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Realistic exposure scenarios to study nanoparticle-lung cell interactions

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The exponential growth and economical success of nanotechnology-based products requires their detailed hazard evaluation to confirm their safety from health and environmental perspective. However, despite the significant progress made in the field of nanosafety assessment, the possible health risks and environmental fate of nanomaterials (NMs) remains relative unknown. In particular, big knowledge gaps remain on NMs short- and long-term health effects i.e. low realistic doses, repeated and chronic exposures.

Focusing on carbon nanotubes (CNTs), they offer great opportunities for various applications due to their unique physicochemical properties. Therefore the overall aim of the first two projects of the present PhD thesis was to realistically and reliably assess the biological consequences of aerosolised multi-walled CNTs (MWCNTs) and predict possible real-life hazards following acute, short-term, or long-term repeated administration on advanced in vitro models at the air-liquid interphase.

In addition, serious concerns have been raised regarding the potential of MWCNTs to cause lung fibrosis, a severe pathological effect greatly associated with the inhalation of asbestos and crystalline silica. Consequently, the purpose of the third project was to investigate the early fibrotic and inflammatory activity of MWCNTs in vitro using monocultures of human lung alveolar epithelial cells, macrophages and fibroblasts.

Moreover, the recent advances in the development of NMs for biomedical purposes have led to the discovery of various potential therapeutics due to the efficient NM interaction with the different lung compartments, the possibility of surface modifications, their ability to carry various bio-agents and modulate immune responses and their relative low to toxicity. Among the existing NMs, gold (Au) NPs hold great promise for such applications due to their unique physico-chemical characteristics. Thereby, in the fourth project the biological impact of well-characterised aerosolised functionalised AuNPs was examined in terms of cellular toxicity and internalisation as well as potential immunomodulatory effects following realistic single NP aerosolisation). Importantly, most existing in vivo and in vitro studies focus on the acute effects of single AuNPs administration thus only limited information is available regarding the impact of repeated AuNP inhalation. In fact, investigation of the biodistribution and biological response after repeated AuNP exposure upon realistic experimental settings is of importance as inhaled drugs or vaccines may have to be administrated repeatedly for an effective disease treatment. Thus, the aim of the last project was to investigate the potential of aerosol delivered biomedical AuNPs, on the sophisticated in vitro lung co-culture model, upon realistic short-term repeated experimental settings.

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