Cultured macrophages help predict lung toxicity of inhaled nanoparticles

Many small particles of industrial or occupational origin are believed to infer an inflammatory or otherwise toxic potential to human health upon inhalation. Knowledge on this issue is especially important for the very small nanoparticles, which measure less than 100 nm and easily enter deep lung regions. Up to now OECD approved animal studies appear indispensable for the toxicological investigation of respirable nanomaterial and for making a final conclusion as to whether or not a material is regarded hazardous or even toxic.

Certainly, animal studies give an insight into the distribution of nanoparticles in the lung and allow to investigate other organs which might become affected. However, adverse reactions to inhaled nanoparticles are mostly confined to the lung. An important class of lung cells which collect microorganisms and also particles in all regions of the lung are the so-called alveolar macrophages. These cells take-up microorganisms and destroy them within intracellular compartments (phagosomes) whereas particles resisting this process are often enriched in phagosomes of these cells (Fig. 1). A particle laden alveolar macrophages can travel along the airways, leave the lungs and, by this, removes non-destroyable matter. These cells, therefore, are "real professionals" in clearing the lung from particle loads.

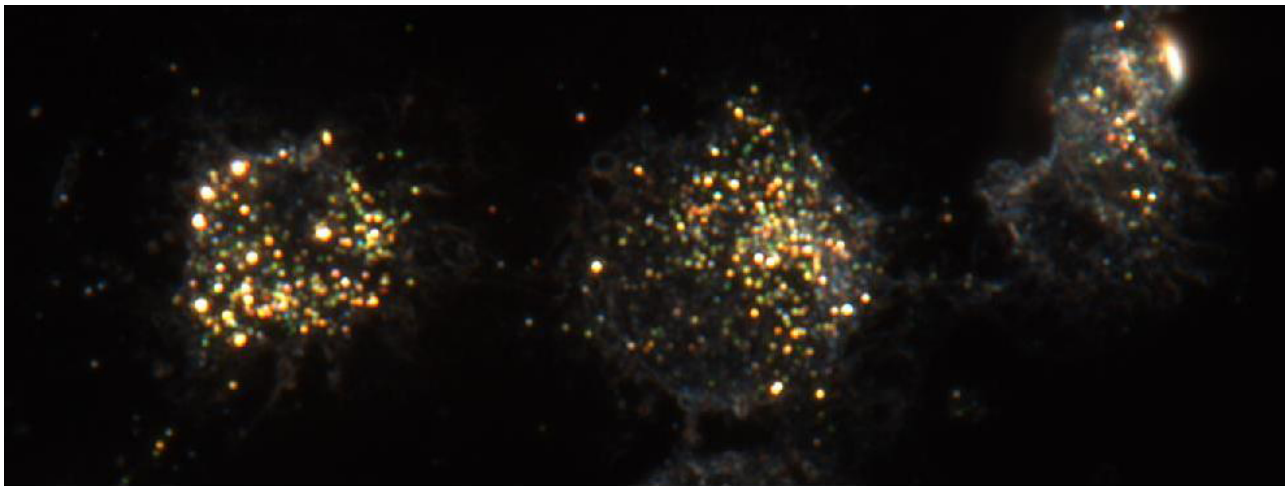

Fig. 1. Cultured alveolar macrophages with gold nanoparticles imaged by darkfield microscopy.

Since more than 20 years scientist have studied isolated alveolar macrophages from animals' lungs to see how these cells act and also how their rigorous behaviour contributes to the effects of (nano)particles on the lung. However, no standardized testing strategy has yet evolved. Furthermore, macrophage tests have not been systematically compared to inhalation studies in

vivo.

In a common research project, partly sponsored by the German Federal Ministry of Education and Research (BMBF), the non-profit company IBE R&D gGmbH together with BASF SE analysed effects of eighteen nanomaterials on the rat lung secondary to inhalation. These studies were carried out according to the highest industrial standards of toxicology so that data sets could be used as a basis for interpreting the responses of alveolar macrophages. These cells were subjected to various concentrations of nanoparticles. From a set of cellular responses we extracted evaluation criteria which allowed to clearly distinguish non-toxic from apparently toxic nanomaterials with an accuracy of 95%. The test is currently used to assess the safety of nanomaterials in a tiered decision-making framework.

It is important to note that the cells used for the assay multiply in culture so that donor animals for alveolar macrophages are no longer needed. Considering on the one hand, the tremendously number of nanomaterials along with the need for a reliable risk assessment and, on the other hand, the ethical imperative to reduce animal experiments, the benefit of this new macrophage assay is immediately obvious.

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Publication

[An in vitro alveolar macrophage assay for predicting the short-term inhalation toxicity of nanomaterials.](#)
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