Abstract Book

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3.21. A preliminary study of engineered nanoparticles effects on barrier function of airway epithelial monolayers

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The increasing development of technologies related to the production and use of nanoparticles (NP) has promoted various studies concerning their physico-chemical properties, the possible interactions with biological systems and the consequent impact on the environment and human health. The lung is one of the key targets for the possible NP toxic effects as a result of environmental, occupational or medicinal exposure. Nevertheless, little is known upon the effects of engineered NP on the barrier properties of the airways.

In this study we evaluate the effects of different NP (obtained from Joint Research Centre – JRC-, Institute of Health and Consumer Protection, Nanobiosciences Unit (Ispra, Italy): ZnO uncoated (Zn1), ZnO coated (Zn2), "small" SiO_2 (Si1), "large" SiO_2 (Si2), hydrophobic TiO_2 (Ti1) and hydrophilic TiO_2 (Ti2) on the trans-epithelial electrical resistance (TEER) of monolayers of human lung Calu-3 epithelial cells. Cells were treated with increasing doses of NP (from 2.5 to 80 μg/cm^2) for 24, 48 and 72h. Cytotoxicity was assessed with two viability assays, resazurin and neutral red, based on different principles. Measurements of TEER were made with an epithelial voltohmmeter.

The two cytotoxicity tests yielded consistent results, although neutral red was slightly less sensitive. Toxicity of Ti1 and Ti2 was modest with a slightly higher effect for Ti2. Si1 and Si2 induced a mild time-dependent toxicity. Both ZnO NP produced a marked loss of viability at the highest doses. As far as TEER was concerned, TiO_2 NPs slightly changed the permeability in a time-dependent manner only at the highest doses, causing a decrease of 30% in TEER after 16d, with a slightly higher effect for Ti2. On the contrary, ZnO NP produced a progressive increase in permeability of monolayer corresponding to a decrease in TEER in a time- and dose-dependent manner. The effect produced by Zn1 NP (20 and 40 μg/cm^2) was almost the same, with a decrease in TEER approximately of 40% after the last days of treatment. The decrease in TEER, induced by Zn2, was instead markedly larger at 40 μg/cm^2 than at 20 μg/cm^2 with a decrease of more than 50% from the eleventh day of exposure. The TEER of monolayers exposed to SiO_2 NP were not significantly different from that of control monolayers.

In summary, these data indicate that ZnO, but neither TiO_2 nor SiO_2 NP, cause a damage to airway epithelial cell monolayers in vitro, suggesting that these materials may impair the competence of airway barrier. Moreover, the strict correlation existing between viability data and TEER, indicates that TEER determination provides a simple and sensitive device for the evaluation of NP toxic effects in cultured tight epithelial cell models. Further studies will be required to define the immunological changes that match with the impairment of Calu-3 monolayers.

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