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3D human co-cultures for predicting nanomaterial possible adverse effects on human health with a focus on multi-walled carbon nanotubes

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Increasing production of nanomaterials raises concerns about the associated hazard. The main concern about nanomaterial hazard is linked to their small sizes, allowing them deep penetration into the body. Although human exposures to nanomaterials can follow different pathways (i.e., dermal, gastrointestinal, etc.), the main route of entry is *via* the respiratory tract, where they can even reach alveoli or cross the air-blood tissue barrier and enter the bloodstream.

Therefore, there is an increasing need for reliable testing strategies to investigate the potential human health effects of nanomaterials under realistic conditions. Occupational exposures occur likely repeatedly at low doses. Therefore the aim of my thesis was to develop an *in vitro* testing strategy including reliable and responsive human alveolar cell culture models, and exposure scenario for repeated long-term exposures of nanomaterials at the air-liquid interface. Several cell culture models have been tested, including monoculture of adenocarcinoma cell line A549 (human type II-like alveolar epithelial cell line), co-cultures combining A549 and immune cells, or fibroblasts, and finally commercially available co-culture model consisting of human primary cells EpiAlveolar^{TM} (MatTek Corporation, USA).

The experimental setup including EpiAlveolar^{TM} model and three weeks of repeated nanomaterial exposures presented the most promising tool for future assessment of the fibrotic potential of inhaled nanomaterials.

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