica nanoparticles on various complex *in vitro* organ models.

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Abstract:
Nanoparticle-cell interactions have been investigated since years and their evaluation in terms of health and safety is of essential importance. However, effects on single cells are not reflecting the effects on organs or even living organisms. A sophisticated approach to analyse and predict their impact on humans much more precisely is the use of complex *in vitro* multiculture systems. These model systems have many advantages since it is known that cell communication could play a pivotal role in the effect of NPs to organs (inflammatory response, cell stress, etc.) [1]. In principal, two main concerns of nanoparticles exposure should be considered in detail and can be summarized as following: (1) Uptake routes of nanoparticles into the body (lung, skin, intestine) and (2) the impact on organs (e.g. brain). Thus, we decided to utilize our expertise in the development of complex cell culture model systems (co- and triple-cultures under standard and air-liquid-interface conditions) simulating the major physiological barriers for the investigation of the effects of nanoparticles and nanoparticle-cell-interactions [2-4].
We started our examinations with amorphous silica nanoparticles of different sizes (30nm, 70nm) and various surface modifications (carboxy-, amino, hydroxyl groups) and used these particles as model nanoparticles due to the monodispersity, good fluorescent properties and standardized synthesis procedures.
Our aim was not to compare the different model systems but to generate as much data as possible to predict how those nanoparticles could affect living organisms.
The results show that silica particles regardless which size (30nm or 70nm) or surface modification did not overcome the stratum corneum of the skin. Histological analysis indicated that the nanoparticles stacked to the stratum corneum but did not interact with viable keratinocytes. In contrast, bronchial epithelial cells internalized all kinds of nanoparticles. However, the amounts of nanoparticles that were internalized and located in the perinuclear region were different dependent from their surface modification. Moreover it could be demonstrated that a smaller size of the particles allowed a transcytosis across the epithelial cell layer following an interaction with fibroblasts. In addition to that we also investigated the effect of the particles on the blood-brain barrier that is one of the tightest barriers in our body and protects the brain from xenobiotic and endobiotic substances by expressing tight junctions and ABC efflux transporters. The results indicated that the barrier built by endothelial cells is not affected and that the nanoparticles did not induce an expression of pro-inflammatory mediators in endothelial cells even the particles have been internalized.
This study shows that highly complex *in vitro* barrier models represent an excellent tool to assess the impact of nanoparticles on animals or humans more precisely. More detailed experiments will furthermore enable the examination of the effects and functionality of nanoparticles designed for medical applications (drug delivery, improved imaging, etc.).

References

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