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0092
Chemotaxis of alveolar macrophages: a new model of lung inflammation

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The first step of lung inflammation by inhaled particles is the induction of chemotaxis from alveolar macrophages. Supernatants of particle challenged NR8383 rat alveolar macrophages induce migration of other leukocytes (PMN) and this effect may serve as an *in vitro*-model for particle-induced inflammation of the lung. In the present study we investigated metal oxides of different solubility according to the strength of their chemotactic effects in this model.

NR8383 rat alveolar macrophages were challenged with metal oxide particles up to 164 µg/cm2. The cell supernatants were than used to induce migration of unexposed NR8383 rat macrophages and differentiated HL-60 cells (as a surrogate of PMN). Cytotoxicity was determined using LDH test.

The highly soluble ZnO exerted the strongest cytotoxicity and chemotaxis of the investigated metal oxides, followed by Cu(I)O, Cu(II)O, TiO2 as micro rutile and nano rutile particles inducing similar, moderate effects. TiO2 in the form of micro anatase and nano anatase induced weak chemotaxis. ZrO2 and Fe3O4 (magnetite) were inert.

With the exception of ZnO all investigated metal oxides showed intermediate, weak or no chemotaxis *in vitro* – which is consistent with a rather weak toxicity *in vivo*. The soluble ZnO however acted strongly cytotoxic and chemotactic *in vitro*. On one hand this strong inflammatory stimulus may not lead to strong chronic toxicity *in vivo* due to the rapid elimination of dissolved ZnO from the lung but may lead on the other hand to the widely known systemic pyrogenic effect of the Zn2+ ion. The particle sizes of TiO2 had no or only a slight effect on chemotaxis in this assay.